Studie 032a

(CTN032-FCE20124)

Studienbericht

Pharmacia Document 9550087

Reboxetine	CLINICAL STUDY 032	November 15, 1995

Double-blind activity and tolerability study of reboxetine *vs* placebo in elderly patients with depressive disorders (Phase III)

Final report of study
CTN032-FCE20124

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LIST OF ABBREVIATIONS AND TERMS

b.i.d.	twice daily
ADH	antidiuretic hormone
BUN	blood urea nitrogen
CGI	clinical global impression
CRF	case record form
CI	confidence interval
DSM-III-R	diagnostic and statistical manual - 3rd edition - revised
ECG	electrocardiogram
EEG	electroencephalogram
gamma GT	gamma glutamyl transpeptidase
GDS	geriatric depression scale
HAM-D	Hamilton depression rating scale
MMS	Mini Mental State examination
PL	placebo
RBX	reboxetine
REM	rapid eye movement
SCAG	Sandoz clinical assessment geriatric
SGOT	serum glutamic-oxaloacetic transaminase
SGPT	serum glutamic-pyruvic transaminase
T_4	thyroxine
TSH	thyroid-stimulating hormone

REBOXETINE - PROTOCOL 20124/032

SYNOPSIS

Name of Company: Pharmacia Spa **Name of finished product:** **Name of active ingredient(s):** Reboxetine	**Individual study table referring to part IV of the dossier** **Ref.:** **Vol.:** **Page:**	**(For national authority use only)**
Title of study: Double-blind activity and tolerability study of reboxetine versus placebo in elderly patients with depressive disorders. (Protocol 20124/032, Report n°9550087)		
Investigators: Prof V Andreoli, Dr G Carbognin.		
Study centre: Ospedale Provinciale Lungodegenti, Negrar, Verona, Italy.		
Publication (reference): None		
Study period: June 91-November 91	**Clinical phase:** III	
Objectives: To assess the activity and tolerability of reboxetine in comparison with placebo in elderly patients suffering from Depressive Disorders.		
Methodology: The study was carried out according to a double-blind, randomized, parallel group design in a population under in-patient care. After a wash-out period of 4 days-3 weeks, patients received reboxetine 2 mg b.i.d. or placebo for 8 weeks. In case of good tolerance but inefficacy, the daily dose was increased to 6 mg reboxetine or placebo. The response to treatment was assessed using the HAM-D scale, Clinical Global Impression (CGI) and two geriatric scales: Sandoz Clinical Assessment Geriatric (SCAG) and Geriatric Depression Scale (GDS). Safety and tolerability were assessed by the reporting of any adverse events and assessment of vital signs (supine and standing blood pressure and heart rate), laboratory tests, ECG and EEG.		
Number of subjects (planned and analysed): 70 patients were to be recruited but, after a selection of 50 patients, the recruitment was discontinued due to low response rate in the overall sample.		
Diagnosis and main criteria for inclusion : Patients were diagnosed according to the DSM-III-R classification. The severity of depression was evaluated using the HAM-D scale. Criteria for inclusion were as follows: patients of either sex, aged over 65 years; diagnosis of Major Depressive Disorders not accompanied by psychotic features (DSM-III-R); initial (pre-treatment) total score for the 21-item HAM-D of ≥ 18 and for the Mini Mental State of ≥ 20.		
Test product: tablets containing reboxetine methanesulphonate **Unit dose:** 2 mg reboxetine (free base). From day 28, in case of increased dose, the morning tablets were of 4 mg reboxetine **Mode of administration:** by oral route, b.i.d. **Batch no:** SF1105 (2 mg), SF1106 (4 mg)		
Duration of treatment: 8 weeks		
Reference therapy: Placebo (excipients alone) indistinguishable tablets **Unit dose:** 2 or 4 mg **Mode of administration:** by oral route, b.i.d. **Batch no:** SF1205 (2 mg), SF1030 (4 mg)		

Name of Company: Pharmacia Spa	**Individual study table referring to part IV of the dossier**	**(For national authority use only)**
Name of finished product:	**Ref.:**	
Name of active ingredient(s): Reboxetine	**Vol.:** **Page:**	

Criteria for evaluation:

Efficacy

Response. HAM-D total score decreases equal to or greater than 50% compared to the baseline value (Day 0 visit).

Remission. HAM-D total score lower than or equal to 10 (absolute value).

Response rate. Proportion of randomized patients treated at least for 4 weeks and experiencing a response at last assessment.

Safety

Reporting of adverse events, measurements of vital signs (supine and standing blood pressure and heart rate), laboratory tests, ECG and EEG.

Statistical Method: The primary objective of the study was the estimation of the difference in response rate between reboxetine and placebo calculated as the ratio between the number of patients treated for at least 4 weeks and experiencing a response at last assessment and all the randomized patients. The 95% confidence interval of the between treatment difference in response rate was estimated. The very low response rate caused the study interruption, then the inferential analysis foreseen by the protocol, on the results obtained from the administered rating scales, was not performed. Descriptive statistics for laboratory tests were provided

Results

After the accrual of 50 of the 70 expected patients, the study was discontinued owing to the very low frequency of occurrence of the study end-point in the total sample (18%). As for the 50 patients entered the study, 39 were females and 11 males, with a mean age of 80 years. 24 patients received reboxetine and 26 received placebo. 38 patients completed the 8 weeks treatment period, 17 under reboxetine and 21 under placebo. 7 patients on reboxetine and 5 on placebo withdrew from the study owing to adverse events, intercurrent illnesses and uncooperativeness.

Efficacy: No difference between the two treatments was apparent as for the study end-point (18% on reboxetine, 19% on placebo) and the results of the rating scales. Two possible explanations are: the relatively short treatment duration and the overall high rate of co-morbidity. In addition, all patients received concomitant medications for somatic complaints already present at baseline.

Safety: During the study, 16.6% patients under reboxetine and 15.4% under placebo reported adverse events and 12.5% on reboxetine and 7.7% on placebo withdrew from the study due to adverse events. 4/24 patients on reboxetine reported 10 adverse events compared with 4/26 patients on placebo who reported 5 adverse events. Most frequently affected were the psychiatric, cardiovascular and gastrointestinal systems under reboxetine and the gastrointestinal system under placebo. There was one serious adverse event during the study on reboxetine (syndrome of inappropriate secretion of ADH), leading to treatment interruption. There was no indication of modifications in laboratory tests that were of clinical significance in all patients but one. This patient had abnormal decrease of serum electrolytes associated with the inappropriate ADH secretion syndrome.

Vital signs were not modified to a significant extent. The only difference of possible clinical relevance between reboxetine and placebo concerned the heart rate values higher than 100 beats/min: they were present, only in standing position, at least once during the treatment in 8 patients on reboxetine and in 2 on placebo.

No indication of effect on cardiac function emerged from ECG tracings. No modifications were apparent in EEG recordings.

Conclusions: The study does not provide evidence of the activity of reboxetine in elderly patients suffering of Major Depressive Disorders with coexisting somatic complaints, while indicate a satisfactory tolerability of the compound at the administered doses in the population studied.

1. INTRODUCTION AND RATIONALE

RBX (FCE 20124 or (2RS, αRS)-2-[α-(2-ethoxy-phenoxy)benzyl]morpholine) is a new chemical compound which is highly potent in pharmacological and biochemical tests predictive of antidepressant efficacy: reserpine antagonism, norepinephrine re-uptake inhibition and REM sleep latency increase. In addition, RBX has been found to be able to prevent clonidine effects after single oral administration in an animal model where tricyclic monoamine uptake inhibitors were active only upon repeated doses. RBX was therefore hypothesized to exert antidepressant efficacy of faster onset with respect to available antidepressants in patients [1].

In phase I studies [2, 3] single doses of 0.5 - 5 mg of compound were administered orally to healthy volunteers. After 5 mg, orthostatic hypotension, accompanied by tachycardia and by subjective symptomatology consistent with the disturbed circulatory regulation, was observed. In these studies single doses of 1 and 3 mg of the compound showed dose-dependent central nervous system effects with EEG modifications (decreased power of ϑ and fast-β waves in the fronto-central derivative), performance improvement (peg-board test) and growth hormone increase, the latter reportedly sensitive to hypothalamic noradrenergic stimulation by norepinephrine re-uptake inhibitors.

The comparison with the positive control, imipramine 75 mg, associated to similar EEG modifications in the fronto-central derivative, to modifications indicative of sedative activity in the occipitotemporal derivative and to deterioration of the Pauli performance test, in the absence of growth hormone modifications, indicate that RBX does not possess the marked sedative activity of imipramine, but rather psychostimulating properties. After treatment, standing heart rate increase and salivation decrease were apparent. No other modifications of tolerability parameters were observed.

The pharmacokinetics of the compound was evaluated in the above mentioned studies as well as after administration of 2 mg ^{14}C-FCE 20124 to 3 healthy volunteers [4]. Most of the radioactivity circulating in plasma (73% in terms of AUC) was accounted for by unchanged RBX; the average peak levels were observed at 2h, with remarkably stable levels 1-6 hours after administration; its plasma half-life was estimated as 13.2 h, slightly lower than that of total radioactivity.

On the basis of the results of the phase I studies, a 6-center early phase II study was carried out aimed at assessing tolerability and activity of progressively increased doses of RBX, administered over a 4-week period to hospitalized patients suffering from Major Depressive Episodes [5].

Ninety-eight patients were admitted to the study to be treated with maximum RBX daily doses of 4 mg (29 pts), 6 mg (27 pts), 8 mg (18 pts), 10 mg (12 pts) and 12 mg (12 pts). Dosage decrease was almost only present in the 12 mg group where in 5/12 cases, due to hypotension and tachycardia, the daily dose was decreased to 10 mg until completion of the treatment period.

The rating scales applied show a dose-related improvement of the clinical picture both as average changes *vs* basal conditions as well as frequencies of relevant modifications (defined as ≥50% decrease of HAM-D) up to the 10 mg/day dose, whereas slight deterioration, concomitant to signs/symptoms of intolerance, was observed in the highest dose group.

The compound was well tolerated when administered at doses up to 10 mg/day, as shown by newly observed signs and symptoms, mainly of mild to moderate severity and transient, and by vital signs, laboratory tests assessments and ECG.

A double-blind, placebo and standard-controlled, parallel group study was subsequently carried out in 10 centers (France, Hungary, Italy and Latin America) in 258 patients hospitalized due to a Major Depressive Episode [6]. The experimental treatment had to be administered for 4 weeks, with maximum doses of 8 mg RBX or 200 mg desipramine (DMI).

Of the 80, 82 and 81 cases evaluable for efficacy in the RBX, DMI and PL group, 63%, 46% and 36% respectively showed a decrease >50% of the total HAM-D score at the end of treatment; in 31%, 22% and 21% of these patients, respectively, the decrease was present within the 14th day of treatment. After 2 and 4 weeks of treatment, an average decrease of 23% and 34% of the HAM-D was present in the PL group; the corresponding figures were 34% and 49% in the DMI group and 39% and 57% in the RBX group.

As for signs/symptoms, the more frequent in the RBX group were headache, complained of by 33% of the patients (*vs* 20% and 21% in the DMI and PL groups, respectively), and urinary hesitancy/retention, present in 12% of the cases (*vs* 4% and 1% in the DMI and PL groups, respectively). The more frequent in the DMI group were dry mouth (45% *vs* 26% *vs* 21%, DMI *vs* RBX *vs* PL, respectively), sweating (28% *vs* 18% *vs* 22%, respectively), blurred vision (17% *vs* 4% reported in both RBX and PL groups). Cardiovascular signs/symptoms were relatively rare, and appeared with slightly higher frequency in the DMI group: hypotension 13%, *vs* 6% in the RBX and 8% in the PL group, and tachycardia 19% *vs* 12% and 8% in the RBX and PL group, respectively.

An open scaling-up repeated doses study was carried out to evaluate the activity, tolerability and pharmacokinetics of RBX administered for 4 weeks at daily doses increased at weekly intervals from 1 to 4 mg b.i.d. to 12 elderly patients suffering from depressive disorders [7]. The pharmacokinetic results indicated dose-proportionality over the explored range, and C_{max} and $AUC_{0\text{-}12h}$ higher than those found in healthy young subjects having received RBX at the same doses. The maximum foreseen dose of 4 mg b.i.d. was well tolerated in 8 out of the 9 exposed patients. However, the attainment of this dose was prevented in 3 patients because of the emergence of cardiac acceleration or other rhythm disorders. The results of this study suggested daily doses of 2 to 3 mg b.i.d. to be used in subsequent controlled studies of the antidepressant efficacy and tolerability of RBX in the elderly population.

Phase II results obtained in controlled conditions in patients suffering from a Major Depressive Episode indicate that RBX is an effective antidepressant agent, with a favorable therapeutic

index with respect to DMI. Confirmation of this evidence in the elderly population was needed. The presently reported study was designed accordingly.

2. STUDY OBJECTIVES

The present study was designed to evaluate the activity and tolerability of RBX in comparison with PL in elderly patients suffering from depressive disorders.

3. INVESTIGATIONAL PLAN

The study protocol is enclosed (Appendix 12.1.1).

3.1 Study Design and Plan

The study was carried out according to a double-blind parallel group design in one single investigational center. The center was expected to recruit 70 patients suffering from a Major Depressive Episode.

After the initial wash-out period lasting 4-7 days (14 days in case of previous MAOI administration and 3-4 weeks in case of previous fluoxetine treatment), patients received experimental treatment for 8 weeks, at the dose of 4 mg/day RBX or PL. The dose could be increased to 6 mg/day of RBX or matching PL for the final 4 weeks in case of unsatisfactory response. Efficacy was assessed by means of the HAM-D scale. Clinically relevant improvement (at least 50% decrease of the HAM-D total score) was the study end-point; patients not completing at least 4 weeks of treatment were classified as failures. Tolerability (vital signs, ECG, EEG, laboratory tests) was monitored.

After recruitment of 50 of the 70 expected patients, the study was discontinued under blind conditions because of the very low frequency of occurrence of the study end-point. In fact only 9 patients of the 50 recruited (18%) completed at least 4 weeks of treatment while showing 50% decrease of the HAM-D at the end of treatment, a figure not consistent with a sensitive experimental setting.

3.2 Ethics

The study protocol was approved by the Institutional Review Board of the investigational center (Ospedale Provinciale Lungodegenti-Negrar, Verona, Italy). The approval is enclosed (Appendix 12.1.3).

The study was conducted according to the principles of the Declaration of Helsinki and its Venice and Hong Kong amendments (Enclosure 11 of Appendix 12.1.1).

Before screening, patients were informed about characteristics of the investigational new compound and protocol procedures by the Principal Investigator or the Co-investigators. Only

consenting patients were admitted. The consent form is enclosed to the protocol (Enclosure 12 of Appendix 12.1.1). The translation in local language is filed in the Trial Master File.

3.3 Study Population

Patients were selected from the population under in-patient care of the participating center according to the following inclusion/exclusion criteria.

3.3.1 INCLUSION CRITERIA

Inclusion criteria were the following:

- Patients of either sex, aged over 65 years
- Diagnosis of Major Depressive Disorder not accompanied by psychotic features according to DSM III-R
- The total score for the 21-item HAM-D had to be ≥ 18 at admission
- The total score for the Mini Mental State Examination had to be ≥ 20 at admission
- Informed consent had to be obtained from the patient or next of kin

3.3.2 EXCLUSION CRITERIA

Exclusion criteria were the following:

- Dysthymia or Cyclothymia
- History of resistance to antidepressant therapy
- History of Major Depressive Disorder associated with endocrine disorders (e.g. hypo or hyperthyroidism confirmed by TSH and T_4 level at admission).
- History of drug hypersensitivity
- History or presence of gastrointestinal, hepatic, renal disease (the latter confirmed by a creatinine clearance <30 ml/min) or other diseases that could interfere with the metabolism of drugs
- History or presence of chronic respiratory insufficiency
- History of seizures or brain injury
- Evidence of substance or drug abuse at present or within the past 6 months
- Evidence of clinically important hematopoietic or cardiovascular diseases
- Evidence of urinary retention
- Evidence of glaucoma
- Electroconvulsive therapy in the previous 6 months
- Participation in a clinical trial with an investigational compound in the 4 weeks preceding the study
- Clinically relevant abnormal findings in the physical examination, laboratory tests, ECG and EEG at admission
- High risk of suicide

3.3.3 SAMPLE SIZE

On the basis of the absence of previous efficacy results from phase II trials in the relevant population and of consistent evidence from published trials, the study had to be considered as explorative. Therefore, the sample size was not defined on a statistical basis, but was based on the center accrual capability. Seventy patients were considered a suitable sample size to provide with a rough estimation of the size of the between treatment difference. In fact, interval estimates (95% CI) provided by such a sample would have been as wide as 0.47 under the worst hypothesis of an equal response rate of 0.50 in both treatments. This is the case in which the variance is maximised and so it is the width of the interval.

3.4 Treatments

3.4.1 TREATMENTS TO BE COMPARED

Patients received either RBX in the daily dose of 4 mg (2 mg b.i.d.) or PL b.i.d. for 56 days. The treatment was administered in the morning and in the evening. In the case of good tolerance but inefficacy or minimal improvement, the daily dose was to be increased from day 28 on to "dose 2", i.e. 6 mg of RBX (4 mg in the morning and 2 mg in the evening) or PL b.i.d.

3.4.2 IDENTITY OF TEST MATERIAL

The experimental treatments consisted of indistinguishable tablets of either RBX 2 mg (batch SF 1105) and 4 mg (batch SF 1106), or PL for RBX 2 mg (batch SF 1205) and for RBX 4 mg (batch SF 1030). Experimental treatments were prepared by Pharmacia, Pharmaceutical Development Department, Milan. Analytical certificates are enclosed (Appendix 12.1.5).

3.4.3 RANDOMIZATION

Allocation of patients to either of the two treatments (Appendix 12.1.6) was done according to a computer generated randomization list. SAS software (release 6.04/DOS) was used in order to generate the list which was kept at Biometrics and Data Management Department of Pharmacia Milan, until the study data were completely cleaned.
Patients found eligible for the study, fulfilling the inclusion/exclusion criteria, were identified by progressive number and they were given the corresponding experimental treatment according to their temporal entry into the study.

3.4.4 TREATMENT PACKAGE AND BLINDING

Medication was supplied as capsules, indistinguishable in shape and colour, containing either RBX 2 mg and 4 mg tablets or PL. Capsules were supplied in amber-glass bottles separately for morning and evening administration, labelled with the patient number and week number. Each bottle contained medication necessary for 1 week of treatment. Bottles for the whole 8-week-treatment period were packed in small cartons labelled with the patient number. Additional 4

bottles for optional dose increase ("dose 2") labelled with the patient number and the indication "Dose 2" were also supplied.

Sealed individual treatment codes were provided for any emergency situation necessitating treatment identification. They were returned to the Sponsor at the end of the study.

3.4.5 CONCOMITANT THERAPY

Only drugs considered essential for the management of the patients were allowed during the study. These drugs were to be administered at stable doses before the start of the study.

The following drugs were not allowed: psychotropics (neuroleptics, antidepressants, psychostimulants, tranquilizers - with the exception of sleep medication -), anti-Parkinson and anticholinergic agents, sympathomimetic drugs, hormones and anesthetic agents. In the case of insomnia, a short-acting benzodiazepine (for instance temazepam 5 - 10 mg) as a sleep inducer on the p.r.n. basis at bed-time was allowed.

In the case of events arising during the course of the treatment concomitant non-psychotropic medication considered necessary for patient's welfare was allowed.

3.5 Efficacy and Safety Variables

3.5.1 EFFICACY

Patients were seen at regular intervals throughout the study and the following efficacy assessments were carried out at the specified intervals.

Hamilton Depression Rating Scale
The severity of depression was measured using the HAM-D scale [8] at screening, days 0, 14, 28 and 56 or last assessment.

Mini Mental State
The Mini Mental State was administered at screening and day 56 or last assessment.

Sandoz Clinical Assessment Geriatric and Geriatric Depression Scale
Two geriatric evaluation scales were administered: the Sandoz Clinical Assessment Geriatric [9] and Geriatric Depression Scale [10].
The SCAG and GDS scales were applied at days 0, 14, 28 and 56 or last assessment.

Clinical Global Impression
The Clinical Global Impression (Severity of Illness, Global Improvement and Efficacy Index) was applied according to the ECDEU manual [11] at days 0, 14, 28 and 56 or last assessment.

All the evaluations and ratings were to be carried out by the same observer and in the same setting for a given patient.

3.5.2 SAFETY

At screening, a full medical history and physical examination were carried out, including chest X-ray, ECG, EEG, laboratory tests and vital signs assessment, including respiratory rate.

Adverse Events
The occurrence of adverse events was recorded at days 0, 14, 28 and 56.

For each adverse event, the following information was recorded: description, date of onset and end, severity, effect of interruption of treatment and rechallange, treatment relationship, outcome and action taken regarding the treatment (such as none, dose reduced or discontinued). Any medication given as a result of the adverse event and the possible opening of double-blind code had to be reported.
The criteria of Karch and Lasagna served as guidelines for the evaluation of the relationship between the event and the treatment (Enclosure 10 of Appendix 12.1.1).

All serious and/or unexpected adverse events had to be reported to the sponsor according to the detailed instructions given in the protocol (Section 12.0 of Appendix 12.1.1). The same procedure was applied for patients who died during the study or within 30 days of completion. The definition of serious and unexpected adverse event is given in the protocol (Section 12.0 of Appendix 12.1.1).

Vital Signs
Arterial blood pressure in lying and standing position, heart rate, body temperature and body weight were recorded at screening, on days 0, 14, 28 and 56 or at last assessment as per protocol. In the CRF, blood pressure and heart rate could be also recorded on days 7 and 21. Lying blood pressure and heart rate were measured after 5 minutes in the supine position and standing blood pressure and heart rate were measured in standing position 2 minutes after standing-up.

Body temperature and body weight were recorded at screening, day 0, 14, 28 and 56 or at last assessment as per protocol. In the CRF, body temperature and body weight could be recorded also on days 7 and 21.

Laboratory Tests
Laboratory tests were recorded at screening, on days 28 and 56 and included: full blood cells count, serum electrolytes, liver enzymes, blood sugar, serum alkaline phosphatase, blood urea nitrogen (BUN), serum creatinine, uric acid, total and direct bilirubin, total serum protein and electrophoresis, serum cholesterol and triglycerides, and, at screening only, TSH, T_4 and creatinine clearance.
Urinalysis was performed at screening, on days 28 and 56.

Laboratory tests and urinalysis were also to be recorded for patients who withdrew from the study.

ECG
An ECG was recorded at screening, on days 28 and 56. ECG was also to be recorded for patients who withdrew from the study.

EEG
An EEG was performed at screening and at the end of treatment.

3.6 Evaluation Criteria

3.6.1 EFFICACY

The following criteria apply to the set of data analyzed:
- Response: HAM-D total score decrease ≥50% compared to the baseline value (Day 0 visit).
- Remission: HAM-D total score ≤ 10 points (absolute value).

3.6.2 SAFETY

Vital Signs
As for blood pressure, patients were classified according to presence/absence of an increase (≥20 mmHg) or decrease (≤20 mmHg) of possible clinical relevance *vs* baseline (Day 0 visit) and of presence of absolute lying and standing heart rate values >100 beats/min.
Orthostatic hypotension was defined as a decrease >20 mmHg of standing systolic blood pressure as compared to lying.

Laboratory Tests
Results of laboratory examinations were classified as normal or abnormal according to the normal range (Appendix 12.2.2). In addition, abnormal values were classified as clinically relevant according to the criteria reported in Appendix 12.1.7.

ECG
The ECG tracings were classified as normal or abnormal according to the cardiologist's report. The abnormalities were coded and subsequently grouped as reported in Appendix 12.1.8.

EEG
The EEG were classified as normal or abnormal basing on the judgment of the investigator and according to the neurological report.

3.7 Statistical Analysis (Planned and Carried Out)

3.7.1 EFFICACY ANALYSIS

The primary objective of the study was the estimation of difference in response rate between RBX and PL. In each treatment, response rate was calculated as the ratio between the number of patients treated for at least 4 weeks and experiencing a response at their last valid observation and all randomized patients. This was an "intention to treat" approach and patients treated for less than 4 weeks were considered as failures. The 95% confidence interval of the between treatment difference in response rate was estimated.

In addition, results obtained from the administered rating scales (HAM-D, CGI, SCAG, GDS) should have been analysed comparing the score at last assessment and the baseline in the two treatments by using a two tailed Student's test. At variance with what stated in the protocol, no inferential statistics was applied to the secondary end points because of the very low response rate in both groups of treatment which caused the study interruption.

3.7.2 SAFETY ANALYSIS

Adverse Events
Adverse events have been presented by patient and treatment and grouped by body systems.

Vital Signs
Frequency of patients showing changes of possible clinical relevance *vs* baseline, occurred at least once during treatment, as well as frequency of heart rate > 100 beats/min, and of orthostatic hypotension in the two treatment groups were calculated and compared.

Laboratory Tests
The Wilcoxon Rank Signed test for paired data was applied to all the laboratory results, to compare median values observed during treatment with those recorded at baseline and $p<0.01$ was assumed as significance level. Patients showing clinically relevant changes were listed. The criteria used to define the modifications of laboratory values with respect to baseline as clinically relevant are reported in Appendix 12.1.7.

ECG
ECG results have been summarised in frequency tables showing normal/abnormal findings at each assessment time. Changes from baseline and newly appeared abnormalities have been displayed.

Reasons for discontinuation
Early interruptions of the study were grouped by reason and the proportion of patients who withdrew from the study in the two groups of treatment was compared.

3.8 Data Management

Data Management was carried out in the Biometrics and Data Management Departiment of Pharmacia, Milan.

CRFs data were entered into an IBM 3090 computer (according to the arrival flow) through data entry masks generated by SAS FSP release 5.18-6.07.

ECG tracings were classified and subsequently grouped according to the codes reported in Appendix 12.1.8. Previous and concomitant diseases were coded according to ICD9 dictionary [12]: concomitant drugs were coded according to the Drug Reference List [13]; and adverse events according to the WHO-ART dictionary [14].

Subsequently, individual data listings were produced, reviewed by clinical personnel and editing of CRFs was requested at the Investigator site, whenever appropriate. Corrections were entered, repeating the loop until the files were clean.

Reporting , as well as statistical analyses, were carried out with SAS PROCs (version 6.07).

3.9 GCP compliance, Data Quality Assurance

The study was initiated before the formal adoption of Good Clinical Practice guidelines by European Regulatory Authorities and in the absence of Company Standard Operating Procedures. However, operating procedures for study monitoring and co-ordination were defined and are described in Attachment A of Appendix 12.1.1. These procedures for training on assessment instruments and study monitoring were agreed upon with the investigators before study start.
During the monitoring visits, which were made at regular intervals, the monitor validated the content of the CRFs against source documents on the basis of the agreed procedure.

4. STUDY PATIENTS

4.1 Study Interruption

After the accrual of 50 of the 70 expected patients, the study was discontinued under blind conditions because of the very low frequency of occurrence of the study end-point. In fact, only 9 patients of the 50 recruited (18%) showed a 50% or greater decrease of the HAM-D at the end of treatment, while completing at least 4 weeks of treatment, a figure not compatible with the expected response rate, on the basis of the results obtained in controlled conditions in the adult.

4.2 Disposition of Patients

A total of 50 patients (11 males, 39 females) were admitted to the study within a period of 6 months, from June 1991 to November 1991. RBX treatment was allocated to 24 patients and PL to 26 patients.

The patients' classification at the end of the study is reported in Table 1. A total of 38 (76%) patients completed the 8 weeks of treatment as per protocol: 17 (70.8%) under RBX and 21 (80.7%) under PL. Twelve (24%) patients withdrew from the study: 7 (29.2%) under RBX and 5 (19.2%) under PL. Main reasons for withdrawal are shown in Table 2. Adverse events and intercurrent medical problems caused withdrawal of 4 patients under RBX and of 3 under PL. These cases are commented in the Adverse Events section. Other reasons of discontinuation are consent-withdrawal in 4 patients, 3 under RBX and 1 under PL, and patient's request in 1 under PL.

4.3 Protocol Deviations

Non-compliance with inclusion/exclusion criteria was frequently related to abnormalities of thyroid function tests (20% of patients), suggestive of a non diagnosed endocrine disorder (see Appendix 12.2.2-Individual Data Listings).

Nine patients (18%) had values of creatinine clearance under 30 ml/min, possibly leading to interference with the elimination of drugs (see Appendix 12.2.2-Individual Data Listings).

One patient was under 65 years when entered the study.

Most patients (94%) received medications during the wash-out period essentially for co-morbidity. The most frequently used drugs are listed by active principle in Table 9.

4.4 Demography

Demographic data are given in Table 3. Female patients represented the majority of the study population: 79.2% in the RBX group and 76.9% in the PL group. The RBX and PL groups were well matched for age, height and weight.

4.5 History of Depression

Diagnosis and history of the mental disorder are shown in Table 4. The majority of the patients was diagnosed as single major depressive episode in both arms: 75% and 69.2% in RBX and PL groups, respectively. The two groups were similar for all the parameters considered except for the number of previous episodes of depression, higher in the RBX than in PL groups (median 6.0 *vs* 4.5 respectively).

In most patients, the present episode of depression was the first episode and the onset was subacute. External events precipitating the onset of present depressive episode were definitely present in 12 out of 24 patients of RBX group (50.0%) and 8 out of 26 of PL group (30.7%).

Previous antidepressant treatments are listed in Appendix 12.2.2. Only 5 patients (20.8%) of RBX group and 4 (15.4%) of PL group were previously treated with antidepressants mostly tricyclics.

4.6 Severity of Depression

Most patients were judged, by the investigator, moderately ill at admission: 79.2% in RBX arm and 76.9% in PL arm (Table 20).

4.7 Medical History

Most frequent illnesses are listed in Table 5 and grouped by body systems in Table 6. The most frequent illnesses were osteoarthrosis (12 patients in RBX and 10 in the PL group), diabetes mellitus (3 and 6 cases, respectively) and essential hypertension (5 and 3 patients, respectively). Musculoskeletal, connective tissue and circulatory system disorders were the most frequent in both groups of patients. Circulatory system disorders affected 13 patients (54.2%) in the RBX group, and 9 (34.6%) in the PL group.

4.8 Chest X-ray and Respiratory Rate

Chest X-ray abnormalities are listed by patient in Appendix 12.2.2 and grouped by more frequently present abnormalities in Table 7. At admission, 36 patients (72%) had chest X-ray abnormalities. Senile emphysema was present in 66.6% and 50.0% of patients in the RBX and PL group, respectively. Few other abnormalities were similarly represented in both groups, except for arcus aortae calcification, present only in RBX group.

Median respiratory rate was 20 breaths/min both in RBX and PL group (Table 8).

5. STUDY MEDICATION

Details of the treatment period and the administered dosages are given in the Appendix 12.2.2.

The treatment was administered as per protocol to 38 patients out of 50: 17 received RBX (70.8%) and 21 PL (80.7%). Early termination occurred in 12 patients out of 50: 7 received RBX (29.2%) and 5 PL (19.2%).

The dose was increased from 4 mg/day to 6 mg/day of RBX or PL in 16 patients out of 50: 11 received RBX (45.8%) and 5 PL (19.2%).

The dose was reduced from 6 mg/day to 4 mg/day in 1 patient (#33), for fourteen days, and from 4 mg/day to 2 mg/day, for only one day, in another patient (#34): in both cases because of adverse event and under PL. The treatment was temporarily interrupted in 2 patients (#28 and #43; for 4 and 3 days, respectively), both under RBX, owing to adverse events.

Compliance to prescribed treatment schedule and dose, both per protocol and prescribed by the investigator, occurred for most patients (92%). Exceptions were: patient #10, under PL, who assumed one week less of the experimental drug and 3 patients, 2 under RBX and 1 under PL, whose compliance was judged unknown by the investigator (Table 1).

6. CONCOMITANT MEDICATION

Most of the concomitant medications were administered to the patients before the beginning of the study and also during the wash-out period. These medications are listed in Table 9.

The frequency of patients treated at least once with newly administered medications is reported in Table 10. Most frequently newly administered were tenoxicam in 6 patients (4 under RBX and 2 under PL), hydrochlorothiazide and captopril in 3 patients (1 under RBX and 2 under PL). The majority of the newly administered medications were given for associated pathologies and following the emergence of adverse events. No relevant differences in the frequency of administration between RBX and PL occurred.

Newly observed signs/symptoms required additional medications during the treatment period in patient # 15, who received metoclopramide for heartburn and vomiting, and patients # 43 and # 28, who received nifedipine for hypertension. All were under RBX treatment.

7. FOLLOW-UP

At the end of the treatment period 10 patients continued the double-blind treatment, 6 in the RBX group and 4 in the PL group (Table 1). The results of the follow-up assessment are not included in the present report.

8. EFFICACY RESULTS

8.1 Data Set Analysed

All 50 randomized patients were included for the evaluation of the results according to an "intent to treat" criterion.

8.2 Study End Point Analysis

Table 11 reports the classification of patients at last visit, according to protocol criteria. Among the patients treated at least for 4 weeks, which represent 90% of total patients, responders under RBX were 16.7% and under PL 19.2%. (Between treatment difference: -2.6 %, 95% CI -23.8% ÷ 18.7%).

Remission rate was 12.5% and 11.5% under RBX and PL, respectively.

8.3 Analysis of Rating Scales

8.3.1 HAMILTON DEPRESSION RATING SCALE

Summary statistics of HAM-D total score are presented in Table 12 by assessment times and treatment. Under RBX, mean HAM-D total score at baseline (Day 0) was 23.2 and at day 56 was 16.6. Under PL mean HAM-D total score at baseline was 23.1 and at day 56 was 15.5.

Summary statistics at last assessment are reported in Table 13. No difference between the two groups is apparent.

8.3.2 MINI MENTAL STATE

Summary statistics of MMS scale by assessment times and treatment are reported in Table 14 and the summary of results at last assessment in Table 15. No modifications or differences between the two treatments are apparent.

8.3.3 SANDOZ CLINICAL ASSESSMENT GERIATRIC

Summary statistics of SCAG scale by assessment times and treatment are presented in Table 16 and the summary of results at last assessment in Table 17.
At baseline a slight difference was recorded between the two groups: mean total score was 56..9 and 59.0 for RBX and PL, respectively. At the end of the study the mean total score was 47.1 and 47.2 under RBX and PL, respectively. During the study and at last assessment, neither important reductions nor relevant differences between the two groups are observed.

8.3.4 GERIATRIC DEPRESSION SCALE

Summary statistics of GDS scale by assessment times and treatment are presented in Table 18 and summary of results at last assessment in Table 19. During the study and at last assessment, neither important reductions nor differences between the two groups are observed.

8.3.5 CLINICAL GLOBAL IMPRESSION

Severity of Illness
The distribution of the severity scores by assessment times is presented in Table 20 and results at last assessment are given in Table 21.

At baseline, the distribution of the scores is similar in the two groups of treatment. Most patients were judged moderately ill: 79.2% and 76.9% in RBX and PL groups, respectively. Only 12.5% and 15.4% were judged markedly ill. There is a shift towards low severity of both groups of patients but only 23.5% and 19.0%, respectively under RBX and PL, were judged borderline at the end of the study and no patient was evaluated as normal. At last assessment 22.7% and 16%, respectively under RBX and PL, were judged borderline. A shift table of the last value *vs* baseline (Table 22) showed that, on RBX, the severity decreased in 50% of patients and was unchanged in all the remaining patients and, on PL, decreased in 60% and remained unchanged in 40%.

Global Improvement
The distribution of the global improvement scores by assessment times is shown in Table 23 and results at last assessment are given in Table 24. The much improved patients increased, from the second week to the eighth week of treatment, from 18.2% to 41.2% under RBX, and from 12.0% to 71.4% under PL. Only 1 patient was judged very much improved and was under RBX. The rate of much improved cases at last assessment was 36.4% and 60.0% on RBX and PL, respectively.

Efficacy Index
Summary statistics of the efficacy index are shown in Table 25. No difference was seen between the two groups, either after 4 weeks or 8 weeks of treatment.

8.4 Dose Response Relationship

In the RBX group no difference in response rate was apparent in patients completing the study and treated with the daily dose of 4 mg (n = 6) or 6 mg (n = 11).

9. SAFETY RESULTS

9.1 Adverse Events

Adverse events are presented, by patient, in Appendix 12.2.2 (Individual Data Listings).
Adverse events were complained of by 4 patients (16.6%) under RBX and 4 (15.4%) under PL. In the 5 patients listed below, adverse events caused withdrawal from the study.

Fifteen events occurred throughout the study: 10 (66.7%) on RBX and 5 (33.3%) on PL. The events occurred within the fifth week of RBX treatment and within the sixth week of PL, with

no difference in occurrence in the different weeks. The events are grouped by body systems in Table 26. Most frequently affected were the psychiatric, cardiovascular and gastrointestinal systems under RBX, and the gastrointestinal system under PL .

Under RBX 4 events (40%) required symptomatic treatment: heartburn, vomiting and 2 cases of hypertension. The concomitant therapy exerted full recovery in all cases.

Three events under RBX (30%) required treatment interruption: agitation, nervousness and paraesthesia. The interruption did not lead to recovery within the observation period. Two events under PL (40%) required modification of treatment dosage: vertigo and asthenia. Recovery followed only in this latter case.

Maximal severity occurred in 4 events (40%) under RBX and in 2 under PL (40%).

Under RBX no event was judged by the investigator as probably or definitely related to study medication. Three out of 5 events occurred under PL were judged probably or definitely related: agitation, vertigo and asthenia.

Serious adverse events

One adverse event was reported as serious during the study. Patient #15, on 4 mg/day RBX for 7 days, suffered from clinical symptoms leading to the diagnosis of syndrome of inappropriate secretion of ADH. The experimental treatment was interrupted. Details are given in Appendix 12.2.1.

Adverse events leading to withdrawal

Five patients withdrew from the study because of adverse events: 3 on RBX (12.5%) and 2 on PL (7.7%), as indicated below:

Pat. #15	SIADH	possible	RBX
Pat. #20	agitation	probable	PL
Pat. #21	anxiety/hypochondriasis	possible	RBX
Pat. #43	hypertension	possible	RBX
Pat. #50	abdominal pain/dyspepsia	possible	PL

More details are given in Appendix 12.2.2 (Individual Data Listings).

9.2 Vital Signs

9.2.1 BLOOD PRESSURE AND HEART RATE

Table 27 shows the number of patients evaluated for systolic, diastolic blood pressure and heart rate in standing and lying position by assessment time and treatment groups.
Mean and median blood pressures and heart rates are presented in Tables 28-33. There were no important trends toward modification in mean and median blood pressures. A slight increase was apparent in heart rate values both in standing and lying position under RBX.

The percent frequency of changes *vs* baseline at each assessment interval are reported in Tables 34 and 35. At few assessment intervals a slightly higher percentage of patients showed blood pressure values lower and heart rate values higher than at baseline under RBX than under PL. In Tables 36 and 37 the frequency of patients with possibly relevant variations of blood pressure, occurred at least once during the treatment, is presented. No important differences between RBX and PL are apparent.

The frequency of absolute heart rate values >100 beats/min in lying and standing position at each assessment time is shown in Table 38. Throughout the study, the event was present only in standing position, at least once during treatment in 8 patients on RBX and in 2 patients on PL.

Orthostatic hypotension occurred in 2 patients under RBX and 1 under PL within the first 2 weeks of treatment.

9.2.2 BODY TEMPERATURE

Mean and median body temperatures are shown in Table 39. No trend towards modification and no difference between the two treatments is apparent.

9.2.3 BODY WEIGHT

Mean and median body weights are shown in Table 40. No trend towards modification and no difference between the two treatments is apparent.

9.3 Laboratory Tests

9.3.1 HAEMATOLOGY AND CLINICAL CHEMISTRY

Summary statistics

Summary statistics of laboratory values are shown by variables and assessment time in Table 41 and 42 respectively for the RBX and PL arm.

In the RBX group, no significant ($p<0.01$) differences *vs* baseline were observed during the study period.

In the PL group, differences *vs* baseline indicate a significant increase of serum calcium at day 28 (median differences 0.2 mmol/l) and a significant decrease of total proteins (median differences -3.2 g/l), total and direct bilirubin (median differences -1.7 µmol/l and -0.6 µmol/l, respectively) and serum phosphate (median differences -0.1 mmol/l), all at the assessment of day 56.

Clinically relevant abnormalities

In Table 43 the patients with relevant abnormalities are listed, with the indication whether the abnormalities are above or below the maximum/minimum value according to the criteria reported in Appendix 12.1.7.

On RBX, the following patients showed a relevant increase/decrease of at least one test at last assessment: patients #45 and #46 showed increased blood urea nitrogen (BUN), patient #15 increased direct bilirubin, patient #8 increased SGPT and patient #13 increased γ-GT. Patient #15 had a relevant decrease of serum chloride and sodium at last assessment. These abnormalities were associated with the inappropriate ADH secretion syndrome that caused patient's withdrawal from the study (Appendix 12.2.1). The same patient showed a decrease of the percentage of lymphocytes. Another patient (#18) showed a decrease of serum phosphates at last assessment. All the listed abnormalities, with the exception of those observed in patient #15, were judged as not relevant by the investigator.

On PL, the following patients showed a relevant increase of at least one test at last assessment: patient #42 had an increase of BUN, patients #10, #41 and #50 an increase of γ-GT, patient #10 an increase of α_2-globulins, patients #10 and #33 an increase of blood sugar. Patient #10 suffered from compensated diabetes mellitus and withdrew from the study due to worsening of diabetic arteriopathy. The following patients had a relevant decrease of one or more tested variables at last assessment: patients #11 and #24 had a decrease of red blood cells, patient #33 a decrease of the percentage of lymphocytes and patient #31 a decrease of serum chloride.

9.3.2 URINALYSIS

Urinalysis results are listed by patient in Appendix 12.2.2 (Individual Data Listings).
No abnormalities were detected in all patients, but patient #15 on RBX, previously commented, who had abnormal specific gravity as well as albumin and red blood cells abnormally present at day 8. These abnormalities were probably associated with the syndrome of inappropriate ADH secretion that caused the patient's withdrawal from the study (Appendix 12.2.1).

9.4 Electrocardiogram

The number of patients evaluated for ECG is summarised in Table 44 by assessment times. The individual patients findings are detailed by assessment times in Table 45. At screening the two treatment groups were well matched as for frequency of abnormal findings, present in the vast majority of patients in both groups (79.2% in the RBX and 84.6% in the PL group).

In Table 46 frequency of abnormal/normal findings at last assessment in patients with abnormal/normal baseline tracings are reported. Two patients under RBX and 3 under PL, with abnormal baseline, showed normal ECG at last assessment. Only 1 subject with normal tracing at baseline showed at least one abnormality at last assessment. This patient, #28, was under RBX and the abnormalities concerned rhythm disorders (sinus tachycardia and occasional atrial ectopic beats).

The frequency of individual abnormalities at baseline and during the study is reported in Tables 47 and 48, respectively. At baseline and during the study, the frequency of patients with at least one abnormality in each abnormality group is similar in the two treatment groups, except for ischemic signs, more frequent in the PL group.

The abnormalities newly appeared during treatment are summarized by group of abnormalities in Table 49. Among the newly appeared abnormalities, no major differences between the two treatment groups are apparent.

9.5 Electroencephalogram

The number of patients evaluated for EEG were 17 (70.8%) on RBX and 21 (80.8%) on PL. EEG results are listed in Appendix 12.2.2. In the RBX group, no modifications in comparison with the screening assessment were apparent. In the PL group, only 1 patient, #27, showed a slight modification in comparison with the screening assessment, with increased generalized θ activity.

10. DISCUSSION

The objective of the study was the evaluation of the efficacy and tolerability of RBX in elderly depressed patients.

On the basis of the objective, the study was carried out according to a double-blind, parallel group, PL-controlled design organized in one center.

Selection of the study end-point was made in the absence of published data on the pattern of the assessment instruments in the study experimental conditions, though response and remission were defined according to widely accepted criteria. On the basis of the above, the study was seen as an exploratory one, and the sample size was decided on the basis of center's recruitment capacity. After recruiting 50 of the 70 planned patients the recruitment was stopped because of the low response rate in the overall sample (18%), not compatible with the study being informative on the basis of the adopted end-points.

Out of 50 patients admitted to the study, 24 entered the RBX group and 26 the PL group. A total of 38 patients completed the 8 weeks treatment period: 17 in RBX group and 21 in PL group. The treatment was discontinued in 7 patients treated with RBX and 5 with PL, due to adverse events (3 and 2 in RBX and PL group respectively), intercurrent medical problems (1 patient in RBX and 1 in PL group) and uncooperativeness (3 patients in RBX group and 2 in PL group).

The clinical response rate was very low, and similar to both treatments. One possible reason may be the relatively low treatment duration: expected response to active antidepressant medication is 50-60% in the elderly (ranging from 22 to 75%) [15], but the clinical improvement often requires up to 12 weeks of treatment [16]. This is not comparable to the experimental study conditions where the treatment period was restricted to 8 weeks only.

A further reason of the lack of difference in efficacy between the two treatment groups may be the high rate of co-morbidity in the whole sample. It is an obvious fact that depression in old age is associated with a high rate of somatic complaints and co-morbidity with physical illnesses [17,

18], which usually entail the administration of a large number of concomitant medication. This fact was also observed in this study population and determined a clinical picture which hardly allowed to discriminate the effect of the active treatment. The treatment of depressive symptoms rarely relieves somatic complaints, and demonstration of efficacy could be problematic, particularly when selecting the criterion of 50% decrease of the HAM-D as study end-point. Recent reports suggest that coexisting physical illness, among other factors, predicts poor prognosis in elderly depression [19]. This leads to the general rule that regardless of treatment 1/3 of aged depressive patients show improvement, 1/3 are unchanged and 1/3 get worse [19].

The study demonstrated good overall tolerability of RBX in elderly depressed patients. With the exception of one serious adverse reaction (syndrome of inappropriate secretion of ADH), other adverse events were trivial (anxiety, hypochondriasis, hypertension, agitation, facial paresthesia, heartburn and vomiting). The profile of these reactions is similar to the already known side effects which occurred under RBX treatment in younger patients [1].

In the previous RBX studies it was found that the treatment with RBX may cause orthostatic hypotension with compensatory tachycardia [1]. Although in the present study a slight increase of mean and median heart rate were found, the modifications were modest, and no patient discontinued treatment because of orthostatic hypotension. However, 8 patients on RBX compared to 2 on PL had heart rate values >100 beats/min at least once during the study period.

The overall laboratory test results following RBX did not show relevant abnormalities with the exception of the case, above commented, of syndrome of inappropriate ADH secretion which was accompanied by serum electrolytes decrease. Among most relevant side-effects of tricyclic antidepressants in the elderly are ECG modifications, sedation and anticholinergic effects [20]: these events were never reported in the present study suggesting a satisfactory tolerability profile of RBX in elderly depressed patients.

Nine patients with values of creatinine clearance (under 30 ml/min) possibly leading to interference with the elimination of drugs were admitted to the study and 5 of them received RBX. In these subjects newly observed signs/symptoms were not observed to a grater extent compared to the other patients treated with RBX, suggesting a good tolerability of RBX also when a possible accumulation of the experimental drug could occur.

In conclusion, the results of the study, while inconclusive on the study end-point, chosen on the basis of theoretical considerations in the absence of established methodology, do provide indications on the good tolerability of RBX in elderly depressed patients. No difference between RBX and PL was found regarding efficacy, most probably due to the selection of a study end-point, difficult to be verified, particularly in patients with high frequency of associated physical complaints. However, in view of the available evidence on the efficacy of the product in Major Depressive Disorders in the adult, further controlled studies in the elderly population appear to be warranted.

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TABLES

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 1

CLASSIFICATION AT END OF STUDY

	TREATMENT	
	REBOXETINE	PLACEBO
TREATMENT COMPLETED AS PER PROTOCOL		
no	7	5
yes	17	21
DRUG COMPLIANCE		
as prescribed	22	25
unknown	2	1
TREATMENT CONTINUED		
no	18	22
yes	6	4

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TABLE No.: 2

REASONS FOR DISCONTINUATION

	TREATMENT	
	REBOXETINE	PLACEBO
ADVERSE EVENT	3	2
INTERCURRENT MEDICAL PROBLEMS	1	1
PATIENT UNCOOP./UNRELIABLE/NOT COMPLIANT	3	2
TOTAL	7	5

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TABLE No.: 3

DEMOGRAPHIC DATA

		TREATMENT	
		REBOXETINE	PLACEBO
SEX: MALE	N	5	6
	%	20.83	23.08
SEX: FEMALE	N	19	20
	%	79.17	76.92
AGE(years):	mean	79.75	80.15
	stdev	7.11	4.51
	median	82.00	80.00
	min	63	72
	max	90	89
	N	24	26
	unk.	0	0
HEIGHT(cm):	mean	162.29	159.27
	stdev	6.36	10.25
	median	161.50	157.50
	min	153	132
	max	178	178
	N	24	26
	unk.	0	0
WEIGHT(kg):	mean	66.02	63.63
	stdev	12.04	13.56
	median	66.00	64.50
	min	44	38
	max	90	96
	N	24	26
	unk.	0	0

TABLE No.: 4

DIAGNOSIS AND HISTORY OF MENTAL DISORDERS

			TREATMENT	
			REBOXETINE	PLACEBO
DIAGNOSIS	296.2	N	18	18
		%	75.00	69.23
	296.3	N	6	8
		%	25.00	30.77
	unk.	N	0	0
		%	0.00	0.00
AGE OF ONSET (years)		mean	72.90	73.29
		stdev	19.17	19.26
		median	79.50	80.00
		min	20	20
		max	90	89
		N	20	21
		unk.	4	5
NUMBER OF PREVIOUS EPISODES		mean	5.67	4.13
		stdev	3.27	1.96
		median	6.00	4.50
		min	2	1
		max	10	6
		N	6	8
DURATION OF LAST EPISODE (months)		mean	2.29	2.88
		stdev	0.95	0.35
		median	3.00	3.00
		min	1	2
		max	3	3
		N	7	8
DURATION OF PRESENT EPISODE (months)		mean	1.92	2.12
		stdev	0.72	1.03
		median	2.00	2.00
		min	1.00	1.00
		max	4	6
		N	24	26
CHARACT. OF PRESENT EPISODE	exacerbation	N	5	8
	recurrence	N	5	6
	different	N	0	0
	first occurr.	N	14	12
ONSET OF PRESENT EPISODE	acute	N	2	2
	subacute	N	19	19
	insidious	N	3	5
PRECIPIT. EXTERNAL STRESS	absent	N	1	0
	prob.present	N	11	18
	def.present	N	12	8
DSM III-R	A present	N	24	26
DSM III-R	B present	N	24	26
DSM III-R	C present	N	24	26
DSM III-R	D present	N	24	26

DIAGNOSIS: 296.2=Major Depressive Disorder,Single Episode

296.3=Major Depressive Disorder,Recurrent Episode

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TABLE No.: 5

MEDICAL HISTORY

	TREATMENT	
	REBOXETINE	PLACEBO
PREVIOUS DISEASES		
PULMONARY TUBERCULOSIS	1	3
GENITOURINARY TB	1	
MALIGNANT NEOPLASM COLON	1	
OTH MALIG NEO GI/PERITON	1	
MALIG NEO FEMALE BREAST	2	
DISEASE OF HODGKIN		1
UTERINE LEIOMYOMA		1
DIABETES MELLITUS	3	6
DIS CARBOHYDRATE METABOL		1
DIS OF LIPOID METABOLISM		1
SPINAL CORD DISEASE NEC	1	
DISORDERS OF EAR NEC		1
ESSENTIAL HYPERTENSION	5	3
HYPERTENSIVE HEART DIS	4	1
OTH CHR ISCHEMIC HRT DIS		3
OTH ENDOCARDIAL DISEASE	1	
CONDUCTION DISORDERS	1	
CARDIAC DYSRHYTHMIAS	1	
ILL-DEFINED HEART DIS	1	1
PRECEREBRAL OCCLUSION		1
THROMBOPHLEBITIS	1	2
VARICOSE VEINS, LEG	1	
BRONCOPNEUMONIA ORG NOS	1	
CHRONIC BRONCHITIS		2

(CONTINUED)

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TABLE No.: 5

MEDICAL HISTORY

	TREATMENT	
	REBOXETINE	PLACEBO
PREVIOUS DISEASES		
GASTRIC ULCER	1	
GASTRITIS AND DUODENITIS		1
OTHER ABDOMINAL HERNIA	1	1
INTESTINAL OBSTRUCTION		1
CHR LIVER DIS/CIRRHOSIS		1
CHOLELITHIASIS	3	4
GENITAL PROLAPSE	1	
CHRONIC ULCER OF SKIN	1	1
OTH INFLAMM POLYARTHROP	1	
OSTEOARTHROSIS ET AL	12	10
OTHER JOINT DERANGEMENT		1
JOINT DISORDER NEC NOS		1
SPONDYLOSIS ET AL	4	2
OSTEITIS DEFORMANS	1	
OTHER BONE AND CARTILAGE DISEASE	1	4
SENILITY W/O PSYCHOSIS	1	

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TABLE No.: 6

MEDICAL HISTORY BY BODY SYSTEM

	TREATMENT	
	REBOXETINE	PLACEBO
BODY SYSTEM		
INFECTIOUS AND PARASTITIC DISEASE	2	3
NEOPLASM	4	2
ENDOCR.,NUTRIT. AND METAB. DISEASES	3	7
NERVOUS SYSTEM AND SENSE ORGANS	1	1
CIRCULATORY SYSTEM	13	9
RESPIRATORY SYSTEM	1	2
DIGESTIVE SYSTEM	5	8
GENITOURINARY SYSTEM	1	
SKIN AND SUBCUTANEOUS TISSUE	1	1
MUSCOLOSKELETAL SYS.AND CONNETIVE TISSUE	16	13
SYMPT.,SIGNS AND ILL DEFINED CONDITIONS	1	
TOTAL	48	46

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TABLE No. : 7

CHEST X-RAY: PATIENTS WITH MOST FREQUENT ABNORMALITIES

	Total	Treatment			
		RBX (n=24)		PL (n=26)	
Abnormalities	N	N	%	N	%
Senile emphisema	29	16	66.6	13	50.0
Enlarged cardiac shadow	10	4	16.6	6	23.1
Arcus aortae calcification	4	4	16.6	0	0.0
Other	8	4	16.6	4	15.4

Other=tuberculoma, scars, bronchiectasic picture, interstice reiforcement, pleuric veil.

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PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 8

VITAL SIGNS: RESPIRATORY RATE

			VISIT -1
TREATMENT			
REBOXETINE	N		24
	MEAN		19.88
	STDEV		1.92
	MEDIAN		20.00
	MIN		16.00
	MAX		24.00
	MISS		0
PLACEBO	N		26
	MEAN		20.15
	STDEV		2.11
	MEDIAN		20.00
	MIN		16.00
	MAX		24.00
	MISS		0

TABLE No.: 9
PATIENTS TREATED AT LEAST ONCE DURING WASH OUT PERIOD

DRUG	N
DIGOXINE	16
HYDROCHLOROTHIAZIDE	16
TRIAZOLAM	14
AMILORIDE HYDROCHLORIDE	13
ASCORBIC ACID	9
CALCIUM CARBONATE	9
ERGOCALCIFEROL	9
PYRIDOXINE HYDROCHLORIDE	9
AMLODIPINE	6
RANITIDINE HYDROCHLORIDE	6
NIFEDIPINE	5
FUROSEMIDE	4
HEPARIN CALCIUM	4
INDOBUFEN SODIUM	4
SPIRONOLACTONE	4
THEOPHYLLINE	4
GLIBENCLAMIDE	3
NITROGLYCERIN	3
PENTOXIFYLLINE	3
PHENFORMIN HYDROCHLORIDE	3
PIROXICAM	3
VERAPAMIL HYDROCHLORIDE	3
BUFLOMEDIL HYDROCHLORIDE	2
CAPTOPRIL	2
ENALAPRIL MALEATE	2
GLIBENCLAMIDE	2
INSULIN	2
LACTULOSE	2
NICARDIPINE HYDROCHLORIDE	2
ALLOPURINOL	1
ATENOLOL	1
BETAHISTINE HYDROCHLORIDE	1
CARNITINE HYDROCHLORIDE	1
CINNARIZINE	1
CISAPRIDE	1
DICLOFENAC SODIUM	1
DILTIAZEM HYDROCHLORIDE	1
DIMETICONE	1

(continued)

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 9
PATIENTS TREATED AT LEAST ONCE DURING WASH OUT PERIOD

DRUG	N
DOMPERIDONE	1
FENDILINE HYDROCHLORIDE	1
FUROSEMIDE	1
INDAPAMIDE	1
ISOSORBIDE MONONITRATE	1
NIMODIPINE	1
PRAVASTATIN	1
QUINAPRIL HYDROCHLORIDE	1
TENOXICAM	1
THYMUS EXTRACT	1
TICLOPIDINE HYDROCHLORIDE	1
TOLBUTAMIDE	1
VITAMIN D	1

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 10
NEWLY ADMINISTERED MEDICATION BY ACTIVE PRINCIPLE
Number of patients treated at least once during treatment

DRUG	TOTAL	RBX	PL
HYDROCHLOROTHIAZIDE	3	1	2
TENOXICAM	6	4	2
CAPTOPRIL	3	1	2
ENALAPRIL MALEATE	2	1	1
ACETYL-SALICYLIC ACID	2	1	1
CAFFEIN	2	1	1
NIFEDIPINE	2	2	
PARACETAMOL	2	1	1
PIROXICAM	2	1	1
ALUMINIUM HYDROXIDE GEL	1	1	
AMILORIDE HYDROCHLORIDE	1	1	
CISAPRIDE	1		1
CORTICOSTEROID NOS	1		1
FUROSEMIDE	1		1
MAGNESIUM HYDROXIDE	1	1	
METOCLOPRAMIDE HYDROCHLORIDE	1	1	
NORFLOXACIN	1		1
PENTOXIFYLLINE	1	1	
PROMETHAZINE HYDROCHLORIDE	1		1
RANITIDINE HYDROCHLORIDE	1		1
TRIAZOLAM	1		1
VERAPAMIL HYDROCHLORIDE	1	1	

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 2024/032

TABLE No.: 11

CLASSIFICATION AT LAST VISIT ACCORDING TO PROTOCOL CRITERIA

	RESPONSE						REMISSION					
	ONLY BASELINE		PRESENCE		ABSENCE		ONLY BASELINE		PRESENCE		ABSENCE	
	N	%	N	%	N	%	N	%	N	%	N	%
TREATMENT												
REBOXETINE	2	8.33	4	16.67	18	75.00	2	8.33	3	12.50	19	79.17
PLACEBO	1	3.85	5	19.23	20	76.92	1	3.85	3	11.54	22	84.62

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PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 12

HAMILTON DEPRESSION RATING SCALE

		VISIT				
TREATMENT		-1	0	14	28	56
REBOXETINE	N	24	24	22	20	17
	MEAN	23.21	23.21	20.82	18.75	16.59
	STDEV	2.69	2.69	3.05	3.80	4.73
	MEDIAN	23.00	23.00	21.00	19.00	17.00
	MIN	19	19	14	10	6
	MAX	31	31	28	25	23
PLACEBO	N	26	26	25	24	21
	MEAN	23.08	23.12	20.72	18.50	15.52
	STDEV	2.23	2.21	2.62	3.74	4.78
	MEDIAN	23.00	23.00	21.00	19.50	14.00
	MIN	19	19	15	9	6
	MAX	28	28	26	25	25

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 2024/032

TABLE No.: 13

HAMILTON DEPRESSION RATING SCALE - SUMMARY STATISTICS AT LAST ASSESSMENT

		VISIT				
		14	28	36	56	TOTAL
TREATMENT						
REBOXETINE	N	1	4		17	22
	MEAN	23.00	18.25		16.59	17.18
	STDEV		4.86		4.73	4.75
	MEDIAN	23.00	20.50		17.00	17.50
	MIN	23	11		6	6
	MAX	23	21		23	23
PLACEBO	N	1	2	1	21	25
	MEAN	22.00	20.50	26.00	15.52	16.60
	STDEV		2.12		4.78	5.14
	MEDIAN	22.00	20.50	26.00	14.00	16.00
	MIN	22	19	26	6	6
	MAX	22	22	26	25	26

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PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 2012A/032

TABLE No.: 14

TOTAL SCORE MINI MENTAL STATE

		VISIT	
		-1	56
TREATMENT			
REBOXETINE	N	24	17
	MEAN	22.04	22.35
	STDEV	1.37	1.46
	MEDIAN	22.00	22.00
	MIN	20	20
	MAX	25	25
PLACEBO	N	26	21
	MEAN	21.81	22.29
	STDEV	1.52	1.93
	MEDIAN	21.00	22.00
	MIN	20	20
	MAX	28	29

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 15

TOTAL SCORE MINI MENTAL STATE - LAST ASSESSMENT

		VISIT		
		36	56	TOTAL
TREATMENT				
REBOXETINE	N		17	17
	MEAN		22.35	22.35
	STDEV		1.46	1.46
	MEDIAN		22.00	22.00
	MIN		20	20
	MAX		25	25
PLACEBO	N	1	21	22
	MEAN	19.00	22.29	22.14
	STDEV		1.93	2.01
	MEDIAN	19.00	22.00	22.00
	MIN	19	20	19
	MAX	19	29	29

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PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 16

TOTAL SCORE SCAG

		VISIT			
TREATMENT		0	14	28	56
REBOXETINE	N	24	22	20	17
	MEAN	56.88	54.05	50.65	47.12
	STDEV	4.30	4.02	5.56	7.21
	MEDIAN	55.00	54.00	52.00	49.00
	MIN	51	45	38	34
	MAX	68	62	59	55
PLACEBO	N	26	25	24	21
	MEAN	59.00	55.24	50.92	47.19
	STDEV	4.77	5.45	7.45	8.40
	MEDIAN	58.50	56.00	53.50	47.00
	MIN	50	43	32	25
	MAX	68	64	62	64

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 2012A/032

TABLE No.: 17

TOTAL SCORE SCAG - LAST ASSESSMENT

		VISIT				
TREATMENT		14	28	36	56	TOTAL
REBOXETINE	N	1	4		17	22
	MEAN	59.00	51.25		47.12	48.41
	STDEV		8.85		7.21	7.68
	MEDIAN	59.00	55.50		49.00	50.50
	MIN	59	38		34	34
	MAX	59	56		55	59
PLACEBO	N	1	2	1	21	25
	MEAN	57.00	50.50	73.00	47.19	48.88
	STDEV		10.61		8.40	9.65
	MEDIAN	57.00	50.50	73.00	47.00	48.00
	MIN	57	43	73	25	25
	MAX	57	58	73	64	73

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PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 18

TOTAL SCORE GDS

		VISIT			
TREATMENT		0	14	28	56
REBOXETINE	N	24	22	20	17
	MEAN	20.17	19.64	17.90	17.18
	STDEV	2.20	2.46	3.02	4.52
	MEDIAN	20.00	20.00	18.50	18.00
	MIN	15	13	10	8
	MAX	25	25	22	24
PLACEBO	N	26	25	24	21
	MEAN	20.96	19.80	18.04	17.00
	STDEV	2.84	2.78	3.14	3.61
	MEDIAN	21.00	19.00	18.00	16.00
	MIN	15	15	11	10
	MAX	26	25	23	25

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PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 19

TOTAL SCORE GDS - LAST ASSESSMENT

		VISIT			
TREATMENT		14	28	56	TOTAL
REBOXETINE	N	1	4	17	22
	MEAN	20.00	16.50	17.18	17.18
	STDEV		4.36	4.52	4.33
	MEDIAN	20.00	18.50	18.00	18.00
	MIN	20	10	8	8
	MAX	20	19	24	24
PLACEBO	N	1	3	21	25
	MEAN	22.00	18.00	17.00	17.32
	STDEV		1.73	3.61	3.48
	MEDIAN	22.00	17.00	16.00	17.00
	MIN	22	17	10	10
	MAX	22	20	25	25

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 20

CLINICAL GLOBAL IMPRESSION : SEVERITY OF ILLNESS

		SEVERITY OF ILLNESS										TOTAL
		Borderline mentally ill		Mildly ill		Moderately ill		Markedly ill				
		N	ROW %	N	ROW %	N	ROW %	N	ROW %	N		
VISIT	TREATMENT											
0	REBOXETINE			2	8.33	19	79.17	3	12.50			24
	PLACEBO			2	7.69	20	76.92	4	15.38			26
14	REBOXETINE			6	27.27	15	68.18	1	4.55			22
	PLACEBO			5	20.00	18	72.00	2	8.00			25
28	REBOXETINE	2	10.00	5	25.00	13	65.00					20
	PLACEBO	1	4.35	8	34.78	13	56.52	1	4.35			23
56	REBOXETINE	4	23.53	8	47.06	5	29.41					17
	PLACEBO	4	19.05	11	52.38	6	28.57					21

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 21

CLINICAL GLOBAL IMPRESSION : SEVERITY OF ILLNESS - LAST ASSESSMENT

		SEVERITY OF ILLNESS						TOTAL
		Borderline mentally ill		Mildly ill		Moderately ill		
		N	ROW %	N	ROW %	N	ROW %	N
VISIT	TREATMENT							
14	REBOXETINE					1	100.00	1
	PLACEBO					1	100.00	1
28	REBOXETINE	1	25.00			3	75.00	4
	PLACEBO			1	50.00	1	50.00	2
36	PLACEBO					1	100.00	1
56	REBOXETINE	4	23.53	8	47.06	5	29.41	17
	PLACEBO	4	19.05	11	52.38	6	28.57	21
TOTAL	TREATMENT							
	REBOXETINE	5	22.73	8	36.36	9	40.91	22
	PLACEBO	4	16.00	12	48.00	9	36.00	25

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PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 22

SHIFT TABLE (LAST VALUE VS VISIT 0) SEVERITY

	SEVERITY				TOTAL
	DECREASED		NO CHANGE		
TREATMENT	N	ROW %	N	ROW %	N
REBOXETINE	11	50.00	11	50.00	22
PLACEBO	15	60.00	10	40.00	25

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 23

CLINICAL GLOBAL IMPRESSION : GLOBAL IMPROVEMENT

		GLOBAL IMPROVEMENT										TOTAL
		Very much improved		Much improved		Minimally improved		No change		Minimally worse		
VISIT	TREATMENT	N	ROW %	N	ROW %	N	ROW %	N	ROW %	N	ROW %	N
14	REBOXETINE			4	18.18	5	22.73	13	59.09			22
	PLACEBO			3	12.00	6	24.00	16	64.00			25
28	REBOXETINE			6	30.00	9	45.00	4	20.00	1	5.00	20
	PLACEBO			9	39.13	6	26.09	8	34.78			23
56	REBOXETINE	1	5.88	7	41.18	5	29.41	4	23.53			17
	PLACEBO			15	71.43	2	9.52	3	14.29	1	4.76	21

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 24

CLINICAL GLOBAL IMPRESSION : GLOBAL IMPROVEMENT - LAST ASSESSMENT

		GLOBAL IMPROVEMENT												TOTAL	
		Very much improved		Much improved		Minimally improved		No change		Minimally worse					
VISIT	TREATMENT	N	ROW %	N	ROW %	N	ROW %	N	ROW %	N	ROW %	N			
14	REBOXETINE							1	100.00					1	
	PLACEBO							1	100.00					1	
28	REBOXETINE			1	25.00			2	50.00	1	25.00			4	
	PLACEBO					1	50.00	1	50.00					2	
36	PLACEBO							1	100.00					1	
56	REBOXETINE	1	5.88	7	41.18	5	29.41	4	23.53					17	
	PLACEBO			15	71.43	2	9.52	3	14.29	1	4.76			21	
TOTAL	TREATMENT														
	REBOXETINE	1	4.55	8	36.36	5	22.73	7	31.82	1	4.55			22	
	PLACEBO			15	60.00	3	12.00	6	24.00	1	4.00			25	

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 25

STATISTICAL ANALISYS OF EFFICACY INDEX

		N	MEAN	STDEV	MEDIAN	MIN	MAX
TREATMENT	VISIT						
REBOXETINE	14	22	1.59	0.80	1.00	1.00	3.00
	28	20	2.05	0.76	2.00	1.00	3.00
	56	17	2.53	1.12	3.00	1.00	4.00
PLACEBO	14	25	1.52	0.71	1.00	1.00	3.00
	28	23	2.01	0.92	2.00	0.33	3.00
	56	21	2.71	0.96	3.00	1.00	4.00

EFFICACY INDEX: computed from the vector activity by the vector side effects

TABLE No.: 26

FREQUENCY OF ADVERSE EVENTS GROUPED BY BODY SYSTEM AND EXPERIMENTAL TREATMENT

		TREATMENT	
		REBOXETINE	PLACEBO
BODY SYSTEM	ADVERSE EVENT		
BODY AS A WHOLE-GENERAL	ASTHENIA		1
CARDIOVASCUL-AR, GENERAL	HYPERTENSION	2	
CENTRAL AND PERIPHERAL NERVOUS SYSTEM	PARAESTHESIA	1	
	VERTIGO		1
ENDOCRINE	SIADH	1	
GASTRO-INTESTINAL SYSTEM	VOMITING	1	
	ABDOMINAL PAIN		1
	DYSPEPSIA	1	1
PSYCHIATRIC	AGITATION	1	1
	ANXIETY	1	
	NERVOUSNESS	1	
	NEUROSIS	1	
TOTAL		10	5

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 27

NUMBER OF SUBJECTS EVALUATED FOR BLOOD PRESSURE AND HEART RATE AT EACH VISIT, ACCORDING TO TREATMENT

		VISIT														
		-1	0	7	8	14	21	23	24	28	30	33	36	56	
TREATMENT															
REBOXETINE	LYING S.B.P.	24	24	6	1	23	2		1	21	1	1			17
	LYING D.B.P.	24	24	6	1	23	2		1	21	1	1			17
	LYING HEART RATE	24	24	6	1	23	2		1	21	1	1			17
	STANDING S.B.P.	24	24	6	1	22	2		1	21	1	1			17
	STANDING D.B.P	24	24	6	1	22	2		1	21	1	1			17
	STANDING HEART RATE	24	24	6	1	22	2		1	21	1	1			17
PLACEBO	LYING S.B.P.	26	26	8		25	1	1		24			1	22	
	LYING D.B.P.	26	26	8		25	1	1		24			1	22	
	LYING HEART RATE	26	26	8		25	1	1		24			1	22	
	STANDING S.B.P.	25	26	8		25	1	1		24			1	22	
	STANDING D.B.P	25	26	8		25	1	1		24			1	22	
	STANDING HEART RATE	25	26	8		25	1	1		24			1	22	

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 28

VITAL SIGNS: 5m. LYING SYSTOLIC BLOOD PRESSURE

		VISIT				
		-1	0	1-14	15-28	29-56
TREATMENT						
REBOXETINE	N	24	24	24	22	19
	MEAN	145.21	142.92	141.46	146.36	136.32
	STDEV	19.97	14.29	22.38	17.74	18.92
	MEDIAN	140.00	140.00	137.50	142.50	130.00
	MIN	110.00	120.00	115.00	115.00	110.00
	MAX	180.00	170.00	210.00	180.00	180.00
	MISS	0	0	0	0	0
PLACEBO	N	26	26	26	25	23
	MEAN	143.85	144.04	145.58	150.20	143.26
	STDEV	18.56	21.17	17.28	16.04	15.20
	MEDIAN	142.50	140.00	145.00	150.00	140.00
	MIN	110.00	110.00	120.00	125.00	110.00
	MAX	180.00	190.00	180.00	185.00	175.00
	MISS	0	0	0	0	0

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 29

VITAL SIGNS: 5m. LYING DIASTOLIC BLOOD PRESSURE

		VISIT				
		-1	0	1-14	15-28	29-56
TREATMENT						
REBOXETINE	N	24	24	24	22	19
	MEAN	80.42	80.00	78.96	81.14	77.37
	STDEV	7.65	6.08	11.42	9.63	7.88
	MEDIAN	80.00	80.00	77.50	80.00	80.00
	MIN	60.00	70.00	60.00	70.00	60.00
	MAX	100.00	90.00	100.00	100.00	90.00
	MISS	0	0	0	0	0
PLACEBO	N	26	26	26	25	23
	MEAN	75.38	76.73	77.50	77.40	76.52
	STDEV	7.61	8.12	7.65	7.52	8.04
	MEDIAN	77.50	80.00	80.00	80.00	80.00
	MIN	60.00	60.00	70.00	60.00	60.00
	MAX	90.00	100.00	100.00	95.00	90.00
	MISS	0	0	0	0	0

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 30

VITAL SIGNS: 2m. STANDING SYSTOLIC BLOOD PRESSURE

		VISIT				
TREATMENT		-1	0	1-14	15-28	29-56
REBOXETINE	N	24	24	23	22	19
	MEAN	138.54	136.04	133.48	138.18	130.53
	STDEV	19.92	14.44	22.43	17.76	18.33
	MEDIAN	135.00	135.00	130.00	135.00	125.00
	MIN	100.00	110.00	105.00	110.00	105.00
	MAX	175.00	165.00	200.00	175.00	175.00
	MISS	0	0	1	0	0
PLACEBO	N	25	26	26	25	23
	MEAN	138.20	139.23	138.08	142.00	136.74
	STDEV	19.03	19.78	17.27	17.26	15.35
	MEDIAN	140.00	135.00	140.00	140.00	135.00
	MIN	100.00	115.00	110.00	115.00	110.00
	MAX	175.00	185.00	185.00	180.00	170.00
	MISS	1	0	0	0	0

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 31

VITAL SIGNS: 2m. STANDING DIASTOLIC BLOOD PRESSURE

		VISIT				
TREATMENT		-1	0	1-14	15-28	29-56
REBOXETINE	N	24	24	23	22	19
	MEAN	78.96	78.54	78.70	79.32	77.89
	STDEV	6.42	5.21	11.50	8.06	6.31
	MEDIAN	80.00	80.00	75.00	75.00	75.00
	MIN	65.00	70.00	60.00	70.00	65.00
	MAX	95.00	90.00	105.00	100.00	90.00
	MISS	0	0	1	0	0
PLACEBO	N	25	26	26	25	23
	MEAN	77.00	77.88	77.88	77.40	77.17
	STDEV	6.45	7.24	6.35	6.79	6.37
	MEDIAN	75.00	75.00	75.00	75.00	75.00
	MIN	65.00	70.00	70.00	65.00	65.00
	MAX	95.00	105.00	90.00	95.00	90.00
	MISS	1	0	0	0	0

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 32

VITAL SIGNS: 5m. LYING HEART RATE

		VISIT				
		-1	0	1-14	15-28	29-56
TREATMENT						
REBOXETINE	N	24	24	24	22	19
	MEAN	77.50	75.42	81.17	79.64	81.16
	STDEV	5.24	4.62	8.65	7.14	9.20
	MEDIAN	76.50	76.00	78.00	77.00	78.00
	MIN	70.00	68.00	70.00	70.00	72.00
	MAX	90.00	88.00	100.00	98.00	100.00
	MISS	0	0	0	0	0
PLACEBO	N	26	26	26	25	23
	MEAN	77.54	74.08	74.31	77.36	78.00
	STDEV	7.78	8.53	5.65	3.04	7.53
	MEDIAN	76.00	74.00	76.00	78.00	76.00
	MIN	60.00	58.00	64.00	72.00	70.00
	MAX	100.00	100.00	84.00	84.00	100.00
	MISS	0	0	0	0	0

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PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 33

VITAL SIGNS: 2m. STANDING HEART RATE

		VISIT				
		-1	0	1-14	15-28	29-56
TREATMENT						
REBOXETINE	N	24	24	23	22	19
	MEAN	83.50	81.75	87.87	86.36	89.16
	STDEV	5.99	5.05	9.80	8.25	10.80
	MEDIAN	84.00	82.00	84.00	84.00	84.00
	MIN	72.00	74.00	76.00	76.00	78.00
	MAX	96.00	92.00	110.00	110.00	112.00
	MISS	0	0	1	0	0
PLACEBO	N	25	26	26	25	23
	MEAN	82.72	79.38	80.69	84.32	85.39
	STDEV	8.38	8.65	6.86	4.11	10.29
	MEDIAN	84.00	78.00	82.00	84.00	82.00
	MIN	68.00	60.00	66.00	76.00	76.00
	MAX	108.00	104.00	98.00	96.00	120.00
	MISS	1	0	0	0	0

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 34

NUMBER AND PERCENTAGE OF SUBJECTS WITH BLOOD PRESSURE AND HEART RATE VALUES LOWER , EQUAL OR HIGHER THAN VISIT 0

TREATMENT REBOXETINE	VISIT		
	1-14	15-28	29-56
LYING S.B.P EVALUATED	24	22	19
% UP	41.7	45.5	26.3
% SAME	12.5	18.2	15.8
% DOWN	45.8	36.4	57.9
LYING D.B.P. EVALUATED	24	22	19
% UP	29.2	36.4	26.3
% SAME	29.2	27.3	26.3
% DOWN	41.7	36.4	47.4
LYING H.R. EVALUATED	24	22	19
% UP	66.7	72.7	57.9
% SAME	16.7	13.6	10.5
% DOWN	16.7	13.6	31.6
STANDING S.B.P EVALUATED	23	22	19
% UP	39.1	40.9	36.8
% SAME	17.4	18.2	0.0
% DOWN	43.5	40.9	63.2
STANDING D.B.P. EVALUATED	23	22	19
% UP	30.4	31.8	21.1
% SAME	26.1	22.7	31.6
% DOWN	43.5	45.5	47.4
STANDING H.R. EVALUATED	23	22	19

(CONTINUED)

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 34

NUMBER AND PERCENTAGE OF SUBJECTS WITH BLOOD PRESSURE AND HEART RATE VALUES LOWER , EQUAL OR HIGHER THAN VISIT 0

TREATMENT REBOXETINE	VISIT		
	1-14	15-28	29-56
% UP	73.9	68.2	68.4
% SAME	8.7	22.7	10.5
% DOWN	17.4	9.1	21.1

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 35

NUMBER AND PERCENTAGE OF SUBJECTS WITH BLOOD PRESSURE AND HEART RATE VALUES LOWER , EQUAL OR HIGHER THAN VISIT 0

TREATMENT PLACEBO	VISIT		
	1-14	15-28	29-56
LYING S.B.P EVALUATED	26	25	23
% UP	34.6	68.0	47.8
% SAME	26.9	4.0	8.7
% DOWN	38.5	28.0	43.5
LYING D.B.P. EVALUATED	26	25	23
% UP	26.9	36.0	34.8
% SAME	46.2	32.0	34.8
% DOWN	26.9	32.0	30.4
LYING H.R. EVALUATED	26	25	23
% UP	53.8	64.0	56.5
% SAME	11.5	8.0	13.0
% DOWN	34.6	28.0	30.4
STANDING S.B.P EVALUATED	26	25	23
% UP	38.5	56.0	39.1
% SAME	15.4	12.0	13.0
% DOWN	46.2	32.0	47.8
STANDING D.B.P. EVALUATED	26	25	23
% UP	30.8	40.0	34.8
% SAME	34.6	28.0	34.8
% DOWN	34.6	32.0	30.4
STANDING H.R. EVALUATED	26	25	23

(CONTINUED)

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PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 35

NUMBER AND PERCENTAGE OF SUBJECTS WITH BLOOD PRESSURE AND HEART RATE VALUES LOWER , EQUAL OR HIGHER THAN VISIT 0

TREATMENT PLACEBO	VISIT		
	1-14	15-28	29-56
% UP	46.2	68.0	60.9
% SAME	26.9	12.0	8.7
% DOWN	26.9	20.0	30.4

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 36
PATIENTS WITH AN INCREASE < = 20 MMHG AT LEAST ONCE DURING TREATMENT *vs* DAY 0

TREATMENT	BLOOD PRESSURE	EVALUATED	N	%
RBX	LYING S.B.P.	24	7	29.2
	LYING D.B.P.	24	2	8.3
	STANDING S.B.P.	23	5	21.7
	STANDING D.B.P.	23	3	13.0
PL	LYING S.B.P.	26	11	42.3
	LYING D.B.P.	26	3	11.5
	STANDING S.B.P.	26	9	34.6
	STANDING D.B.P.	26	0	0.0

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 37
PATIENTS WITH A DECREASE < = 20 MMHG AT LEAST ONCE DURING TREATMENT vs DAY 0

TREATMENT	BLOOD PRESSURE	EVALUATED	N	%
RBX	LYING S.B.P.	24	6	25.0
	LYING D.B.P.	24	3	12.5
	STANDING S.B.P.	23	7	30.4
	STANDING D.B.P.	23	1	4.3
PL	LYING S.B.P.	26	5	19.2
	LYING D.B.P.	26	3	11.5
	STANDING S.B.P.	26	7	26.9
	STANDING D.B.P.	26	2	7.7

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 38

PATIENTS WITH LYING OR STANDING HEART RATE > 100 FROM VITAL SIGNS ACCORDING TO TREATMENT AND VISITS

		VISIT				
		-1	0	1-14	15-28	29-56
TREATMENT						
REBOXETINE	5M L.H.R. EVALUATED	24	24	24	22	19
	>100	0	0	0	0	0
	2M S.H.R. EVALUATED	24	24	23	22	19
	>100	0	0	3	2	4
PLACEBO	5M L.H.R. EVALUATED	26	26	26	25	23
	>100	0	0	0	0	0
	2M S.H.R. EVALUATED	25	26	26	25	23
	>100	1	1	0	0	2

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 39

VITAL SIGNS: BODY TEMPERATURE

		VISIT				
		-1	0	1-14	15-28	29-56
TREATMENT						
REBOXETINE	N	24	24	24	22	19
	MEAN	36.41	36.37	36.49	36.58	36.58
	STDEV	0.27	0.47	0.24	0.15	0.17
	MEDIAN	36.40	36.40	36.40	36.60	36.60
	MIN	35.70	35.70	35.70	36.40	36.40
	MAX	36.80	37.60	36.80	36.80	36.80
	MISS	0	0	0	0	0
PLACEBO	N	26	26	26	25	23
	MEAN	36.44	36.47	36.55	36.57	36.47
	STDEV	0.27	0.28	0.13	0.16	0.30
	MEDIAN	36.50	36.50	36.60	36.60	36.50
	MIN	35.60	35.80	36.40	36.40	35.80
	MAX	36.80	36.80	36.80	37.00	36.80
	MISS	0	0	0	0	0

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 40

VITAL SIGNS: BODY WEIGHT

		VISIT			
TREATMENT		0	1-14	15-28	29-56
REBOXETINE	N	24	24	22	19
	MEAN	66.21	65.75	65.36	64.63
	STDEV	11.98	12.03	11.45	11.31
	MEDIAN	67.00	66.50	64.50	66.00
	MIN	45.00	43.00	41.00	40.00
	MAX	90.00	89.00	86.00	84.00
	MISS	0	0	0	0
PLACEBO	N	26	26	25	22
	MEAN	63.50	63.50	62.92	63.14
	STDEV	13.42	13.24	13.58	14.33
	MEDIAN	64.00	64.50	65.00	66.00
	MIN	38.00	38.00	37.00	37.00
	MAX	96.00	95.00	94.00	92.00
	MISS	0	0	0	1

PHARMACIA CNS 9950087
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 41

HEMATOLOGY AND BLOOD CHEMISTRY : MEAN AND MEDIAN VALUES AT EACH VISIT AS COMPARED TO VISIT -1

REBOXETINE		VISIT		
		SCREENING	1-28	29-56
HB	Evaluated	24	23	17
	Mean	12.51	12.73	12.85
	STD	1.13	1.38	1.00
	Min	10.60	10.20	11.60
	Max	15.10	17.10	15.20
	Median	12.30	12.70	12.70
	Median diff.		0.30	0.40
	P value		0.2610	0.0260
HTC	Evaluated	24	23	17
	Mean	38.15	38.34	39.62
	STD	3.38	3.29	3.37
	Min	30.90	30.30	33.60
	Max	44.30	45.40	47.10
	Median	37.50	37.70	39.10
	Median diff.		0.80	3.30
	P value		0.5350	0.0887
RBC	Evaluated	24	23	17
	Mean	4.20	4.29	4.43
	STD	0.42	0.46	0.50
	Min	3.19	3.31	3.58
	Max	5.00	5.27	5.41
	Median	4.17	4.22	4.38
	Median diff.		0.13	0.37
	P value		0.1894	0.0638
PLATELETS	Evaluated	24	23	17
	Mean	229.00	238.39	242.76
	STD	71.01	68.26	51.10
	Min	123.00	122.00	140.00
	Max	425.00	408.00	354.00
	Median	217.00	229.00	253.00
	Median diff.		19.00	14.00
	P value		0.1118	0.3289
WBC	Evaluated	24	23	17

(CONTINUED)

P value: probability from the Wilcoxon signed rank test

PHARMACIA CNS 9850087
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 41

HEMATOLOGY AND BLOOD CHEMISTRY : MEAN AND MEDIAN VALUES AT EACH VISIT AS COMPARED TO VISIT -1

REBOXETINE		VISIT		
		SCREENING	1-28	29-56
WBC	Mean	6.86	7.55	8.15
	STD	1.69	1.60	2.84
	Min	4.00	4.31	4.95
	Max	10.30	10.20	16.47
	Median	6.62	7.38	7.96
	Median diff.		1.15	0.91
	P value		0.0155	0.0348
NEUTROPHILS	Evaluated	24	23	17
	Mean	58.68	58.00	57.91
	STD	10.11	11.48	10.14
	Min	39.10	40.00	39.80
	Max	81.90	91.10	74.80
	Median	59.40	57.20	58.50
	Median diff.		-1.70	-0.20
	P value		0.1973	0.6029
MONOCYTES	Evaluated	24	23	17
	Mean	6.90	7.00	7.17
	STD	1.32	1.46	1.25
	Min	3.40	4.40	5.20
	Max	9.20	10.70	9.30
	Median	6.95	6.90	7.50
	Median diff.		0.00	0.10
	P value		0.6543	0.3550
BASOPHILS	Evaluated	24	23	17
	Mean	0.69	0.63	0.74
	STD	0.22	0.27	0.28
	Min	0.40	0.20	0.40
	Max	1.00	1.40	1.40
	Median	0.70	0.60	0.70
	Median diff.		0.00	0.10
	P value		0.0663	0.2693
LYMPHOCYTES	Evaluated	24	23	17
	Mean	28.53	29.17	29.30

(CONTINUED)

P value: probability from the Wilcoxon signed rank test

TABLE No.: 41

HEMATOLOGY AND BLOOD CHEMISTRY : MEAN AND MEDIAN VALUES AT EACH VISIT AS COMPARED TO VISIT -1

REBOXETINE		VISIT		
		SCREENING	1-28	29-56
LYMPHOCYTES	STD	8.45	10.18	9.39
	Min	11.90	3.40	14.90
	Max	47.50	47.00	47.20
	Median	27.25	30.30	27.90
	Median diff.		0.20	-0.30
	P value		0.5081	0.5874
EOSINOPHILS	Evaluated	24	23	17
	Mean	3.20	2.92	2.65
	STD	2.13	1.96	1.59
	Min	0.10	0.10	0.50
	Max	7.70	8.30	6.50
	Median	2.10	2.50	2.20
	Median diff.		0.00	0.00
	P value		0.8406	0.6780
CREATININE	Evaluated	24	23	17
	Mean	90.79	94.15	88.60
	STD	18.35	20.19	15.72
	Min	63.70	59.40	64.30
	Max	131.00	136.60	116.90
	Median	87.75	93.00	88.70
	Median diff.		1.70	1.60
	P value		0.1995	0.2582
BUN	Evaluated	24	23	17
	Mean	6.50	7.81	7.31
	STD	2.13	2.82	1.36
	Min	0.20	3.80	4.80
	Max	11.20	14.20	10.00
	Median	6.35	7.10	7.40
	Median diff.		0.60	0.50
	P value		0.0768	0.1176
URIC ACID	Evaluated	24	23	17
	Mean	0.30	0.29	0.28
	STD	0.09	0.08	0.08

(CONTINUED)

P value: probability from the Wilcoxon signed rank test

TABLE No.: 41

HEMATOLOGY AND BLOOD CHEMISTRY : MEAN AND MEDIAN VALUES AT EACH VISIT AS COMPARED TO VISIT -1

REBOXETINE		VISIT		
		SCREENING	1-28	29-56
URIC ACID	Min	0.20	0.20	0.20
	Max	0.50	0.50	0.40
	Median	0.30	0.30	0.30
	Median diff.		0.00	0.00
	P value		0.5156	0.7500
TOTAL PROTEINS	Evaluated	24	23	17
	Mean	63.60	65.19	63.45
	STD	5.29	6.73	6.57
	Min	51.70	50.40	51.70
	Max	74.20	81.20	73.80
	Median	62.10	64.30	62.60
	Median diff.		1.40	1.60
	P value		0.1048	0.5966
ALBUMIN	Evaluated	24	23	17
	Mean	59.42	58.40	58.23
	STD	5.75	5.60	5.29
	Min	49.30	47.10	47.90
	Max	70.80	67.10	65.60
	Median	61.85	58.20	58.40
	Median diff.		-1.10	-1.40
	P value		0.2566	0.2069
TOTAL BILIRUBIN	Evaluated	24	23	17
	Mean	9.63	9.49	7.91
	STD	4.82	6.39	3.54
	Min	4.70	4.00	2.60
	Max	21.90	30.70	16.50
	Median	7.95	7.00	8.10
	Median diff.		-0.50	-0.80
	P value		0.0571	0.1711
DIRECT BILIRUBIN	Evaluated	24	23	17
	Mean	4.69	4.67	3.89
	STD	2.69	4.56	1.52
	Min	1.70	1.10	1.60

(CONTINUED)

P value: probability from the Wilcoxon signed rank test

PHARMACIA CNS S&D
REBOXETINE - PROTOCOL 20124/032

3590087

TABLE No.: 41

HEMATOLOGY AND BLOOD CHEMISTRY : MEAN AND MEDIAN VALUES AT EACH VISIT AS COMPARED TO VISIT -1

REBOXETINE		VISIT		
		SCREENING	1-28	29-56
DIRECT BILIRUBIN	Max	10.70	22.30	7.30
	Median	3.65	3.40	3.70
	Median diff.		-0.50	-0.20
	P value		0.1431	0.6031
SGOT	Evaluated	24	23	17
	Mean	17.00	18.65	16.88
	STD	7.66	6.06	6.40
	Min	7.00	7.00	7.00
	Max	46.00	30.00	35.00
	Median	15.00	18.00	16.00
	Median diff.		1.00	0.00
	P value		0.1554	0.7139
SGPT	Evaluated	24	23	17
	Mean	18.00	21.35	20.35
	STD	9.98	11.66	15.58
	Min	6.00	8.00	8.00
	Max	50.00	58.00	74.00
	Median	15.00	19.00	17.00
	Median diff.		1.00	0.00
	P value		0.2833	0.8911
GAMMA-GT	Evaluated	24	23	17
	Mean	39.88	44.13	40.76
	STD	59.66	57.93	50.18
	Min	13.00	9.00	11.00
	Max	301.00	274.00	224.00
	Median	21.00	19.00	23.00
	Median diff.		1.00	2.00
	P value		0.7623	0.6023
ALKALINE PHOSPHATASE	Evaluated	24	23	17
	Mean	94.79	97.96	95.24
	STD	48.69	20.77	20.41
	Min	55.00	76.00	64.00
	Max	314.00	174.00	136.00

(CONTINUED)

P value: probability from the Wilcoxon signed rank test

PHARMACIA CNS R&D 9530087
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 41

HEMATOLOGY AND BLOOD CHEMISTRY : MEAN AND MEDIAN VALUES AT EACH VISIT AS COMPARED TO VISIT -1

REBOXETINE		VISIT		
		SCREENING	1-28	29-56
ALKALINE PHOSPHATASE	Median	85.50	92.00	98.00
	Median diff.		8.00	-2.00
	P value		0.0139	0.5390
GLOBULINS: ALFA1	Evaluated	24	23	17
	Mean	2.58	2.75	2.73
	STD	0.75	0.71	0.60
	Min	1.60	1.50	2.00
	Max	4.30	4.60	3.90
	Median	2.40	2.70	2.80
	Median diff.		0.20	0.30
	P value		0.2444	0.3959
GLOBULINS: ALFA2	Evaluated	24	23	17
	Mean	9.85	9.70	9.64
	STD	2.14	1.05	1.52
	Min	6.10	7.60	7.20
	Max	15.50	11.70	12.40
	Median	9.35	9.70	9.10
	Median diff.		-0.10	0.00
	P value		0.8714	0.7531
GLOBULINS: BETA	Evaluated	24	23	17
	Mean	11.08	11.73	11.86
	STD	1.87	1.79	1.74
	Min	7.70	8.10	8.40
	Max	14.80	15.50	14.90
	Median	11.00	11.80	12.00
	Median diff.		0.40	0.70
	P value		0.0271	0.0773
GLOBULINS: GAMMA	Evaluated	24	23	17
	Mean	17.07	17.40	17.54
	STD	3.60	4.43	3.73
	Min	10.80	8.90	10.50
	Max	24.00	27.60	24.10
	Median	16.90	17.20	17.60

(CONTINUED)

P value: probability from the Wilcoxon signed rank test

TABLE No.: 41

HEMATOLOGY AND BLOOD CHEMISTRY : MEAN AND MEDIAN VALUES AT EACH VISIT AS COMPARED TO VISIT -1

REBOXETINE		VISIT		
		SCREENING	1-28	29-56
GLOBULINS: GAMMA	Median diff.		0.20	0.30
	P value		0.5079	0.2199
TOTAL CHOLESTEROL	Evaluated	24	22	17
	Mean	5.00	4.99	5.21
	STD	1.11	1.16	0.89
	Min	3.10	3.30	3.90
	Max	6.90	7.70	7.30
	Median	5.00	4.65	5.20
	Median diff.		-0.05	-0.20
	P value		0.8274	0.5863
TRIGLYCERIDES	Evaluated	24	22	17
	Mean	1.35	1.38	1.58
	STD	0.53	0.57	0.47
	Min	0.60	0.80	0.70
	Max	2.80	2.80	2.40
	Median	1.20	1.20	1.70
	Median diff.		-0.15	0.10
	P value		0.9625	0.1927
BLOOD SUGAR	Evaluated	24	23	17
	Mean	4.95	4.78	5.21
	STD	0.79	0.77	0.69
	Min	3.90	3.10	3.60
	Max	7.10	6.30	6.70
	Median	4.80	4.80	5.10
	Median diff.		0.00	0.00
	P value		0.9490	0.5035
NA+	Evaluated	24	23	17
	Mean	142.29	138.74	141.41
	STD	3.09	8.77	2.55
	Min	138.00	101.00	136.00
	Max	152.00	147.00	145.00
	Median	142.00	141.00	141.00
	Median diff.		-1.00	0.00

(CONTINUED)

P value: probability from the Wilcoxon signed rank test

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 41

HEMATOLOGY AND BLOOD CHEMISTRY : MEAN AND MEDIAN VALUES AT EACH VISIT AS COMPARED TO VISIT -1

REBOXETINE		VISIT		
		SCREENING	1-28	29-56
NA+	P value		0.0518	0.3262
CL-	Evaluated	24	23	17
	Mean	102.42	98.61	101.35
	STD	3.76	8.75	3.00
	Min	93.00	61.00	97.00
	Max	110.00	108.00	108.00
	Median	102.00	100.00	101.00
	Median diff.		-3.00	-2.00
	P value		0.0185	0.0945
K+	Evaluated	24	23	17
	Mean	4.30	4.41	4.22
	STD	0.54	0.49	0.58
	Min	2.90	3.30	3.30
	Max	5.30	5.20	5.40
	Median	4.35	4.40	4.20
	Median diff.		0.10	-0.10
	P value		0.4245	0.5332
CA++	Evaluated	24	23	17
	Mean	2.30	2.37	2.33
	STD	0.19	0.21	0.13
	Min	1.90	1.90	2.10
	Max	2.60	2.90	2.50
	Median	2.30	2.40	2.40
	Median diff.		0.10	0.00
	P value		0.1409	0.7094
PO4-	Evaluated	24	23	17
	Mean	1.07	0.97	1.04
	STD	0.23	0.15	0.23
	Min	0.70	0.70	0.60
	Max	1.80	1.20	1.80
	Median	1.00	0.90	1.00
	Median diff.		-0.10	0.00
	P value		0.1198	0.4281

P value: probability from the Wilcoxon signed rank test

PHARMACIA CNS 880
REBOXETINE - PROTOCOL 20124032

TABLE No.: 42

HEMATOLOGY AND BLOOD CHEMISTRY : MEAN AND MEDIAN VALUES AT EACH VISIT AS COMPARED TO VISIT -1

PLACEBO		VISIT		
		SCREENING	1-28	29-56
HB	Evaluated	26	25	23
	Mean	12.08	12.22	12.17
	STD	1.47	1.35	1.40
	Min	8.30	8.20	7.80
	Max	15.20	15.00	14.10
	Median	12.30	12.50	12.40
	Median diff.		0.00	-0.10
	P value		0.8023	0.8140
HTC	Evaluated	26	25	23
	Mean	37.92	37.74	37.37
	STD	4.61	3.80	4.00
	Min	27.20	27.60	26.60
	Max	49.50	44.40	45.60
	Median	37.80	38.00	38.30
	Median diff.		-0.40	-1.50
	P value		0.7395	0.3896
RBC	Evaluated	26	25	23
	Mean	4.20	4.19	4.17
	STD	0.42	0.44	0.47
	Min	3.17	3.52	3.35
	Max	5.08	5.11	5.26
	Median	4.20	4.23	4.24
	Median diff.		-0.06	-0.14
	P value		0.4229	0.3339
PLATELETS	Evaluated	26	25	23
	Mean	252.12	237.00	240.26
	STD	77.91	64.27	64.63
	Min	134.00	122.00	144.00
	Max	419.00	357.00	378.00
	Median	225.50	226.00	211.00
	Median diff.		-13.00	0.00
	P value		0.0488	0.5927

(CONTINUED)

P value: probability from the Wilcoxon signed rank test

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 42

HEMATOLOGY AND BLOOD CHEMISTRY : MEAN AND MEDIAN VALUES AT EACH VISIT AS COMPARED TO VISIT -1

PLACEBO		VISIT		
		SCREENING	1-28	29-56
WBC	Evaluated	26	25	23
	Mean	6.97	7.60	7.57
	STD	2.09	2.65	2.32
	Min	3.19	3.17	3.19
	Max	11.20	13.99	13.58
	Median	6.74	7.42	7.18
	Median diff.		0.34	0.60
	P value		0.0328	0.0851
NEUTROPHILS	Evaluated	26	25	23
	Mean	57.32	57.91	57.29
	STD	7.48	8.15	8.03
	Min	43.00	41.20	40.50
	Max	71.90	79.00	72.80
	Median	57.95	56.10	56.70
	Median diff.		-0.40	-1.50
	P value		0.7940	0.5748
MONOCYTES	Evaluated	26	25	23
	Mean	6.96	7.06	7.12
	STD	2.28	2.13	1.67
	Min	1.30	2.10	4.00
	Max	10.50	10.80	10.70
	Median	7.35	7.50	6.90
	Median diff.		-0.20	-0.50
	P value		0.7639	0.1340
BASOPHILS	Evaluated	26	25	23
	Mean	0.75	0.74	0.77
	STD	0.32	0.31	0.26
	Min	0.10	0.40	0.20
	Max	1.60	1.40	1.50
	Median	0.70	0.60	0.80
	Median diff.		0.00	0.10
	P value		0.9488	0.2789

(CONTINUED)

P value: probability from the Wilcoxon signed rank test

PHARMACIA CNS 880
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 42

HEMATOLOGY AND BLOOD CHEMISTRY : MEAN AND MEDIAN VALUES AT EACH VISIT AS COMPARED TO VISIT -1

PLACEBO		VISIT		
		SCREENING	1-28	29-56
LYMPHOCYTES	Evaluated	26	25	23
	Mean	29.07	28.84	29.33
	STD	7.50	8.23	8.05
	Min	16.80	13.50	12.40
	Max	44.00	45.90	48.40
	Median	27.85	28.90	30.50
	Median diff.		-0.80	1.00
	P value		0.8859	0.3813
EOSINOPHILS	Evaluated	26	25	23
	Mean	3.49	3.10	3.13
	STD	1.81	1.47	1.61
	Min	0.70	1.00	0.80
	Max	8.40	7.30	7.20
	Median	3.20	3.00	3.10
	Median diff.		-0.10	-0.30
	P value		0.2695	0.4412
CREATININE	Evaluated	26	25	23
	Mean	93.35	93.72	95.38
	STD	27.58	26.59	27.36
	Min	65.20	62.10	66.80
	Max	190.40	181.00	194.00
	Median	88.45	90.60	93.40
	Median diff.		-0.40	-1.40
	P value		0.9896	0.8599
BUN	Evaluated	26	25	23
	Mean	7.60	7.46	7.99
	STD	2.83	2.61	3.31
	Min	3.70	3.80	3.60
	Max	15.30	14.30	19.80
	Median	6.90	7.10	7.60
	Median diff.		0.40	0.60
	P value		0.3565	0.4149

(CONTINUED)

P value: probability from the Wilcoxon signed rank test

PHARMACIA CNS 9500087
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 42

HEMATOLOGY AND BLOOD CHEMISTRY : MEAN AND MEDIAN VALUES AT EACH VISIT AS COMPARED TO VISIT -1

PLACEBO		VISIT		
		SCREENING	1-28	29-56
URIC ACID	Evaluated	26	25	23
	Mean	0.27	0.28	0.27
	STD	0.12	0.09	0.10
	Min	0.10	0.10	0.10
	Max	0.60	0.40	0.40
	Median	0.30	0.30	0.30
	Median diff.		0.00	0.00
	P value		0.5791	0.8633
TOTAL PROTEINS	Evaluated	26	25	23
	Mean	65.42	63.19	62.71
	STD	5.14	5.83	4.32
	Min	53.50	53.00	51.70
	Max	75.70	79.40	69.10
	Median	65.20	63.80	62.90
	Median diff.		-1.60	-3.20
	P value		0.1046	0.0069
ALBUMIN	Evaluated	26	25	23
	Mean	58.28	57.75	57.28
	STD	5.13	5.10	4.60
	Min	47.30	46.00	46.40
	Max	66.40	66.20	66.00
	Median	59.10	57.20	57.00
	Median diff.		-0.70	-1.50
	P value		0.2441	0.2083
TOTAL BILIRUBIN	Evaluated	26	25	23
	Mean	8.07	7.24	6.33
	STD	2.61	2.56	2.34
	Min	3.90	3.50	3.00
	Max	15.00	13.60	12.70
	Median	7.85	6.70	5.70
	Median diff.		-1.00	-1.70
	P value		0.1383	0.0006

(CONTINUED)

P value: probability from the Wilcoxon signed rank test

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 42

HEMATOLOGY AND BLOOD CHEMISTRY : MEAN AND MEDIAN VALUES AT EACH VISIT AS COMPARED TO VISIT -1

PLACEBO		VISIT		
		SCREENING	1-28	29-56
DIRECT BILIRUBIN	Evaluated	26	25	23
	Mean	3.76	3.49	3.01
	STD	1.59	1.34	1.50
	Min	1.70	1.00	0.80
	Max	9.20	5.50	7.40
	Median	3.65	3.40	2.90
	Median diff.		-0.30	-0.60
	P value		0.6852	0.0077
SGOT	Evaluated	26	25	23
	Mean	17.50	17.32	18.13
	STD	8.71	6.56	6.37
	Min	8.00	9.00	10.00
	Max	54.00	36.00	34.00
	Median	16.00	16.00	17.00
	Median diff.		0.00	0.00
	P value		0.9293	0.4069
SGPT	Evaluated	26	25	23
	Mean	19.04	17.16	17.65
	STD	10.65	9.53	10.04
	Min	5.00	6.00	5.00
	Max	54.00	48.00	40.00
	Median	16.50	15.00	14.00
	Median diff.		-2.00	-1.00
	P value		0.2927	0.6578
GAMMA-GT	Evaluated	26	25	23
	Mean	24.38	28.36	30.43
	STD	12.63	20.95	31.77
	Min	9.00	8.00	8.00
	Max	62.00	104.00	137.00
	Median	19.50	22.00	23.00
	Median diff.		-1.00	-1.00
	P value		0.9063	0.8143

(CONTINUED)

P value: probability from the Wilcoxon signed rank test

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 42

HEMATOLOGY AND BLOOD CHEMISTRY : MEAN AND MEDIAN VALUES AT EACH VISIT AS COMPARED TO VISIT -1

PLACEBO		VISIT		
		SCREENING	1-28	29-56
ALKALINE PHOSPHATASE	Evaluated	26	25	23
	Mean	109.27	107.60	103.00
	STD	63.14	56.33	48.14
	Min	51.00	52.00	49.00
	Max	356.00	316.00	278.00
	Median	90.50	88.00	96.00
	Median diff.		-1.00	2.00
	P value		0.6190	0.8482
GLOBULINS: ALFA1	Evaluated	26	25	23
	Mean	2.63	2.44	2.52
	STD	0.61	0.51	0.44
	Min	1.20	1.70	1.80
	Max	3.90	3.70	3.60
	Median	2.75	2.40	2.50
	Median diff.		-0.10	0.00
	P value		0.1829	0.6944
GLOBULINS: ALFA2	Evaluated	26	25	23
	Mean	10.27	10.22	10.43
	STD	1.91	2.28	2.46
	Min	7.20	7.40	7.60
	Max	14.50	18.30	18.40
	Median	10.00	9.60	10.00
	Median diff.		0.20	0.00
	P value		0.9272	0.7897
GLOBULINS: BETA	Evaluated	26	25	23
	Mean	11.39	11.57	11.78
	STD	1.68	1.70	1.74
	Min	8.10	8.70	8.90
	Max	14.10	16.20	15.80
	Median	11.30	11.40	11.50
	Median diff.		0.10	0.20
	P value		0.6375	0.1333

(CONTINUED)

P value: probability from the Wilcoxon signed rank test

PHARMACIA CNS 98-0087
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 42

HEMATOLOGY AND BLOOD CHEMISTRY : MEAN AND MEDIAN VALUES AT EACH VISIT AS COMPARED TO VISIT -1

PLACEBO		VISIT		
		SCREENING	1-28	29-56
GLOBULINS: GAMMA	Evaluated	26	25	23
	Mean	17.42	18.02	18.01
	STD	4.24	4.82	4.34
	Min	9.80	10.50	10.30
	Max	31.20	33.60	31.60
	Median	16.55	17.40	17.00
	Median diff.		0.60	0.40
	P value		0.0213	0.2027
TOTAL CHOLESTEROL	Evaluated	26	25	23
	Mean	4.99	4.96	5.06
	STD	0.76	0.67	0.98
	Min	3.30	3.70	3.60
	Max	6.50	6.30	7.10
	Median	5.10	5.10	4.80
	Median diff.		-0.10	0.10
	P value		0.6049	0.7754
TRIGLYCERIDES	Evaluated	26	25	23
	Mean	1.30	1.33	1.34
	STD	0.47	0.48	0.57
	Min	0.60	0.50	0.50
	Max	2.40	2.60	3.20
	Median	1.20	1.20	1.20
	Median diff.		0.00	0.10
	P value		0.8628	0.5892
BLOOD SUGAR	Evaluated	26	25	23
	Mean	5.10	4.88	5.35
	STD	1.29	1.02	1.57
	Min	3.70	2.60	3.30
	Max	8.40	7.30	9.30
	Median	4.40	4.70	4.80
	Median diff.		0.00	0.10
	P value		0.5109	0.3880

(CONTINUED)

P value: probability from the Wilcoxon signed rank test

PHARMACIA CNS, R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 42

HEMATOLOGY AND BLOOD CHEMISTRY : MEAN AND MEDIAN VALUES AT EACH VISIT AS COMPARED TO VISIT -1

PLACEBO		VISIT		
		SCREENING	1-28	29-56
NA+	Evaluated	26	25	23
	Mean	141.77	140.00	140.65
	STD	2.76	5.29	3.84
	Min	135.00	120.00	129.00
	Max	148.00	146.00	148.00
	Median	142.00	141.00	140.00
	Median diff.		-1.00	0.00
	P value		0.2693	0.3296
CL-	Evaluated	26	25	23
	Mean	101.35	100.20	101.09
	STD	4.18	4.68	5.53
	Min	93.00	88.00	84.00
	Max	108.00	107.00	109.00
	Median	101.50	101.00	101.00
	Median diff.		-1.00	-1.00
	P value		0.2454	0.8007
K+	Evaluated	26	25	23
	Mean	4.38	4.41	4.37
	STD	0.53	0.50	0.54
	Min	3.30	3.30	3.30
	Max	5.30	5.20	5.50
	Median	4.50	4.50	4.30
	Median diff.		-0.10	-0.10
	P value		0.7535	0.5493
CA++	Evaluated	26	25	23
	Mean	2.22	2.37	2.33
	STD	0.28	0.16	0.21
	Min	1.60	2.10	1.90
	Max	2.70	2.80	2.70
	Median	2.30	2.30	2.40
	Median diff.		0.20	0.10
	P value		0.0047	0.0488

(CONTINUED)

P value: probability from the Wilcoxon signed rank test

PHARMACIA CNS 99990087
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 42

HEMATOLOGY AND BLOOD CHEMISTRY : MEAN AND MEDIAN VALUES AT EACH VISIT AS COMPARED TO VISIT -1

PLACEBO		VISIT		
		SCREENING	1-28	29-56
PO4-	Evaluated	26	25	23
	Mean	1.07	0.94	0.88
	STD	0.34	0.17	0.16
	Min	0.60	0.60	0.60
	Max	2.50	1.20	1.20
	Median	1.02	1.00	0.90
	Median diff.		-0.10	-0.10
	P value		0.0978	0.0023

P value: probability from the Wilcoxon signed rank test

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 43

LABORATORY TEST: PATIENTS WITH CLINICALLY RELEVANT ABNORMALITIES AT BASELINE, DURING THE STUDY AND/OR AT LAST ASSESSMENT

			patient					
Laboratory test	Treatment	Sex	Baseline below min	Baseline above max	During study below min	During study above max	Last visit below min	Last visit above max
ALK. PHOSPH.	PLACEBO	Female		11		11		
				24		24		
								24
	REBOXETINE	Female		14				
BUN	PLACEBO	Female		11		11		
								42
		Male		44		44		
								44
	REBOXETINE	Female						45
		Male						46
CA++	PLACEBO	Female	24					
		Male	29					
CL-	PLACEBO	Female					31	

(*) patients listed only under the columns last visit had clinically relevant abnormalities at last assessment only

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 43

LABORATORY TEST: PATIENTS WITH CLINICALLY RELEVANT ABNORMALITIES AT BASELINE, DURING THE STUDY AND/OR AT LAST ASSESSMENT

			patient					
Laboratory test	Treatment	Sex	Baseline below min	Baseline above max	During study below min	During study above max	Last visit below min	Last visit above max
CL-	REBOXETINE	Female					15	
DIR BILIRUBIN	REBOXETINE	Female						15
GAMMA-GT	PLACEBO	Female						41
								50
		Male						10
	REBOXETINE	Female				8		
								13
				14				
						14		
								14
		Male		39				
								39
GLOBULINS: ALPHA 2	PLACEBO	Male				10		
								10
GLOBULINS: GAMMA	PLACEBO	Male		44				
						44		
								44
	REBOXETINE	Female				37		

(*) patients listed only under the columns last visit had clinically relevant abnormalities at last assessment only

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 43

LABORATORY TEST: PATIENTS WITH CLINICALLY RELEVANT ABNORMALITIES AT BASELINE, DURING THE STUDY AND/OR AT LAST ASSESSMENT

			patient					
Laboratory test	Treatment	Sex	Baseline below min	Baseline above max	During study below min	During study above max	Last visit below min	Last visit above max
GLUCOSE	PLACEBO	Female		42				
		Male						10 33
HB	PLACEBO	Female	7 11		11		11	
		Male	9 10 44		10 44		10 44	
	REBOXETINE	Male	40		40			
HTC	PLACEBO	Female	7 11		11		11	
		Male	9 10 44					

(*) patients listed only under the columns last visit had clinically relevant abnormalities at last assessment only

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 43

LABORATORY TEST: PATIENTS WITH CLINICALLY RELEVANT ABNORMALITIES AT BASELINE, DURING THE STUDY AND/OR AT LAST ASSESSMENT

			patient					
Laboratory test	Treatment	Sex	Baseline below min	Baseline above max	During study below min	During study above max	Last visit below min	Last visit above max
HTC	PLACEBO	Male			44		44	
	REBOXETINE	Female	6		28			
		Male	18		18			
			40					
K+	REBOXETINE	Female	28					
NA+	PLACEBO	Female			24			
	REBOXETINE	Female					15	
PO4-	PLACEBO	Female		27	22			
					42			
		Male	20		20		20	
	REBOXETINE	Male					18	

(*) patients listed only under the columns last visit had clinically relevant abnormalities at last assessment only

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 43

LABORATORY TEST: PATIENTS WITH CLINICALLY RELEVANT ABNORMALITIES AT BASELINE, DURING THE STUDY AND/OR AT LAST ASSESSMENT

			patient					
Laboratory test	Treatment	Sex	Baseline below min	Baseline above max	During study below min	During study above max	Last visit below min	Last visit above max
RBC	PLACEBO	Female	7		11		11	
							24	
		Male	10		10		10	
			44		44		44	
	REBOXETINE	Female	6		28			
		Male	40		40			
			46					
SGPT	REBOXETINE	Female						8
URIC ACID	PLACEBO	Female		11				
WBC	PLACEBO	Female	19		19		19	
WBC: L	PLACEBO	Male					33	

(*) patients listed only under the columns last visit had clinically relevant abnormalities at last assessment only

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 43

LABORATORY TEST: PATIENTS WITH CLINICALLY RELEVANT ABNORMALITIES AT BASELINE, DURING THE STUDY AND/OR AT LAST ASSESSMENT

			patient					
Laboratory test	Treatment	Sex	Baseline below min	Baseline above max	During study below min	During study above max	Last visit below min	Last visit above max
WBC: L	REBOXETINE	Female	28				15	

(*) patients listed only under the columns last visit had clinically relevant abnormalities at last assessment only

9550087

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 44

TOTAL SUBJECTS EVALUATED FOR ECG

		DAYS OF TREATMENT		
TREATMENT		SCREENING	1-28	29-56
REBOXETINE	ON TREATMENT		24	20
	EVALUATED	24	23	17
PLACEBO	ON TREATMENT		26	23
	EVALUATED	26	24	22

9550087

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 45

NUMBER AND PERCENTAGE OF PATIENTS WITH ECG NORMAL OR ABNORMAL

			DAYS OF TREATMENT		
			SCREENING	1-28	29-56
TREATMENT					
REBOXETINE	EVALUATED	n	24	23	17
	ABNORMAL	n	19	19	11
		%	79.17	82.61	64.71
	NORMAL	n	5	4	6
		%	20.83	17.39	35.29
PLACEBO	EVALUATED	n	26	24	22
	ABNORMAL	n	22	17	17
		%	84.62	70.83	77.27
	NORMAL	n	4	7	5
		%	15.38	29.17	22.73

9550087

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 46

SHIFT TABLE - NUMBER OF PATIENTS WITH NORMAL OR ABNORMAL ECG VALUE AT LAST ASSESSMENT AS COMPARED TO SCREENING, BY TREATMENT

Assigned treatment	ECG at screening	LAST ASSESSMENT					
		MISSING		ABNORMAL		NORMAL	
		No.	%	No.	%	No.	%
REBOXETINE	ABNORMAL	5	26.32	12	63.16	2	10.53
	NORMAL			1	20.00	4	80.00
PLACEBO	ABNORMAL	2	9.09	17	77.27	3	13.64
	NORMAL					4	100.00

PHARMACIA CNS 95050087
REBOXETINE - PROTOCOL 20124/032

TABLE No.: 47

ECG ABNORMALITIES OBSERVED AT BASELINE BY GROUP
frequency of patients with abnormalities reported at least once

		TREATMENT			
		REBOXETINE		PLACEBO	
		n	%	n	%
GROUP OF ABNORMALITIES	ABNORMALITIES				
RHYTHM DISORDERS	SINUS BRADYCARDIA (< 60)	2	7.41	2	5.71
	SINUS TACHYCARDIA (> 100)	1	3.70		
	ATRIAL ECTOPIC BEATS - OCCASIONAL	1	3.70	4	11.43
	ATRIAL ECTOPIC BEATS - FREQUENT (> 6/MN)			1	2.86
	VENTRICULAR ECTOPIC BEATS - OCCASIONAL	1	3.70	1	2.86
	VENTRIC. ECTOPIC BEATS- FREQUENT (>6/MN)			2	5.71
	ATRIAL FIBRILLATION / FLUTTER	3	11.11	1	2.86
CONDUCTION DISORDERS	A-V BLOCK 1ST DEGREE			1	2.86
	RIGHT BUNDLE BRANCH BLOCK	3	11.11	1	2.86
	LEFT BUNDLE BRANCH BLOCK	1	3.70	1	2.86
	LEFT ANTERIOR HEMIBLOCK	6	22.22	6	17.14
	LEFT AXIAL DEVIATION			4	11.43
ISCHEMIC SIGNS	MYOCARDIAL ISCHEMIA			3	8.57
OTHER DISORDERS	LEFT VENTRICULAR HYPERTROPHY	5	18.52	7	20.00
	PREVIOUS MYOCARDIAL INFARCTION			1	2.86
	OTHER	4	14.81		
TOTAL		27	100.00	35	100.00

PHARMACIA CNS 9950087
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TABLE No.: 48

ECG ABNORMALITIES OBSERVED DURING THE STUDY BY GROUP
frequency of patients with abnormalities reported at least once while on treatment

		TREATMENT			
		REBOXETINE		PLACEBO	
		n	%	n	%
GROUP OF ABNORMALITIES	ABNORMALITIES				
RHYTHM DISORDERS	SINUS BRADYCARDIA (< 60)			1	2.94
	SINUS TACHYCARDIA (> 100)	2	6.67		
	ATRIAL ECTOPIC BEATS - OCCASIONAL	4	13.33	4	11.76
	VENTRICULAR ECTOPIC BEATS - OCCASIONAL	3	10.00	2	5.88
	VENTRIC. ECTOPIC BEATS- FREQUENT (>6/MM)			1	2.94
	VENTRIC. ECTOPIC BEATS - COUPLETS			1	2.94
	ATRIAL FIBRILLATION / FLUTTER	2	6.67	2	5.88
CONDUCTION DISORDERS	RIGHT BUNDLE BRANCH BLOCK	4	13.33		
	LEFT BUNDLE BRANCH BLOCK	2	6.67	2	5.88
	LEFT ANTERIOR HEMIBLOCK	3	10.00	6	17.65
	LEFT AXIAL DEVIATION	1	3.33	2	5.88
ISCHEMIC SIGNS	MYOCARDIAL ISCHEMIA			4	11.76
	RIPOLARIZATION DISTURBANCES	1	3.33		
OTHER DISORDERS	LEFT VENTRICULAR HYPERTROPHY	4	13.33	6	17.65
	RIGHT VENTRICULAR HYPERTROPHY	1	3.33		
	PREVIOUS MYOCARDIAL INFARCTION			1	2.94
	OTHER	3	10.00	2	5.88
TOTAL		30	100.00	34	100.00

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TABLE No.: 49
ECG ABNORMALITIES NEWLY OBSERVED DURING THE STUDY BY GROUP
FREQUENCY OF PATIENTS WITH AT LEAST ONE ABNORMALITY WITHIN EACH GROUP

GROUP OF ABNORMALITIES	TREATMENT			
	RBX		PL	
	N	%	N	%
RHYTHM DISORDERS	5	41.6	5	50.0
CONDUCTION DISORDERS	3	25.0	2	20.0
ISCHEMIC SIGNS	1	8.3	1	10.0
OTHER DISORDERS	3	25.0	2	20.0
TOTAL	12	100.0	10	100.0

12. APPENDICES

12.1 Study Information

12.1.1 PROTOCOL

9550087

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R & D, CNS LINE

COMPOUND	:	Reboxetine
PROTOCOL N°	:	20124/032
VERSION	:	Final; May 16, 1991
PHASE	:	III
TITLE	:	Double blind activity and tolerability study of reboxetine vs placebo in elderly patients with depressive disorders.
INVESTIGATORS	:	Prof. Vittorino Andreoli Primario, Dpt di Psichiatria Ospedale di Soave (Verona) via Mare 7, SOAVE (Verona) phone: 045/7680166 Dott. Giorgio Carbognin Primario Divisione Medica Ospedale Provinciale Lungodegenti Negrar, VERONA phone: 045/7500044
PRODUCT LEADER	:	Dr. Marek Jarema Farmitalia Carlo Erba R & D, CNS Dpt via Carlo Imbonati 24 20159 Milano phone: 02/69959081
STUDY MONITOR	:	Dr. Silvio Tazzari Farmitalia Carlo Erba R & D, CNS Dpt via Carlo Imbonati 24 20159 Milano phone: 02/69959069
DATA MANAGEMENT CENTER	:	Farmitalia Carlo Erba, R & D via Carlo Imbonati 24 20159 Milano phone: 02/69952759

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I N D E X

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1.0 Protocol Summary

The study will be carried out in order to evaluate the activity and tolerability of reboxetine, a new potential antidepressant agent, in elderly depressed patients. After the initial washout period of 1-2 weeks 70 patients over 65 years suffering from depressive disorders will receive either reboxetine in repeated doses of 4 to 6 mg/day or placebo for a 2 months period. Patients could then enter a follow-up treatment on a long-term basis. The effectiveness will be measured by use of the rating scales (HAMD, CGI, SCAG, GDS). The tolerability will be evaluated on the basis of the appearance of newly observed signs/symptoms, vital signs, laboratory tests and ECG.

2.0 Introduction

Reboxetine (FCE 20124 or RS, RS 2-[µ-(2-ethoxy-phenoxy) benzyl] morpholine methanesulphonate) is a chemically new compound highly potent in pharmacological and biochemical tests predictive of antidepressant effectiveness: reserpine antagonism, norepinephrine reuptake inhibition, REM sleep latency increase. In addition reboxetine has been found to be able to prevent clonidine effects in rodents after single oral administration, in contrast with what observed following tricyclic monoamine uptake inhibitors, which were found to be active only upon repeated doses: these results indicate that the compound is able to decrease the sensitivity of µ2 noradrenergic receptors, one of the biochemical correlates of chronic antidepressant treatment, after single oral dose; therefore it was expected to exert antidepressant effectiveness of faster onset with respect to available antidepressants in patients (1).

In phase I studies healthy volunteers were orally administered single doses of 0.5 - 5 mg of the compound (2,3). After 5 mg orthostatic hypotension, accompanied by tachycardia and by subjective symptomatology consistent with the disturbed circulatory regulation was observed.

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In these studies single doses of 1 & 3 mg of the compound showed dose-dependent CNS effects with EEG modifications (decreased power of theta and fast-beta waves in the fronto-central derivate), performance improvement (peg-board test) and growth hormone increase, the latter reportedly sensitive to hypothalamic noradrenergic stimulation by norepinephrine reuptake inhibitors.

The comparison with the positive control, imipramine 75mg, associated to similar EEG modifications in the fronto-central derivative, to modifications indicative of sedative activity in the occipito-temporal derivative and to deterioration of the Pauli performance test, in the absence of growth hormone modifications, indicate that reboxetine does not possess the marked sedative activity of imipramine, but rather psychostimulating properties. After all treatment standing heart rate increase and salivation decrease was apparent. No other modifications of tolerability parameters were observed.

The pharmacokinetics of the compound was evaluated in the above mentioned studies as well as after administration of 2 mg 14C-FCE 20124 to 3 healthy volunteers (4). Most of the radioactivity circulating in plasma (73% in terms of AUC) was accounted for by unchanged reboxetine; the average peak levels were observed at 2 hours, with remarkably stable levels 1-6 hours after administration; its plasma half-life was estimated as 13.2 h, slightly lower than that of total radioactivity.

Antidepressant efficacy of reboxetine has been demonstrated in a controlled study in Major Depressive Disorders carried out vs desipramine and placebo.
Frequency of response (50% decrease of Hamilton Depression Rating Scale, study end point) was significantly higher in the reboxetine (60%) than in the placebo (35%) group. As to the time course of the response, significant differences vs placebo in the average values of the rating scales applied were observed from day 10-14 of the treatment on in the reboxetine group and from day 14-21 on in the desimipramine group. The overall superiority of reboxetine over desimipramine in the administered dose range reached statistical significance for one of the rating scales at the end of treatment, confirming the trend seen in the other scales.

3.0 Rationale

Phase II results obtained in controlled conditions in patients suffering from Major Depressive Disorders indicate that reboxetine is an effective anti-depressant agent. A dose-finding study in 12 elderly depressed patients showed the overall good tolerability of reboxetine in the dose range of 4 to 8 mg. Only 3 out of 12 patients did not reach the maximal foreseen dose of 8 mg because of slight to moderate side effects (report in preparation). The activity and the tolerability of the compound in the elderly need now to be tested in controlled conditions vs placebo.

4.0 Objective

The study is carried cut in order to evaluate the efficacy and tolerability of reboxetine in elderly in-patients suffering from depressive disorders.

5.0 Design

5.1 Description

This Phase III study will be carried out in a single center according to a double blind parallel group design, controlled vs placebo, with random allocation of patients to one of the two treatments.

5.2 Number of Subjects Proposed

The center will recruit enough patients to collect a sample of 70 patients fulfilling the criteria for entering the study.

5.3 Logistics

The study will be carried out at the Ospedale Provinciale Lungodegenti Negrar (Verona) under the specialistic supervision of Prof. Vittorino Andreoli, Department of Psychiatry, Ospedale di Soave (Verona).

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6.0 Study Population

6.1 Source of Subjects

Depressed patients in good physical condition selected from the population of in-patients of the Psychiatric Department of the participating center will participate in the study.

6.2 Inclusion Criteria

- Patients aged over 65 years
- Normal body weight/height ratio
- Fulfillment of the DSM-III-R criteria for Major Depressive Episode
- Total score of 18 or more in the 21-HAMD
- Total score of 20 or more in the MMS (enclosure 1)
- Informed written consent

6.3 Exclusion Criteria

- Dysthymia, Cyclothymia
- Resistance to antidepressive treatment (lack of response to at least two courses of previous antidepressants given at full doses for more than 1 month).
- Clinically relevant abnormal findings in the physical examination and/or laboratory tests at admission (see Safety Assessments);
- History of Major Depressive Episodes associated to endocrine disorders: hypo and hyper-thyroidism tested by TSH and T4 at screen and defined as at least 10% abnormal values of the laboratory norms; adrenal insufficiency, etc.
- Past history of any drug hypersensitivity.
- History or presence of gastrointestinal disease causing possible impairment of the gastrointestinal absorption, liver disease (hepatic insufficiency defined as clinically relevant abnormal findings of following tests: hematolytic markers - SGOT and SGPT; cholestasis markers - total and direct bilirubin,

gamma-GT, alkaline phosphatase; mesenchymal activations markers - serum protein electrophoresis) or kidney disease (renal insufficiency defined as moderate to medium renal impairment with creatinine clearance not lower than 30 $ml.min^{-1}$) or other conditions known to interfere with the absorption, distribution, metabolism and excretion of drugs.

- Participation in any clinical study with an investigational compound in the 4 weeks preceeding the study.

- Evidence of Substance Use Disorder (DSM-III-R) within past 6 months or currently.

- Chronic respiratory insufficiency in the physical examination and X-ray.

- History of seizures or serious brain injury; current evidence of urinary retention or glaucoma. Current evidence of clinically important hemato-poietic or cardiovascular diseases.

- ECT in the previous 6 months.

- High risk of suicide.

6.4 Identification of Subjects

Patients will be identified by their initials and by the number in the trial.

7.0 Randomization Procedures

A randomization list will be prepared for patient allocation to one of the 2 possible treatments (reboxetine or placebo). On this basis the experimental treatment will be prepared and labelled with the corresponding patient number.

8.0 Experimental Treatment

8.1 Test Preparations

Indistinguishable tablets of reboxetine 2 mg (batch N° SF 1105) or 4 mg (batch N° SF 1106) or placebo (tablets for reboxetine 2 mg and 4 mg batches N° SF 1025 and SF 1030) will be used. The experimental treatments will be administered according to fixed-flexible dose schedules as indicated under Study Conduct. Test preparations will consist of:

	morning	evening
- reboxetine	1 tabl 2 mg	1 tabl 2 mg
- reboxetine DOSE 2 (weeks 4 - 8)	1 tabl 4 mg	1 tabl 2 mg
- placebo	1 tabl	1 tabl
- placebo DOSE 2	as above	as above

8.2 Labelling

The experimental treatments will be contained in glass amber bottles labelled with the indication of the N° of subject and the treatment week (enclosure 2).

8.3 Packaging

Twelve glass amber bottles (six for the "morning" and six for the "evening") labelled with the patient's number and the indication week 1, week 2, week 3, week 4, weeks 5-6 and weeks 7-8 will be prepared for each patient. Each "morning" and "evening" bottle for the treatment week 1, 2, 3, and 4 will contain the medication necessary for 7 days of treatment, i.e. 8 tablets (7 tablets plus 1 tablet for possible losses). For the treatment weeks 5-6 and 7-8 each bottle will contain the medication necessary for 14 treatment days, i.e. 16 tablets (14+2). In addition for each patient a carton labelled with the patient number and the indication "week 4 - dose 2" "week 5-6 - dose 2" and "week 7-8 - dose 2" will be provided for the possible dosage increase during treatment period starting 4th week.

8.4 **Drug Supplies Storage**

Drug supplies will be stored at room temperature. All drug supplies will be handled under the direct responsibility of the Investigator and held by the hospital pharmacy.

The Study Monitor will check drug storage conditions during the visit. The Investigator will be also responsible for drug accountability and will keep a record of the test compounds received from the Sponsor as well as of the dispensed drug (see enclosure 3).

8.5 **Dispensing, Use and Disposal of the Preparation during and at the End of the Study**

Medication will be dispensed to the patient on the occasion of each visit; the Investigator will detach the upper label from each of the weekly bottles and will attach them in the appropriate space in the Case Record Form. Used bottles will be returned to the study Monitor during site visits. All unused medication has to be returned to Farmitalia Carlo Erba at the end of the study.

9.0 **Study Conduct**

9.1 **Pre-treatment Period**

Patients will be checked for eligibility according to the inclusion and exclusion criteria. A washout period of 4-7 days (14 days in case of MAOI administration and 3 - 4 weeks in the case of treatment with fluoxetine) will then be undertaken, during which only a short-acting benzodiazepine (see 8.6) as sleep inducer on p.r.n. basis will be allowed.

Informed consent will be obtained from each patient. Eligible patients will be randomized to one of the two treatment groups and will then undergo baseline assessments.

Information on patients screened for the study, including those not eligible, will be collected in the Screening Form - enclosure 4).

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9.2 Treatment Schedule

Patients will receive 2 tablets of reboxetine or placebo (one in the morning and one in the evening).

Treatment intake will take place at least 2 hours before or after meals.

In case of inefficacy or unsatisfactory response (slight worsening or no change or minimal improvement at the CGI - see assessments) but of good tolerance, after 3 weeks of treatment the dose can be increased up to 6 mg (4 mg in the morning and 2 mg in the evening).
In case of intolerance the dose will be reduced to the previously well tolerated dosage level.

The daily dose can be reduced by half tablet in case of emergence of non tolerable signs or symptoms.

9.3 Duration of Treatment

Treatment will be administered for two months.

9.4 Indications for Early Termination of Therapy

Termination of test therapy prior to completion of the treatment period may be considered under the following circumstances:

- Patient's request.

- Unacceptable toxicity: this is defined as the occurrence of serious and unexpected (see Adverse Events) adverse events or the persistence of non tolerable signs or symptoms which are not alleviated by reducing the dose to the lower dosage level.

- Inefficacy during the treatment: this will apply to patients who after completion of at least 4 weeks of treatment will show worsening of the global clinical picture (CGI - Global Improvement, see assessments).

- Switch to mania.

In case of treatment discontinuation the final complete battery of assessments will be carried out.

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9.5 Dropouts/Replacement of Subjects

Patients who drop out of the study for any reason during the treatment will not be substituted.

For those patients who have been selected for the study who drop out at any time, even before the entrance to the treatment period, documentation will be provided.

9.6 Concomitant Therapy

Only drugs considered essential for the management of the patients will be allowed. These should be given at stable doses for at least one month before admission to the study. However, drugs that may interfere with the pharmacokinetics/pharmacodynamics of Reboxetine will be discontinued for a period at least 5 times their elimination half life before the study start and throughout the study.

In particular the following drugs should not be used during the trial: neuroleptics, antidepressants, psychostimulants, tranquillizers (with the exception of sleep medication, see below), antiparkinson and anticholinergic agents, sympathomimetic drugs, hormones and anesthetic agents.

In case of events arising during the course of the study non psychotropic medications which are considered necessary for the patient's welfare may be administered. The drugs, dosage and frequency of administration will be recorded on the CRF. Only a short-acting benzodiazepine (for instance temazepam 5-10 mg tablet) as a sleep inducer on the p.r.n. basis at bed-time will be allowed.

9.7 Indications for opening the code

The Investigator will be given individual sealed envelopes containing the information on each patient's treatment. These latter may be opened only in case of emergency necessitating treatment identification; the Investigator will immediately (within 24 hours) inform the study Monitor at FICE Milan (Dr. Silvio Tazzari, Farmitalia Carlo Erba R&D, via Imbonati 24, 20159 Milano, tel. 02/69959069) and will report full description of reasons for opening the code in the CRF (Adverse Event Form).

9.8 Follow-up

A follow-up visit will be carried out for each patient one month after treatment discontinuation in order to monitor possible withdrawal reactions and collect information on possible adverse events.

Patients willing to continue receiving the experimental treatment after completion of the 8 week treatment period, and having demonstrated at least moderate improvement (CGI) at the end of the 8th week vs day 0, will be maintained under the experimental treatment on a long-term basis in double-blind conditions up to completion of the 2 months experimental treatment in the last patient of the study. Afterwards patients may continue the treatment in open conditions according to the protocol 20124/032 Follow-up.

9.9 Study Timetable

Foreseen start date:	May 1991
Duration of the study:	1 year
Foreseen end date:	July 1992

10.0 Efficacy Assessments

10.1 Variables to be Measured for Efficacy Assessment

On days 0, 14, 28 and 56 the following scales will be applied:

- 21-items Hamilton Depression Rating Scale /HAMD/ (see enclosure 5)

- Clinical Global Impression /CGI/ (see enclosure 6)

- Sandoz Clinical Assessment-Geriatric / SCAG / (see enclosure 7)

- The Geriatric Depression Scale /GDS/ (see enclosure 8)

All psychiatric evaluations and ratings will be carried out by the same observer for a given patient.

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10.2 Efficacy Definition

Decrease of at least 50% in the total HAMD score vs day 0 will be considered index of response whereas total HAMD score of 10 or less will be considered index of remission.

10.3 Criteria for Efficacy Evaluability

Every randomized patient will be included in the analysis.

11.0 Safety Assessment

11.1 Variables to be Measured for Safety Assessment

- Standard medical history: pre-treatment screen

- Standard clinical examination: full physical examination; chest X-ray: pre-treatment screen

- Blood pressure and pulse will be measured in the lying position (after 5 minutes lying) and in the standing position (1-2 minutes after standing up) in the morning: at screen, at day 0, 14, 28 and at the end of the treatment

- ECG: at screen, day 28 and at the end of treatment

- EEG: at screen and at the end of treatment

- Creatinine clearance, TSH and T4 at screen; laboratory tests (full blood count, serum electrolytes, liver enzymes, blood sugar, SAP, BUN, serum creatine, uric acid, total and direct bilirubin, total serum proteins and electrophoresis, serum cholesterol and triglycerides, urine analysis): at screen, day 28 and at the end of treatment

- Adverse events: a check list will be administered at each visit (see enclosure 9).

11.2 Criteria for Safety Evaluability

Every patient who has received at least one dose of the experimental treatment will be included in the safety evaluation.

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12.0 Adverse Events

Patients will be notified of possible adverse events they could experience and instructed to immediately report them to the Investigator.

Any adverse event, noticed by the Investigator or complained of by the patient, including clinically relevant lab abnormalities, will be recorded in the appropriate section of the CRF, regardless of presumed relationship to study medication.

For each event, the following information will be entered in the CFR: description, onset date, disappearance date, severity (1 = mild, awareness of sign or symptom, but easily tolerated; 2 = moderate, discomfort enough to cause interference with usual activity; 3 = severe, incapacitating with inability to do usual activity; 4 = unknown), drug cause-effect relationship (according to Karch and Lasagna modified criteria; see enclosure 10), outcome, dechallenge (what happened to the adverse event when the drug was stopped or the dose decreased?), rechallenge (what happened when the drug was restarted after the adverse event had disappeared?). The Investigator will also note if the double-blind code has been opened, the action taken regarding the test drug (none, discontinued, dosage reduced) and any treatment applied because of the adverse reactions.

All serious * ("any experience that is (potentially) fatal or life-threatening, disabling, incapacitating, requires inpatient hospitalization, or causes a congenital anomaly or cancer or is due to overdose") and/or unexpected * ("any adverse experience that is not identified in nature, severity or frequency in the current investigator's brochure for the study) adverse events must be immediately (within 24 hours) reported by telephone to the Adverse Reaction Center of FICE (Dr. Osman Bawa, tel. 02/69952153).

Adverse Event Form must be filled in immediately and mailed to the same address. The same applies to all patients who died, irrespective of whether the event was judged as related to treatment, during the course of the study or within 30 days of completion of treatment.

In case of death, if an autopsy is performed, copy of the pathological report should be sent to the Adverse Reaction Center of FICE.

13.0 Evaluation Schedule

It is reported in table 1.

14.0 Statistical Considerations

14.1 Sample size

The main evaluation of the treatment effectiveness will be based on the estimation of the difference between the response rates of the two treatment groups.
Owing to the fact that there are no previous efficacy results from phase II trials in elderly patients or from documentation, this trial must be considered as explorative.

Therefore the sample size is not defined on a statistical basis and taking into consideration the center accrual capability, 70 patients seem to be a suitable sample size.

With this sample size of 70 patients (35 in each treatment arm) in the most unfavourable conditions one can expect to provide an estimate of the difference between response rates with a confidence interval not larger than 0,47.

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* Code of Federal Regulation, Vol 21 Part 312. Revised as of April 1, 1987, pg. 75.

* J. L. Bem et al.: Review of yellow cards (1986): Report to the Committee on the Safety of Medicines. Br. J. Clin. Pharmac. (1988), 26, 679-689.

14.2 Statistical analysis

The primary efficacy objective of the study will be to estimate the difference in response rate between reboxetine and placebo.

In each treatment response rate will be calculated as ratio between the number of patients treated for at least four weeks and experiencing a response (see definition 10.2) at their last valid observation and all randomized patients. This is an "intention to treat" approach and patients treated less than four weeks are considered as failures. The difference between the success rates will be point-estimated and the 95% confidence interval will be provided.

The results obtained from the administered scales (HAMD, CGI, SCAG and GDS) will be analysed. The difference between the last post baseline and the baseline score in the two treatments will be compared by using a two tailed Student's test. Descriptive statistics for laboratory data will be provided as well as frequency of abnormal values with respect to normal ranges at the end of treatment in each gruop.

Adverse events will be presented by patient by patient listing and tabulated by treatment group both on a patient and on an event basis.
All the other efficacy and safety variables will be described by presenting tables of frequency or by using descriptive statistics (mean, standard deviation, range).

15.0 Ethical Aspects

The study will be carried out according to the Helsinki Declaration (Venice and Hong-Kong revisions, enclosure 11).

15.1 Ethical Committee

This study will not be undertaken until approval is obtained from the Ethical Committee ("Consiglio dei Sanitari") of the participating center. It is responsibility of the Investigator to submit the study protocol with its attachments to the Committee.

The Investigator is committed, in compliance with local requirements, to inform the Committee of any

emergent problems, serious adverse reactions or protocol amendments.

15.2 Informed Consent

Before entering the study each patient will be explained nature, duration and purpose of the study and the action of the compound in such a manner that the patient is aware of the potential risks, inconveniencies or adverse effects that may occur and can express his/her informed consent to participation.

The consent form (enclosure 12) will be signed by the patient or by the next of kin and/or by the Investigator. In the latter case, the signature of a witness will testify that full information was given to the patient.

16.0 Protocol Amendments

After the protocol has been signed, no changes will be made without the agreement of both the Investigator and the Sponsor. Any change will be recorded on a written agreement which will be signed and dated by both parties and attached to the original protocol.

17.0 Study Monitoring

Monitor to the study is Dr. Silvio Tazzari, Farmitalia Carlo Erba, via Imbonati 24, 20159 Milano, phone 02/69959069.

A prestudy visit will be made by the Monitor to the Investigator in order to discuss problems, if any, and the obligations of both the Sponsor and the Investigator. During the trial monitoring visits will be paid to the site by the study Monitor monthly. The trial can be also monitored by the Sponsor's Quality Assurance. During the visits the Monitor will assess the progress of the study, review the compliance with the study protocol, discuss any problem, check the CRFs for legibility, accuracy and completeness, assess the status of drug storage dispensing and retrieval.

18.0 Supply and Inventory

Test preparation will be supplied by Farmitalia Carlo Erba in the form described in 6.1. Records will be kept by the Investigator as to the disposition of study drug for each patient. A disposition from accounting for all study supplies will be signed by the Investigator.

19.0 Administrative Aspects

19.1 Insurance Policy

Farmitalia Carlo Erba Company declares to have a group insurance cover (policy NO. 4W8102 - Fondiaria Assicurazioni) which provides indemnity to the Investigator, to the co-Investigators and to the subjects participating in the trial (enclosure 13).

19.2 Curriculum Vitae

The Investigator will provide the Sponsor with signed copies of his/her and co-Investigators CVs.

19.3 Data Collection in the Case Record Form

All study data will be recorded in the CRF supplied by the Sponsor (Attachment B). A black ink ball point pen should be used for entering the data to ensure the good quality of the reproduced CRFs copies.

Only the Principal Investigator and the duly authorized co-Investigators can make entires in the CRF. In case of errors corrections must be made by crossing out the incorrect entry (that must remain legible) and entering the correction followed by the Investigator's initials and the date of the correction.

On the occasion of the monitoring visits the Monitor will take away the original and one copy of each page, while the Investigator will retain a copy for his files, together with the drug disposition records, for ten years after the discontinuation of the investigation.

19.4 Use of the Information related to the Study

All unpublished documentation including the protocol, the CRF and the Investigator's Brochure, given to the Investigator is confidential. These documents cannot be disclosed to a third party without the written consent of FICE R&D. The submission of these documents to the Ethical Committee is expressly permitted.

The Investigator agrees that FICE R&D maintains the right to utilize the results of this study, in their original form and/or in a global report, for submission to the governmental and regulatory authorities of any country.

20.0 Study Report

20.1 Clinical Study Final Report

The final Medical Study Report will be written by the Product Leader and will be submitted to the Investigator for approval and signature.

20.2 Publication of Study Results

The results of the study will be published in a common publication, agreed upon between Investigator and FICE R&D.

The Investigator, whilst free to use the data resulting from this study for individual publications (subsequent to the common one), is asked to discuss any paper with Farmitalia Carlo Erba prior to submission; to this purpose copy of manuscript / abstract has to be available for FICE R&D Approval Procedure 30 days prior to publication.

21.0 End of the Study

Either the Investigator or FICE R&D could terminate this study at any time for well documented reasons. In this event the other party will be immediately notified.

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22.0 References

1. Reboxetine Investigator Brochure, FICE, CNS Line, June 1988

2. /602i - Herrman W.M. et al. (AFB - Berlin) Safety and tolerance of reboxetine in healthy male volunteers - A single rising dose tolerance study. June 15, 1984.

3. /603i - Herrman W.M. (AFB - Berlin) Reboxetine - Quantitative pharmaco EEG pharmacopsychological study. January, 1985.

4. /604i - Dubini A. et al. Disposition and fate of 14C- reboxetine administered orally to healthy volunteers. March, 1985.

5. /118i - Strolin Benedetti et al. A new HPLC method for the determination of FCE 20124 and its metabolite FCE 22930 in human plasma. September, 1987.

23.0 Signatures

Signatures of the:

Investigator Giorgio Carbognin

Study Monitor [illegible]

* Product Leader Adriana Dubini

Line Medical Head Adriana Dubini

X Biostatisticians [illegible]

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2. EXPERIMENTAL TREATMENT LABELLING
3. DRUG ACCOUNTABILITY FORM
4. SCREENING FORM
5. HAMILTON DEPRESSION RATING SCALE (HAMD)
6. CLINICAL GLOBAL IMPRESSION (CGI)
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ATTACHMENT A

PROTOCOL 20124/032: OPERATING PROCEDURES FOR TRAINING ON ASSESSMENT INSTRUMENTS, STUDY MONITORING AND COORDINATION

ATTACHMENT B

CASE RECORD FORM

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Table 1

EVALUATION SCHEDULE

Period	: Screen	Treatment					
Day	:	0	7	14	21	28	56
Assessment							
Medical History	: X						
Physical Examination	: X						
Chest X-ray	: X						
ECG	: X					X	X
EEG	: X						X
MMS	: X						X
Vital Signs	: X	X	X	X	X	X	X
Laboratory	: X					X	X
HAMD	: X	X	X	X	X	X	X
CGI	:	X	X	X	X	X	X
SCAG	:	X		X		X	X
GDS	:	X		X		X	X
Adverse Events	:	X	X	X	X	X	X

22

FARMITALIA CARLO ERBA
Erbamont Group

Compound **REBOXETINE**

Protocol No. 20124/032

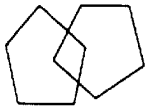
Pat. Initials

Visit: S C R E E N

Date D M Y

THE MINI-MENTAL STATE EXAMINATION

		Score	Maximum Points
Orientation			
1. What is the	Year?	___	1
	Seasons?	___	1
	Date?	___	1
	Day?	___	1
	Month?	___	1
2. Where are we?	State?	___	1
	County?	___	1
	Town or city?	___	1
	Hospital?	___	1
	Floor?	___	1
Registration			
3. Name three objects: taking one second to say each. Then ask the patient all three after you have said them. Give one point for each correct answer. Repeat the answers until the patient learns all three		___	3
Attention and calculation			
4. Serial sevens. Give one point for each correct answer. Stop after five answers. ALTERNATE: Spell WORLD backwards		___	5
Recall			
5. Ask for names of three objects learned in Question 3. Give one point for each correct answer		___	3
Language			
6. Point to a pencil and a watch. Have the patient name them as you point		___	2
7. Have the patient repeat "No ifs, ands, or buts"		___	1
8. Have the patient follow a three-stage command: "Take the paper in your right hand. Fold the paper in half. Put the paper on the floor"		___	3
9. Have the patient read and obey the following: "CLOSE YOUR EYES" (Write it in large letters)		___	1
10. Have the patient write a sentence of his or her own choice. (The sentence should contain a subject and an object and should make sense. Ignore spelling errors when scoring)		___	1
11. Enlarge the design printed below to 1-5 cm per side and have the patient copy it. (Give one point if all sides and angles are preserved and if the intersecting sides form a quadrangle)		___	1
		___	= Total 30



Investigator's signature .....

9550087

Enclosure 2

FARMITALIA CARLO ERBA
ERBAMONT GROUP

Prot. FCE 20124/032
REBOXETINA
8 Compresse
PAZIENTE N°: ___ - SETTIMANA 1 - MATTINO
Lotto N°: F R 0 3 6 Scadenza: 6/92
AVVERTENZA: Nuovo farmaco in sperimentazione clinica, da usare sotto controllo medico.

Prot. FCE 20124/032
REBOXETINA
8 Compresse
PAZIENTE N°: ___ - SETTIMANA 1 - SERA
Lotto N°: F R 0 3 6 Scadenza: 6/92
AVVERTENZA: Nuovo farmaco in sperimentazione clinica, da usare sotto controllo medico.

Prot. FCE 20124/032
REBOXETINA
8 Compresse
PAZIENTE N°: ___ - SETTIMANA 2 - MATTINO
Lotto N°: F R 0 3 6 Scadenza: 6/92
AVVERTENZA: Nuovo farmaco in sperimentazione clinica, da usare sotto controllo medico.

Prot. FCE 20124/032
REBOXETINA
8 Compresse
PAZIENTE N°: ___ - SETTIMANA 2 - SERA
Lotto N°: F R 0 3 6 Scadenza: 6/92
AVVERTENZA: Nuovo farmaco in sperimentazione clinica, da usare sotto controllo medico.

Prot. FCE 20124/032
REBOXETINA
8 Compresse
PAZIENTE N°: ___ - SETTIMANA 3 - MATTINO
Lotto N°: F R 0 3 6 Scadenza: 6/92
AVVERTENZA: Nuovo farmaco in sperimentazione clinica, da usare sotto controllo medico.

Prot. FCE 20124/032
REBOXETINA
8 Compresse
PAZIENTE N°: ___ - SETTIMANA 3 - SERA
Lotto N°: F R 0 3 6 Scadenza: 6/92
AVVERTENZA: Nuovo farmaco in sperimentazione clinica, da usare sotto controllo medico.

Prot. FCE 20124/032
REBOXETINA
8 Compresse
PAZIENTE N°: ___ - SETTIMANA 4 - MATTINO
Lotto N°: F R 0 3 6 Scadenza: 6/92
AVVERTENZA: Nuovo farmaco in sperimentazione clinica, da usare sotto controllo medico.

Prot. FCE 20124/032
REBOXETINA
8 Compresse
PAZIENTE N°: ___ - SETTIMANA 4 - SERA
Lotto N°: F R 0 3 6 Scadenza: 6/92
AVVERTENZA: Nuovo farmaco in sperimentazione clinica, da usare sotto controllo medico.

Prot. FCE 20124/032
REBOXETINA
16 Compresse
PAZIENTE N°: ___ - SETTIMANE 5-6 - MATTINO
Lotto N°: F R 0 3 6 Scadenza: 6/92
AVVERTENZA: Nuovo farmaco in sperimentazione clinica, da usare sotto controllo medico.

Prot. FCE 20124/032
REBOXETINA
16 Compresse
PAZIENTE N°: ___ - SETTIMANE 5-6 - SERA
Lotto N°: F R 0 3 6 Scadenza: 6/92
AVVERTENZA: Nuovo farmaco in sperimentazione clinica, da usare sotto controllo medico.

Prot. FCE 20124/032
REBOXETINA
16 Compresse
PAZIENTE N°: ___ - SETTIMANE 7-8 - MATTINO
Lotto N°: F R 0 3 6 Scadenza: 6/92
AVVERTENZA: Nuovo farmaco in sperimentazione clinica, da usare sotto controllo medico.

Prot. FCE 20124/032
REBOXETINA
16 Compresse
PAZIENTE N°: ___ - SETTIMANE 7-8 - SERA
Lotto N°: F R 0 3 6 Scadenza: 6/92
AVVERTENZA: Nuovo farmaco in sperimentazione clinica, da usare sotto controllo medico.

FARMITALIA CARLO ERBA
ERBAMONT GROUP

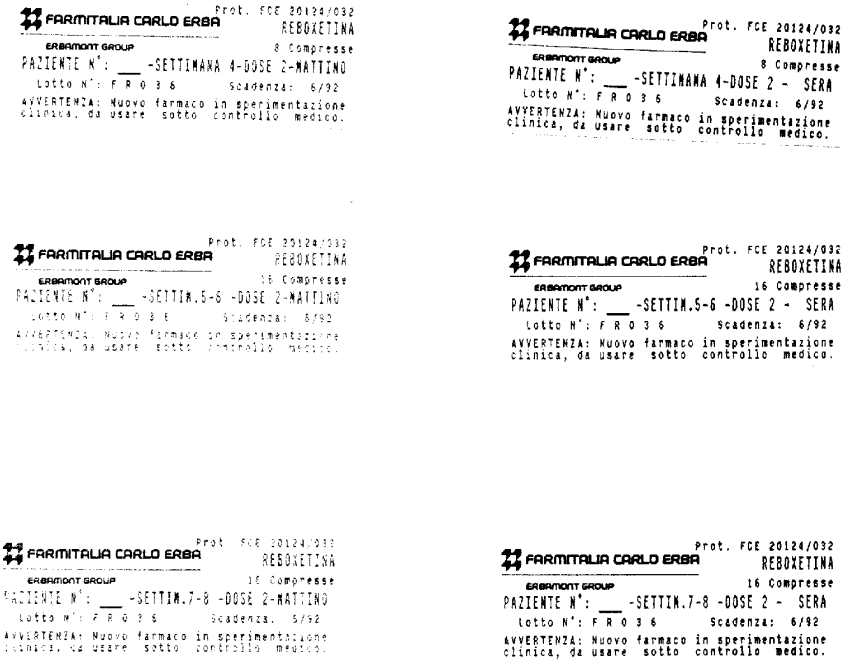
Prot. FCE 20124/032
REBOXETINA
128 Compresse
PAZIENTE N°.: ___
SETTIMANE 1-8
Lotto N°.: F R 0 3 6 Scadenza: 6/92
AVVERTENZA: nuovo prodotto in sperinentazione clinica, da usare sotto controllo medico.

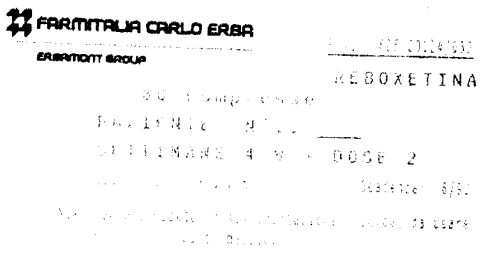
R. Bard

135

9550087

Enclosure 2 cont'd





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Enclosure 2 cont'd

FARMITALIA CARLO ERBA
ERBAMONT GROUP

Prot. FCE 20124/032

REBOXETINA

208 Compresse

PAZIENTE N°: ___

Lotto N°.: F R 0 3 6 Scadenza: 6/92

AVVERTENZA: nuovo prodotto in sperimentazione clinica, da usare sotto controllo medico.

FARMITALIA CARLO ERBA
ERBAMONT GROUP
CNS LINE

9550087

Enclosure 3

DRUG ACCOUNTABILITY

Compound: **REBOXETINE**

Protocol N°: **20124/032**

Title: The double-blind activity and tolerability study of Reboxetine vs Placebo in elderly patients with Depressive Disorders.

City: ______________

Investigator: ______________

Treatm. received: |__|__|__| (d m y) for pat. N°____ to pat. N°____ Receipt N°__________

Bottles per patient received: **12 + 6 (dose 2)**

Pat. N°	Pat. Init.	Date Start	N° of bottles given	N° of remaining bottles	N° of remaining tablets
			___ + ___ (dose 2)	___ + ___ (dose 2)	___ + ___ (dose 2)
			___ + ___ (dose 2)	___ + ___ (dose 2)	___ + ___ (dose 2)
			___ + ___ (dose 2)	___ + ___ (dose 2)	___ + ___ (dose 2)
			___ + ___ (dose 2)	___ + ___ (dose 2)	___ + ___ (dose 2)
			___ + ___ (dose 2)	___ + ___ (dose 2)	___ + ___ (dose 2)
			___ + ___ (dose 2)	___ + ___ (dose 2)	___ + ___ (dose 2)
			___ + ___ (dose 2)	___ + ___ (dose 2)	___ + ___ (dose 2)
			___ + ___ (dose 2)	___ + ___ (dose 2)	___ + ___ (dose 2)
			___ + ___ (dose 2)	___ + ___ (dose 2)	___ + ___ (dose 2)
			___ + ___ (dose 2)	___ + ___ (dose 2)	___ + ___ (dose 2)
			___ + ___ (dose 2)	___ + ___ (dose 2)	___ + ___ (dose 2)
			___ + ___ (dose 2)	___ + ___ (dose 2)	___ + ___ (dose 2)

Date: __________

Investigator's signature: ______________________

- The present form, duly filled out, should be kept as record by the investigator, together with his/her copy of CRFs.
- A photocopy of the present form should be given to the monitor of Farmitalia Carlo Erba, together with the unused drug at the end of the study.

9550087 Enclosure 4

FARMITALIA CARLO ERBA
Erbamont Group

Compound **REBOXETINE**

Protocol No. 20124/032

Pat. Initials

Visit: S C R E E N

Investigator's name

Monitor's name

Date D M Y

PATIENT IDENTIFICATION

Hospital File N°

Initials Sex M F Age (years) Weight (kg) Height (cm)

Birth date D M Y

Ethnic group: Caucasian Black Asian Other Specify

Hospitalized on D M Y

DIAGNOSIS

– DMS-III-R AXIS I

HISTORY OF THE MENTAL DISORDER: Unknown If known:

– Age of onset of disease years

– Number of previous episodes

– Approximate duration of last episode weeks months years

PRESENT EPISODE

– Approximate duration at the time of admission to the study days weeks months years

THE PRESENT EPISODE IN BEST CHARACTERIZED AS:

– Exacerbation of chronic condition 1

– Recurrence of similar previous conditions 2

– Significantly different from any previous conditions 3

– First occurrence, no previous psychiatric diagnosis 4

ONSET OF PRESENT EPISODE WAS:

– Acute (< 2 weeks) 1

– Subacute (≥ 2 weeks) 2

– Insidious (≥ 3 months) 3

PRECIPITATING EXTERNAL STRESS WAS:

– Absent 1

– Probably present 2

– Definitely present 3

Investigator's signature

FARMITALIA CARLO ERBA
Erbamont Group

Compound **REBOXETINE**

Protocol No. 20124/032

Pat. Initials

Visit: S C R E E N

Date D M Y

DSM-III-R: DIAGNOSTIC CRITERIA FOR THE *MAJOR DEPRESSIVE EPISODE*

Note: all A, B, C and D must be marked as "present"

Mark "X" if present

A. At least five of the following symptoms have been present during the same two-week period and represent a change from previous functioning: at least one of the symptoms is either 1) depressed mood or 2) loss of interest or pleasure.

1) depressed mood most of the day, nearly every day, as indicated by subjective account or observation by others
2) markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated either by subjective account or observation by others of apathy most of the time)
3) significant weight loss or weight gain when not dieting (e.g. more than 5% of body weight in a month), or decrease or increase in appetite nearly every day
4) insomnia or hipersomnia nearly every day
5) psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)
6) fatigue or loss of energy nearly every day
7) feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick)
8) diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others)
9) recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide

"A" present ....

B. 1) It cannot be established that an organic factor initiated and maintained the disturbance
2) The disturbance is not a normal reaction to the death of a loved one

"B" present.....

C. At no time during the disturbance have there been delusions or hallucinations for as long as two weeks in the absence of prominent mood symptoms (i.e., before the mood symptoms developed or after they have remitted)

"C" present.....

D. Not superimposed on Schizophrenia, Schizophreniform, Disorder, Delusional Disorder, or Psychotic Disorder NOS.

"D" present.....

Investigator's signature

FARMITALIA CARLO ERBA
Erbamont Group

Compound **REBOXETINE**

Protocol No. 20124/032

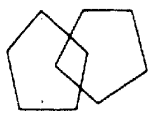
Pat. Initials

Visit: S C R E E N

Date: D M Y

THE MINI-MENTAL STATE EXAMINATION

		Score	Maximum Points
Orientation			
1. What is the	Year?	—	1
	Seasons?	—	1
	Date?	—	1
	Day?	—	1
	Month?	—	1
2. Where are we?	State?	—	1
	County?	—	1
	Town or city?	—	1
	Hospital?	—	1
	Floor?	—	1
Registration			
3. Name three objects, taking one second to say each. Then ask the patient all three after you have said them. Give one point for each correct answer. Repeat the answers until the patient learns all three		—	3
Attention and calculation			
4. Serial sevens. Give one point for each correct answer. Stop after five answers. ALTERNATE: Spell WORLD backwards		—	5
Recall			
5. Ask for names of three objects learned in Question 3. Give one point for each correct answer		—	3
Language			
6. Point to a pencil and a watch. Have the patient name them as you point		—	2
7. Have the patient repeat "No ifs, ands, or buts"		—	1
8. Have the patient follow a three-stage command: "Take the paper in your right hand. Fold the paper in half. Put the paper on the floor"		—	3
9. Have the patient read and obey the following: "CLOSE YOUR EYES" (Write it in large letters)		—	1
10. Have the patient write a sentence of his or her own choice. (The sentence should contain a subject and an object and should make sense. Ignore spelling errors when scoring)		—	1
11. Enlarge the design printed below to 1-5 cm per side and have the patient copy it. (Give one point if all sides and angles are preserved and if the intersecting sides form a quadrangle)		—	1
			___ = Total 30



14.

Investigator's signature _____

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Erbamont Group

Compound **REBOXETINE**

Protocol No. 20124/032

Pat. Initials

Visit: S C R E E N

Date
D M Y

HAMD: HAMILTON DEPRESSION RATING SCALE

1. Depressed mood ***(Sadness, hopeless, helpless, worthless)***

0 Absent
1 These feeling states indicated only on questioning
2 These feeling states spontaneously reported verbally
3 Communicates feeling states non-verbally - i.e., through facial expression, posture, voice, and tendency to weep
4 Patient reports VIRTUALLY ONLY these feeling states in his spontaneous verbal and non-verbal communication

2. Feelings of guilt

0 Absent
1 Self reproach, feels he has let people down
2 Ideas of guilt or rumination over past errors or sinful deeds
3 Present illness is a punishment. Delusions of guilt
4 Hears accusatory or denunciatory voices and/or experiences threatening visual hallucinations

3. Suicide

0 Absent
1 Feels life is not worth living
2 Wishes he were dead or any throughts of possible death to self
3 Suicide ideas or gesture
4 Attempts at suicide *(any serious attempt rates 4)*

4. Insomnia early

0 No difficulty falling asleep
1 Complains of occasional difficulty falling asleep - i.e., more than ½ hour
2 Complains of nightly difficulty falling asleep

5. Insomnia middle

0 No difficulty
1 Patient complains of being restless and disturbed during the night
2 Waking during the night - any getting out of bed rates 2 *(except for purposes of voiding)*

6. Insomnia late

0 No difficulty
1 Waking in early hours of the morning but goes back to slepp
2 Unable to fall asleep again if he gets out of bed

7. Work and activities

0 No difficulty
1 Thoughts and feelings of incapacity, fatigue or weakness related to activities; work or hobbies
2 Loss of interest in activity; hobbies or work - either directly reported by patient, or indirect in listlessness, indecision and vacillation *(feels he has to push self to work or activities)*
3 Decrease in actual time spent in activities or decrease in productivity. In hospital, rate 3 if patient does not spend at least three hours a day in activities *(hospital job or hobbies)* exclusive of ward chores
4 Stopped working because of present illness. In hospital, rate 4 if patient engages in no activities except ward chores, or if patient fails to perform ward chores unassisted

Investigator's signature

FARMITALIA CARLO ERBA
Erbamont Group

Compound **REBOXETINE**

Protocol No. 20124/032

Pat. Initials ☐☐☐

Visit: SCREEN

Date ☐☐/☐☐/☐☐ D M Y

8. Retardation ***(Slowness of thought and speech; impaired ability to concentrate; decreased motor activity)***

- [0] Normal speech and thought
- [1] Slight retardation at interview
- [2] Obvious retardation at interview
- [3] Interview difficult
- [4] Complete stupor ☐

9. Agitation

[0] None [1] Fidgetiness [2] Playing with hands, hair, etc.
[3] Moving about, can't sit still [4] Hand wringing, nail biting, hair-pulling, biting of lips ☐

10. Anxiety psychic

[0] No difficulty [1] Subjective tension and irritability
[2] Worrying about mirror matters [3] Apprehensive attitude apparent in face or speech
[4] Fears expressed without questioning ☐

11. Anxiety somatic
Physiological concomitants of anxiety, such as: Gastro-intestinal *(dry mouth, wind, indigestion, diarrhea, cramps, belching)*; Cardio-vascular *(palpitations, headaches)*; Respiratory *(hyperventilation, sighing)*; Urinary frequency; Sweating

[0] Absent [1] Mild [2] Moderate
[3] Severe [4] Incapacitating ☐

12. Somatic symptoms gastrointestinal

- [0] None
- [1] Loss of appetite but eating without staff encouragement. Heavy feelings in abdomen
- [2] Difficulty eating without staff urging. Requests or requires laxatives or medication for bowels or medication for G.I. symptoms ☐

13. Somatic symptoms general

- [0] None
- [1] Heaviness in limbs, back or head. Backaches, headache, muscle aches. Loss of energy and fatigability
- [2] Any clear-cut symptoms rates 2 ☐

14. Genital symptoms (Such as: *Loss of libido; Menstrual disturbances*

[0] Absent [1] Mild [2] Severe ☐

15. Hipochondriasis

[0] Non present [1] Self-absorption (bodily)
[2] Preoccupation with health [3] Frequent complaints, requests for help, etc.
[4] Hypocondriacal delusions ☐

Investigator's signature _____

FARMITALIA CARLO ERBA
Erbamont Group

Compound **REBOXETINE**

Protocol No. 20124/032

Pat. Initials

Visit: S C R E E N

Date D M Y

16. Loss of weight ***Rate either A or B***

A. When Rating By History:

0 No weight loss
1 Probable weight loss associated with present illness
2 Definite (according to patient) weight loss
3 Not assessed

B. On Weakly Ratings By Ward Psychiatrist, When Actual Weight Changes Are Measured:

0 Less than 1 lb. weight loss in week
1 Greater than 1 lb. weight loss in week
2 Greater than 2 lb. weight loss in week
3 Not assessed

17. Insight

0 Acknowledges being depressed and ill
1 Acknowledges illness but attributes cause to bad food, climate, overwork, virus, need for rest, etc.
2 Denies being ill at all

18. Diurnal variation

0 None 1 Mild 2 Severe

19. Depersonalization and derealization (Such as: *Feelings of unreality, Nihilistic ideas)*

0 Absent 1 Mild 2 Moderate
3 Severe 4 Incapacitating

20. Paranoid symptoms

0 None
1 Suspicious
2 Ideas of reference
3 Delusions of reference and persecution

21. Obsessional and compulsive symptoms

0 Absent 1 Mild 2 Severe

Total score

Investigator's signature

FARMITALIA CARLO ERBA
Erbamont Group

Compound **REBOXETINE**

Protocol No. 20124/032

Pat. Initials .....

Visit: S C R E E N

Date ..... D M Y

ADMISSION EXAMINATION

CHEST X-RAY taken on ..... D M Y normal abnormal

If abnormal, detail .....

VITAL SIGNS

– Body temperature (°C) .....

– Respiratory rate (breaths/min) .....

– 5 min lying arterial blood pressure (mmHg) systolic ..... diastolic .....

– 5 min lying heart rate (beats/min) .....

– 2 min standing arterial blood pressure (mmHg) systolic ..... diastolic .....

– 2 min standing heart rate (beats/min) .....

MEDICAL HISTORY

– Important previous diseases .....

Investigator's signature .....

FARMITALIA CARLO ERBA
Erbamont Group

Compound **REBOXETINE**

Protocol No. 20124/032

Pat. Initials

Visit: S C R E E N

Date D M Y

ECG

HEART RATE

- Normal
- Abnormal

if abnormal check one or more boxes as appropriate:

1 Sinus bradycardia (<60)
2 Sinus tachycardia (>100)
3 Sick Sinus Syndrome

- Atrial ectopic beats:
  - Occasional
  - Frequent (>6/mm)
  - Couplets
  - Supraventricular Tachycardia
- Ventricular ectopic beats:
  - Occasional
  - Frequent (>6/mm)
  - Polymorphic
  - Couplets
  - Ventricular Tachycardia
- Atrial fibrillation/flutter
- A-V Block 1st degree
  - 2nd degree - Mobitz 1
  - Mobitz 2
  - Complete
- Left ventricular hypertrophy
- Right ventricular hypertrophy
- Myocardial ischemia
- Previous Myocardial infarction
- Acute Myocardial infarction
- Right bundle branch block
- Left bundle branch block
- Left anterior hemiblock
- Left posterior hemiblock
- Bifascicular Block (specify)
- Trifascicular Block (specify)
- Other

(specify)

Investigator's signature

9550087 Enclosure 4 cont.'d
Page 9

FARMITALIA CARLO ERBA
Erbamont Group

Compound **REBOXETINE**

Protocol No. 20124/032

Pat. Initials

Visit: S C R E E N

Date
D M Y

CONT' ECG

Please, add here the ORIGINAL TRACING AND MEDICAL REPORT

Investigator's signature

FARMITALIA CARLO ERBA
Erbamont Group

Compound **REBOXETINE**

Protocol No. 20124/032

Pat. Initials

Visit: S C R E E N

Date
D M Y

EEG REPORT

Description:

RESULT: Normal

Slight abnormal/Borderline

Abnormal: generalized abnormally (specify:)

lateralized abnormality (specify:)

focal abnormality (specify:)

Other (please give detailed description):

Note: please, check always 1 box only: even when giving detailed description.

Investigator's signature

FARMITALIA CARLO ERBA
Erbamont Group

Compound **REBOXETINE**

Protocol No. 20124/032

Pat. Initials

Visit: S C R E E N

Date D M Y

LABORATORY TESTS

VIROLOGY *

Date of blood sample collection	D M Y
HBa Ag negative?	yes , no
HBc Ab negative?	yes , no
"ELISA" HIV negative?	yes , no

* To be carried out within 2 weeks prior to the beginning of the study.

Tests	Value	Clinically Significant abnormality *	Tests	Value	Clinically Significant abnormality *
BLOOD TESTS			BUN		
HB			Creatinine		
HCT			Uric acid		
RBC			Total bilirubin		
WBC			Direct bilirubin		
Neutrophils			Total protein		
Lymphocytes			Blood albumin		
Eosinophils			Cholesterol		
Monocytes			Triglycerides		
Basophils			Globulins α 1		
Platelets			α 2		
Na^+			β		
K^+			γ		
Cl^-			CLcr		
Ca^{++}			TSH		
PO_4^{--}			T_4		
SGOT			**URINALYSIS**	Normal	Abnormal
SGPT			Specific gravity	☐	☐
γ-GT			Albumin	☐	☐
LDH			Sugar	☐	☐
Alkaline phosphatase			RBC	☐	☐
Blood sugar			WBC	☐	☐

* Cross in case of clinically significant abnormality.

Observation: .....

Investigator's signature .....

FARMITALIA CARLO ERBA
Erbamont Group

Compound **REBOXETINE**

Protocol No. 20124/032

Pat. Initials

Visit: S C R E E N

Date D M Y

PREVIOUS ANTIDEPRESSIVE TREATMENTS

NAME*	EFFICACY (Very poor, Poor, Fair, Good, Very good)	SIDE EFFECTS (if any)
	VP P F G VG	
	VP P F G VG	
	VP P F G VG	
	VP P F G VG	
	VP P F G VG	

Last treatment taken: name* Last day of treatment D M Y

Drug free, Wash-Out Period: from D M Y to D M Y

CONCOMITANT DRUGS (during the drug free, wash-out period)

NAME*	Daily Dose (mg)	Started on (date)			Discontinued on (date)			Reason for the administration
		D	M	Y	D	M	Y	

* Please use trade name

Observations:

Investigator's signature

FARMITALIA CARLO ERBA
Erbamont Group

Compound **REBOXETINE**

Protocol No. 20124/032

Pat. Initials .....

Visit: SCREEN

Date ..... D M Y

ELEGIBILITY OF THE PATIENT

INCLUSION CRITERIA

FOLLOWING QUESTIONS NEED TO BE ANSWERED **YES**:	YES	NO
– Aged over 65 years?		
– Normal body weight/height ratio?		
– Are the DSM-III-R criteria for Major Depressive Episodes present?		
– Total score of 18 or above in the 21-HAMD?		
– Total score of 20 or above in the MMS?		
– Able and willing (he/she or the next of kin) to give Informed Consent?		

EXCLUSION CRITERIA

FOLLOWING QUESTIONS NEED TO BE ANSWERED **NO**:		
– Cyclothymia? Dysthymia?		
– History of Major Depressive Episodes, associated to Endocrine Disorders?		
– History of drug hypersensitivity?		
– History of seizures or serious brain injury?		
– Evidence of substance use disorder within past 6 months or currently?		
– ECT in the previous 6 months?		
– Participation in a clinical trial with an investigational compound in the 4 weeks preceding the study?		
– Resistance to previous antidepressive treatments?		
– Psychotropic treatment during wash-out period?		
– Need of chronic treatment with wathever drug?		
– High risk of suicide?		
– Chronic respiratory insufficiency?		
– Current evidence of urinary retention?		
– Current evidence of glaucoma?		
– Important clinical illness in the 4 weeks preceding the study?		
– Clinically significant lab values abnormality?		
– Clinically significant physical abnormality?		

If yes, please specify: .....

CONCLUSION

Is the patient elegible for this study? yes ☐ no ☐

If yes, this patient will receive the following patient number: ☐☐

Investigator's signature .....

FARMITALIA CARLO ERBA
Erbamont Group

Compound **REBOXETINE**

Protocol No. 20124/032

Pat. Initials .....

Visit: S C R E E N

Date .. / .. / .. (D M Y)

HAMD: HAMILTON DEPRESSION RATING SCALE

1. Depressed mood ***(Sadness, hopeless, helpless, worthless)***

0 Absent
1 These feeling states indicated only on questioning
2 These feeling states spontaneously reported verbally
3 Communicates feeling states non-verbally - i.e., through facial expression, posture, voice, and tendency to weep
4 Patient reports VIRTUALLY ONLY these feeling states in his spontaneous verbal and non-verbal communication

2. Feelings of guilt

0 Absent
1 Self reproach, feels he has let people down
2 Ideas of guilt or rumination over past errors or sinful deeds
3 Present illness is a punishment. Delusions of guilt
4 Hears accusatory or denunciatory voices and/or experiences threatening visual hallucinations

3. Suicide

0 Absent
1 Feels life is not worth living
2 Wishes he were dead or any throughts of possible death to self
3 Suicide ideas or gesture
4 Attempts at suicide *(any serious attempt rates 4)*

4. Insomnia early

0 No difficulty falling asleep
1 Complains of occasional difficulty falling asleep - i.e., more than ½ hour
2 Complains of nightly difficulty falling asleep

5. Insomnia middle

0 No difficulty
1 Patient complains of being restless and disturbed during the night
2 Waking during the night - any getting out of bed rates 2 *(except for purposes of voiding)*

6. Insomnia late

0 No difficulty
1 Waking in early hours of the morning but goes back to slepp
2 Unable to fall asleep again if he gets out of bed

7. Work and activities

0 No difficulty
1 Thoughts and feelings of incapacity, fatigue or weakness related to activities; work or hobbies
2 Loss of interest in activity; hobbies or work - either directly reported by patient, or indirect in listlessness, indecision and vacillation *(feels he has to push self to work or activities)*
3 Decrease in actual time spent in activities or decrease in productivity. In hospital, rate 3 if patient does not spend at least three hours a day in activities *(hospital job or hobbies)* exclusive of ward chores
4 Stopped working because of present illness. In hospital, rate 4 if patient engages in no activities except ward chores, or if patient fails to perform ward chores unassisted

Investigator's signature .....

FARMITALIA CARLO ERBA
Erbamont Group

Compound **REBOXETINE**

Protocol No. 20124/032

Pat. Initials .....

Visit: S C R E E N

Date ..... D M Y

---

8. Retardation ***(Slowness of thought and speech; impaired ability to concentrate; decreased motor activity)***

0 Normal speech and thought
1 Slight retardation at interview
2 Obvious retardation at interview
3 Interview difficult
4 Complete stupor

---

9. Agitation

0 None
1 Fidgetiness
2 Playing with hands, hair, etc.
3 Moving about, can't sit still
4 Hand wringing, nail biting, hair-pulling, biting of lips

---

10. Anxiety psychic

0 No difficulty
1 Subjective tension and irritability
2 Worrying about mirror matters
3 Apprehensive attitude apparent in face or speech
4 Fears expressed without questioning

---

11. Anxiety somatic
Physiological concomitants of anxiety, such as: Gastro-intestinal *(dry mouth, wind, indigestion, diarrhea, cramps, belching)*; Cardio-vascular *(palpitations, headaches)*; Respiratory *(hyperventilation, sighing)*; Urinary frequency; Sweating

0 Absent
1 Mild
2 Moderate
3 Severe
4 Incapacitating

---

12. Somatic symptoms gastrointestinal

0 None
1 Loss of appetite but eating without staff encouragement. Heavy feelings in abdomen
2 Difficulty eating without staff urging. Requests or requires laxatives or medication for bowels or medication for G.I. symptoms

---

13. Somatic symptoms general

0 None
1 Heaviness in limbs, back or head. Backaches, headache, muscle aches. Loss of energy and fatigability
2 Any clear-cut symptoms rates 2

---

14. Genital symptoms (Such as: *Loss of libido; Menstrual disturbances*

0 Absent
1 Mild
2 Severe

---

15. Hipochondriasis

0 Non present
1 Self-absorption (bodily)
2 Preoccupation with health
3 Frequent complaints, requests for help, etc.
4 Hypocondriacal delusions

Investigator's signature .....

FARMITALIA CARLO ERBA
Erbamont Group

Compound **REBOXETINE**

Protocol No. 20124/032

Pat. Initials .....

Visit: SCREEN

Date ... ...
D M Y

16. Loss of weight ***Rate either A or B***

A. When Rating By History:

0 No weight loss
1 Probable weight loss associated with present illness
2 Definite (according to patient) weight loss
3 Not assessed

B. On Weakly Ratings By Ward Psychiatrist, When Actual Weight Changes Are Measured:

0 Less than 1 lb. weight loss in week
1 Greater than 1 lb. weight loss in week
2 Greater than 2 lb. weight loss in week
3 Not assessed

17. Insight

0 Acknowledges being depressed and ill
1 Acknowledges illness but attributes cause to bad food, climate, overwork, virus, need for rest, etc.
2 Denies being ill at all

18. Diurnal variation

0 None 1 Mild 2 Severe

19. Depersonalization and derealization (Such as: *Feelings of unreality, Nihilistic ideas)*

0 Absent 1 Mild 2 Moderate
3 Severe 4 Incapacitating

20. Paranoid symptoms

0 None
1 Suspicious
2 Ideas of reference
3 Delusions of reference and persecution

21. Obsessional and compulsive symptoms

0 Absent 1 Mild 2 Severe

Total score ...

Investigator's signature .....

FARMITALIA CARLO ERBA
Erbamont Group

Compound **REBOXETINE**

Protocol No. 20124/032

Patient No.

Visit: D A Y 0

Date
D M Y

CLINICAL GLOBAL IMPRESSION (CGI)

A. SEVERITY OF ILLNESS

Considering your clinical experience with this particular population, how mentally ill is the patient at this time?

1 Normal, not at all ill
2 Borderline mentally ill
3 Mildly ill
4 Moderately ill
5 Markedly ill
6 Severely ill
7 Among the most extremely ill patients

Investigator's signature .....

9550087 Enclosure 7 Page 5

FARMITALIA CARLO ERBA
Erbamont Group

Compound REBOXETINE

Protocol No. 20124/032

Patient No.

Visit: D A Y 0

Date D M Y

SCAG: SANDOZ CLINICAL ASSESSMENT GERIATRIC

(Please circle one number for each simptom)*

Symptom	Severity						
1. Mood depression	1	2	3	4	5	6	7
2. Confusion	1	2	3	4	5	6	7
3. Mental alertness	1	2	3	4	5	6	7
4. Motivation/Initiative	1	2	3	4	5	6	7
5. Irritability	1	2	3	4	5	6	7
6. Hostility	1	2	3	4	5	6	7
7. Bothersome	1	2	3	4	5	6	7
8. Indifference to surroundings	1	2	3	4	5	6	7
9. Unsociability	1	2	3	4	5	6	7
10. Uncooperativeness	1	2	3	4	5	6	7
11. Emotional lability	1	2	3	4	5	6	7
12. Fatigue	1	2	3	4	5	6	7
13. Self-care	1	2	3	4	5	6	7
14. Appetite	1	2	3	4	5	6	7
15. Dizziness	1	2	3	4	5	6	7
16. Anxiety	1	2	3	4	5	6	7
17. Impairment of recent memory	1	2	3	4	5	6	7
18. Disorientation	1	2	3	4	5	6	7
19. Overall impression of patient	1	2	3	4	5	6	7

Total score:

*: Scoring: «1»=normal ----- «7»=severe

Investigator's signature

FARMITALIA CARLO ERBA
Erbamont Group

Compound **REBOXETINE**

Protocol No. 20124/032

Patient No.

Visit: D A Y 0

Date
D M

GDS: GERIATRIC DEPRESSION SCALE

Please ask patient the following questions:

1. Are you basically satisfied with your life?	YES	NO
2. Have you dropped many of your activities and interest?	YES	NO
3. Do you feel that your life is empty?	YES	NO
4. Do you often get bored?	YES	NO
5. Are you hopefull about the future?	YES	NO
6. Are you bothered by thoughts you can't get out of your head?	YES	NO
7. Are you in good spirits most of the time?	YES	NO
8. Are you afraid that something bad is going to happen to you?	YES	NO
9. Do you feel happy most of the time?	YES	NO
10. Do you often feel helpless?	YES	NO
11. Do you often get restless and fidgety?	YES	NO
12. Do you prefer to stay at home rather than going out and doing new things?	YES	NO
13. Do you frequently worry about the future?	YES	NO
14. Do you feel you have more problems with memory than most?	YES	NO
15. Do you think it is wonderful to be alive now?	YES	NO
16. Do you often feel downhearted and blue?	YES	NO
17. Do you feel pretty worthless the way you are now?	YES	NO
18. Do you worry a lot about the past?	YES	NO
19. Do you find life very exciting?	YES	NO
20. Is it hard for you to get started on new project?	YES	NO
21. Do you feel full of energy?	YES	NO
22. Do you feel that your situation is hopeless?	YES	NO
23. Do you think that most people are better off than you are?	YES	NO
24. Do you frequently get upset over little things?	YES	NO
25. Do you frequently feel like crying?	YES	NO
26. Do you have trouble concentrating?	YES	NO
27. Do you enjoy getting up in the morning?	YES	NO
28. Do you prefer to avoid social gatherings?	YES	NO
29. Is it easy for you to make decisions?	YES	NO
30. Is your mind as clear as it used to be?	YES	NO

Total score:

*: Please, score 1 point for each answer marked in white (not shaded) box.

Investigator's signature

FARMITALIA CARLO ERBA
Erbamont Group

Compound **REBOXETINE**

Protocol No. 20124/032

Patient No.

Visit: D A Y 0

Date
D M Y

ADVERSE EVENTS: CHECK-LIST

1. AUTONOMIC

- Dry mouth
- Nasal congestion
- Blurred vision
- Constipation
- Urinary hesitancy
- Urinary retention
- Increased salivation
- Sweating
- Vomiting
- Diarrhoea
- Sexual disturbances
- Nausea

2. BEHAVIORAL TOXICITY

- Confusional reaction
- Excitement/agitation
- Increased motor activity
- Decreased motor activity
- Insomnia
- Drowsiness
- Lassitude

3. CARDIOVASCULAR

- Hypotension
- Dizziness
- Circulatory collapse
- Tachycardia
- Hypertension
- Precordial pain

4. NEUROLOGICAL

- Rigidity
- Tremor
- Akathisia
- Dystonia
- Paresthesias
- Seizures
- Myoclonus
- Muscular pain

5. OTHER

- Skin-rash
- Urticaria
- Decreased appetite
- Headache
- Dyspnea

Investigator's signature

9550087

Enclosure 10

ADVERSE DRUG REACTION - A CRITICAL REVIEW

CAUSE-EFFECT RELATIONSHIP

F.E.KARCH, L.LASAGNA
(JAMA Dec. 22, 1975-Vol.234)

1. DEFINITE (or CERTAIN)
A reaction that follows a reasonable temporal sequence from administration of the drug or in which the drug level has been established in body fluids or tissues; that follows a known response pattern to the suspected drug; and that is confirmed by improvement on stopping the drug (dechallenge), and reappearance of the reaction on repeated exposure (rechallenge).

2. PROBABLE
A reaction that follows a reasonable temporal sequence from administration of the drug; that follows a known response pattern to the suspected drug; that is confirmed by dechallenge; and that could not be reasonably explained by the known characteristics of the patient's clinical state.

3. POSSIBLE
A reaction that follows a reasonable temporal sequence from administration of the drug; that follows a known response pattern to the suspected drug; but that could have been produced by the patient's clinical state or other modes of therapy administered to the patient.

4. DOUBTFUL
Any reaction that does not meet the criteria above.

5. UNKNOWN
Relationship for which no evaluation can be made.

6. NOT RELATED
A reaction for which sufficient information exists to indicate tha the aetiology is unrelated to the study drug.

Enclosure 11

Declaration of Helsinki IV (Hong Kong - September 1989)

WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI

Recommendations guiding physicians
in biomedical research involving human subjects

Adopted by the 18th World Medical Assembly,
Helsinki, Finland, June 1964,

and amended by the
29th World Medical Assembly,
Tokyo, Japan, October 1975,
35th World Medical Assembly,
Venice, Italy, October 1983
and the
41st World Medical Assembly
Hong Kong, September 1989

INTRODUCTION

It is the mission of the physician to safeguard the healthy of the people. His or her knowledge and conscience are dedicated to the fulfillment of this mission.

The Declaration of Geneva of the World Medical Association binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act only in the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient." The purpose of biomedical research involving human subjects must be to improve diagnostic, therapeutic and prophylactic procedures and the understanding of the aetiology and pathogenesis of disease.
In current medical practice most diagnostic, therapeutic or prophylactic procedures involve hazards. This applies especially to biomedical research.

Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects.

In the field of biomedical research a fundamental distinction must be recognized between medical research in which the aim is essentially diagnostic or therapeutic for a patient, and medical research, the essential object of which is purely scientific and without implying direct diagnostic or therapeutic value to the person subjected to the research.

Special caution must be exercised in the conduct of research which may affect the environment and the welfare of animals used for research must be respected.

Because it is essential that the results of laboratory experiments be applied to human beings to further scientific knowledge and to help suffering humanity, the World Medical Association has prepared the following recommendations as a guide to every physician in biomedical research involving human subjects. They should be kept under review in the future. It must be stressed that the standards as drafted are only a guide to physicians all over the world. Physicians are not relieved from criminal, civil and ethical responsibilities under the laws of their own countries.

I. BASIC PRINCIPLES

1. Biomedical research involving human subjects must conform to generally accepted scientific principles and should be based on adequately performed laboratory and animal experimentation and on a thorough knowledge of the scientific literature.
2. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol which should be transmitted for consideration, comment and guidance to a specially appointed committee independent of the investigator and the sponsor provided that this independent committee is in conformity with the laws and regulations of the country in which the research experiment is performed.
3. Biomedical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research , even though the subject has given his or her consent.
4. Biomedical research involving human subjects cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.
5. Every biomedical research project involving human subjects should be preceded by careful assessment of predictable risks in comparison with foreseable benefits to the subject or to others. Concern for the interests of the subject must always prevail over the interests of science and society.
6. The right of the research subject to safeguard his or her integrity must always be respected. Every precaution should be taken to respect the privacy of the subject and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.
7. Physicians should abstain from engaging in research projects involving human subject unless they are satisfied that the hazard involved are believed to be predictable. Physicians should cease any investigation if the hazards are found to outweigh the potential benefits.
8. In publication of the results of his or her research, the physician is obliged to preserve the accuracy of the results. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.
9. In any research on human beings, each potential subject must be adequately informed of the aims, methods, anticipated benefits and potential hazard of the study and the discomfort it may entail. He or she should be informed that he or she is at liberty to abstain from participation in the study and that he or she is free to withdraw his or her consent to participation at any time. The physician should then obtain the subject's freely-given informed consent, preferably in writing.
10. When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in a dependent relationship to him or her or may consent under duress. In that case the informed consent should be obtained by a physician who is not engaged in the investigation and who is completely independent of this official relationship.
11. In case of legal incompetence, informed consent should be obtained from the legal guardian in accordance with national legislation. Where physical or mental incapacity makes it impossible to obtain informed consent, or when the subject is a minor, permission from the responsible relative replaces that of the subject in accordance with national legislation. Whenever the minor child is in fact able to give a consent, the minor's consent must be obtained in addition to the consent of the minor's legal guardian.
12. The research protocol should always contain a statement of the ethical considerations involved and should indicate that the principles enunciated in the present Declaration are complied with.

II. MEDICAL RESEARCH COMBINED WITH PROFESSIONAL CARE
(Clinical research)

1. In the treatment of the sick person, the physician must be free to use a new diagnostic and therapeutic measure, if in his or her judgement it offers hope of saving life, reestablishing health or alleviating suffering.

2. The potential benefits, hazards and discomfort of a new method should be weighed against the advantages of the best current diagnostic and therapeutic methods.

3. In any medical study, every patient - including those of a control group, if any - should be assured of the best proven diagnostic and therapeutic method.

4. The refusal of the patient of participate in a study must never interfere with the physician-patient relationship.

5. If the physician considers it essential not to obtain informed consent, the specific reasons for this proposal should be stated in the experimental protocol for transmission to the independent committee (1, 2).

6. The physician can combine medical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that medical research is justified by its potential diagnostic or therapeutic value for the patient.

III. NON-THERAPEUTIC BIOMEDICAL RESEARCH INVOLVING HUMAN SUBJECTS (Non-clinical biomedical research)

1. In the purely scientific application of medical research carried out on a human being, it is the duty of the physician to remain the protector of the life and health of that person on whom biomedical research is being carried out.

2. The subjects should be volunteers - either healthy persons or patients for whom the experimental design is not related to the patient's illness.

3. The investigator or the investigating team should discontinue the research if in his/her or their judgement it may, if continued, be harmful to the individual.

4. In research on man, the interest of science and society should never take precedence over considerations related to the wellbeing of the subject.

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Enclosure 12

REBOXETINE PROTOCOL 20124/032

Multicenter double blind activity and tolerability study of reboxetine vs placebo in elderly patients with depressive disorders.

CONSENT FORM

Principal Investigator:

_____

_____

EXPLANATION

Purpose of the study

Reboxetine, a new potential antidepressant agent, has effects in animals which suggest that it may exert therapeutic efficacy of faster onset, in comparison with established antidepressant drugs, in patients suffering from depressive disorders. The trial is proposed in order to learn about the antidepressant effectiveness and the tolerability of the compound in the elderly depressed patients.

Plan of the study

After an initial drug free wash out period of at least one week, patients will receive either reboxetine or a harmless inactive treatment (placebo). Neither patients nor doctors will know which treatment will be administered in individual cases until after the study is completed. The identity of the treatments can anyhow be determined immediately if any medical problem will develop and it will become important to learn which of the two possible treatment is being given.

Treatment will be administered for a maximum period of six months. It will be discontinued in case of re-emerge of psychiatric symptomatology or in case of significant side-effects. In addition patients participating in the study may withdraw their consent at any time without prejudice to their continued medical treatment.

During treatment, physical and psychiatric examinations will be done on frequent occasions, in order to determine possible side-effects and benefits of treatments. Blood tests, urinalysis, ECG will be undertaken at bi-weekly to monthly intervals during the treatment. Blood pressure and pulse will be taken very frequently.

Possible discomforts and risks

Antidepressant drugs can cause dry mouth, blurred vision, dizziness, mild difficulty in voiding urine, postural hypotension and electrocardiographic changes.

Reboxetine has been so far administered for 28 days to about 180 patients and was well tolerated up to the dose of 5 mg twice daily. In the dose range of 3-5 mg twice daily clinically relevant improvement of depressive condition was present in the majority of patients; symptoms complained off by patients were mainly mild and transient and included most frequently headache, sweating, lassitude, nasal congestion, constipation and urinary hesitancy. At higher doses orthostatic hypotension, tachycardia, dizziness, blurred vision and nausea were reported.

Patients participating in the study will be carefully monitored to detect early signs of such side-effects.

Possible benefits

Other drugs are available for treatment of depressive disorders but none has been of proven value in all cases. This study will allow the evaluation of the antidepressant activity of reboxetine upon long-term administration for elderly depressed patients.

Alternative treatment

Patients would receive alternative pharmacological therapy with an antidepressant drug chosen on the basis of response during previous episodes, if any. Risks and benefits of receiving treatment with any of the available antidepressant drugs can be explained by the Investigator.

Confidentiality

Participation in the study will be kept confidential to the extent permitted by law.

Problems and questions

Should any problem or question arise with regard to the study, patients can contact the Principal Investigator:

_____

or the other staff members also involved in the study:

_____

_____

_____

In addition any problem or question can be discussed with a member of the Institutional Review Board (..... .....), the Committee which has evaluated the potential risks and possible benefits of the study.

Payments and policy regarding research-related injuries.

Patients will not be paid for the participation in the study. The Clinical Center will provide short-term medical care for any physical injury resulting from participation in the study. No long-term medical care or financial compensation for such injuries will be provided except as it may be through whatever remedies are normally available under law. Insurance coverage is granted through the Sponsor Company.

PATIENTS CONSENT

I have read the explanation about this study and I have been given the opportunity to discuss it and to ask questions. I hereby consent to take part in this study.

_____ _____

Patient Signature date

I have explained all the above indicated aspects of the study to the patient, who expressed his/her consent to the participation.

_____ _____

Investigator Signature date

_____ _____

Witness Signature date

9550087

Enclosure 13

Milano 12.

Spett.le
FARMITALIA C. ERBA SRL
Via C. Imbonati 24

20159 MILANO

DICHIARAZIONE
DECLARATION
To whom it may concern

La sottoscritta LA FONDIARIA ASS.NI S.p.A. con sede in Firenze-Via L. Il Magnifico 1
The undersigned LA FONDIARIA ASS.NI S.p.A., with head office in Firenze - Via Lorenzo il Magnifico 1

dichiara a tutti gli effetti che la Spett.le FARMITALIA CARLO ERBA SRL
hereby declares to all intents and purposes that the firma FARMITALIA CARLO ERBA SRL

con sede in Milano - Via C. Imbonati 24, e' assicurata contro la
with head office in Milan - Via C. Imbonati 24, is insured against

responsabilita' civile verso terzi per danni derivanti dalla sua attivita' (ivi compresa "produzione"
third party liability for damage deriving from their activities (including "production"

e "smercio") e dalle sue proprieta' con polizza n.4W8102, scadente il 31.12.1991
and "sales") and its properties, under policy No.4W8102, expiring on 31.12.1991

e tacitamente rinnovabile di anno in anno, per il massimale unico
di L. 10.000.000.000.=(diecimiliardi) per sinistro,
automatically renewable for one year at a time, to cover up
to L. 10.000.000.000 (ten thausand millions Lire) as a singleanyone claim,

nei termini tutti di cui alla polizza stessa.
in all terms concerning the policy itself.

La garanzia e'valida per il mondo intero e prevede, tra l'altro, anche l'estensione della copertura ai seguenti:
This coverage is applicable through out the world, and includes the following:

- danni causati da specialita' medicinali e prodotti medicinali che secondo la
- damage arising from medicinal specialities and products which, according to

  comune prassi, prima della loro registrazione sanitaria e della loro
  normal practice, before they are officially registered and

  immissione in commercio, vengono consegnati a cliniche, ospedali,
  put on the market, are giving to clinics, hospitals

  case di cura ed esercenti professioni sanitarie per sperimentazioni e
  nursing homes and professional healt workers for clinical trials and

9550087

ITALIA ASSICURAZIONI

Enclosure 13 cont'd

prove cliniche, nonche'ai danni causati a seguito di somministrazione
tests and damage arising following administration for pharmacological tests

per ricerche di farmacologia ed esperimenti con farmaci e preparazioni gia' registrate in Italia
experiments of drugs or preparations already registered in Italy

e/o all'estero, ma con posologie diverse da quelle
and/or in other countries but using dosages different from these

indicate dalle case produttrici e con nuovi farmaci in fase di studio;
indicated by the manufacturer and of new drugs in the study stage;

comprese tutte le attivita' inerenti e connesse alle sperimentazioni stesse,
including all activities connected with and inherent to tests and trials

quali la tecnica di somministrazione dei farmaci ed il prelievo del
such as the methods of administering drugs and withdrawing

sangue dai soggetti per studio; il tutto con prodotti
blood samples from subjects under study; all with products

sia ad uso umano che non, propri e/o di terzi;
for human use or not, own and/or of the third party.

- connessi a responsabilita' civile che possa derivare personalmente
- damage relating to third party liability which may result personally

agli esperimentatori sia nel paese dell'Assicurata che all'estero
to the experimenters both in the country of Insured and/or in other countries

in ragione degli esperimenti effettuati su richiesta e/o per conto dell'Assicurata stessa.
because of the experiments effected at request and/or for account of the Insured.

La presente viene rilasciata a richiesta della Spett.le FARMITALIA C. ERBA SRL
This declaration is issued in response to a request by FARMITALIA C.ERBA SRL

Relativamente alla presente dichiarazione redatta sia in lingua italiana che in
Relatively to the present declaration drawn up both in italian language and

lingua inglese, viene convenuto che, in caso di divergenza tra i due testi,
English language, it is agreed that, in case of divergence between the two texts,

9550087

ITALIA ASSICURAZIONI

Enclosure 13 cont'd

prevarra', ai fini interpretativi, il testo in lingua italiana.
the one in Italian language will prevail for the purpose of interpretation.

In fede

LA FONDIARIA ASSICURAZIONI SPA
B.U.GRANDI OCEANICI-CONVENZIONI E GERENZE
GRANDI CLIENTI
G. Perrone

9550087

Attachment A

REBOXETINE PROTOCOL 20124/032: OPERATING PROCEDURES FOR TRAINING ON ASSESSMENT INSTRUMENTS, STUDY MONITORING AND COORDINATION.

Aim

The purpose of these procedures is to assure data uniformity and compatibility by appropriate interventions during data gathering.

Study monitoring

During the course of the study (1 year) monthly monitoring visits will be conducted by Study Monitors from Farmitalia Carlo Erba.

The start-up visit will take place after approval of the protocol by the Institutional Review Board (IRB) or Ethical Committee. On this visit the following documents will be collected:

- copy of the protocol signed by the Principal Investigator;
- the written approval of the study (typed on the Institute's letter head) by the Hospital or University Center Review Board and the IRB members list;
- an IRB approved blank copy of the consent form;

These documents will be sent to FICE-Milan. On the occasion of this visit the monitor will also check that the CRFs and the drug supply have been delivered to the Clinical Investigator and the accompanying letter, signed by the Clinical Investigator, will be collected. In addition the Monitor will identify the staff members who will be involved in the study conduct and the monitoring visits schedule will be agreed.

Following the start-up visit the monitoring form A (enclosed) will be filled in. The original page will be sent to FICE in Milan.

The first monitoring visit will be done immediately after the recruitment of the first two, three patients.

The periodic monitoring visits are carried out in order to:

1 verify protocol adherence: patient eligibility (page 13 of screening form), times of assessments, completeness of data, pill count;

2 verify data consistency looking for inconsistencies or errors in the data recorded on the CRF;

3 verify the accuracy of data collection in CRFs against the original clinic or hospital records for:

- pt initials and hospital record N°
- signed informed consent
- study medication administration and concomitant medications
- physician notes on adverse events
- 20% of data for laboratory tests, patient history and vital signs; in case of an error rate > 15% all data need to be monitored;
- total Hamilton score reported in the hospital record.

Source-verified data can be initialled by the study monitor in the CRF.

4 review all adverse events including laboratory abnormalities, occurred since the previous visit. Should the information of a serious, or unexpected adverse event newly emerge, the local study Monitor must immediately (within two working days) inform the Product Leader in Milan;

5 evaluate patient recruitment rate and treatment discontinuations;

6 verify study medication storage and accountability and collect bottles of completed treatments;

7 ensure continued acceptability of the facilities and of the staff.

CRFs will be completed in black ink and corrections, if needed, made only by the Clinical Investigator with a single line throughout; the corrections will be initialled by Clinical Investigator and dated. Each page of each completed CRF will be signed by Clinical Investigator.

After review for accuracy and completeness, the original and first copy of each page of the CRF will be removed (leaving the second copy with the Investigator) and be sent to Milan for data processing.

After each monitoring visit the periodic site visit report and the patients progress report form (form B and C enclosed) will be filled in. The original pages will be sent to FICE Milan.

The study termination visit will be performed upon Investigator's completion of all CRFs of treated patients. During this visit:

1 the monitor will check and collect the remaining completed CRFs and will perform a final data review;

2 a final check and review of drug accounting, inventorying of remaining drug supplies and arrangement to send them to FICE will be done;

3 a time frame for study reporting will be discussed;

The study termination visit form (form D) will be filled in and the original page sent to FICE Milan.

Study coordination

In order to obtain uniformity and standardization in the carrying out of the study a Steering Committee is established. All questions arising during the conduct of the study will be submitted to the Committee for advice and action taking.

In particular the Committee will take care of:

- queries about patients acceptability
- possible need of protocol amendments
- possible need of premature termination of the study
- acceptability of particular cases of protocol violations
- evaluation of clinically relevant adverse events and their scientific and ethical consequences in terms of issues raised or study discontinuation.

Members of the Committee will be: Prof. V. Andreoli (Italy), Prof. T. Ban (USA), Prof. V. Caillard (France), Prof. S. Levine (UK), Prof. D. Rüther (Germany).

Any problem or issue arising during the conduct of the study will be submitted to the Committee in writing by the Clinical Investigators or by the study Monitors. "Ad hoc" meetings of the Committee will be organized when needed. File note of the meeting with conclusions about action taking will be circulated to Clinical Investigators and study Monitors.

12.1.2 CRF SAMPLE

A complete CRF is filed in the Study Master File.

Pharmacia

12.1.3 INSTITUTIONAL REVIEW BOARD : APPROVAL

9550087

OSPEDALE GENERALE DI ZONA
« SACRO CUORE »
37024 NEGRAR (Verona) - Tel. 750.00.44

Direzione Sanitaria

Negrar, 17 settembre 1990

ADRIANA DUBINI

Responsabile Medico
R&S - Dip. SNC
Via Carlo Imbonati, 24
20159 MILANO

Oggetto: Studio clinico prodotto farmeceutico FCE 20124

In riferimento alla Vs. lettera del 4 settembre 1990, questa Direzione Sanitaria rilascia l'autorizzazione ad effettuare uno studio clinico con il preparato etichettato FCE 20124 (Reboxetina) da parte del reparto di Lungodegenza di questo Ospedale, diretto dal Dr. Carbognin.

Con l'occasione porgiamo distinti saluti.

OSPEDALE S. CUORE - NEGRAR -

Il Direttore Sanitario
Dr. Gastone Orio

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12.1.4 CLINICAL INVESTIGATORS LIST, SIGNATURES AND CURRICULUM VITAE

INVESTIGATORS

Prof V Andreoli
Department of Psychiatry, Hospital of Soave, Soave (Verona), Italy

Dr G Carbognin
Medical Department, Ospedale Provinciale Lungodegenti, Negrar (Verona), Italy

Dr G Vantini
Medical Department, Ospedale Provinciale Lungodegenti, Negrar (Verona), Italy

Dr A Abati
Department of Psychiatry, Hospital of Soave, Soave (Verona), Italy

The signature of the main Investigator is enclosed in the protocol (Appendix 12.1.1)

9550087

Prof. Dott. VITTORINO ANDREOLI

Curriculum

Laureato in medicina presso l'Università di Padova, Vittorino Andreoli si è specializzato in psichiatria e successivamente in neurologia presso l'Università di Milano; è attualmente primario presso i Servizi Psichiatrici di Verona e professore di antropologia medica presso l'Università di Verona. Prima di dedicarsi all'attività clinica aveva conseguito la libera docenza in farmacologia e tossicologia all'Istituto di Farmacologia dell'Università di Milano ed è stato ricercatore nel campo dell'attività normale e patologica del sistema nervoso centrale presso il Department of Biochemistry dell'Università di Cambridge (UK), presso il Department of Neuroanatomy del Cornell Medical College di New York e al Department of Psychiatry del Massachusetts General Hospital della Harvard University di Boston.

E' autore di numerosi lavori d'argomento biologico e clinico inerenti i problemi del comportamento e della sua patologia. Tra i volumi più noti:

La terza via della psichiatria (Mondadori, 1980).

La norma e la scelta (Mondadori, 1984).

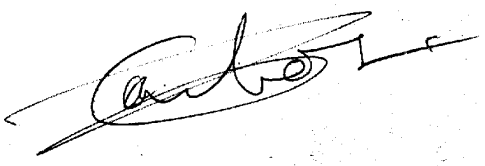
E' coautore de Il ciclo della droga (Mondadori, 1978) e di Forze armate e droga (Masson, 1985).

Prof.dr. Vittorino Andreoli

37129 Verona - Via XX Settembre, 35

9550087

Il Dott. GIORGIO CARBOGNIN è nato a Verona il 27-02-1938.
Ha conseguito la Laurea in Medicina e Chirurgia presso l'Università di Bologna nel 1965. E' stato allievo interno presso l'Istituto di Patologia Speciale Medica e Metodologia Clinica diretto dal Prof. Campanacci e successivamente presso la Clinica Medica diretta dal Prof. Sotgin.
Divenuto assistente e quindi aiuto della divisione di Medicina Generale dell'Ospedale di Negrar (Verona), ha conseguito le idoneità nazionali di aiuto e quindi di Primario di Medicina tramite concorso a Roma.
Si è specializzato in Medicina Interna presso l'Università di Parma nel 1971. Nel 1974 ha conseguito la specializzazione in Cardiologia presso l'Università di Bologna.
E' membro della Società Italiana di Geriatria e Gerontologia.
Dal Dicembre del 1973 è Primario della divisione di Medicina Riabilitativa dell'Ospedale Provinciale Lungodegenti di Negrar.
Oltre all'attività professionale e scientifica, si è occupato e si occupa del problema degli anziani e dei tossicodipendenti.
E' stato presidente del corso per la formazione di animatori Socio Sanitari con particolare apertura ai problemi dell'assistenza geriatrica promosso dall'OARI.
E' stato insegnante di farmacologia presso la Scuola Infermieri di Negrar.
E' cofondatore e vicepresidente del CeIS (Centro Italiano di Solidarietà) di Verona e membro del Consiglio di Amministrazione della "Cooperativa Grola", due enti che si occupano del recupero e della riabilitazione dei tossicodipendenti.
Attualmente è impegnato nella creazione di un centro, sempre nell'ambito della divisione da lui diretta, per la terapia subintensiva dei traumatizzati cranici e midollari.



9550087

1) Cosentina - Bouvet - Carbognin - Castoldi - Della Croce - Schinco

Trattamento con S-Carbossimetilcisteina lisina dell'ipersecrezione bronchiale nell'anziano.

2) Carbognin - Zamboni - Rossi - Cosentina

Patologie reumatiche e loro trattamento.

3) Carbognin - Rossi

Valutazione dell'effetto antidolorifico del B.I.2611 - studio acuto.

4) Gruppo Italiano per lo studio della Nicergolina
Buttolo - Carbognin - Crolla - Sega ed altri.

Attività della Nicergolina nel deterioramento cerebrale senile.

5) Castellani - Colafelice - Carbognin - Perbellini - Rigoli - Fichera Marsiai

Clinical Experiments with brain cortex phospholipids in Psychogeriatrics.

6) Lavezzari - Bottino - Carbognin

Indoprofene per via intramuscolare nel trattamento a breve termine dell'osteoartrosi.

7) Carbognin - Castellani - Rossi

Trattamento della patologia vascolare cerebrale cronica con RU 12128 DL alfa, nicotinoilossifenilacetico acido CIS 3.3.5. Trimetilcicloesilestere.

8) Andreoli - Carbognin - Guerani - Carrieri - Abati - Berto - Vantini Righetti

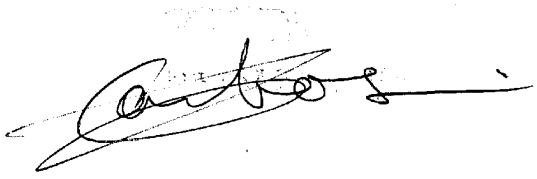
Buspirone as a tool to better understand and modify cognitive processes.

9) Carbognin - Ferrari - Benedetti

L'alcool ed il suo abuso. CeIS Verona.

10) Carbognin - Ferrari - Benedetti

AIDS - Informazione e Prevenzione. CeIS Verona.



9550087

Dott. Alberto Abati
Via Carpagnon, 18
36025 Noventa Vicentina (VI)
Tel. 0444/887220

CURRICULUM VITAE

Nato a Verona il 12.9.1941.
Laurea in Lettere presso l'Università di Padova nel 1966.
Attività di ricerca presso il Centro di Studi per le Ricerche di Fonetica C.N.R. dell'Università di Padova dal 1966 al 1972.
Laurea in Medicina e Chirurgia presso l'Università di Padova nel 1972.
Specializzazione in Psichiatria presso l'Università di Padova nel 1976.
Assistente di ruolo di Neurologia e Psichiatria presso l'Ospedale di Noventa VIcentina (VI) dal 1973 al 1979.
Aiuto di ruolo di Psichiatria presso la suddetta struttura dal 1979 al 1985.
Aiuto di ruolo di Psichiatria presso l'U.L.S.S. N° 24 Regione Veneto dal 1985 a tutt'oggi.
Idoneità nazionale a Primario di Psichiatria nel 1985 (sessione 1983).
Altri titoli professionali:
Diploma in Ipnosi Clinica (Corso biennale dell' Istituto "H. Bernheim" di Verona 1977-1979);
Diploma in Tecniche di Analisi e Modificazione del Comportamento (Corso biennale dell'A.I.A.M.C. Verona 1981-1982).
Lavori pubblicati: v. elenco allegato.

Alberto Abati

26.10.1990

9550087

Dr. Alberto Abati

ELENCO DELLE PUBBLICAZIONI

1) E. Magno Caldognetto, A. Abati, L. Dossi, "Differenziazioni elettroacustiche delle consonanti sorde e sonore della lingua italiana", Bollettino di Audiologia e Foniatria, XIX, 1-2, 1970.

2) E. Magno Caldognetto, A. Abati, L. Dossi, "Consonanti occlusive sorde e sonore della lingua italiana", Quaderni del Centro di Studio per le Ricerche di Fonetica del C.N.R. presso l'Università di Padova, 1, 1971.

3) E. Magno Caldognetto, A. Abati, L. Dossi, "Introduzione all'analisi ed alla sintesi strumentale della parola", Quaderni del Centro di Studio per le Ricerche di Fonetica del C.N.R. presso l'Università di Padova, 2, 1971.

4) E. Schergna, A. Abati, "Percezione dei fonemi della lingua italiana in cerebrolesi", in R. Simone, U. Vignuzzi, G. Ruggiero (a cura di) "Studi di Fonetica e Fonologia", Bulzoni, Roma, 1976, pp. 173-185.

5) F. Denes, C. Semenza, A. Abati, "Analisi fonemica di un caso di sordità verbale",ibidem, pp. 23-33.

6) E. Schergna, A. Abati, "Evoluzione dei sintomi schizofrenici in un gruppo di lungodegenti istituzionalizzate", Rivista Sperimentale di Freniatria, CII, III, 1978.

7) A. Abati, F. Chiesa, "Per una risposta razionale all'etilismo dei Servizi Psichiatrici (legge 180)", Giornale di Neuropsicofarmacologia, IV, 3, 1982.

8) V. Andreoli, A. Abati, "Alcool etilico: effetti socio ambientali" in P. Avogaro, M. Trabucchi, E. Tremoli, "Alcool salute e malattia", Masson Italia, Milano, 1984, pp. 81-92.

9) A. Abati, P. Giovacchini, "Un caso di abuso di amineptina", Giornale di Neuropsicofarmacologia, VIII, 1, 1986.

10) V. Andreoli, A. Abati, "La concezione della schizofrenia nel DSM-III", Quaderni Italiani di Psichiatria, V, 1, 1986.

(11) A. Abati, F. Chiesa, D. Ferremi, "I servizi di tutela della salute mentale in un'ottica preventiva" in R. Zerbetto (a cura di), "Realtà e prospettive della riforma dell'assistenza psichiatrica", Ist. Pol., Roma, 1985.

(12) V. Andreoli, A. Abati, "Per un razionale uso dei farmaci nelle sindromi schizofreniche", Psichiatria Gen. Età Evol., 25, 1987.

(13) A. Abati, "Il ruolo dei neurolettici dopo la riforma psichiatrica: il caso del benperidolo", Giornale di neuropsicofarmacologia, IX, 1, 1987.

(14) A. Abati, L. Fabbri, "Per un intervento farmacologico sulla cognitività dell'anziano: l'azione della fipexide", La riforma medica, 101, 12, 1986.

(15) A. Abati, D. Berto, L. Crestoni, R. Carcereri, A. Forgione, "Miglioramento farmacologico delle funzioni cognitive dell'anziano", Rivista Sperimentale di Freniatria, CXII,I, 1988.

(16) Andreoli V., Abati A., "La schizofrenia. Orientamenti diagnostici", Psichiatria e Medicina, 3, 5, 1989.

(17) Rossi M., Abati A., "La realtà operativa di un Servizio Psichiatrico a dieci anni dalla Legge 180", Psychopathologia, 8, 1, 1990.

(18) Andreoli V., Olivieri D.N., Ferremi D., Berto D., Abati A., Berti Taini A., Zammichele R., "La condizione giovanile e le mitologie cliniche", Rivista Sperimentale di Freniatria, CXIV, 3, 1990.

(19) Andreoli V., Carbognin G., Guerani G., Carrieri M.P., Abati A., Righetti C.A., Berto D., Vantini G., " Buspirone as tool to better understand and modify cognitive processes"; (IN CORSO DI STAMPA)

Seminari del Prof. V. Andreoli raccolti e con note del Dr. A. Abati in Quaderni Italiani di Psichiatria 1987 - 1990 (TOTALE: 18).

9550087

OSPEDALE « Don G. CALABRIA »
37024 NEGRAR (Verona) - Tel. 750.00.44

DIVISIONE DI LUNGODEGENZA RIABILITATIVA
Primario Dr. GIORGIO CARBOGNIN

Negrar, 23-10-90

IL DOTT. GIOVANNI VANTINI È NATO IL 30-8-49.
LAUREATO IN MEDICINA E CHIRURGIA PRESSO LA UNIVERSITÀ DI PADOVA IL 9-3-76 –
ABILITATO ALL'ESERCIZIO PROFESSIONALE NELLO APRILE 76.
ISCRITTO ALL'ALBO PROFESSIONALE DEI MEDICI CHIRURGHI DELLA PROVINCIA DI VERONA IL 3-6-76,
SI È SPECIALIZZATO IN GERIATRIA E GERONTOLOGIA PRESSO L'UNIVERSITÀ DI PAVIA IL 11-3-86 –
È ASSISTENTE PRESSO LA DIVISIONE DI LUNGODEGENZA RIABILITATIVA DELL'OSPEDALE PROVINCIALE DON G. CALABRIA DI NEGRAR (VR)
DALL'ANNO 1978.
DAL 76 AL 88 HA SVOLTO ANCHE ATTIVITÀ COME MEDICO GENERICO CONVENZIONATO COL S.S.N.

PUBBLICAZIONI:

ACTA GERONTOLOGICA, 33; FASCIC. 1; 14-20, 1983
DAL TITOLO: "ANEMIA ED IPOSIDEREMIE NELL'ANZIANO-STUDIO STATISTICO E CLINICO DI 626 PAZIENTI IN UN OSPEDALE PER LUNGODEGENTI".

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Vantini

Mod. 031/L

Pharmacia Document 9550087

12.1.5 CERTIFICATES OF ANALYSIS

9550087

VIA CARLO IMBONATI, 24
20159 MILANO

TELEFONO (02) 6995.1 (CENTRALINO)
TELEGRAMMI ERBACAR MILANO
CASELLA POSTALE 10519
C.C. POSTALE 619205
TELEX 330314 ERBA I-

FARMITALIA CARLO ERBA

March 11th, 1992

DATA

VS. RIF.

NS. RIF.

TEL. DIRETTO

CERTIFICATE OF ANALYSIS

REBOXETINE 2 mg tablets

Batch SF 1105

Manufacturing date	: July, 1990
Expiry date	: December, 1992
Appearance	: white, round, convex, 6 mm diameter tablet, marked S.F. on one surface
Identification	: positive
Average weight	: mg 100.43
Assay	: mg 1.975 of Reboxetine/tablet
Related substances	: 0.64%
Uniformity of content	: complies, according to Eur. Ph., 2nd Ed., requirements
Dissolution	: 95.5% of the L.A. after 15 minutes
Microbial contamination	: total viable aerobic count < 1000 moulds and yeasts < 100 E. Coli and Salmonellae : absent

Note : this certificate replaces the previous one

Approved by : Virginio Busnelli

S.R.L. - SEDE LEGALE IN MILANO
CAPITALE L. 528.732.127.000 I.V.
TRIBUNALE DI MILANO R.S. N. 38246
VOL. 9366 - FASC. 46 - C.C.I.A.A. N. 1171077
COD. FISC. E PART. IVA N. 07508290154

GRUPPO ERBAMONT

9550087

FARMITALIA CARLO ERBA

TELEFONO (02) 6995 1 (CENTRALINO)
TELEGRAMMI ERBACARLO MILANO
CASELLA POSTALE 10519
C.C. POSTALE 616205
TELEX 330314 ERBA I

November 16th, 1992

CERTIFICATE OF ANALYSIS

REBOXETINE 4 mg tablets

Batch SF 1106

Manufacturing date	: July, 1990
Expiry date	: June, 1993
Active drug substance	: RR 17L015
Appearance	: white, round, convex, 8 mm diameter tablet, with a breakline on one surface
Identification	: positive
Average weight	: mg 200.80
Assay	: mg 3.880 of Reboxetine/tablet
Related substances	: 0.61%
Uniformity of content	: complies, according to Eur. Ph., 2nd Ed., requirements
Dissolution	: 93.9% of the L.A. after 15 minutes
Microbial contamination	: total viable aerobic count < 1000 moulds and yeasts < 100 E. Coli and Salmonellae : absent

Note : this certificate replaces the previous one, in order to extend the shelf-life, having already obtained stability data after 36 months storage at 25°C, for two other 4 mg batches

Approved by 186 : Virginio Busnelli

GRUPPO ERBAMONT

9550087

FARMITALIA CARLO ERBA

VIA CARLO IMBONATI, 24
20159 MILANO

TELEFONO (02) 6905 1 (CENTRALINO)
TELEGRAMMI ERBACAR MILANO
CASELLA POSTALE 1059
C.C. POSTALE 6/9205
TELEX 320314 ERBA I

May 9th, 1991

CERTIFICATE OF ANALYSIS

Placebo for Reboxetine 2 mg tablets

Batch SF 1205

Manufacturing date	: May, 1991
Appearance	: round, convex, 6 mm diameter, white tablet, marked S.F. on a side.
Identification	: negative
Average weight	: mg 99.92
Uniformity of weight	: complies, according to Eur. Ph. 2nd Ed., Section V.5.2.1
Disintegration time	: 1 minute
Approved by	: V. Busnelli

9550087

VIA CARLO IMBONATI, 24
20159 MILANO

TELEFONO (02) 6095 1 (CENTRALINO)
TELEGRAMMI ERBACAR-MILANO
CASELLA POSTALE 10519
C.C. POSTALE 6/9205
TELEX 330314 ERBA I-

FARMITALIA CARLO ERBA

DATA April 26, 1990

VS. RIF.

NS. RIF.

DESTINATO

ANALYSIS CERTIFICATE

Placebo for Reboxetine 4 mg tablets

Batch SF 1030

Manufacturing date	: May, 1989
Appearance	: round, convex, 8 mm diameter, white tablet with a breakline on one surface, and marked S.F. on the other
Identification	: negative
Average weight	: mg 202.47
Uniformity of weight	: complies, according to Eur. Ph. 2nd Ed., Section V.5.2.1
Disintegration time	: 25 seconds
Approved by	: Virginio Busnelli

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12.1.6 RANDOMIZATION LIST

FARMITALIA * C[illegible]

REBOXETINE - PROTOCOL 20124/032

RANDOMIZATION LIST

PATIENT NO.	TREATMENT
1	REBOXETINE
2	PLACEBO
3	PLACEBO
4	PLACEBO
5	REBOXETINE
6	REBOXETINE
7	PLACEBO
8	REBOXETINE
9	PLACEBO
10	PLACEBO
11	PLACEBO
12	PLACEBO
13	REBOXETINE
14	REBOXETINE
15	REBOXETINE
16	REBOXETINE
17	REBOXETINE
18	REBOXETINE
19	PLACEBO
20	PLACEBO
21	REBOXETINE
22	PLACEBO
23	REBOXETINE
24	PLACEBO
25	REBOXETINE
26	REBOXETINE
27	PLACEBO
28	REBOXETINE
29	PLACEBO
30	REBOXETINE
31	PLACEBO
32	PLACEBO
33	PLACEBO
34	PLACEBO
35	PLACEBO
36	REBOXETINE
37	REBOXETINE
38	PLACEBO
39	REBOXETINE
40	REBOXETINE
41	PLACEBO
42	PLACEBO
43	REBOXETINE
44	PLACEBO
45	REBOXETINE
46	REBOXETINE
47	REBOXETINE
48	PLACEBO
49	PLACEBO
50	PLACEBO

12.1.7 CRITERIA USED TO JUDGE LABORATORY ABNORMALITIES AS CLINICALLY RELEVANT

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

CRITERIA USED TO CONSIDER LABORATORY ABNORMALITIES CLINICALLY RELEVANT

Laboratory test	Percent variation above or below normal range (*)
HB	- 15
HTC	- 15
RBC	- 15
PLATELETS	- 30
WBC	- 30
WBC: N	- 30
WBC: M	not defined
WBC: B	not defined
WBC: L	- 30
WBC: E	not defined
CREATININE	+ 50
BUN	+ 50
URIC ACID	+ 30
TOT. PROTEINS	-+ 30
ALBUMINE	-+ 30
TOT BILIRUBIN	+ 100
DIR BILIRUBIN	+ 100
SGOT	+ 100
SGPT	+ 100
GAMMA-GT	+ 100
LDH	+ 100
ALK. PHOSPH.	+ 100
GLOBULINS: ALPHA 1	-+ 30
GLOBULINS: ALPHA 2	-+ 30
GLOBULINS: BETA	-+ 30
GLOBULINS: GAMMA	-+ 30
TOT. CHOLESTEROL	+ 30
TRIGLYCERIDES	-+ 30
GLUCOSE	-+ 30
NA+	-+ 10
CL-	-+ 10
K+	-+ 15
CA++	-+ 15
PO4-	-+ 15

(*) MINUS INDICATES BELOW THE LOWER LIMIT OF NORMAL RANGE, AND PLUS ABOVE THE UPPER LIMIT OF NORMAL RANGE

12.1.8 ECG CODES

APPENDIX No.: 12.1.8

ECG CODES

0 Normal

1 Rhythm disorders

10 Sinus bradycardia (<60)

20 Sinus tachycardia (>100)

30 Sick Sinus Syndrome

40 • Atrial ectopic beats:
- 41 - Occasional
- 42 - Frequent (>6/mm)
- 43 - Couplets
- 44 - Supraventricular Tachycardia

50 • Ventricular ectopic beats:
- 51 - Occasional
- 52 - Frequent (>6/mm)
- 53 - Polymorphic
- 54 - Couplets
- 55 - Ventricular Tachycardia

60 • Atrial fibrillation/flutter

105 • Vagotonia

108 • Atrial-ventricular dissociation

2 Conduction disorders

70 • A-V Block
- 71 - 1st degree
- 72 - 2nd degree - Mobitz 1
- 73 - - Mobitz 2
- Complete

85 • Right bundle branch block

86 • Left bundle branch block

87 • Left anterior hemiblock

88 • Left posterior hemiblock

89 • Bifascicular Block (specify)

90 • Trifascicular Block (specify)

91 • Conduction disorders

103 • Left axial deviation

106 • Right incomplete bundle branch block

3 Ischemic signs

102 • Ripolarization disturbances

107 • Non specific ST-T changes

82 • Myocardial ischemia

84 • Acute Myocardial infarction

4 Other

80 • Left ventricular hypertrophy

81 • Right ventricular hypertrophy

83 • Previous Myocardial infarction

93 • Other
(specify)_____

104 • Right axial deviation

Pharmacia Document 9550087

12.2 Patient Information

Pharmacia Document 9550087

12.2.1 SERIOUS ADVERSE EVENTS - CASE HISTORY

Pharmacia Document 9550087

Narrative of Event No IT 1096 **Protocol No 20124/ 032** **Patient No 15**
Center: Verona (Italy) **Investigator: Andreoli**

Adverse event: syndrome of inappropriate ADH secretion (date of the event: 16.07.91)

Patient's history: the patient was a 84 years old female and she was suffering from a Major Depressive Episode for 2 months when she entered the study 20124/032 on July 1st, 1991. She had had the onset of depressive disorder at the age of 83 years.

The patient had been suffering from chronic obstructive bronchopulmonary disease, hiatus hernia with dyspepsia, cervical arthrosis and tachycardia. She was treated with theophylline (400 mg/day), domperidone (20 mg/day), verapamil (80 mg/day). All these drugs started on June 25th, 1991.

At the baseline visit ECG findings were consistent with a diagnosis of cor pulmonale. Chest X-ray showed generalized hyperdiaphania due to emphysema, calcified lesions in the apical region and signs of previous pleuritis. Laboratory tests did not show any clinical relevant abnormalities. The Mini- Mental State Examination showed a cognitive impairment and signs of diffuse brain disturbance (low voltage activity) were consistently found in EEG recording.

Experimental period: the patient entered the 20124/032 study on July 1st, 1991 and received the experimental treatment as follows:

treatment from - to		days	dose (mg/day)
09.07.91	15.07.91	7	4

On July 3rd, 1991 she started a therapy with hydrochlorothiazide/amiloride (25/2.5 mg/day) because of peripheral oedema.

From July 11th, 1991 the patient complained of multiple episodes of gastric burning sensation exiting in vomiting that required symptomatic treatment (metoclopramide 10 mg single dose i.m.) on 14.07.91. These symptoms recovered on the same day.

On July 16th, 1991 the patient withdrew from the study because of fatiguability, slowness and orthostatic hypotension. Ataxic gait, miosis, bilateral Babinsky were also apparent. Reflexes were absent and generalized muscle hypotonia was observed.
Laboratory tests were performed and lymphocytes, Na+, K+ and Cl- were found to be abnormal (lymphocytes 3.4%, n.r. 19-48%; Na+ 101 mmol/l, n.r. 135-150; K+ 3.3 mmol/l, n.r. 3.5-5.3; Cl- 61 mmol/l, n.r. 96-112) as well as plasma osmolarity (200 mosmol/Kg). Urinalysis showed abnormal specific gravity and abnormal albumin and RBC.Urinary sodium concentration was not evaluated.

A diagnosis of "syndrome of inappropriate antidiuretic hormone secretion" (SIADH) was made by the Investigator on the basis of the laboratory tests results and of the clinical signs/symptoms.

Follow-up information indicates that the patient stayed in the hospital ward till her death (03.11.91) due to cardiac failure. A pontine myelinolysis was diagnosed by the neurologist on a clinical basis as a possible consequence of the occurring electrolyte imbalance.

During the study the patient had received the experimental treatment for 7 days, taking a cumulative amount of 28 mg of reboxetine.

Comments: the Investigator judged the adverse event possibly drug related. According to literature, SIADH has been observed as a rare adverse event following drug administration, included psychotropic drugs, in the elderly. For instance, this syndrome has been reported under fluoxetine, imipramine and amitriptyline, among others.

As far as pontine myelinolysis is concerned, electrolyte imbalance and, particularly, rapid changes in electrolyte abnormalities can be associated with neurologic disease, so that a rapid correction of the hyponatremia which is present in SIADH could have played a role in its pathogenesis. No direct relationship between drug administration and pontine myelinolysis has been reported so far in the literature.
Furthermore only two cases of drug induced hyponatremia secondary to amitriptyline and thioridazine were reported, followed by irreversible neurological symptoms in one case and a coma in the other.

12.2.2 INDIVIDUAL DATA LISTINGS

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

DEMOGRAPHIC DATA

Patient No.	Initials	Visit No.	Date of Visit	Sex	Birth Date	Age (years)	Weight (kg)	Height (cm)	Etnic Group	Date of Hospitalization	Patient Eligibility
1	TR	-1	20MAY91	F	03DEC08	82	75.0	162	CAUCASIAN	20MAY91	YES
2	FB	-1	25MAY91	F	03JAN08	83	65.0	158	CAUCASIAN	15MAY91	YES
3	BI	-1	25MAY91	F	25AUG15	75	52.0	155	CAUCASIAN	13MAY91	YES
4	PC	-1	25MAY91	F	08DEC19	72	56.0	178	CAUCASIAN	07MAY91	YES
5	BL	-1	25MAY91	F	04JAN25	66	52.0	160	CAUCASIAN	18APR91	YES
6	SM	-1	29MAY91	F	21JAN11	80	67.0	160	CAUCASIAN	29MAY91	YES
7	DA	-1	25MAY91	F	01AUG10	80	49.0	155	CAUCASIAN	17MAY91	YES
8	SC	-1	25MAY91	F	11APR16	75	82.0	168	CAUCASIAN	14MAY91	YES
9	PA	-1	25MAY91	M	04DEC16	74	70.0	172	CAUCASIAN	19APR91	YES
10	PE	-1	30MAY91	M	11MAR16	75	61.0	170	CAUCASIAN	30MAY91	YES
11	CL	-1	31MAY91	F	21JUL10	80	82.0	165	CAUCASIAN	31MAY91	YES
12	ML	-1	01JUL91	F	10JAN10	81	70.0	152	CAUCASIAN	21JUN91	YES
13	DSC	-1	01JUL91	F	01DEC21	70	59.0	156	CAUCASIAN	17JUN91	YES
14	BM	-1	01JUL91	F	05MAR04	87	60.0	165	CAUCASIAN	23MAY91	YES
15	GI	-1	01JUL91	F	09FEB07	84	48.0	154	CAUCASIAN	25JUN91	YES
16	PJ	-1	01JUL91	F	13APR09	82	72.0	161	CAUCASIAN	14JUN91	YES
17	MM	-1	01JUL91	F	16OCT05	85	54.0	160	CAUCASIAN	01JUL91	YES
18	VM	-1	02JUL91	M	23MAR08	83	78.0	171	CAUCASIAN	02JUL91	YES
19	NI	-1	05JUL91	F	26JUN08	83	45.0	150	CAUCASIAN	05JUL91	YES
20	BE	-1	01JUL91	M	02AUG11	79	73.0	167	CAUCASIAN	17JUN91	YES
21	SE	-1	01JUL91	F	10JUL05	86	73.0	164	CAUCASIAN	05JUN91	YES
22	BA	-1	31AUG91	F	05OCT04	86	77.0	165	CAUCASIAN	16AUG91	YES
23	UT	-1	13AUG91	F	11JUL04	87	67.0	168	CAUCASIAN	13AUG91	YES
24	BEA	-1	31AUG91	F	03AUG02	89	38.0	150	CAUCASIAN	16AUG91	YES
25	GA	-1	31AUG91	F	12JAN08	83	82.0	160	CAUCASIAN	29AUG91	YES
26	PR	-1	31AUG91	M	19MAY28	63	74.0	170	CAUCASIAN	31JUL91	YES
27	GA	-1	31AUG91	F	13AUG05	86	83.0	161	CAUCASIAN	26AUG91	YES
28	MR	-1	31AUG91	F	31OCT05	85	65.0	162	CAUCASIAN	28AUG91	YES
29	TR	-1	31AUG91	M	10NOV12	78	64.0	175	CAUCASIAN	26AUG91	YES
30	PA	-1	30SEP91	F	12JAN09	82	53.0	155	CAUCASIAN	20SEP91	YES
31	CC	-1	03OCT91	F	19AUG07	84	42.0	132	CAUCASIAN	03OCT91	YES
32	CE	-1	04SEP91	F	19SEP08	82	73.0	158	CAUCASIAN	04SEP91	YES
33	VA	-1	02OCT91	M	20JUL08	83	96.0	170	CAUCASIAN	02OCT91	YES
34	BA	-1	01OCT91	F	21AUG15	76	64.0	154	CAUCASIAN	26SEP91	YES
35	SB	-1	04OCT91	F	23FEB18	73	76.0	172	CAUCASIAN	04OCT91	YES
36	SM	-1	02OCT91	F	13DEC17	73	59.0	153	CAUCASIAN	02OCT91	YES
37	SE	-1	01OCT91	F	18MAY12	79	64.0	170	CAUCASIAN	17SEP91	YES
38	LO	-1	01OCT91	F	13JUL15	76	65.0	150	CAUCASIAN	30SEP91	YES
39	CP	-1	04OCT91	M	27JUL11	80	67.0	163	CAUCASIAN	04OCT91	YES
40	PO	-1	02NOV91	M	05JAN16	75	83.0	178	CAUCASIAN	28OCT91	YES
41	FE	-1	29OCT91	F	06MAR14	77	65.0	152	CAUCASIAN	29OCT91	YES
42	LI	-1	31OCT91	F	19JAN08	83	48.0	152	CAUCASIAN	29OCT91	YES
43	PA	-1	30OCT91	F	24OCT13	78	59.5	166	CAUCASIAN	30OCT91	YES
44	MZ	-1	30OCT91	M	28APR07	84	55.0	154	CAUCASIAN	15OCT91	YES
45	PG	-1	30OCT91	F	15JUL01	90	90.0	154	CAUCASIAN	04OCT91	YES
46	AD	-1	24OCT91	M	14SEP20	71	57.0	160	CAUCASIAN	14OCT91	YES
47	SG	-1	06NOV91	F	17OCT03	88	44.0	155	CAUCASIAN	06NOV91	YES
48	FA	-1	30OCT91	F	18AUG05	86	65.0	165	CAUCASIAN	15OCT91	YES
49	SA	-1	30OCT91	F	11OCT12	79	63.0	152	CAUCASIAN	21OCT91	YES
50	ZZ	-1	07NOV91	F	12SEP11	80	57.5	157	CAUCASIAN	07NOV91	YES

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

DIAGNOSIS AND HISTORY OF MENTAL DISORDER

Patient No.	Initials	Visit Date	DSM3 Axis I	Men. Dis. Unknown	Onset Age (years)	Number of Prev. Epis.	Last Epis. Duration	Duration at Admiss. Date	Present Episode Characterization	Onset of Pres. Epis.	Precip. External Stress	DSM3-R A	DSM3-R B	DSM3-R C	DSM3-R D
1	TR	20MAY91	296.2	Y	.	.		2months	exac. chron. cond.	subacute	defin. pres.	Y	Y	Y	Y
2	FB	25MAY91	296.2	Y	.	.		3months	exac. chron. cond.	subacute	prob. pres.	Y	Y	Y	Y
3	BI	25MAY91	296.2	Y	.	.		2months	exac. chron. cond.	subacute	prob. pres.	Y	Y	Y	Y
4	PC	25MAY91	296.3		20	6	3months	2months	rec. prev. cond.	subacute	prob. pres.	Y	Y	Y	Y
5	BL	25MAY91	296.2	Y	.	.		2months	first occurrence	subacute	prob. pres.	Y	Y	Y	Y
6	SM	29MAY91	296.2	Y	.	.		2months	exac. chron. cond.	subacute	prob. pres.	Y	Y	Y	Y
7	DA	25MAY91	296.2	Y	.	.		2months	exac. chron. cond.	subacute	prob. pres.	Y	Y	Y	Y
8	SC	25MAY91	296.2	Y	.	.		2months	first occurrence	subacute	prob. pres.	Y	Y	Y	Y
9	PA	25MAY91	296.2	Y	.	.		2months	exac. chron. cond.	subacute	prob. pres.	Y	Y	Y	Y
10	PE	30MAY91	296.2	Y	.	.		1month	exac. chron. cond.	subacute	prob. pres.	Y	Y	Y	Y
11	CL	31MAY91	296.3		20	6	3months	3months	rec. prev. cond.	insidious	prob. pres.	Y	Y	Y	Y
12	ML	01JUL91	296.2		81	.		3months	exac. chron. cond.	subacute	prob. pres.	Y	Y	Y	Y
13	DSC	01JUL91	296.3		55	7	3months	2months	rec. prev. cond.	subacute	prob. pres.	Y	Y	Y	Y
14	BM	01JUL91	296.2		87	.		2months	first occurrence	subacute	defin. pres.	Y	Y	Y	Y
15	BI	01JUL91	296.3		83	2	1month	2months	rec. prev. cond.	subacute	prob. pres.	Y	Y	Y	Y
16	PJ	01JUL91	296.2		82	.		2months	first occurrence	acute	prob. pres.	Y	Y	Y	Y
17	MM	01JUL91	296.2		85	.		2months	first occurrence	acute	defin. pres.	Y	Y	Y	Y
18	VM	02JUL91	296.3		25	10	3months	3months	rec. prev. cond.	subacute	absent	Y	Y	Y	Y
19	NI	05JUL91	296.2		82	.		6months	first occurrence	subacute	defin. pres.	Y	Y	Y	Y
20	BE	01JUL91	296.2		79	.		2months	first occurrence	subacute	prob. pres.	Y	Y	Y	Y
21	SE	01JUL91	296.3		75	5	2months	2months	rec. prev. cond.	subacute	prob. pres.	Y	Y	Y	Y
22	BA	31AUG91	296.2		86	.		2months	first occurrence	subacute	prob. pres.	Y	Y	Y	Y
23	UT	13AUG91	296.2		87	.		2months	first occurrence	subacute	prob. pres.	Y	Y	Y	Y
24	BEA	31AUG91	296.2		89	.		1month	first occurrence	insidious	defin. pres.	Y	Y	Y	Y
25	GA	31AUG91	296.2		83	.		4months	first occurrence	insidious	prob. pres.	Y	Y	Y	Y
26	PR	31AUG91	296.2		68	.		2months	first occurrence	subacute	defin. pres.	Y	Y	Y	Y
27	GA	31AUG91	296.2		86	.		1month	first occurrence	insidious	prob. pres.	Y	Y	Y	Y
28	MR	31AUG91	296.3		20	8	3months	1month	rec. prev. cond.	subacute	prob. pres.	Y	Y	Y	Y
29	TR	31AUG91	296.2		78	.		3months	first occurrence	subacute	prob. pres.	Y	Y	Y	Y
30	PA	30SEP91	296.2		82	.		3months	first occurrence	subacute	defin. pres.	Y	Y	Y	Y
31	CC	03OCT91	296.3		80	1	3months	2months	exac. chron. cond.	subacute	defin. pres.	Y	Y	Y	Y
32	CE	04SEP91	296.2		82	.		1month	first occurrence	subacute	prob. pres.	Y	Y	Y	Y
33	VA	02OCT91	296.3		80	3	2months	2months	rec. prev. cond.	subacute	prob. pres.	Y	Y	Y	Y
34	BA	01OCT91	296.3		56	5	3months	2months	rec. prev. cond.	acute	defin. pres.	Y	Y	Y	Y
35	SB	04OCT91	296.3		68	4	3months	2months	rec. prev. cond.	subacute	prob. pres.	Y	Y	Y	Y
36	SM	02OCT91	296.2		73	.		2months	exac. chron. cond.	subacute	prob. pres.	Y	Y	Y	Y
37	SE	01OCT91	296.2		79	.		1month	first occurrence	subacute	defin. pres.	Y	Y	Y	Y
38	LO	01OCT91	296.3		66	6	3months	2months	rec. prev. cond.	subacute	prob. pres.	Y	Y	Y	Y
39	CP	04OCT91	296.2		80	.		1month	exac. chron. cond.	subacute	defin. pres.	Y	Y	Y	Y
40	PO	02NOV91	296.2		75	.		2months	first occurrence	subacute	defin. pres.	Y	Y	Y	Y
41	FE	29OCT91	296.2		77	.		3months	first occurrence	subacute	defin. pres.	Y	Y	Y	Y
42	LI	31OCT91	296.2		83	.		2months	first occurrence	subacute	prob. pres.	Y	Y	Y	Y
43	PA	30OCT91	296.3		70	2	3months	1month	exac. chron. cond.	subacute	defin. pres.	Y	Y	Y	Y
44	MZ	30OCT91	296.2		84	.		1month	first occurrence	subacute	defin. pres.	Y	Y	Y	Y
45	PG	30OCT91	296.2		90	.	1month	1month	first occurrence	insidious	defin. pres.	Y	Y	Y	Y
46	AD	24OCT91	296.2		71	.		1month	first occurrence	subacute	defin. pres.	Y	Y	Y	Y
47	SG	06NOV91	296.2		88	.		2months	first occurrence	insidious	defin. pres.	Y	Y	Y	Y
48	FA	30OCT91	296.2		86	.		2months	first occurrence	insidious	defin. pres.	Y	Y	Y	Y
49	SA	30OCT91	296.3		76	2	3months	2months	exac. chron. cond.	insidious	defin. pres.	Y	Y	Y	Y
50	ZZ	07NOV91	296.2		80	.		1month	first occurrence	acute	prob. pres.	Y	Y	Y	Y

DSM3 Axis I: 296.2=Major Depressive Disorder, Single Episode
296.3=Major Depressive Disorder, Recurrent Episode

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20126/032

CHEST X-RAY AND MEDICAL HISTORY

Patient No.	Initials	Screening Date	X-Ray	Previous Disease				
1	TR	20MAY91	NORMAL	ESSENTIAL HYPERTENSION	OSTEOARTHROSIS ET AL			
2	FB	25MAY91	ABNORMAL	OSTEOARTHROSIS ET AL	PULMONARY TUBERCULOSIS			
3	BI	25MAY91	NORMAL	OSTEOARTHROSIS ET AL	ESSENTIAL HYPERTENSION	DIS OF LIPOID METABOLISM		
4	PC	25MAY91	ABNORMAL	PULMONARY TUBERCULOSIS				
5	BL	25MAY91	NORMAL	DIABETES MELLITUS				
6	SM	29MAY91	ABNORMAL	PULMONARY TUBERCULOSIS	OSTEOARTHROSIS ET AL			
7	DA	25MAY91	ABNORMAL	OTHER BONE AND CARTILAGE DISEASE				
8	SC	25MAY91	ABNORMAL	CHRONIC ULCER OF SKIN				
9	PA	25MAY91	NORMAL	DIABETES MELLITUS				
10	PE	30MAY91	NORMAL	INTESTINAL OBSTRUCTION	DIABETES MELLITUS		UTERINE LEIOMYOMA	
11	CL	31MAY91	NORMAL	SPONDYLOSIS ET AL	OSTEOARTHROSIS ET AL	CHOLELITHIASIS		
12	ML	01JUL91	NORMAL	THROMBOPHLEBITIS	CHRONIC ULCER OF SKIN	DISORDERS OF EAR NEC		
13	DSC	01JUL91	ABNORMAL	OSTEOARTHROSIS ET AL	HYPERTENSIVE HEART DIS	DIABETES MELLITUS		
14	BM	01JUL91	ABNORMAL	ILL-DEFINED HEART DIS	THROMBOPHLEBITIS			
15	GI	01JUL91	ABNORMAL	OTHER ABDOMINAL HERNIA	SPONDYLOSIS ET AL			
16	PJ	01JUL91	NORMAL	OSTEOARTHROSIS ET AL	ESSENTIAL HYPERTENSION			
17	MM	01JUL91	NORMAL	MALIG NEO FEMALE BREAST				
18	VM	02JUL91	ABNORMAL	OTH MALIG NEO GI/PERITON				
19	NI	05JUL91	NORMAL					
20	BE	01JUL91	ABNORMAL	DIABETES MELLITUS	ILL-DEFINED HEART DIS	DIABETES MELLITUS	OTH CHR ISCHEMIC HRT DIS	
21	SE	01JUL91	NOT DONE	VARICOSE VEINS, LEG	GENITAL PROLAPSE			
22	BA	31AUG91	ABNORMAL	OSTEOARTHROSIS ET AL	OTHER BONE AND CARTILAGE DISEASE	GASTRITIS AND DUODENITIS		
23	UT	13AUG91	ABNORMAL	MALIGNANT NEOPLASM COLON	ESSENTIAL HYPERTENSION	SPONDYLOSIS ET AL	CHOLELITHIASIS	
24	BEA	31AUG91	NORMAL	CHRONIC BRONCHITIS	HYPERTENSIVE HEART DIS			
25	GA	31AUG91	ABNORMAL	OSTEOARTHROSIS ET AL	SPONDYLOSIS ET AL			
26	PR	31AUG91	NORMAL	SPINAL CORD DISEASE NEC	BRONCOPNEUMONIA ORG NOS			
27	GA	31AUG91	ABNORMAL	OSTEOARTHROSIS ET AL				
28	MR	31AUG91	ABNORMAL	GENITOURINARY TB	CHOLELITHIASIS	OSTEOARTHROSIS ET AL	OTHER BONE AND CARTILAGE DISEASE	
29	TR	31AUG91	NOT DONE	CHRONIC BRONCHITIS	PULMONARY TUBERCULOSIS	PRECEREBRAL OCCLUSION		
30	PA	30SEP91	ABNORMAL	OSTEOARTHROSIS ET AL	OSTEOARTHROSIS ET AL	HYPERTENSIVE HEART DIS		
31	CC	03OCT91	ABNORMAL	ESSENTIAL HYPERTENSION				
32	CE	06SEP91	ABNORMAL	OSTEOARTHROSIS ET AL	CHOLELITHIASIS			
33	VA	02OCT91	ABNORMAL	OTH CHR ISCHEMIC HRT DIS	CHR LIVER DIS/CIRRHOSIS	DIS CARBOHYDRATE METABOL		CHOLELITHIASIS
34	BA	01OCT91	ABNORMAL	DISEASE OF HODGKIN	DIABETES MELLITUS	OTHER BONE AND CARTILAGE DISEASE	JOINT DISORDER NEC NOS	
35	SB	04OCT91	ABNORMAL	OSTEOARTHROSIS ET AL				
36	SM	02OCT91	ABNORMAL	CHOLELITHIASIS	OSTEOARTHROSIS ET AL	SENILITY W/O PSYCHOSIS		
37	SE	01OCT91	ABNORMAL	OSTEOARTHROSIS ET AL	ESSENTIAL HYPERTENSION			
38	LD	01OCT91	ABNORMAL					
39	CP	04OCT91	ABNORMAL	DIABETES MELLITUS	ESSENTIAL HYPERTENSION			
40	PD	02NOV91	ABNORMAL	OSTEOARTHROSIS ET AL	CARDIAC DYSRHYTHMIAS			
41	FE	29OCT91	ABNORMAL	OTH CHR ISCHEMIC HRT DIS	SPONDYLOSIS ET AL	OTHER BONE AND CARTILAGE DISEASE		
42	LT	31OCT91	ABNORMAL	DIABETES MELLITUS				
43	FA	30OCT91	ABNORMAL	SPONDYLOSIS ET AL				
44	NZ	30OCT91	ABNORMAL	OTHER ABDOMINAL HERNIA	OSTEOARTHROSIS ET AL			
45	PG	30OCT91	ABNORMAL	MALIG NEO FEMALE BREAST	CONDUCTION DISORDERS	OSTEITIS DEFORMANS		
46	AD	24OCT91	ABNORMAL	GASTRIC ULCER	HYPERTENSIVE HEART DIS	OSTEOARTHROSIS ET AL		
47	SS	06NOV91	ABNORMAL	HYPERTENSIVE HEART DIS	OTH ENDOCARDIAL DISEASE	OTH INFLAMM POLYARTHROP		
48	FA	30OCT91	ABNORMAL	OTHER JOINT DERANGEMENT	CHOLELITHIASIS	OSTEOARTHROSIS ET AL		
49	SA	30OCT91	ABNORMAL	ESSENTIAL HYPERTENSION	OSTEOARTHROSIS ET AL	THROMBOPHLEBITIS		
50	ZZ	07NOV91	ABNORMAL					

PHARMACIA CNS R&D
REBOXETINE - PROTOCOL 20124/032

CHEST X-RAY: PATIENTS WITH ABNORMAL FINDINGS AT SCREENING

Patient No.	Initials	Abnormalities
2	FB	other
4	PC	senile emphysema
6	SM	senile emphysema
7	DA	senile emphysema
8	SC	senile emphysema
13	DSC	senile emphysema, enlarged cardiac shadow
14	BM	senile emphysema
15	GI	senile emphysema
18	VM	senile emphysema
20	BE	senile emphysema
22	BA	senile emphysema, enlarged cardiac shadow
23	UT	other
25	GA	senile emphysema
27	GA	enlarged cardiac shadow
28	MR	senile emphysema, arcus aortae calcifications, other
30	PA	senile emphysema
31	CC	other
32	CE	senile emphysema
33	VA	enlarged cardiac shadow, other
34	BA	senile emphysema
35	SB	senile emphysema, enlarged cardiac shadow
36	SM	senile emphysema, arcus aortae calcifications
37	SE	senile emphysema
38	LO	senile emphysema
39	CP	senile emphysema, arcus aortae calcifications
40	PO	senile emphysema, enlarged cardiac shadow, other
41	FE	senile emphysema
42	LI	senile emphysema, enlarged cardiac shadow
43	PA	senile emphysema
44	MZ	enlarged cardiac shadow, other
45	PG	senile emphysema (+ pace maker)
46	AD	senile emphysema, enlarged cardiac shadow, arcus aortae calcifications
47	SG	enlarged cardiac shadow, other
48	FA	senile emphysema
49	SA	senile emphysema
50	ZZ	senile emphysema

other = tuberculoma, scars, bronchiectasic picture, interstice reinforcement, pleuric veil.

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

PREVIOUS TREATMENTS

Patient No.	Initials	Visit Date	Treatment	Efficacy	Last Treatment Date	Last Treatment Taken	
1	TR	20MAY91	MUTABON ANTIDEPRESSIVO	GOOD	28MAY91	MUTABON ANTIDEPRESSIVO	_____
4	PC	25MAY91	LANTANON	POOR	22SEP90	LANTANON	_____
11	CL	31MAY91	LAROXYL	POOR	25MAY91	LAROXYL	_____
13	DSC	01JUL91	DALMADORM	GOOD	03JUL91	DALMADORM	_____
18	VM	02JUL91	SURVECTOR LIMBITRYL SAMYR	POOR POOR POOR	30JUN91 . .	SURVECTOR	LIMBITRYL
19	NI	05JUL91	LANTANON	POOR	30JUN91	LANTANON	_____
21	SE	01JUL91	MUTABON ANTIDEPRESSIVO	POOR	15JUN91	MUTABON ANTIDEPRESSIVO	_____
26	PR	31AUG91	LAROXYL SURVECTOR	. .	31AUG91 .	SURVECTOR	_____
37	SE	01OCT91	CANTOR TAVOR	GOOD GOOD	03OCT91 .	CANTOR	_____
38	LO	01OCT91	MUTABON ANTIDEPRESSIVO	FAIR	02OCT91	MUTABON ANTIDEPRESSIVO	_____

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CONCOMITANT DRUGS STARTED BEFORE STUDY TREATMENT

Patient No.	Initials	Wash Out Period From	Wash Out Period To	Concomitant Drug	Starting Date	Discontinuation Date
1	TR	29MAY91	04JUN91	HALCION	29MAY91	
				ADALAT	20MAY91	
				MODURETIC	20MAY91	
				CALCITONIN	20MAY91	
				CALCIDON	20MAY91	
3	BI	13MAY91	04JUN91	MODURETIC	13MAY91	
				PRAVASTATIN	13MAY91	
				CALCITONIN	13MAY91	
				VITAMIN D	13MAY91	
4	PC	30MAY91	04JUN91	THEOPHYLLINE	07MAY91	
				ACEPLUS	07MAY91	
5	BL	30MAY91	04JUN91	IBUSTRIN	18JUL90	
				IRRODAN	18JUL90	
				EUGLUCON	18JUL90	
				TRENTAL	18JUL90	
6	SM	29MAY91	04JUN91	SUGUAN	29MAY91	
				MODURETIC	29MAY91	
				LANOXIN	29MAY91	
7	DA	30MAY91	04JUN91	NATRILIX	17MAY91	
				LANOXIN	17MAY91	
8	SC	25MAY91	04JUN91	ADALAT	14MAY91	
				LOPIVL	14MAY91	
				ACEPLUS	14MAY91	
				CALCIPARINE	14MAY91	
9	PA	25MAY91	04JUN91	TRENTAL	19APR91	
				CALCIPARINE	19APR91	
11	CL	31MAY91	04JUN91	RANIDIL	31MAY91	
				CALCITONIN	31MAY91	
				CALCIDON	31MAY91	
12	ML	21JUN91	08JUL91	LANOXIN	21JUN91	
				IBUSTRIN	21JUN91	
13	DSC	03JUL91	08JUL91	TENORMIN	17JUN91	
				NITRO	17JUN91	
				CALCIDON	17JUN91	
				CALCITONIN	17JUN91	
				HALCION	03JUL91	
14	BM	01JUL91	08JUL91	TRENTAL	23MAY91	
				AMLODIPINE	23MAY91	
				INSULIN	26JUN91	

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CONCOMITANT DRUGS STARTED BEFORE STUDY TREATMENT

Patient No.	Initials	Wash Out Period From	Wash Out Period To	Concomitant Drug	Starting Date	Discontinuation Date
14	BM	.	.	LASITONE	26JUN91	.
15	GI	25JUN91	08JUL91	ISOPTIN	25JUN91	.
		.	.	THEOPHYLLINE	25JUN91	.
		.	.	MOTILIUM	25JUN91	.
		.	.	MODURETIC	03JUL91	.
16	PJ	28JUN91	08JUL91	AMLODIPINE	14JUN91	.
		.	.	SENSIT	14JUN91	.
		.	.	STUGERON	14JUN91	.
17	MM	01JUL91	08JUL91	CALCITONIN	01JUL91	.
		.	.	CALCIDON	01JUL91	.
18	VM	02JUL91	08JUL91	LAEVOLAC	02JUL91	.
		.	.	HALCION	06JUL91	.
19	NI	30JUN91	08JUL91	HALCION	05JUL91	.
20	BE	30JUN91	08JUL91	LANOXIN	17JUN91	.
		.	.	LASITONE	20JUN91	.
		.	.	THEOPHYLLINE	20JUN91	.
		.	.	HALCION	30JUN91	.
21	SE	01JUL91	10JUL91	NIMOTOP	05JUN91	.
		.	.	MODURETIC	05JUN91	.
		.	.	HALCION	05JUN91	.
22	BA	24AUG91	10SEP91	MODURETIC	16AUG91	.
		.	.	ADALAT	16AUG91	.
		.	.	CALCITONIN	16AUG91	.
		.	.	CALCIDON	16AUG91	.
23	UT	13AUG91	09SEP91	ADALAT	13AUG91	.
		.	.	MODURETIC	13AUG91	.
		.	.	LANOXIN	13AUG91	.
24	BEA	31AUG91	10SEP91	LANOXIN	16AUG91	.
		.	.	MODURETIC	16AUG91	.
		.	.	ADALAT	16AUG91	.
		.	.	NITRO-DUR	16AUG91	.
25	GA	31AUG91	10SEP91	ISOPTIN	20AUG90	.
		.	.	MICROSER	29AUG91	.
		.	.	GEFFER	20AUG90	.
26	PR	01SEP91	10SEP91	LANOXIN	31JUL91	.
		.	.	MODURETIC	31JUL91	.
		.	.	CALCIPARINE	31JUL91	.

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CONCOMITANT DRUGS STARTED BEFORE STUDY TREATMENT

Patient No.	Initials	Wash Out Period From	Wash Out Period To	Concomitant Drug	Starting Date	Discontinuation Date
27	GA	02SEP91	09SEP91	NICARDAL	26AUG91	
				RANIDIL	26AUG91	
				LAEVOLAC	26AUG91	
				CISAPRIDE	26AUG91	
28	MR	28AUG91	10SEP91	RANIDIL	28AUG91	
				CALCITONIN	28AUG91	
				CALCIDON	28AUG91	
29	TR	31AUG91	10SEP91	THEOPHYLLINE	26AUG91	
				IBUSTRIN	26AUG91	
				LANITOP	26AUG91	
30	PA	30SEP91	07OCT91	LANOXIN	20SEP91	
				QUINAPRIL HYDROCHLORIDE	20SEP91	24SEP91
				HALCION	23SEP91	
				ENALAPRIL	25SEP91	
				HYDROCHLOROTHIAZIDE	25SEP91	
31	CC	03OCT91	07OCT91	PERDIPINE	03OCT91	
				HODURETIC	03OCT91	
				IBUSTRIN	03OCT91	
				CALCITONIN	03OCT91	
				CALCIDON	03OCT91	
32	CE	04SEP91	09SEP91	LANOXIN	04SEP91	
				HODURETIC	04SEP91	
				RANIDIL	04SEP91	
				FELDENE	04SEP91	
33	VA	28SEP91	07OCT91	LANOXIN	01JAN88	
				SPIROFUR	01JAN88	
				HALCION	02OCT91	
34	BA	01OCT91	07OCT91	ACTRAPHANE HM	26SEP91	
				RANIDIL	26SEP91	
				FELDENE	26SEP91	02OCT91
36	SM	02OCT91	07OCT91	HALCION	02OCT91	
37	SE	03OCT91	07OCT91	CALCITONIN	17SEP91	
				CALCIDON	17SEP91	
				FELDENE	28SEP91	07OCT91
38	LO	02OCT91	07OCT91	RASTINON	30SEP91	
				HALCION	30SEP91	
39	CP	04OCT91		SUGUAN	09JAN90	
				HALCION	04OCT91	

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CONCOMITANT DRUGS STARTED BEFORE STUDY TREATMENT

Patient No.	Initials	Wash Out Period From	Wash Out Period To	Concomitant Drug	Starting Date	Discontinuation Date
40	PO	28OCT91	08NOV91	RANIDIL	28OCT91	.
		.	.	TILCOTIL	28OCT91	04NOV91
41	FE	29OCT91	08NOV91	ALTIAZEM	28SEP91	.
		.	.	ISMO	28SEP91	.
		.	.	EUGLUCON	01JAN90	.
		.	.	HALCION	29OCT91	.
		.	.	ZYLORIC	28SEP91	.
42	LI	31OCT91	08NOV91	SUGUAN	29OCT91	.
		.	.	CALCITONIN	29OCT91	.
		.	.	CALCIDON	29OCT91	.
		.	.	AMLODIPINE	29OCT91	.
43	PA	30OCT91	08NOV91	HALCION	01NOV91	.
44	MZ	30OCT91	08NOV91	LANOXIN	15OCT91	.
		.	.	LASIX	15OCT91	.
		.	.	CALCITONIN	15OCT91	.
		.	.	AMLODIPINE	19OCT91	.
45	PG	01NOV91	08NOV91	LANOXIN	01JUN90	.
		.	.	ENAPREN	01JUN90	.
		.	.	MODURETIC	01JUN90	.
		.	.	TIKLID	04JUN91	.
		.	.	CALCITONIN	01NOV91	.
46	AD	30OCT91	08NOV91	LANOXIN	28OCT91	.
		.	.	NITRO-DUR	28OCT91	.
		.	.	ISOPTIN	28OCT91	.
		.	.	MODURETIC	28OCT91	.
47	SG	30OCT91	08NOV91	EUDIGOX	06NOV91	.
		.	.	LASITONE	06NOV91	.
		.	.	AMLODIPINE	06NOV91	.
48	FA	30OCT91	08NOV91	LANOXIN	15OCT91	.
		.	.	VOLTAREN	07NOV91	08NOV91
49	SA	30OCT91	08NOV91	CALCIPARINE	21OCT91	.
		.	.	HALCION	21OCT91	.
		.	.	AMLODIPINE	21OCT91	.
50	ZZ	01NOV91	08NOV91	LANOXIN	01JAN78	.
		.	.	CARNITENE	01NOV91	.
		.	.	LEUCOTROFINA	01NOV91	.

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REBOXETINE - PROTOCOL 20124/032

CONCOMITANT DRUGS STARTED AND/OR STOPPED DURING STUDY TREATMENT

Treatment	Patient No.	Initials	Treatment Started on	Concomitant Drug	Starting Date	Discontinuation Date	Days of Administration	Interval Conc.Drug-Treat
REBOXETINE	1	TR	05JUN91	FELDENE	01JUL91	01JUL91	1	26
REBOXETINE	5	BL	05JUN91	NISIDINA	13JUN91	13JUN91	1	8
				NISIDINA	15JUN91	15JUN91	1	10
				NISIDINA	17JUN91	17JUN91	1	12
				NISIDINA	27JUN91	27JUN91	1	22
				NISIDINA	30JUN91	01JUL91	2	25
				NISIDINA	04JUL91	04JUL91	1	29
				NISIDINA	08JUL91	08JUL91	1	33
				NISIDINA	20JUL91	20JUL91	1	45
				NISIDINA	27JUL91	27JUL91	1	52
				NISIDINA	30JUL91	30JUL91	1	55
REBOXETINE	8	SC	05JUN91	ACEPLUS	14MAY91	06JUN91	24	-22
REBOXETINE	15	GI	09JUL91	PLASIL	14JUL91	14JUL91	1	5
REBOXETINE	16	PJ	09JUL91	MODURETIC	30JUL91	.	35	21
REBOXETINE	23	UT	10SEP91	MAALOX	24OCT91	.	12	44
REBOXETINE	25	GA	10SEP91	ACEDIUR	20OCT91	.	16	40
REBOXETINE	28	MR	10SEP91	ADALAT	22SEP91	22SEP91	1	12
				TILCOTIL	01NOV91	.	4	52
REBOXETINE	30	PA	08OCT91	HYDROCHLOROTHIAZIDE	25SEP91	11NOV91	48	-13
				ENALAPRIL	25SEP91	11NOV91	48	-13
				NAPRILENE	28NOV91	.	5	51
				TILCOTIL	06NOV91	08NOV91	3	29
REBOXETINE	37	SE	08OCT91	ISOPTIN	20OCT91	.	44	12
				TILCOTIL	03NOV91	07NOV91	5	26
REBOXETINE	39	CP	08OCT91	TRENTAL	05NOV91	.	5	28
REBOXETINE	40	PO	09NOV91	TILCOTIL	19NOV91	24NOV91	6	10
REBOXETINE	43	PA	09NOV91	ADALAT	01DEC91	01DEC91	1	22
PLACEBO	3	BI	05JUN91	VITAMIN D	13MAY91	22JUL91	71	-23
				CALCITONIN	13MAY91	22JUL91	71	-23
PLACEBO	4	PC	05JUN91	ACEPLUS	25JUN91	.	36	20
PLACEBO	10	PE	05JUN91	NISIDINA	27JUN91	27JUN91	1	22
				NISIDINA	30JUN91	01JUL91	2	25
PLACEBO	11	CL	05JUN91	LASIX	10JUN91	.	51	5

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REBOXETINE - PROTOCOL 20124/032

CONCOMITANT DRUGS STARTED AND/OR STOPPED DURING STUDY TREATMENT

Treatment	Patient No.	Initials	Treatment Started on	Concomitant Drug	Starting Date	Discontinuation Date	Days of Administration	Interval Conc.Drug-Treat
PLACEBO	19	NI	09JUL91	CISAPRIDE	25JUL91	.	40	16
PLACEBO	24	BEA	10SEP91	FARGAN	29OCT91	29OCT91	1	49
				TILCOTIL	23SEP91	27SEP91	5	13
PLACEBO	29	TR	10SEP91	CORTICOSTEROID NOS	22SEP91	06OCT91	15	12
PLACEBO	32	CE	10SEP91	HALCION	21SEP91	.	45	11
PLACEBO	42	LI	09NOV91	HYDROCHLOROTHIAZIDE	11NOV91	14NOV91	4	2
				ENALAPRIL	11NOV91	14NOV91	4	2
				NOROXIN	15NOV91	22NOV91	8	6
				ACEDIUR	15NOV91	.	50	6
				AMLODIPINE	07NOV91	09NOV91	3	-2
PLACEBO	44	MZ	09NOV91	CALCITONIN	15OCT91	16NOV91	33	-25
				AMLODIPINE	19OCT91	20NOV91	33	-21
PLACEBO	49	SA	09NOV91	FELDENE	21NOV91	25NOV91	5	12
				RANIDIL	21NOV91	.	44	12
PLACEBO	50	ZZ	09NOV91	TILCOTIL	20NOV91	26NOV91	7	11

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REBOXETINE - PROTOCOL 20124/032

EXPERIMENTAL TREATMENT

Patient No.	Initials	Treatment	Week No.	Dose 2 Taken?	Week From	Week To	Days of Treatment	Total Returned Tablets
1	TR	REBOXETINE	1		05JUN	11JUN	7	2
			2		12JUN	18JUN	7	2
			3		19JUN	25JUN	7	2
			4	NO	26JUN	02JUL	7	2
			5-8	YES	03JUL	30JUL	28	8
2	FB	PLACEBO	1		05JUN	11JUN	7	2
			2		12JUN	18JUN	7	2
			3		19JUN	25JUN	7	2
			4	NO	26JUN	02JUL	7	2
			5-8	NO	03JUL	30JUL	28	8
3	BI	PLACEBO	1		05JUN	11JUN	7	2
			2		12JUN	18JUN	7	.
			3		19JUN	25JUN	7	2
			4	NO	26JUN	02JUL	7	2
			5-8	NO	03JUL	30JUL	28	2
4	PC	PLACEBO	1		05JUN	11JUN	7	2
			2		12JUN	18JUN	7	2
			3		19JUN	25JUN	7	2
			4	NO	26JUN	02JUL	7	2
			5-8	NO	03JUL	30JUL	28	7
5	BL	REBOXETINE	1		05JUN	11JUN	7	2
			2		12JUN	18JUN	7	2
			3		19JUN	25JUN	7	2
			4	NO	26JUN	02JUL	7	2
			5-8	YES	03JUL	30JUL	28	8
6	SM	REBOXETINE	1		05JUN	11JUN	7	2
			2		12JUN	18JUN	7	2
			3		19JUN	25JUN	7	2
			4	NO	26JUN	02JUL	7	2
			5-8	YES	03JUL	30JUL	28	8
7	DA	PLACEBO	1		05JUN	11JUN	7	2
			2		12JUN	18JUN	7	2
			3		19JUN	25JUN	7	2
			4	NO	26JUN	02JUL	7	2
			5-8	YES	03JUL	30JUL	28	7
8	SC	REBOXETINE	1		05JUN	11JUN	7	.
			2		12JUN	18JUN	7	2
			3		19JUN	25JUN	7	2
			4	NO	26JUN	02JUL	7	2
			5-8	YES	03JUL	30JUL	28	7
9	PA	PLACEBO	1		05JUN	11JUN	7	2
			2		12JUN	18JUN	7	2

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EXPERIMENTAL TREATMENT

Patient No.	Initials	Treatment	Week No.	Dose 2 Taken?	Week From	Week To	Days of Treatment	Total Returned Tablets
9	PA	PLACEBO	3		19JUN	25JUN	7	2
			4	NO	26JUN	02JUL	7	2
			5-8	NO	03JUL	30JUL	28	7
10	PE	PLACEBO	1		05JUN	11JUN	7	2
			2		12JUN	18JUN	7	2
			3		19JUN	25JUN	0	0
			4	NO	26JUN	02JUL	7	2
			5-8	NO	03JUL	11JUL	9	.
11	CL	PLACEBO	1		05JUN	11JUN	7	2
			2		12JUN	18JUN	7	2
			3		19JUN	25JUN	7	2
			4	NO	26JUN	02JUL	7	2
			5-8	YES	03JUL	30JUL	28	8
12	ML	PLACEBO	1		09JUL	15JUL	7	2
			2		16JUL	22JUL	7	2
			3		23JUL	29JUL	7	2
			4	NO	30JUL	05AUG	7	2
			5-8	YES	06AUG	02SEP	28	8
13	DSC	REBOXETINE	1		09JUL	15JUL	7	2
			2		16JUL	22JUL	7	2
			3		23JUL	29JUL	7	2
			4	NO	30JUL	05AUG	7	2
			5-8	YES	06AUG	02SEP	28	8
14	BM	REBOXETINE	1		09JUL	15JUL	7	2
			2		16JUL	22JUL	7	2
			3		23JUL	29JUL	7	2
			4	NO	30JUL	05AUG	7	2
			5-8	NO	06AUG	02SEP	28	7
15	GI	REBOXETINE	1		09JUL	15JUL	7	1
			2		16JUL	16JUL	0	16
16	PJ	REBOXETINE	1		09JUL	15JUL	7	2
			2		16JUL	22JUL	7	2
			3		23JUL	29JUL	7	2
			4	NO	30JUL	05AUG	7	2
			5-8	YES	06AUG	02SEP	28	8
17	MM	REBOXETINE	1		09JUL	15JUL	7	2
			2		16JUL	22JUL	7	2
			3		23JUL	29JUL	7	2
			4		30JUL	05AUG	7	2
			5-8	YES	06AUG	02SEP	28	4
18	VM	REBOXETINE	1		09JUL	15JUL	7	2

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REBOXETINE - PROTOCOL 20124/032

EXPERIMENTAL TREATMENT

Patient No.	Initials	Treatment	Week No.	Dose 2 Taken?	Week From	Week To	Days of Treatment	Total Returned Tablets
18	VM	REBOXETINE	2		16JUL	22JUL	7	2
			3		23JUL	29JUL	7	2
			4	NO	30JUL	05AUG	7	2
			5-8	NO	06AUG	02SEP	28	4
19	NI	PLACEBO	1		09JUL	15JUL	7	2
			2		16JUL	22JUL	7	2
			3		23JUL	29JUL	7	2
			4	NO	30JUL	05AUG	7	2
			5-8	NO	06AUG	02SEP	28	4
20	BE	PLACEBO	1		09JUL	15JUL	7	2
			2		16JUL	22JUL	7	2
			3		23JUL	29JUL	7	2
			4	NO	30JUL	05AUG	7	2
			5-8	YES	06AUG	13AUG	8	48
21	SE	REBOXETINE	1		11JUL	15JUL	5	4
			2		16JUL	22JUL	7	2
			3		23JUL	29JUL	7	2
			4	NO	30JUL	05AUG	7	2
			5-8	NO	06AUG	09AUG	4	56
22	BA	PLACEBO	1		10SEP	16SEP	7	2
			2		17SEP	23SEP	7	2
			3		24SEP	30SEP	7	2
			4	NO	01OCT	07OCT	7	2
			5-8	NO	08OCT	04NOV	28	8
23	UT	REBOXETINE	1		10SEP	16SEP	7	2
			2		17SEP	23SEP	7	2
			3		24SEP	30SEP	7	2
			4	NO	01OCT	07OCT	7	2
			5-8	NO	08OCT	04NOV	28	8
24	BEA	PLACEBO	1		10SEP	16SEP	7	2
			2		17SEP	23SEP	7	2
			3		24SEP	30SEP	7	2
			4	NO	01OCT	07OCT	7	2
			5-8	NO	08OCT	04NOV	28	8
25	GA	REBOXETINE	1		10SEP	16SEP	7	2
			2		17SEP	23SEP	7	2
			3		24SEP	30SEP	7	2
			4	NO	01OCT	07OCT	7	2
			5-8	NO	08OCT	04NOV	28	2
26	PR	REBOXETINE	1		10SEP	16SEP	7	2
			2		17SEP	23SEP	7	15

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REBOXETINE - PROTOCOL 20124/032

EXPERIMENTAL TREATMENT

Patient No.	Initials	Treatment	Week No.	Dose 2 Taken?	Week From	Week To	Days of Treatment	Total Returned Tablets
27	GA	PLACEBO	1		10SEP	16SEP	7	2
			2		17SEP	23SEP	7	2
			3		24SEP	30SEP	7	2
			4	NO	01OCT	07OCT	7	2
			5-8	NO	08OCT	04NOV	28	8
28	MR	REBOXETINE	1		10SEP	16SEP	7	2
			2		17SEP	23SEP	7	2
			3		24SEP	30SEP	7	2
			4	NO	01OCT	03OCT	3	.
			4	NO	04OCT	07OCT	0	10
			5-8	NO	08OCT	04NOV	28	8
29	TR	PLACEBO	1		10SEP	16SEP	7	2
			2		17SEP	23SEP	7	2
			3		24SEP	30SEP	7	2
			4	NO	01OCT	07OCT	7	2
			5-8	NO	08OCT	04NOV	28	2
30	PA	REBOXETINE	1		08OCT	14OCT	7	2
			2		15OCT	21OCT	7	2
			3		22OCT	28OCT	7	2
			4	NO	29OCT	04NOV	7	2
			5-8	YES	05NOV	02DEC	28	8
31	CC	PLACEBO	1		08OCT	14OCT	7	2
			2		15OCT	21OCT	7	2
			3		22OCT	28OCT	7	2
			4	NO	29OCT	04NOV	7	2
			5-8	NO	05NOV	02DEC	28	2
32	CE	PLACEBO	1		10SEP	16SEP	7	2
			2		17SEP	23SEP	7	2
			3		24SEP	30SEP	7	2
			4	NO	01OCT	07OCT	7	2
			5-8	NO	08OCT	04NOV	28	8
33	VA	PLACEBO	1		08OCT	14OCT	7	2
			2		15OCT	21OCT	7	2
			3		22OCT	28OCT	7	2
			4	NO	29OCT	04NOV	7	2
			5-6	YES	05NOV	18NOV	14	.
			7-8	NO	19NOV	02DEC	14	8
34	BA	PLACEBO	1		08OCT	10OCT	3	11
35	SB	PLACEBO	1		08OCT	14OCT	7	2
			2		15OCT	21OCT	7	2
			3		22OCT	28OCT	7	2
			4	NO	29OCT	04NOV	7	2

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REBOXETINE - PROTOCOL 20124/032

EXPERIMENTAL TREATMENT

Patient No.	Initials	Treatment	Week No.	Dose 2 Taken?	Week From	Week To	Days of Treatment	Total Returned Tablets
35	SB	PLACEBO	5-8	NO	05NOV	02DEC	28	8
36	SM	REBOXETINE	1		08OCT	14OCT	7	2
			2		15OCT	21OCT	7	2
			3		22OCT	28OCT	7	2
			4	NO	29OCT	04NOV	7	2
			5-8	YES	05NOV	02DEC	28	8
37	SE	REBOXETINE	1		08OCT	14OCT	7	2
			2		15OCT	21OCT	7	2
			3		22OCT	28OCT	7	2
			4	NO	29OCT	04NOV	7	2
			5-8	YES	05NOV	02DEC	28	5
38	LO	PLACEBO	1		08OCT	14OCT	7	2
			2		15OCT	21OCT	7	2
			3		22OCT	28OCT	7	2
			4	NO	29OCT	04NOV	7	2
			5-8	NO	05NOV	02DEC	28	3
39	CP	REBOXETINE	1		08OCT	14OCT	7	2
			2		15OCT	21OCT	7	2
			3		22OCT	28OCT	7	2
			4	NO	29OCT	04NOV	7	2
			5-8	YES	05NOV	09NOV	5	54
40	PO	REBOXETINE	1		09NOV	15NOV	7	2
			2		16NOV	22NOV	7	2
			3		23NOV	29NOV	7	2
			4	NO	30NOV	06DEC	7	2
			5-8	NO	07DEC	03JAN	28	8
41	FE	PLACEBO	1		09NOV	15NOV	7	2
			2		16NOV	22NOV	7	2
			3		23NOV	29NOV	7	2
			4	NO	30NOV	06DEC	7	2
			5-8	NO	07DEC	03JAN	28	7
42	LI	PLACEBO	1		09NOV	15NOV	7	2
			2		16NOV	22NOV	7	2
			3		23NOV	29NOV	7	2
			4	NO	30NOV	06DEC	7	2
			5-8	NO	07DEC	03JAN	28	8
43	PA	REBOXETINE	1		09NOV	15NOV	7	.
			2		16NOV	22NOV	7	2
			3		23NOV	25NOV	3	.
			3		26NOV	28NOV	0	.
			3		29NOV	29NOV	1	8
			4	NO	30NOV	01DEC	2	13

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PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

EXPERIMENTAL TREATMENT

Patient No.	Initials	Treatment	Week No.	Dose 2 Taken?	Week From	Week To	Days of Treatment	Total Returned Tablets
44	MZ	PLACEBO	1		09NOV	15NOV	7	2
			2		16NOV	22NOV	7	2
			3		23NOV	29NOV	7	2
			4	NO	30NOV	06DEC	7	2
			5-8	NO	07DEC	03JAN	28	7
45	PG	REBOXETINE	1		09NOV	15NOV	7	2
			2		16NOV	22NOV	7	2
			3		23NOV	29NOV	7	2
			4	NO	30NOV	06DEC	7	2
46	AD	REBOXETINE	1		09NOV	15NOV	7	2
			2		16NOV	22NOV	7	2
			3		23NOV	29NOV	7	2
			4	NO	30NOV	06DEC	7	2
			5-8	NO	07DEC	11DEC	5	54
47	SG	REBOXETINE	1		09NOV	15NOV	7	2
			2		16NOV	22NOV	7	2
			3		23NOV	29NOV	7	2
			4	NO	30NOV	06DEC	7	2
			5-8	NO	07DEC	03JAN	28	7
48	FA	PLACEBO	1		09NOV	15NOV	7	2
			2		16NOV	22NOV	7	2
			3		23NOV	29NOV	7	2
			4	ND	30NOV	01DEC	2	12
49	SA	PLACEBO	1		09NOV	15NOV	7	2
			2		16NOV	22NOV	7	2
			3		23NOV	29NOV	7	2
			4	NO	30NOV	06DEC	7	2
			5-8	NO	07DEC	03JAN	28	6
50	ZZ	PLACEBO	1		09NOV	15NOV	7	2
			2		16NOV	22NOV	7	2
			3		23NOV	29NOV	7	2
			4	NO	30NOV	06DEC	7	2

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

END OF STUDY
TREATMENT: REBOXETINE

Patient No.	Initials	Visit Date	Treatment Completed as per Protocol	Date of Last Dose	Reason for Discont.	Protocol Violation	Other Reason	Decision to Discontinue	Drug Compliance	Treatment Continued	If no, Prescr. Med.	Prescribed Medication
1	TR	30JUL91	YES	30JUL91	.			.	AS PRESCR.	YES		
5	BL	30JUL91	YES	30JUL91	.			.	AS PRESCR.	NO	NO	
6	SM	30JUL91	YES	30JUL91	.			.	AS PRESCR.	NO	NO	
8	SC	30JUL91	YES	30JUL91	.			.	AS PRESCR.	NO	NO	
13	DSC	02SEP91	YES	02SEP91	.			.	AS PRESCR.	YES		
14	BM	02SEP91	YES	02SEP91	.			.	AS PRESCR.	YES	NO	
15	GI	16JUL91	NO	15JUL91	1			PHYSICIAN	AS PRESCR.	NO	NO	
16	PJ	02SEP91	YES	02SEP91	.			.	AS PRESCR.	YES		
17	MM	02SEP91	YES	02SEP91	.			.	AS PRESCR.	NO	NO	
18	VM	02SEP91	YES	02SEP91	.			.	AS PRESCR.	YES		
21	SE	10AUG91	NO	09AUG91	1			PHYSICIAN	AS PRESCR.	NO	YES	MUTABON MITE 1CPX3; EN GTT
23	UT	04NOV91	YES	04NOV91	.			.	AS PRESCR.	NO	NO	
25	GA	04NOV91	YES	04NOV91	.			.	AS PRESCR.	YES	NO	
26	PR	17SEP91	NO	17SEP91	5	PARAPLEGIA		PHYSICIAN	AS PRESCR.	NO	NO	
28	MR	04NOV91	YES	04NOV91	.			.	AS PRESCR.	NO	YES	CANTOR 100 1 G
30	PA	02DEC91	YES	02DEC91	.			.	AS PRESCR.	NO	NO	
36	SM	02DEC91	YES	02DEC91	.			.	AS PRESCR.	NO	NO	
37	SE	02DEC91	YES	02DEC91	.			.	AS PRESCR.	NO	NO	
39	CP	09NOV91	NO	09NOV91	8			PATIENT	AS PRESCR.	NO	NO	
40	PO	03JAN91	YES	03JAN92	.			.	AS PRESCR.	NO	NO	
43	PA	02DEC91	NO	01DEC91	1			PATIENT	AS PRESCR.	NO	NO	
45	PG	14DEC91	NO	13DEC91	8			PATIENT	UNKNOWN	NO	NO	
46	AD	12DEC91	NO	11DEC91	8			PATIENT	UNKNOWN	NO	NO	
47	SG	03JAN92	YES	03JAN92	.			.	AS PRESCR.	NO	NO	

REASON FOR DISCONTINUATION: 1=adverse event 5=intercurrent medical problems 8=patient uncooperative/unreliable/not compliant
9=other

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PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 2012s/032

END OF STUDY

TREATMENT: PLACEBO

Patient No.	Initials	Visit Date	Treatment Completed as per Protocol	Date of Last Dose	Reason for Discont.	Protocol Violation	Other Reason	Decision to Discontinue	Drug Compliance	Treatment Continued	If no, Prescr. Med.	Prescribed Medication
2	FB	30JUL91	YES	30JUL91	.	.		.	AS PRESCR.	YES		
3	BI	30JUL91	YES	30JUL91	.	.		.	AS PRESCR.	YES		
4	PC	30JUL91	YES	30JUL91	.	.		.	AS PRESCR.	NO	YES	EN
7	DA	30JUL91	YES	30JUL91	.	.		.	AS PRESCR.	NO	NO	
9	PA	30JUL91	YES	30JUL91	.	.		.	AS PRESCR.	NO	NO	
10	PE	11JUL91	NO	11JUL91	5	.		PHYSICIAN	AS PRESCR.	NO	NO	
11	CL	30JUL91	YES	30JUL91	.	.		.	AS PRESCR.	YES		
12	ML	02SEP91	YES	02SEP91	.	.		.	AS PRESCR.	YES		
19	NI	02SEP91	YES	02SEP91	.	.		.	AS PRESCR.	NO	YES	EN
20	BE	13AUG91	NO	13AUG91	1	.		PHYSICIAN	AS PRESCR.	NO	YES	EN GTT XV X5
22	BA	04NOV91	YES	04NOV91	.	.		.	AS PRESCR.	NO	NO	
24	BEA	04NOV91	YES	04NOV91	.	.		.	AS PRESCR.	NO	NO	
27	GA	04NOV91	YES	04NOV91	.	.		.	AS PRESCR.	NO	YES	CANTOR ICPX2
29	TR	04NOV91	YES	04NOV91	.	.		.	AS PRESCR.	NO	YES	SURVECTOR 100X2
31	CC	02DEC91	YES	02DEC91	.	.		.	AS PRESCR.	NO	NO	
32	CE	04NOV91	YES	04NOV91	.	.		.	AS PRESCR.	NO	NO	
33	VA	02DEC91	YES	02DEC91	.	.		.	AS PRESCR.	NO	NO	
34	BA	19OCT91	NO	19OCT91	8	.		PATIENT	UNKNOWN	NO	NO	
35	SB	02DEC91	YES	02DEC91	.	.		.	AS PRESCR.	NO	NO	
38	LD	02DEC91	YES	02DEC91	.	.		.	AS PRESCR.	NO	YES	EN
41	FE	03JAN92	YES	03JAN92	.	.		.	AS PRESCR.	NO	NO	
42	LI	03JAN92	YES	03JAN92	.	.		.	AS PRESCR.	NO	NO	
44	MZ	03JAN92	YES	03JAN92	.	.		.	AS PRESCR.	NO	NO	
48	FA	01DEC91	NO	01DEC91	8	.		PATIENT	AS PRESCR.	NO	NO	
49	SA	03JAN92	YES	03JAN92	.	.		.	AS PRESCR.	NO	NO	
50	ZZ	06DEC91	NO	06DEC91	1	.		PATIENT	AS PRESCR.	NO	NO	

REASON FOR DISCONTINUATION: 1=adverse event 5=intercurrent medical problems 8=patient uncooperative/unreliable/not compliant 9=other

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

HAMILTON DEPRESSION RATING SCALE

Patient No.	Initials	Treatment	Visit No.	It.1	It.2	It.3	It.4	It.5	It.6	It.7	It.8	It.9	It.10	It.11	It.12	It.13	It.14	It.15	It.16	It.17	It.18	It.19	It.20	It.21	Total Score
1	TR	REBOXETINE	-1	2	0	0	2	2	2	2	2	2	2	2	1	1	0	2	0	0	1	0	0	1	24
			0	2	0	0	2	2	2	2	2	2	2	2	1	1	0	2	0	0	1	0	0	1	24
			14	2	0	0	2	2	2	2	2	2	2	2	1	1	0	2	0	0	1	0	0	1	24
			28	1	0	0	1	1	1	2	1	2	2	2	1	1	0	2	0	0	1	0	0	1	19
			56	1	0	0	1	1	1	2	1	2	1	2	1	1	0	2	0	0	1	0	0	1	18
2	FB	PLACEBO	-1	2	1	0	2	2	1	2	1	1	2	2	1	1	0	1	0	0	1	0	1	0	21
			0	2	1	0	2	2	1	2	1	1	2	2	1	1	0	1	0	0	1	0	1	0	21
			14	2	1	0	2	2	1	2	1	1	2	2	1	1	0	1	0	0	1	0	1	0	21
			28	1	1	0	1	0	1	1	0	0	1	1	1	0	0	0	0	0	0	0	0	0	9
			56	1	1	0	0	1	0	1	0	0	0	1	0	1	0	0	0	0	0	0	0	0	6
3	BI	PLACEBO	-1	1	0	0	2	2	2	2	1	2	3	2	0	1	0	3	0	0	1	0	1	0	23
			0	1	0	0	2	2	2	2	1	2	3	2	0	1	0	3	0	0	1	0	1	0	23
			14	1	0	0	1	2	1	1	1	1	2	2	0	1	0	1	0	0	1	0	1	0	16
			28	1	0	0	1	1	0	1	0	1	2	2	0	1	0	1	0	0	1	0	0	0	12
			56	1	0	0	0	1	0	1	0	1	1	2	0	1	0	1	0	0	1	0	0	0	10
4	PC	PLACEBO	-1	2	2	1	2	2	2	3	2	2	3	1	0	1	0	3	0	0	1	0	0	1	28
			0	2	2	1	2	2	2	3	2	2	3	1	0	1	0	3	0	0	1	0	1	0	28
			14	2	1	0	2	2	2	2	2	1	2	1	0	1	0	2	0	0	1	0	0	1	22
			28	1	1	0	2	2	1	2	2	1	2	1	0	1	0	2	0	0	1	0	0	1	20
			56	1	1	0	2	2	1	2	2	1	2	1	0	1	0	2	0	0	1	0	0	1	20
5	BL	REBOXETINE	-1	2	2	0	2	1	1	2	0	2	2	2	1	1	0	3	0	0	1	0	0	0	22
			0	2	2	0	2	1	1	2	0	2	2	2	1	1	0	3	0	0	1	0	0	0	22
			14	2	2	0	2	1	1	2	0	2	2	2	1	1	0	3	0	0	1	0	0	0	22
			28	2	2	0	2	1	1	2	0	2	2	2	1	1	0	2	0	0	1	0	0	0	21
			56	2	2	0	2	2	1	2	0	2	2	2	1	1	0	2	0	0	1	0	0	0	22
6	SM	REBOXETINE	-1	2	0	0	1	1	2	1	2	1	1	2	0	1	0	2	0	1	1	0	0	1	19
			0	2	0	0	1	1	2	1	2	1	1	2	0	1	0	2	0	1	1	0	0	1	19
			14	2	0	0	1	1	2	1	2	1	1	2	0	1	0	2	0	1	1	0	0	1	19
			21	2	0	0	1	1	1	1	2	1	1	1	0	1	0	2	0	1	1	0	1	1	18
			56	2	0	0	1	0	1	1	2	1	1	1	0	1	0	1	0	1	1	0	0	1	15
7	DA	PLACEBO	-1	2	0	0	2	2	2	2	0	2	2	2	0	1	0	2	0	0	1	0	1	1	22
			0	2	0	0	2	2	2	2	0	2	2	2	0	1	0	2	0	0	1	0	1	1	22
			14	2	0	0	2	2	2	2	0	2	2	2	0	1	0	2	0	0	1	0	1	1	22
			28	2	0	0	2	2	2	2	0	2	2	2	0	1	0	2	0	0	1	0	1	1	22
			56	2	0	0	2	2	2	2	1	2	2	2	0	1	0	2	0	0	1	0	1	1	23
8	SC	REBOXETINE	-1	1	0	0	1	2	2	2	1	1	2	2	1	1	0	2	0	0	1	0	0	1	20

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HAMD: It.1=Depressed (0-4) It.2=Guilt (0-4) It.3=Suicide(0-4) It.4=Insomnia Early (0-2)
It.5=Insomnia Middle (0-2) It.6=Insomnia Late (0-2) It.7=Work/Activities (0-4) It.8=Retardation (0-4)
It.9=Agitation (0-4) It.10=Anxiety Psychic (0-4) It.11=Anxiety Somatic (0-4) It.12=Gastroin. Symp. (0-2)
It.13=General Symp. (0-2) It.14=Genital Symp. (0-2) It.15=Hypocondriasis (0-4) It.16=Loss Weight A or B (0-3)
It.17=Insight (0-2) It.18=Diurnal Variation (0-2) It.19=Depersonalization (0-4) It.20=Paranoid Symp. (0-3)
It.21=Obsessional Symp. (0-2)

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

HAMILTON DEPRESSION RATING SCALE

Patient No.	Initials	Treatment	Visit No.	It.1	It.2	It.3	It.4	It.5	It.6	It.7	It.8	It.9	It.10	It.11	It.12	It.13	It.14	It.15	It.16	It.17	It.18	It.19	It.20	It.21	Total Score
8	SC	REBOXETINE	0	1	0	0	1	2	2	2	1	1	2	2	1	1	0	2	0	0	1	0	0	1	20
			14	1	0	0	1	2	2	2	1	1	2	2	1	1	0	2	0	0	1	0	0	2	20
			28	1	0	0	1	1	1	2	1	1	2	2	1	1	0	1	0	0	1	0	1	1	18
			56	1	0	0	1	0	1	2	1	1	2	2	1	1	0	1	0	0	1	0	1	1	17
9	PA	PLACEBO	-1	1	0	0	1	2	2	2	2	1	2	2	1	1	0	2	0	1	0	0	0	1	21
			0	1	0	0	1	2	2	2	2	1	2	2	1	1	0	2	0	1	0	0	0	1	21
			14	1	0	0	1	1	1	1	1	1	2	1	1	1	0	1	0	1	0	0	0	1	15
			28	1	0	0	1	1	1	1	1	1	2	1	1	1	0	1	0	1	0	0	0	1	25
			56	1	0	0	1	0	1	1	1	1	2	1	1	1	0	1	0	1	0	0	0	1	14
10	PE	PLACEBO	-1	1	0	0	1	1	1	2	2	1	2	1	1	1	0	2	0	1	1	0	0	1	19
			0	1	0	0	1	1	1	2	2	1	2	1	1	1	0	2	0	1	1	0	0	1	19
			14	1	0	0	1	1	1	2	2	1	2	1	1	1	0	2	0	1	1	0	0	1	19
			28	1	0	0	1	1	1	2	2	1	2	1	1	1	0	2	0	1	1	0	0	1	19
11	CL	PLACEBO	-1	2	0	0	2	2	2	2	2	1	2	2	1	1	0	3	0	1	1	0	0	1	25
			0	2	0	0	2	2	2	2	2	1	2	2	1	1	0	3	0	1	1	0	0	1	25
			14	2	0	0	2	1	2	1	1	1	2	2	1	1	0	2	0	1	1	0	0	1	21
			28	2	0	0	2	1	2	1	1	1	2	2	1	1	0	2	0	1	1	0	0	1	21
			56	2	0	0	1	1	1	1	1	1	2	2	1	1	0	2	0	1	1	0	0	1	19
12	ML	PLACEBO	-1	3	0	0	2	1	2	1	2	1	3	2	0	2	0	2	0	1	0	0	0	1	23
			0	3	0	0	2	1	2	1	2	1	3	2	0	2	0	2	0	1	0	0	0	1	23
			14	2	0	0	2	1	2	1	3	2	3	2	0	1	0	2	0	1	0	0	0	1	23
			28	1	0	0	2	1	2	1	2	2	3	2	0	1	0	2	0	1	0	0	0	1	21
			56	1	0	0	1	1	2	1	2	2	2	2	0	1	0	2	0	1	0	0	0	1	19
13	DSC	REBOXETINE	-1	2	1	0	2	1	2	2	2	1	3	2	0	1	0	2	0	1	0	0	1	1	24
			0	2	1	0	2	1	2	2	2	1	3	2	0	1	0	2	0	1	0	0	1	1	24
			14	2	1	0	2	2	2	1	1	0	2	2	0	1	0	2	0	1	0	0	1	1	21
			28	2	1	0	2	2	2	1	1	0	2	2	1	1	0	2	0	1	0	0	1	1	22
			56	2	1	0	1	1	2	1	1	0	2	2	1	1	0	2	0	1	0	0	0	1	19
14	BM	REBOXETINE	-1	2	1	0	2	1	2	2	1	1	3	2	1	1	0	2	0	1	0	0	0	1	23
			0	2	1	0	2	1	2	2	1	1	3	2	1	1	0	2	0	1	0	0	0	1	23
			14	2	1	0	2	0	2	2	1	0	2	2	0	1	0	2	0	1	0	0	0	1	19
			28	1	1	0	2	0	1	2	1	0	2	2	0	1	0	2	0	1	0	0	0	1	17
			56	1	1	0	1	0	1	2	1	0	2	2	0	1	0	2	0	1	0	0	0	1	16
15	GI	REBOXETINE	-1	2	2	0	1	2	2	1	0	1	3	2	1	1	0	2	0	1	1	0	0	1	23
			0	2	2	0	1	2	2	1	0	1	3	2	1	1	0	2	0	1	1	0	0	1	23

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HAMD: It.1=Depressed (0-4) It.2=Guilt (0-4) It.3=Suicide(0-4) It.4=Insomnia Early (0-2)
It.5=Insomnia Middle (0-2) It.6=Insomnia Late (0-2) It.7=Work/Activities (0-4) It.8=Retardation (0-4)
It.9=Agitation (0-4) It.10=Anxiety Psychic (0-4) It.11=Anxiety Somatic (0-4) It.12=Gastroin. Symp. (0-2)
It.13=General Symp. (0-2) It.14=Genital Symp. (0-2) It.15=Hypocondriasis (0-4) It.16=Loss Weight A or B (0-3)
It.17=Insight (0-2) It.18=Diurnal Variation (0-2) It.19=Depersonalization (0-4) It.20=Paranoid Symp. (0-3)
It.21=Obsessional Symp. (0-2)

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

HAMILTON DEPRESSION RATING SCALE

Patient No.	Initials	Treatment	Visit No.	It.1	It.2	It.3	It.4	It.5	It.6	It.7	It.8	It.9	It.10	It.11	It.12	It.13	It.14	It.15	It.16	It.17	It.18	It.19	It.20	It.21	Total Score
16	PJ	REBOXETINE	-1	2	0	0	2	2	2	3	2	1	3	2	0	2	0	2	0	0	1	0	0	0	24
			0	2	0	0	2	2	2	3	2	1	3	2	0	2	0	2	0	0	1	0	0	0	24
			14	2	0	0	2	1	2	3	2	1	3	2	0	2	0	2	0	0	1	0	0	0	23
			28	1	0	0	1	2	1	1	1	1	2	2	2	1	0	2	0	0	1	0	0	0	16
			56	1	0	0	0	0	1	1	0	1	2	2	0	1	0	1	0	0	0	0	0	0	10
17	MM	REBOXETINE	-1	2	1	0	2	1	1	2	2	1	2	2	0	1	0	3	0	1	0	0	0	1	22
			0	2	1	0	2	1	1	2	2	1	2	2	0	1	0	3	0	1	0	0	0	1	22
			14	2	1	0	2	1	1	2	2	1	2	2	0	1	0	3	0	1	0	0	0	1	22
			28	2	1	0	2	2	1	2	2	1	2	2	0	1	0	3	0	1	0	0	0	1	23
			56	2	1	0	2	2	1	2	2	1	2	2	0	1	0	3	0	1	0	0	0	1	23
18	VM	REBOXETINE	-1	3	0	0	2	1	2	3	0	1	2	2	1	1	1	2	0	0	2	0	0	1	24
			0	3	0	0	2	1	2	3	0	1	2	2	1	1	1	2	0	0	2	0	0	1	24
			14	1	0	0	1	1	1	1	0	1	2	2	1	1	1	2	0	0	1	0	0	1	17
			28	1	0	0	1	1	1	1	0	1	1	2	1	1	1	1	0	0	1	0	0	1	15
			56	1	0	0	1	0	1	1	0	1	1	1	1	1	0	0	0	0	0	0	0	1	10
19	NI	PLACEBO	-1	3	1	0	2	1	2	3	1	1	2	2	1	1	0	3	1	0	0	0	0	1	25
			0	3	1	0	2	1	2	3	1	1	2	2	1	1	0	3	1	0	0	0	0	1	25
			14	3	1	0	2	1	2	3	0	0	2	2	1	1	0	3	1	1	0	0	0	1	24
			28	2	1	0	1	1	1	2	0	0	1	1	0	1	0	2	1	1	0	0	0	1	16
			56	2	1	0	1	1	1	2	0	0	1	1	0	1	0	2	1	1	0	0	0	1	16
20	BE	PLACEBO	-1	3	0	0	2	2	2	1	1	1	2	2	1	1	1	1	0	1	1	0	0	1	23
			0	3	0	0	2	2	2	1	1	1	2	2	1	1	1	1	0	1	1	0	0	1	23
			14	3	0	0	2	2	2	1	1	1	2	2	1	1	1	1	0	1	1	0	0	1	23
			28	1	0	0	2	2	2	1	1	2	0	2	1	1	1	1	0	1	1	0	0	1	20
			36	1	0	0	2	2	2	2	1	4	3	2	1	1	1	1	0	1	1	0	0	1	26
21	SE	REBOXETINE	-1	3	0	0	1	0	2	1	2	1	3	2	0	1	0	2	0	1	1	0	0	0	20
			0	3	0	0	1	0	2	1	2	1	3	2	0	1	0	2	0	1	1	0	0	0	20
			14	3	0	0	1	1	1	1	2	0	2	1	1	1	0	2	0	1	1	0	0	0	18
			28	3	0	0	2	2	2	1	2	0	2	1	1	1	0	2	0	1	1	0	0	0	21
22	BA	PLACEBO	-1	1	0	0	2	2	1	1	2	1	2	2	0	1	0	2	0	1	1	0	0	1	20
			0	1	0	0	2	2	1	1	2	1	2	2	0	1	0	2	0	1	1	0	0	1	20
			14	1	0	0	1	1	0	1	2	1	2	2	0	1	0	2	0	1	1	0	0	1	17
			28	1	0	0	1	1	0	1	2	1	1	2	0	1	0	2	0	1	1	0	0	1	16
			56	1	0	0	1	0	0	2	1	0	1	2	0	1	0	2	0	1	1	0	0	1	13
23	UT	REBOXETINE	-1	2	0	0	2	1	2	2	3	1	2	2	1	1	0	3	0	1	0	0	0	1	24
			0	2	0	0	2	1	2	2	3	1	2	2	1	1	0	3	0	1	0	0	0	1	24

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HAMD: It.1=Depressed (0-4) It.2=Guilt (0-4) It.3=Suicide(0-4) It.4=Insomnia Early (0-2)
It.5=Insomnia Middle (0-2) It.6=Insomnia Late (0-2) It.7=Work/Activities (0-4) It.8=Retardation (0-4)
It.9=Agitation (0-4) It.10=Anxiety Psychic (0-4) It.11=Anxiety Somatic (0-4) It.12=Gastroin. Symp. (0-2)
It.13=General Symp. (0-2) It.14=Genital Symp. (0-2) It.15=Hypocondriasis (0-4) It.16=Loss Weight A or B (0-3)
It.17=Insight (0-2) It.18=Diurnal Variation (0-2) It.19=Depersonalization (0-4) It.20=Paranoid Symp. (0-3)
It.21=Obsessional Symp. (0-2)

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

HAMILTON DEPRESSION RATING SCALE

Patient No.	Initials	Treatment	Visit No.	It.1	It.2	It.3	It.4	It.5	It.6	It.7	It.8	It.9	It.10	It.11	It.12	It.13	It.14	It.15	It.16	It.17	It.18	It.19	It.20	It.21	Total Score
23	UT	REBOXETINE	14	2	0	0	1	1	1	2	3	1	1	2	1	1	0	3	0	1	0	0	0	1	21
			28	1	0	0	1	1	1	2	3	1	0	1	1	1	0	3	0	1	0	0	0	1	18
			56	1	0	0	1	1	1	1	2	1	0	1	1	2	0	3	0	1	0	0	0	1	16
24	BEA	PLACEBO	-1	2	0	0	2	1	1	1	2	1	3	2	1	1	0	2	2	1	1	0	0	1	24
			0	2	0	0	2	1	1	1	2	1	3	2	1	1	0	2	2	1	1	0	0	1	24
			14	2	0	0	2	1	0	1	2	1	2	2	1	1	0	2	2	1	1	0	0	1	22
			28	1	0	0	1	1	0	1	2	0	1	2	1	1	0	2	2	1	1	0	0	1	18
			56	1	0	0	1	1	0	1	2	0	1	1	1	1	0	1	0	1	1	0	0	1	14
25	GA	REBOXETINE	-1	1	1	0	2	2	1	1	1	1	2	3	1	1	0	3	0	1	1	0	0	1	23
			0	1	1	0	2	2	1	1	1	1	2	3	1	1	0	3	0	1	1	0	0	1	23
			14	1	1	0	2	1	1	1	1	1	1	2	1	1	0	1	0	1	1	0	0	1	18
			28	1	1	0	1	1	1	1	1	1	1	2	1	1	0	1	0	1	1	0	0	1	17
			56	1	0	0	1	1	1	1	1	0	1	1	1	1	0	1	0	1	0	0	0	1	13
26	PR	REBOXETINE	-1	3	0	0	2	1	2	2	2	3	2	1	1	2	2	2	0	0	1	0	0	1	27
			0	3	0	0	2	1	2	2	2	2	3	2	1	1	2	2	0	0	1	0	0	2	27
27	GA	PLACEBO	-1	2	0	0	2	1	2	2	2	1	3	2	1	1	0	2	0	1	0	0	0	1	23
			0	2	0	0	2	1	2	2	2	1	3	2	1	1	0	2	0	1	0	0	0	1	23
			14	2	0	0	1	1	1	2	2	1	3	2	1	1	0	2	0	1	0	0	0	1	21
			28	3	0	0	1	1	1	2	2	0	2	2	1	1	0	2	0	1	0	0	0	1	20
			56	3	0	0	1	1	1	2	2	0	2	2	1	1	0	2	0	1	0	0	0	1	20
28	MR	REBOXETINE	-1	3	1	0	2	2	2	3	2	1	3	2	1	2	0	3	1	1	1	0	0	1	31
			0	3	1	0	2	2	2	3	2	1	3	2	1	2	0	3	1	1	1	0	0	1	31
			14	2	1	0	1	2	2	2	2	1	2	1	1	1	0	2	1	1	1	0	0	1	24
			28	2	1	0	1	1	2	2	2	1	2	1	1	1	0	2	1	1	1	0	0	1	23
			56	2	1	0	1	1	2	2	1	0	2	1	1	1	0	2	0	1	1	0	0	1	20
29	TR	PLACEBO	-1	2	1	0	1	0	1	1	1	1	2	2	1	1	1	1	2	1	1	0	1	1	22
			0	2	1	0	1	0	1	1	1	1	2	2	1	1	1	1	2	1	1	0	1	1	22
			14	2	1	0	1	2	1	1	1	1	2	2	1	1	1	1	0	1	1	0	1	1	22
			28	2	1	0	1	2	1	1	1	1	1	2	1	1	1	1	0	1	1	0	1	1	21
			56	3	1	0	1	2	1	2	1	1	1	2	1	1	1	3	0	1	1	0	1	1	25
30	PA	REBOXETINE	-1	2	0	0	2	1	1	1	1	1	3	2	1	2	0	3	0	1	1	0	0	0	22
			0	2	0	0	2	1	1	1	1	1	3	2	1	2	0	3	0	1	1	0	0	0	22
			14	1	0	0	2	1	1	1	1	1	3	2	1	2	0	3	0	1	1	0	0	0	21
			28	1	0	0	2	1	1	1	1	1	2	2	1	2	0	2	0	1	1	0	0	0	19
			56	1	0	0	2	2	1	1	1	1	2	2	1	2	0	2	0	1	1	0	0	0	20

HAMD: It.1=Depressed (0-4) It.2=Guilt (0-4) It.3=Suicide(0-4) It.4=Insomnia Early (0-2)
It.5=Insomnia Middle (0-2) It.6=Insomnia Late (0-2) It.7=Work/Activities (0-4) It.8=Retardation (0-4)
It.9=Agitation (0-4) It.10=Anxiety Psychic (0-4) It.11=Anxiety Somatic (0-4) It.12=Gastroin. Symp. (0-2)
It.13=General Symp. (0-2) It.14=Genital Symp. (0-2) It.15=Hypocondriasis (0-4) It.16=Loss Weight A or B (0-3)
It.17=Insight (0-2) It.18=Diurnal Variation (0-2) It.19=Depersonalization (0-4) It.20=Paranoid Symp. (0-3)
It.21=Obsessional Symp. (0-2)

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

HAMILTON DEPRESSION RATING SCALE

Patient No.	Initials	Treatment	Visit No.	It.1	It.2	It.3	It.4	It.5	It.6	It.7	It.8	It.9	It.10	It.11	It.12	It.13	It.14	It.15	It.16	It.17	It.18	It.19	It.20	It.21	Total Score
31	CC	PLACEBO	-1	2	2	0	2	1	1	1	2	0	3	2	1	1	0	3	0	1	1	0	0	1	24
			0	2	2	0	2	1	1	1	2	0	3	2	1	1	0	3	0	1	1	0	0	1	24
			14	2	2	0	1	1	1	1	2	0	1	1	1	1	0	2	0	1	1	0	0	1	19
			28	1	1	0	1	1	1	1	2	0	1	1	1	1	0	2	0	1	1	0	0	1	17
			56	1	1	0	0	0	1	1	1	0	1	1	1	1	0	2	0	1	1	0	0	1	14
32	CE	PLACEBO	-1	2	0	0	2	1	1	1	2	1	2	2	1	1	0	2	0	1	1	0	0	1	21
			0	2	0	0	2	1	1	1	0	1	2	2	1	1	0	2	0	1	1	0	0	1	21
			14	2	0	0	2	1	1	1	2	1	2	2	1	1	0	2	0	1	1	0	0	1	21
			28	2	0	0	1	1	1	1	2	1	2	1	1	1	0	2	0	1	1	0	0	1	19
			56	2	0	0	1	1	1	1	1	1	2	1	1	1	0	2	0	1	1	0	0	1	18
33	VA	PLACEBO	-1	1	2	0	2	2	2	2	2	0	2	2	1	1	0	3	0	1	0	0	0	1	24
			0	1	2	0	2	2	2	2	2	0	2	2	1	1	0	3	0	1	0	0	0	1	24
			14	1	2	0	2	1	2	2	2	0	1	2	1	1	0	3	0	1	0	0	0	1	22
			28	1	2	0	2	1	1	2	2	0	1	2	1	1	0	3	0	1	0	0	0	1	21
			56	1	1	0	1	0	1	2	2	0	1	1	1	1	0	1	0	1	0	0	0	1	15
34	BA	PLACEBO	-1	2	1	0	1	2	1	1	0	1	3	2	1	2	0	3	0	0	1	0	0	1	22
			0	2	1	0	1	2	2	1	0	1	3	2	1	2	0	3	0	0	1	0	0	1	23
35	SB	PLACEBO	-1	2	1	0	1	2	1	2	0	1	2	2	1	1	0	3	0	0	2	0	0	0	21
			0	2	1	0	2	1	1	2	0	1	2	2	1	1	0	3	0	0	2	0	0	0	21
			14	1	1	0	1	1	1	1	0	1	2	2	1	1	0	3	0	0	2	0	0	0	18
			28	1	1	0	1	1	1	1	0	1	2	2	1	1	0	3	0	0	2	0	0	0	18
			56	1	1	0	1	1	0	1	0	1	1	1	1	1	0	2	0	0	1	0	0	0	13
36	SM	REBOXETINE	-1	3	2	0	2	2	2	3	2	0	2	2	1	1	0	3	0	1	2	0	0	1	29
			0	3	2	0	2	2	2	3	2	0	2	2	1	1	0	3	0	1	2	0	0	1	29
			14	3	2	0	2	2	2	3	2	0	2	2	1	1	0	2	0	1	2	0	0	1	28
			28	2	2	0	2	2	2	2	2	0	1	2	1	1	0	2	0	1	2	0	0	1	25
			56	1	1	0	1	1	1	2	1	0	1	1	1	1	0	2	0	1	1	0	0	1	17
37	SE	REBOXETINE	-1	2	1	0	2	2	2	1	2	0	2	2	1	2	0	3	0	1	0	0	1	1	24
			0	2	1	0	2	2	2	1	1	0	2	2	1	2	0	3	0	1	1	0	0	1	24
			14	2	1	0	2	2	2	1	1	0	2	2	1	2	0	3	0	1	1	0	0	1	24
			28	2	1	0	2	2	1	1	1	0	1	2	1	2	0	2	0	1	1	0	0	1	21
			56	2	1	0	2	2	1	2	1	0	2	2	1	2	0	2	0	1	1	0	0	1	23
38	LO	PLACEBO	-1	3	0	0	2	2	2	3	2	0	3	2	1	1	0	3	0	1	2	0	0	1	28
			0	3	0	0	2	2	2	3	2	0	3	2	1	1	0	3	0	1	2	0	0	1	28
			7	3	0	0	1	2	2	3	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
			14	3	0	0	1	2	2	3	2	0	3	2	1	1	0	2	0	1	2	0	0	1	26

HAMD: It.1=Depressed (0-4) It.2=Guilt (0-4) It.3=Suicide(0-4) It.4=Insomnia Early (0-2)
It.5=Insomnia Middle (0-2) It.6=Insomnia Late (0-2) It.7=Work/Activities (0-4) It.8=Retardation (0-4)
It.9=Agitation (0-4) It.10=Anxiety Psychic (0-4) It.11=Anxiety Somatic (0-4) It.12=Gastroin. Symp. (0-2)
It.13=General Symp. (0-2) It.14=Genital Symp. (0-2) It.15=Hypocondriasis (0-4) It.16=Loss Weight A or B (0-3)
It.17=Insight (0-2) It.18=Diurnal Variation (0-2) It.19=Depersonalization (0-4) It.20=Paranoid Symp. (0-3)
It.21=Obsessional Symp. (0-2)

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

HAMILTON DEPRESSION RATING SCALE

Patient No.	Initials	Treatment	Visit No.	It.1	It.2	It.3	It.4	It.5	It.6	It.7	It.8	It.9	It.10	It.11	It.12	It.13	It.14	It.15	It.16	It.17	It.18	It.19	It.20	It.21	Total Score
38	LO	PLACEBO	28	2	0	0	1	1	1	2	2	0	2	2	1	1	0	2	0	1	2	0	0	1	21
			56	1	0	0	0	0	1	2	0	0	1	2	1	1	0	1	0	1	1	0	0	0	12
39	CP	REBOXETINE	-1	2	1	0	2	2	2	1	2	0	2	2	1	1	0	2	0	1	0	0	0	0	21
			0	2	1	0	2	2	2	1	2	0	2	2	1	1	0	2	0	1	0	0	0	0	21
			14	3	1	0	2	2	2	1	2	0	2	2	1	1	0	2	0	1	0	0	0	0	22
			28	2	1	0	2	2	2	1	2	0	2	2	1	1	0	2	0	1	0	0	0	0	21
40	PO	REBOXETINE	-1	2	1	0	2	1	2	2	1	0	2	2	1	1	0	3	0	0	1	0	1	0	22
			0	2	1	0	2	1	2	2	1	0	2	2	1	1	0	3	0	0	1	0	1	0	22
			14	1	1	0	0	1	1	1	1	0	1	1	1	1	0	2	0	0	1	0	1	0	14
			28	1	0	0	0	1	0	1	1	0	1	1	1	1	0	1	0	0	0	0	1	0	10
			56	0	0	0	0	1	0	0	1	0	1	1	0	1	0	1	0	0	0	0	0	0	6
41	FE	PLACEBO	-1	2	1	0	2	1	1	2	1	1	3	2	1	1	0	3	0	0	1	0	0	1	23
			0	2	1	0	2	1	1	2	1	1	3	2	1	1	0	3	0	0	1	0	0	1	23
			14	2	1	0	2	1	1	2	1	1	3	2	1	1	0	2	0	0	1	0	0	1	22
			28	2	1	0	2	1	1	2	1	1	2	2	1	1	0	2	0	0	1	0	0	1	21
			56	2	1	0	2	1	1	2	1	1	2	2	1	1	0	2	0	0	1	0	0	1	21
42	LI	PLACEBO	-1	2	0	0	1	2	1	2	1	1	3	1	1	1	0	3	0	1	1	0	1	1	23
			0	2	0	0	1	2	1	2	1	1	3	1	1	1	0	3	0	1	1	0	1	1	23
			14	1	0	0	1	1	1	2	1	1	2	0	0	1	0	2	0	1	1	0	1	1	17
			28	1	0	0	1	1	0	1	1	1	2	0	0	1	0	2	0	1	0	0	1	1	14
			56	1	0	0	1	0	0	1	1	1	2	0	0	1	0	1	0	0	0	0	0	1	10
43	PA	REBOXETINE	-1	2	0	0	2	1	1	2	1	1	3	2	1	1	0	3	0	1	1	0	0	1	23
			0	2	0	0	2	1	1	2	1	1	3	2	1	1	0	3	0	1	1	0	0	1	23
			14	2	0	0	2	1	1	2	1	1	3	2	1	1	0	3	0	1	1	0	0	1	23
44	MZ	PLACEBO	-1	2	1	0	1	2	1	2	1	1	3	1	1	1	0	3	0	1	1	0	1	1	24
			0	2	1	0	1	2	1	2	1	1	3	1	1	1	0	3	0	1	1	0	1	1	24
			14	2	1	0	1	2	1	2	1	1	2	1	1	1	0	3	0	1	1	0	1	1	23
			28	2	0	0	1	2	1	2	1	1	2	1	1	1	0	2	0	1	0	0	0	1	19
			56	1	0	0	1	1	0	1	1	1	2	1	1	1	0	1	0	1	0	0	0	0	13
45	PG	REBOXETINE	-1	1	1	0	1	2	1	2	1	1	3	1	1	1	0	2	0	1	1	0	1	1	22
			0	1	1	0	1	2	1	2	1	1	3	1	1	1	0	2	0	1	1	0	1	1	22
			14	1	1	0	1	2	1	2	1	1	2	1	1	1	0	2	0	1	1	0	1	1	21
			28	1	1	0	1	2	1	2	1	1	2	1	1	1	0	2	0	1	0	0	1	1	20
46	AD	REBOXETINE	-1	2	2	0	1	0	1	2	1	2	3	1	1	1	1	2	0	0	1	0	0	1	22
			0	2	2	0	1	0	1	2	1	2	3	1	1	1	1	2	0	0	1	0	0	1	22

HAMD: It.1=Depressed (0-4) It.2=Guilt (0-4) It.3=Suicide(0-4) It.4=Insomnia Early (0-2)
It.5=Insomnia Middle (0-2) It.6=Insomnia Late (0-2) It.7=Work/Activities (0-4) It.8=Retardation (0-4)
It.9=Agitation (0-4) It.10=Anxiety Psychic (0-4) It.11=Anxiety Somatic (0-4) It.12=Gastroin. Symp. (0-2)
It.13=General Symp. (0-2) It.14=Genital Symp. (0-2) It.15=Hypocondriasis (0-4) It.16=Loss Weight A or B (0-3)
It.17=Insight (0-2) It.18=Diurnal Variation (0-2) It.19=Depersonalization (0-4) It.20=Paranoid Symp. (0-3)
It.21=Obsessional Symp. (0-2)

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

HAMILTON DEPRESSION RATING SCALE

Patient No.	Initials	Treatment	Visit No.	It.1	It.2	It.3	It.4	It.5	It.6	It.7	It.8	It.9	It.10	It.11	It.12	It.13	It.14	It.15	It.16	It.17	It.18	It.19	It.20	It.21	Total Score
46	AD	REBOXETINE	14	1	1	0	1	0	1	2	1	1	1	1	1	1	1	2	0	0	1	0	0	1	17
			28	1	0	0	0	0	1	1	0	1	1	1	1	1	1	1	0	0	0	0	0	1	11
47	SG	REBOXETINE	-1	1	2	0	0	2	1	2	2	1	2	1	1	1	0	3	0	1	0	0	1	1	22
			0	1	2	0	0	2	1	2	2	1	2	1	1	1	0	3	0	1	0	0	1	1	22
			14	1	2	0	0	1	1	2	2	1	2	1	1	1	0	2	0	1	0	0	1	1	20
			28	1	1	0	0	1	1	2	1	1	2	1	1	1	0	2	0	1	0	0	1	1	18
			56	1	1	0	1	0	0	2	1	1	2	1	1	1	0	2	0	1	0	0	1	1	17
48	FA	PLACEBO	-1	1	2	0	1	2	2	2	1	1	2	1	1	1	0	2	0	0	1	0	1	1	22
			0	1	2	0	1	2	2	2	1	1	2	1	1	1	0	2	0	0	1	0	1	1	22
			14	1	2	0	1	2	2	2	1	1	2	1	1	1	0	2	0	0	1	0	1	1	22
49	SA	PLACEBO	-1	3	1	0	1	2	2	2	2	1	3	2	1	1	0	3	0	1	1	0	0	1	27
			0	3	1	0	1	2	2	2	2	1	3	2	1	1	0	3	0	1	1	0	0	1	27
			14	2	1	0	1	1	1	1	1	0	2	2	1	1	0	2	0	1	1	0	0	1	19
			28	1	1	0	0	0	1	1	1	0	1	1	1	1	0	1	0	1	0	0	0	1	12
			56	1	0	0	0	0	1	1	1	0	1	1	1	1	0	1	0	1	0	0	0	1	11
50	ZZ	PLACEBO	-1	1	0	0	2	2	2	1	2	1	3	1	1	1	0	2	0	0	1	0	1	1	22
			0	1	0	0	2	2	2	1	2	1	3	1	1	1	0	2	0	0	1	0	1	1	22
			14	1	0	0	1	2	2	1	2	1	3	1	1	1	0	2	0	0	1	0	1	1	21
			28	1	0	0	1	2	2	1	2	1	3	1	2	1	0	2	0	0	1	0	1	1	22

HAMD: It.1=Depressed (0-4) It.2=Guilt (0-4) It.3=Suicide(0-4) It.4=Insomnia Early (0-2)
It.5=Insomnia Middle (0-2) It.6=Insomnia Late (0-2) It.7=Work/Activities (0-4) It.8=Retardation (0-4)
It.9=Agitation (0-4) It.10=Anxiety Psychic (0-4) It.11=Anxiety Somatic (0-4) It.12=Gastroin. Symp. (0-2)
It.13=General Symp. (0-2) It.14=Genital Symp. (0-2) It.15=Hypocondriasis (0-4) It.16=Loss Weight A or B (0-3)
It.17=Insight (0-2) It.18=Diurnal Variation (0-2) It.19=Depersonalization (0-4) It.20=Paranoid Symp. (0-3)
It.21=Obsessional Symp. (0-2)

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

MINI MENTAL STATE - SCAG - GDS

Patient No.	Initials	Treatment	Visit No.	Total Score Mini Mental State	Total Score GDS (YES + NO)	Total Score SCAG
1	TR	REBOXETINE	-1	21	.	.
			0	.	22	54
			14	.	22	54
			28	.	21	51
			56	21	21	46
2	FB	PLACEBO	-1	24	.	.
			0	.	21	57
			14	.	20	55
			28	.	11	32
			56	24	10	25
3	BI	PLACEBO	-1	22	.	.
			0	.	22	55
			14	.	16	45
			28	.	14	38
			56	23	14	33
4	PC	PLACEBO	-1	28	.	.
			0	.	26	68
			14	.	19	55
			28	.	18	46
			56	29	18	46
5	BL	REBOXETINE	-1	23	.	.
			0	.	23	54
			14	.	22	53
			28	.	21	52
			56	24	22	53
6	SM	REBOXETINE	-1	21	.	.
			0	.	20	51
			14	.	20	51
			21	.	20	49
			56	22	22	47
7	DA	PLACEBO	-1	22	.	.
			0	.	24	55
			14	.	24	53
			28	.	22	53
			56	22	23	52
8	SC	REBOXETINE	-1	21	.	.
			0	.	23	51
			14	.	22	49
			28	.	19	43
			56	21	18	42
9	PA	PLACEBO	-1	21	.	.
			0	.	20	54

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

MINI MENTAL STATE - SCAG - GDS

Patient No.	Initials	Treatment	Visit No.	Total Score Mini Mental State	Total Score GDS (YES + NO)	Total Score SCAG
9	PA	PLACEBO	14	.	17	43
			28	.	15	41
			56	21	15	40
10	PE	PLACEBO	-1	21	.	.
			0	.	21	50
			14	.	19	45
			28	.	17	43
11	CL	PLACEBO	-1	22	.	.
			0	.	24	62
			14	.	22	58
			28	.	21	55
			56	24	19	53
12	ML	PLACEBO	-1	21	.	.
			0	.	19	53
			14	.	20	54
			28	.	19	53
			56	21	19	50
13	DSC	REBOXETINE	-1	21	.	.
			0	.	20	54
			14	.	18	50
			28	.	19	51
			56	21	19	50
14	BM	REBOXETINE	-1	22	.	.
			0	.	18	55
			14	.	16	50
			28	.	14	46
			56	22	24	43
15	GI	REBOXETINE	-1	21	.	.
			0	.	17	54
16	PJ	REBOXETINE	-1	21	.	.
			0	.	21	55
			14	.	21	55
			28	.	18	49
			56	21	10	36
17	NM	REBOXETINE	-1	22	.	.
			0	.	20	54
			14	.	20	55
			28	.	20	53
			56	23	20	53
18	VM	REBOXETINE	-1	25	.	.
			0	.	18	55

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PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

MINI MENTAL STATE - SCAG - GDS

Patient No.	Initials	Treatment	Visit No.	Total Score Mini Mental State	Total Score GDS (YES + NO)	Total Score SCAG
18	VM	REBOXETINE	14	.	13	45
			28	.	13	41
			56	25	12	34
19	NI	PLACEBO	-1	21	.	.
			0	.	21	61
			14	.	22	60
			28	.	18	54
			56	21	16	51
20	BE	PLACEBO	-1	23	.	.
			0	.	19	56
			14	.	19	56
			28	.	20	55
			36	19	.	73
21	SE	REBOXETINE	-1	23	.	.
			0	.	20	53
			14	.	19	50
			28	.	19	56
22	BA	PLACEBO	-1	21	.	.
			0	.	19	61
			14	.	18	55
			28	.	18	54
			56	22	15	44
23	UT	REBOXETINE	-1	22	.	.
			0	.	21	57
			14	.	22	57
			28	.	22	54
			56	22	21	54
24	BEA	PLACEBO	-1	21	.	.
			0	.	21	60
			14	.	22	58
			28	.	20	54
			56	21	18	46
25	GA	REBOXETINE	-1	23	.	.
			0	.	21	62
			14	.	19	54
			28	.	18	52
			56	25	15	45
26	PR	REBOXETINE	-1	23	.	.
			0	.	19	61
27	GA	PLACEBO	-1	21	.	.
			0	.	18	59

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

MINI MENTAL STATE - SCAG - GDS

Patient No.	Initials	Treatment	Visit No.	Total Score Mini Mental State	Total Score GDS (YES + NO)	Total Score SCAG
27	GA	PLACEBO	14	.	19	59
			28	.	21	61
			56	20	21	59
28	MR	REBOXETINE	-1	21	.	.
			0	.	24	68
			14	.	21	62
			28	.	21	59
			56	22	18	55
29	TR	PLACEBO	-1	22	.	.
			0	.	24	63
			14	.	24	64
			28	.	23	62
			56	22	25	64
30	PA	REBOXETINE	-1	22	.	.
			0	.	19	59
			14	.	19	57
			28	.	17	55
			56	22	16	55
31	CC	PLACEBO	-1	22	.	.
			0	.	20	58
			14	.	18	50
			28	.	17	48
			56	22	16	47
32	CE	PLACEBO	-1	22	.	.
			0	.	17	51
			14	.	17	48
			28	.	16	45
			56	22	16	45
33	VA	PLACEBO	-1	21	.	.
			0	.	15	58
			14	.	15	56
			28	.	16	54
			56	21	16	48
34	BA	PLACEBO	-1	22	.	.
			0	.	20	55
35	SB	PLACEBO	-1	21	.	.
			0	.	18	63
			14	.	18	56
			28	.	15	51
			56	21	15	48
36	SM	REBOXETINE	-1	24	.	.

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

MINI MENTAL STATE - SCAG - GDS

Patient No.	Initials	Treatment	Visit No.	Total Score Mini Mental State	Total Score GDS (YES + NO)	Total Score SCAG
36	SM	REBOXETINE	0	.	25	61
			14	.	25	58
			28	.	20	55
			56	24	18	49
37	SE	REBOXETINE	-1	22	.	.
			0	.	15	53
			14	.	17	54
			28	.	15	51
			56	22	13	54
38	LO	PLACEBO	-1	23	.	.
			0	.	23	66
			14	.	23	63
			28	.	20	57
			56	23	18	46
39	CP	REBOXETINE	-1	21	.	.
			0	.	19	55
			14	.	20	57
			28	.	18	55
40	PO	REBOXETINE	-1	23	.	.
			0	.	20	62
			14	.	19	54
			28	.	16	44
			56	23	8	34
41	FE	PLACEBO	-1	21	.	.
			0	.	22	58
			14	.	21	58
			28	.	22	57
			56	21	22	57
42	LI	PLACEBO	-1	22	.	.
			0	.	20	64
			14	.	16	54
			28	.	16	48
			56	23	14	46
43	PA	REBOXETINE	-1	22	.	.
			0	.	20	60
			14	.	20	59
44	MZ	PLACEBO	-1	21	.	.
			0	.	25	62
			14	.	25	61
			28	.	23	58
			56	21	14	50

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PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

MINI MENTAL STATE - SCAG - GDS

Patient No.	Initials	Treatment	Visit No.	Total Score Mini Mental State	Total Score GDS (YES + NO)	Total Score SCAG
45	PG	REBOXETINE	-1	20	.	.
			0	.	19	59
			14	.	18	57
			28	.	19	56
46	AD	REBOXETINE	-1	25	.	.
			0	.	20	55
			14	.	20	50
			28	.	10	38
47	SG	REBOXETINE	-1	20	.	.
			0	.	20	63
			14	.	19	58
			28	.	18	52
			56	20	15	51
48	FA	PLACEBO	-1	20	.	.
			0	.	24	60
			14	.	22	57
49	SA	PLACEBO	-1	21	.	.
			0	.	25	68
			14	.	22	60
			28	.	14	45
			56	24	13	41
50	ZZ	PLACEBO	-1	21	.	.
			0	.	17	57
			14	.	17	58
			28	.	17	58

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CLINICAL GLOBAL IMPRESSION (CGI)

Patient No.	Initials	Treatment	Visit No.	Visit Date	Severity of Illness	Global Improvement	Efficacy Index
1	TR	REBOXETINE	0	04JUN91	Moderately ill	.	.
			14	18JUN91	Moderately ill	No change	1.00
			28	02JUL91	Moderately ill	Minimally improved	2.00
			56	30JUL91	Mildly ill	Much improved	3.00
2	FB	PLACEBO	0	04JUN91	Moderately ill	.	.
			14	18JUN91	Moderately ill	No change	1.00
			28	02JUL91	Borderline mentally ill	Much improved	3.00
			56	30JUL91	Borderline mentally ill	Much improved	4.00
3	BI	PLACEBO	0	04JUN91	Moderately ill	.	.
			14	18JUN91	Mildly ill	Much improved	3.00
			28	02JUL91	Mildly ill	Much improved	3.00
			56	30JUL91	Borderline mentally ill	Much improved	4.00
4	PC	PLACEBO	0	04JUN91	Markedly ill	.	.
			14	18JUN91	Moderately ill	Much improved	3.00
			28	02JUL91	Moderately ill	Much improved	3.00
			56	30JUL91	Moderately ill	Much improved	3.00
5	BL	REBOXETINE	0	04JUN91	Moderately ill	.	.
			14	18JUN91	Moderately ill	No change	1.00
			28	02JUL91	Moderately ill	No change	1.00
			56	30JUL91	Moderately ill	No change	1.00
6	SM	REBOXETINE	0	04JUN91	Mildly ill	.	.
			14	18JUN91	Mildly ill	No change	1.00
			21	25JUN91	Mildly ill	No change	1.00
			56	30JUL91	Mildly ill	Minimally improved	2.00
7	DA	PLACEBO	0	04JUN91	Moderately ill	.	.
			14	18JUN91	Moderately ill	No change	1.00
			28	02JUL91	Moderately ill	No change	1.00
			56	30JUL91	Moderately ill	No change	1.00
8	SC	REBOXETINE	0	04JUN91	Mildly ill	.	.
			14	18JUN91	Mildly ill	No change	1.00
			28	02JUL91	Mildly ill	Minimally improved	2.00
			56	30JUL91	Mildly ill	Minimally improved	2.00
9	PA	PLACEBO	0	04JUN91	Mildly ill	.	.
			14	18JUN91	Mildly ill	Much improved	3.00
			28	02JUL91	Mildly ill	Much improved	3.00
			56	30JUL91	Mildly ill	Much improved	3.00
10	PE	PLACEBO	0	04JUN91	Mildly ill	.	.
			14	18JUN91	Mildly ill	Minimally improved	2.00
			28	02JUL91	Mildly ill	Minimally improved	2.00

EFFICACY INDEX: computed from the vector activity by the vector side effects

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CLINICAL GLOBAL IMPRESSION (CGI)

Patient No.	Initials	Treatment	Visit No.	Visit Date	Severity of Illness	Global Improvement	Efficacy Index
11	CL	PLACEBO	0	04JUN91	Markedly ill	.	.
			14	18JUN91	Markedly ill	Minimally improved	2.00
			28	02JUL91	Markedly ill	Minimally improved	2.00
			56	30JUL91	Mildly ill	Much improved	3.00
12	ML	PLACEBO	0	08JUL91	Moderately ill	.	.
			14	22JUL91	Moderately ill	No change	1.00
			28	05AUG91	Moderately ill	No change	1.00
			56	02SEP91	Mildly ill	Minimally improved	3.00
13	DSC	REBOXETINE	0	08JUL91	Moderately ill	.	.
			14	22JUL91	Moderately ill	Minimally improved	2.00
			28	05AUG91	Moderately ill	Minimally improved	2.00
			56	02SEP91	Mildly ill	Minimally improved	3.00
14	BM	REBOXETINE	0	08JUL91	Moderately ill	.	.
			14	22JUL91	Mildly ill	Much improved	3.00
			28	05AUG91	Mildly ill	Much improved	3.00
			56	02SEP91	Mildly ill	Much improved	3.00
15	GI	REBOXETINE	0	08JUL91	Moderately ill	.	.
16	PJ	REBOXETINE	0	08JUL91	Moderately ill	.	.
			14	22JUL91	Moderately ill	No change	1.00
			28	05AUG91	Moderately ill	Minimally improved	2.00
			56	02SEP91	Borderline mentally ill	Much improved	4.00
17	MM	REBOXETINE	0	08JUL91	Moderately ill	.	.
			14	22JUL91	Moderately ill	No change	1.00
			28	05AUG91	Moderately ill	No change	1.00
			56	02SEP91	Moderately ill	No change	1.00
18	VM	REBOXETINE	0	08JUL91	Moderately ill	.	.
			14	22JUL91	Mildly ill	Much improved	3.00
			28	05AUG91	Mildly ill	Much improved	3.00
			56	02SEP91	Borderline mentally ill	Much improved	4.00
19	NI	PLACEBO	0	08JUL91	Moderately ill	.	.
			14	22JUL91	Moderately ill	No change	1.00
			28	05AUG91	Mildly ill	Much improved	3.00
			56	02SEP91	Mildly ill	Much improved	3.00
20	BE	PLACEBO	0	08JUL91	Moderately ill	.	.
			14	22JUL91	Moderately ill	No change	1.00
			28	05AUG91	Moderately ill	No change	1.00
			36	13AUG91	Moderately ill	No change	0.25
21	SE	REBOXETINE	0	10JUL91	Moderately ill	.	.

EFFICACY INDEX: computed from the vector activity by the vector side effects

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CLINICAL GLOBAL IMPRESSION (CGI)

Patient No.	Initials	Treatment	Visit No.	Visit Date	Severity of Illness	Global Improvement	Efficacy Index
21	SE	REBOXETINE	14	22JUL91	Moderately ill	Minimally improved	2.00
			28	05AUG91	Moderately ill	Minimally worse	1.00
22	BA	PLACEBO	0	09SEP91	Moderately ill	.	.
			14	23SEP91	Mildly ill	Minimally improved	2.00
			28	07OCT91	Moderately ill	Minimally improved	2.00
			56	04NOV91	Mildly ill	Much improved	3.00
23	UT	REBOXETINE	0	09SEP91	Moderately ill	.	.
			14	23SEP91	Moderately ill	No change	1.00
			28	07OCT91	Moderately ill	Minimally improved	2.00
			56	04NOV91	Moderately ill	Minimally improved	2.00
24	BEA	PLACEBO	0	09SEP91	Moderately ill	.	.
			14	23SEP91	Moderately ill	No change	1.00
			28	07OCT91	Moderately ill	Minimally improved	2.00
			56	04NOV91	Mildly ill	Much improved	3.00
25	GA	REBOXETINE	0	09SEP91	Moderately ill	.	.
			14	23SEP91	Mildly ill	Minimally improved	2.00
			28	07OCT91	Moderately ill	Much improved	3.00
			56	04NOV91	Mildly ill	Much improved	4.00
26	PR	REBOXETINE	0	09SEP91	Markedly ill	.	.
27	GA	PLACEBO	0	09SEP91	Moderately ill	.	.
			14	23SEP91	Moderately ill	No change	1.00
			28	07OCT91	Moderately ill	No change	1.00
			56	04NOV91	Moderately ill	No change	1.00
28	MR	REBOXETINE	0	09SEP91	Markedly ill	.	.
			14	23SEP91	Moderately ill	Much improved	3.00
			28	07OCT91	Mildly ill	Much improved	3.00
			56	04NOV91	Mildly ill	Much improved	3.00
29	TR	PLACEBO	0	09SEP91	Moderately ill	.	.
			14	23SEP91	Moderately ill	No change	1.00
			28	07OCT91	Moderately ill	No change	1.00
			56	04NOV91	Moderately ill	Minimally worse	1.00
30	PA	REBOXETINE	0	07OCT91	Moderately ill	.	.
			14	21OCT91	Moderately ill	No change	1.00
			28	04NOV91	Mildly ill	Minimally improved	2.00
			56	02DEC91	Mildly ill	No change	1.00
31	CC	PLACEBO	0	07OCT91	Moderately ill	.	.
			14	21OCT91	Mildly ill	Minimally improved	2.00
			28	04NOV91	Mildly ill	Much improved	3.00

EFFICACY INDEX: computed from the vector activity by the vector side effects

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CLINICAL GLOBAL IMPRESSION (CGI)

Patient No.	Initials	Treatment	Visit No.	Visit Date	Severity of Illness	Global Improvement	Efficacy Index
31	CC	PLACEBO	56	02DEC91	Mildly ill	Much improved	3.00
32	CE	PLACEBO	0	09SEP91	Moderately ill	.	.
			14	23SEP91	Moderately ill	No change	1.00
			28	07OCT91	Moderately ill	Minimally improved	2.00
			56	04NOV91	Moderately ill	Minimally improved	2.00
33	VA	PLACEBO	0	07OCT91	Moderately ill	.	.
			14	21OCT91	Moderately ill	No change	1.00
			28	04NOV91	Moderately ill	No change	1.00
			56	02DEC91	Mildly ill	Much improved	3.00
34	BA	PLACEBO	0	07OCT91	Moderately ill	.	.
35	SB	PLACEBO	0	07OCT91	Moderately ill	.	.
			14	21OCT91	Moderately ill	No change	2.00
			28	04NOV91	Mildly ill	Much improved	3.00
			56	02DEC91	Mildly ill	Much improved	3.00
36	SM	REBOXETINE	0	07OCT91	Markedly ill	.	.
			14	21OCT91	Markedly ill	No change	1.00
			28	04NOV91	Moderately ill	Minimally improved	2.00
			56	02DEC91	Borderline mentally ill	Much improved	3.00
37	SE	REBOXETINE	0	07OCT91	Moderately ill	.	.
			14	21OCT91	Moderately ill	No change	1.00
			28	04NOV91	Moderately ill	Minimally improved	2.00
			56	02DEC91	Moderately ill	No change	1.00
38	LO	PLACEBO	0	07OCT91	Markedly ill	.	.
			14	21OCT91	Markedly ill	No change	1.00
			56	02DEC91	Borderline mentally ill	Much improved	4.00
39	CP	REBOXETINE	0	07OCT91	Moderately ill	.	.
			14	21OCT91	Moderately ill	No change	1.00
			28	04NOV91	Moderately ill	No change	1.00
40	PD	REBOXETINE	0	08NOV91	Moderately ill	.	.
			14	22NOV91	Mildly ill	Much improved	3.00
			28	06DEC91	Borderline mentally ill	Much improved	3.00
			56	03JAN92	Borderline mentally ill	Very much improved	4.00
41	FE	PLACEBO	0	08NOV91	Moderately ill	.	.
			14	22NOV91	Moderately ill	No change	1.00
			28	06DEC91	Moderately ill	No change	1.00
			56	03JAN92	Moderately ill	No change	1.00
42	LI	PLACEBO	0	08NOV91	Moderately ill	.	.

EFFICACY INDEX: computed from the vector activity by the vector side effects

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CLINICAL GLOBAL IMPRESSION (CGI)

Patient No.	Initials	Treatment	Visit No.	Visit Date	Severity of Illness	Global Improvement	Efficacy Index
42	LI	PLACEBO	14	22NOV91	Moderately ill	Minimally improved	2.00
			28	06DEC91	Mildly ill	Much improved	3.00
			56	03JAN92	Borderline mentally ill	Much improved	3.00
43	PA	REBOXETINE	0	08NOV91	Moderately ill	.	.
			14	22NOV91	Moderately ill	No change	1.00
44	MZ	PLACEBO	0	08NOV91	Moderately ill	.	.
			14	22NOV91	Moderately ill	No change	1.00
			28	06DEC91	Moderately ill	Minimally improved	2.00
			56	03JAN92	Mildly ill	Much improved	3.00
45	PG	REBOXETINE	0	08NOV91	Moderately ill	.	.
			14	22NOV91	Moderately ill	No change	1.00
			28	06DEC91	Moderately ill	No change	1.00
46	AD	REBOXETINE	0	08NOV91	Moderately ill	.	.
			14	22NOV91	Moderately ill	Minimally improved	2.00
			28	06DEC91	Borderline mentally ill	Much improved	3.00
47	SG	REBOXETINE	0	08NOV91	Moderately ill	.	.
			14	22NOV91	Moderately ill	Minimally improved	2.00
			28	06DEC91	Moderately ill	Minimally improved	2.00
			56	03JAN92	Moderately ill	Minimally improved	2.00
48	FA	PLACEBO	0	08NOV91	Moderately ill	.	.
			14	22NOV91	Moderately ill	No change	1.00
49	SA	PLACEBO	0	08NOV91	Markedly ill	.	.
			14	22NOV91	Moderately ill	Minimally improved	2.00
			28	06DEC91	Mildly ill	Much improved	3.00
			56	03JAN92	Mildly ill	Much improved	3.00
50	ZZ	PLACEBO	0	08NOV91	Moderately ill	.	.
			14	20NOV91	Moderately ill	No change	1.00
			28	06DEC91	Moderately ill	No change	0.33

EFFICACY INDEX: computed from the vector activity by the vector side effects

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

ADVERSE EVENTS

Patient No.=15 Initials=GI Treatment=REBOXETINE

Adverse Event Verbatim	Report	Onset Date	End Date	Severity	Source	Frequency	No. of Days	History	Hospit.	Study Drug	No. of Days	Other Act.	Code Opened	Dechall./ Rechall.	Predisp. Cond.	Relat to Study Med.	Outco
HEARTBURN	1	11JUL91	14JUL91	1	2	3	.	2	3	1	.	2	NO	N.A./N.A.	3	3	1
VOMITING	1	14JUL91	14JUL91	1	2	1	.	2	3	1	.	2	NO	N.A./N.A.	3	3	1
SYNDROME OF INAPPROPRIATE SECRETION OF ADH	.	16JUL91	.	3	1	2	.	2	3	3	.	.	NO	NO/N.A.	1	5	3

Patient No.=20 Initials=BE Treatment=PLACEBO

Adverse Event Verbatim	Report	Onset Date	End Date	Severity	Source	Frequency	No. of Days	History	Hospit.	Study Drug	No. of Days	Other Act.	Code Opened	Dechall./ Rechall.	Predisp. Cond.	Relat to Study Med.	Outcome
AGITATION	1	12AUG91	.	3	1	1	.	2	3	3	.	2	NO	N.A./N.A.	1	2	3

Patient No.=21 Initials=SE Treatment=REBOXETINE

Adverse Event Verbatim	Report	Onset Date	End Date	Severity	Source	Frequency	No. of Days	History	Hospit.	Study Drug	No. of Days	Other Act.	Code Opened	Dechall./ Rechall.	Predisp. Cond.	Relat to Study Med.	Outcome
ANXIETY	1	09AUG91	10AUG91	3	2	2	.	1	3	3	.	2	NO	YES/N.A.	2	3	1
HYPOCHONDRIASIS	1	09AUG91	10AUG91	3	2	2	.	1	3	3	.	2	NO	YES/N.A.	4	3	1

Patient No.=28 Initials=MR Treatment=REBOXETINE

Adverse Event Verbatim	Report	Onset Date	End Date	Severity	Source	Frequency	No. of Days	History	Hospit.	Study Drug	No. of Days	Other Act.	Code Opened	Dechall./ Rechall.	Predisp. Cond.	Relat to Study Med.	Outcome
HYPERTENSION	1	22SEP91	22SEP91	2	2	1	.	2	3	1	.	2	NO	N.A./N.A.	1	4	1
AGITATION	1	01OCT91	.	2	2	1	.	2	1	4	4	.	NO	NO/N.A.	1	4	2
EXCITEMENT	1	01OCT91	.	2	2	1	.	2	3	4	4	.	NO	NO/N.A.	1	4	3

Patient No.=33 Initials=VA Treatment=PLACEBO

Adverse Event Verbatim	Report	Onset Date	End Date	Severity	Source	Frequency	No. of Days	History	Hospit.	Study Drug	No. of Days	Other Act.	Code Opened	Dechall./ Rechall.	Predisp. Cond.	Relat to Study Med.	Outcome
VERTIGO	1	19NOV91	.	1	1	3	4	3	3	2	.	.	NO	YES/N.A.	1	2	3

REPORT: 1=spontaneously 2=non-leading question 3=check list SEVERITY: 1=mild 2=moderate 3=severe 4=unknown
SOURCE: 1=physician 2=patient 3=other FREQUENCY: 1=single episode 2=continuous 3=multiple episode
HISTORY: 1=observed before 2=not observed before 3=unknown HOSPITALIZATION: 1=required 2=not required 3=not applicable
STUDY DRUG: 1=no change 2=dose reduced 3=definitively withdrawn 4=temporaly interrupted
OTHER ACTION: 1=discontinuation of other medication 2=symptomatic treatment
PREDISPOSING CONDITIONS: 1=no 2=yes 3=gastrite cronica 4=trattasi di soggetto anziano
RELATIONSHIP: 1=definite 2=probable 3=possible 4=doubtful 5=unknown 6=none
OUTCOME: 1=recovered 2=recovered with sequelae 3=still present 4=death

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

ADVERSE EVENTS

Patient No.=34 Initials=BA Treatment=PLACEBO

Adverse Event Verbatim	Report	Onset Date	End Date	Severity	Source	Frequency	No. of Days	History	Hospit.	Study Drug	No. of Days	Other Act.	Code Opened	Dechall./ Rechall.	Predisp. Cond.	Relat to Study Med.	Outcome
ASTHENIA	1	09OCT91	10OCT91	3	2	1	.	2	3	2	.	.	NO	YES/YES	1	1	1

Patient No.=43 Initials=PA Treatment=REBOXETINE

Adverse Event Verbatim	Report	Onset Date	End Date	Severity	Source	Frequency	No. of Days	History	Hospit.	Study Drug	No. of Days	Other Act.	Code Opened	Dechall./ Rechall.	Predisp. Cond.	Relat to Study Med.	Outcom
FACIAL LEFT PARESTHESIA	1	25NOV91	.	1	2	2	.	2	3	4	.	.	NO	NO/N.A.	1	3	3
HYPERTENSION	1	01DEC91	03DEC91	3	2	1	.	2	3	3	.	2	NO	N.A./N.A.	1	3	1

Patient No.=50 Initials=ZZ Treatment=PLACEBO

Adverse Event Verbatim	Report	Onset Date	End Date	Severity	Source	Frequency	No. of Days	History	Hospit.	Study Drug	No. of Days	Other Act.	Code Opened	Dechall./ Rechall.	Predisp. Cond.	Relat to Study Med.	Outco
ABDOMINAL PAIN DYSPEPSIA	1	04DEC91	.	2	2	2	.	2	3	3	.	.	NO	N.A./N.A.	1	3	3
DYSPEPSIA	1	04DEC91	.	2	2	2	.	2	3	3	.	.	NO	N.A./N.A.	1	3	3

REPORT: 1=spontaneously 2=non-leading question 3=check list SEVERITY: 1=mild 2=moderate 3=severe 4=unknown
SOURCE: 1=physician 2=patient 3=other FREQUENCY: 1=single episode 2=continuous 3=multiple episode
HISTORY: 1=observed before 2=not observed before 3=unknown HOSPITALIZATION: 1=required 2=not required 3=not applicable
STUDY DRUG: 1=no change 2=dose reduced 3=definitively withdrawn 4=temporaly interrupted
OTHER ACTION: 1=discontinuation of other medication 2=symptomatic treatment
PREDISPOSING CONDITIONS: 1=no 2=yes 3=gastrite cronica 4=trattasi di soggetto anziano
RELATIONSHIP: 1=definite 2=probable 3=possible 4=doubtful 5=unknown 6=none
OUTCOME: 1=recovered 2=recovered with sequelae 3=still present 4=death

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

LABORATORY NORMAL RANGES

SEX=F

TEST	MIN	MAX	UNIT
LDH	160.00	320.00	UI/L
SGOT	1.00	30.00	UI/L
SGPT	1.00	35.00	UI/L
GAMMA-GT	1.00	35.00	UI/L
TOTAL BILIRUBIN	1.71	17.10	MCMOL/L
DIRECT BILIRUBIN	1.71	6.84	MCMOL/L
ALKALINE PHOSPHATASE	30.00	100.00	UI/L
TOTAL PROTEIN	62.00	80.00	G/L
BLOOD ALBUMIN	55.00	68.00	%
GLOBULINS ALFA 1	1.50	5.00	%
GLOBULINS ALFA 2	7.00	12.00	%
GLOBULINS BETA	9.00	15.00	%
GLOBULINS GAMMA	12.00	20.00	%
BLOOD SUGAR	3.33	6.10	MMOL/L
BUN	1.66	8.32	MCMOL/L
CREATININE	53.00	106.00	MCMOL/L
CREATININE CLEARANCE	100.00	150.00	ML/M
URIC ACID	0.14	0.34	MMOL/L
NA+	135.00	150.00	MMOL/L
K+	3.50	5.30	MMOL/L
CL-	96.00	112.00	MMOL/L
POS	0.80	1.61	MMOL/L
CA++	2.12	2.61	MMOL/L
CHOLESTEROL	5.18	6.19	MMOL/L
TRIGLYCERIDES	0.57	2.85	MMOL/L
T4	4.50	12.00	MCG/DL
TSH	0.45	6.20	MCUI/ML
HB	12.00	16.00	G/DL
HCT	37.00	47.00	%
RBC	4.20	5.40	MLN/CL
WBC	4.80	10.80	TSD/CL
NEUTROPHILS	40.00	74.00	%
LYMPHOCYTES	19.00	48.00	%
MONOCYTES	3.40	9.00	%
EOSINOPHILS	0.00	7.00	%
BASOPHILS	0.00	1.50	%
PLATELETS	130.00	400.00	TSD/CL

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PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

LABORATORY NORMAL RANGES

SEX=M

TEST	MIN	MAX	UNIT
LDH	160.00	320.00	UI/L
SGOT	1.00	30.00	UI/L
SGPT	1.00	35.00	UI/L
GAMMA-GT	1.00	50.00	UI/L
TOTAL BILIRUBIN	1.71	17.10	MCMOL/L
DIRECT BILIRUBIN	1.71	6.84	MCMOL/L
ALKALINE PHOSPHATASE	30.00	100.00	UI/L
TOTAL PROTEIN	62.00	80.00	G/L
BLOOD ALBUMIN	55.00	68.00	%
GLOBULINS ALFA 1	1.69	5.08	%
GLOBULINS ALFA 2	7.00	12.00	%
GLOBULINS BETA	9.00	13.00	%
GLOBULINS GAMMA	12.00	20.00	%
BLOOD SUGAR	3.33	6.10	MMOL/L
BUN	1.66	8.32	MCMOL/L
CREATININE	61.80	132.60	MCMOL/L
CREATININE CLEARANCE	100.00	150.00	ML/M
URIC ACID	0.20	0.41	MMOL/L
NA+	135.00	150.00	MMOL/L
K+	3.50	5.30	MMOL/L
CL-	96.00	112.00	MMOL/L
PO4	0.80	1.61	MMOL/L
CA++	2.12	2.61	MMOL/L
CHOLESTEROL	5.18	6.19	MMOL/L
TRIGLYCERIDES	0.57	2.85	MMOL/L
T4	4.50	12.00	MCG/DL
TSH	0.45	6.20	MCUI/ML
HB	14.00	18.00	G/DL
HCT	42.00	52.00	%
RBC	4.70	6.10	MLN/CL
WBC	4.80	10.80	TSD/CL
NEUTROPHILS	40.00	74.00	%
LYMPHOCYTES	19.80	48.00	%
MONOCYTES	3.40	9.00	%
EOSINOPHILS	0.00	7.00	%
BASOPHILS	0.00	1.50	%
PLATELETS	130.00	400.00	TSD/CL

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CHEMISTRY (1)

PATIENT NO.=1 INITIALS=TR TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	20MAY91	251	7	11	15	5	2.6	81	51.7 (L)	64.7	2.2	10.4	11.2	11.5 (L)
28	02JUL91	246	9	21	18	4.8	1.8	89	50.4 (L)	66.7	1.9	9.7	10.5	11.2 (L)
56	30JUL91	241	7	14	14	6.4	3.4	79	51.7 (L)	65	2.2	10.9	11.4	10.5 (L)

PATIENT NO.=2 INITIALS=FB TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	25MAY91	296	15	13	9	15	9.2 (U)	54	58.6 (L)	65.9	2	7.2	10.5	14.4
28	02JUL91	291	14	15	12	10.3	4.5	62	53 (L)	64.4	1.7	7.4	10	16.5
56	30JUL91	293	15	17	12	12.6	7.4 (U)	57	51.7 (L)	63.6	2.1	7.9	11.5	14.9

PATIENT NO.=3 INITIALS=BI TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	25MAY91	353 (U)	15	12	18	6.7	3.1	62	63.6	62.4	1.9	9	10.5	16.2
28	02JUL91	345 (U)	16	14	22	5.9	2.3	59	55.1 (L)	61.5	2	9.5	11.1	15.9
56	30JUL91	496 (U)	20	14	21	5.4	1.6 (L)	60	58.9 (L)	61.6	1.8	10.5	10.7	15.4

PATIENT NO.=4 INITIALS=PC TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	25MAY91	263	9	5	17	5	3	97	53.5 (L)	64.2	2.9	11.2	11.9	9.8 (L)
28	02JUL91	314	9	8	47 (U)	5.6	2.6	117 (U)	55.5 (L)	66.2	2.1	9.8	11.4	10.5 (L)
56	30JUL91	306	12	7	30	4.7	2.8	112 (U)	56.8 (L)	66	2.2	10.3	11	10.3 (L)

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CHEMISTRY (1)

PATIENT NO.=5 INITIALS=BL TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	25MAY91	246	8	9	18	4.7	2.3	70	62	52.3 (L)	2.5	11.2	12.1	21.9 (U)
28	02JUL91	235	7	11	27	4.1	1.8	81	62.3	50 (L)	3.3	11.5	13.1 (U)	22.1 (U)
56	30JUL91	310	9	9	25	2.6	1.6 (L)	76	57.2 (L)	49.4 (L)	3.2	11.9	13.7 (U)	21.8 (U)

PATIENT NO.=6 INITIALS=SM TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	29MAY91	351 (U)	16	17	49 (U)	5.2	2	79	60.8 (L)	55.2	4.3	13.6 (U)	14.8 (U)	12.1
28	02JUL91	340 (U)	17	19	49 (U)	4.8	1.8	94	61.6 (L)	58	2.6	10.5	15.1 (U)	13.8
56	30JUL91	390 (U)	17	18	48 (U)	4.8	2.3	73	56.2 (L)	58.3	2.8	11	14.9 (U)	13

PATIENT NO.=7 INITIALS=DA TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	04JUN91	345 (U)	14	19	20	3.9	2	194 (U)	63.2	51.4 (L)	3.2	11.6	14.1 (U)	19.7
28	02JUL91	342 (U)	16	9	12	6.5	2.6	124 (U)	65	53.3 (L)	2	9.6	12.1	23 (U)
56	30JUL91	471 (U)	20	11	12	5	1.7 (L)	108 (U)	59.4 (L)	54.5 (L)	2.5	10	14.1 (U)	18.9

PATIENT NO.=8 INITIALS=SC TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	25MAY91	268	11	16	40 (U)	5.8	3.6	76	59.6 (L)	53.6 (L)	3.4	14.3 (U)	12.8	16.1
28	02JUL91	328 (U)	19	25	121 (U)	6.3	3.9	83	56.4 (L)	58.2	3.1	11.7	11.8	15.2
56	30JUL91	292	35 (U)	74 (U)	64 (U)	4.4	3.4	64	53.7 (L)	63.9	2.3	10.4	10.9	12.5

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CHEMISTRY (1)

PATIENT NO.=9 INITIALS=PA TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	25MAY91	218	11	22	19	6.1	3	92	64.8	49.3 (L)	3.9	14.5 (U)	12.3	20
28	02JUL91	300	22	16	22	3.5	1.4 (L)	102 (U)	63.8	54 (L)	2.7	11.7	11.5	20.1 (U)
56	30JUL91	326 (U)	26	29	25	5.6	3.6	110 (U)	63.3	57	2.4	10.8	11.3	18.5

PATIENT NO.=10 INITIALS=PE TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	30MAY91	185	8	9	19	11.5	4.02	79	66.1	53.6 (L)	2.9	14.5 (U)	10	19.2
28	02JUL91	246	18	24	65 (U)	6	3.4	81	64.5	47.4 (L)	3.7	18.3 (U)	10.2	20.4 (U)
56	12JUL91	252	23	36 (U)	114 (U)	6.1	3.4	93	65.8	46.4 (L)	3.6	18.4 (U)	10.2	21.4 (U)

PATIENT NO.=11 INITIALS=CL TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	06JUN91	462 (U)	24	16	19	8.4	1.8	213 (U)	62.3	52.4 (L)	3.1	12.6 (U)	13.2 (U)	18.7
28	02JUL91	409 (U)	22	26	22	3.6	1.9	222 (U)	65.6	54.3 (L)	2.7	11.4	13.3 (U)	18.3
56	30JUL91	491 (U)	24	23	24	3	1.6 (L)	170 (U)	68.4 (L)	55.9	2.5	10.6	13.1 (U)	17.9

PATIENT NO.=12 INITIALS=ML TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	01JUL91	368 (U)	14	11	27	6.7	1.9	95	70	56.5	2.3	10.3	12	18.9
28	05AUG91	309	15	11	35	5.3	1.5 (L)	88	64.7	58.1	2.1	10.1	12.1	17.6
56	02SEP91	345 (U)	18	18	41 (U)	4.6	1.1 (L)	97	61.5 (L)	57.9	2.5	10.1	12	17.5

U = above the upper limit of normal range
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ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CHEMISTRY (1)

PATIENT NO.=13 INITIALS=DSC TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	03JUL91	333 (U)	24	34	51 (U)	9.9	5.2	113 (U)	71.1	64.3	1.7	9.3	7.7 (L)	17
28	05AUG91	356 (U)	26	38 (U)	64 (U)	9.4	4	105 (U)	77	63.2	1.5	9.1	8.1 (L)	18.1
56	02SEP91	362 (U)	24	39 (U)	70 (U)	8.1	3.9	102 (U)	73.8	63.4	2	9.1	8.4 (L)	17.1

PATIENT NO.=14 INITIALS=BM TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	01JUL91	288	16	50 (U)	301 (U)	5.3	1.8	314 (U)	66.7	59.3 (L)	4.1	15.5 (U)	14.1 (U)	16
28	05AUG91	248	16	24	274 (U)	4	2.4	174 (U)	71	56.1	2.8	10.5	13.5 (U)	17.1
56	02SEP91	303	16	25	224 (U)	5.4	2.2	136 (U)	61.4 (L)	58.4	2.4	9.4	12.2	17.6

PATIENT NO.=15 INITIALS=GI TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	04JUL91	465 (U)	22	15	22	16.5	9.4 (U)	66	58.6 (L)	68.6 (U)	1.8	6.1 (L)	11.7	11.6 (L)
8	16JUL91	482 (U)	26	16	24	30.7 (U)	22.3 (U)	110 (U)	61 (L)	67.1	2.7	9.2	12.1	8.9 (L)

PATIENT NO.=16 INITIALS=PJ TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	03JUL91	392 (U)	25	28	46 (U)	21.9 (U)	10.7 (U)	55	59.3 (L)	70.8 (U)	1.6	8.4	8.4 (L)	10.8 (L)
28	05AUG91	360 (U)	21	27	55 (U)	12.5	6.1	76	63.8	64.8	3.1	10.9	10.1	11.1 (L)
56	02SEP91	364 (U)	16	19	39 (U)	16.5	7.3 (U)	68	60.9 (L)	65.6	2	9.6	9.4	13.4

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ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CHEMISTRY (1)

PATIENT NO.=17 INITIALS=MM TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	04JUL91	551 (U)	13	10	17	7.1	2.4	100	59 (L)	59.4	2.4	6.5	12	17.7
28	05AUG91	494 (U)	20	21	19	6	3.1	103 (U)	62.7	62.6	2.1	7.6	10.3	17.4
56	02SEP91	512 (U)	21	19	19	4.1	1.9	98	61.4 (L)	59.5	2.2	8.5	11.4	18.4

PATIENT NO.=18 INITIALS=VM TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	02JUL91	304	13	17	26	9.5	4	89	62.2	61.9	1.9	8.1	10	18.1
28	05AUG91	462 (U)	18	14	17	7.7	1.1 (L)	84	59.5	60.5	2.4	8	10.4	18.7
56	02SEP91	318	15	13	22	8.7	3.7	77	61.8 (L)	62.1	2	7.9	9.6	18.4

PATIENT NO.=19 INITIALS=NI TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	05JUL91	468 (U)	54 (U)	54 (U)	43 (U)	9.8	5.6	131 (U)	66	58.3	2.3	7.3	9.7	22.4 (U)
28	05AUG91	399 (U)	33 (U)	26	39 (U)	8.7	4.9	120 (U)	66.7	57.2	2.1	7.8	9.6	23.3 (U)
56	02SEP91	466 (U)	31 (U)	28	41 (U)	6.2	3	115 (U)	66.9	56.8	2.5	7.5	9.5	23.6 (U)

PATIENT NO.=20 INITIALS=BE TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	04JUL91	313	19	17	33	12.9	5.7	82	75.6	60.6	3	8.7	12.7	15
28	05AUG91	265	20	15	25	13.6	5.4	74	61 (L)	64.8	2.3	8.6	10.2	14.1
36	13AUG91	254	17	14	23	12.7	5.3	75	59.7 (L)	63.2	2.6	8.6	9.5	16.1

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PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CHEMISTRY (1)

PATIENT NO.=21 INITIALS=SE TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	06JUL91	302	21	24	33	13.9	6.1	84	57.4 (L)	62.5	2.8	10.9	10.4	13.4
28	05AUG91	286	22	29	30	14.4	6.9 (U)	76	64.4	63.7	2.3	10.2	11	12.8

PATIENT NO.=22 INITIALS=BA TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	31AUG91	408 (U)	19	20	15	8.1	1.7 (L)	77	61.6 (L)	62.4	1.7	9.7	9.3	16.9
28	07OCT91	337 (U)	16	15	11	7.2	3.3	67	57.9 (L)	57.7	2.5	10.5	10.7	18.6
56	04NOV91	272	13	12	10	8.5	4.4	59	56.9 (L)	60.3	2.4	9.4	10.9	17

PATIENT NO.=23 INITIALS=UT TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	13AUG91	423 (U)	15	12	15	6.5	3.7	90	63.7	61.8	1.7	9.2	9.2	18.1
28	07OCT91	377 (U)	30	41 (U)	18	6.2	2.4	121 (U)	64.7	57.5	2	9.7	12.3	18.5
56	04NOV91	310	20	21	17	5.6	3	114 (U)	62.9	55.9	2.6	9.1	13.8 (U)	18.6

PATIENT NO.=24 INITIALS=BEA TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	31AUG91	372 (U)	20	23	20	7.8	4.3	356 (U)	75.7	53.5 (L)	2.6	11.7	11	21.2 (U)
28	07OCT91	305	14	8	14	6.8	3.1	316 (U)	64.2	53.4 (L)	2.7	10.5	10.6	22.8 (U)
56	04NOV91	259	13	5	15	6.2	3.7	278 (U)	66.5	52.3 (L)	3	10.6	12.2	21.9 (U)

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PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CHEMISTRY (1)

PATIENT NO.=25 INITIALS=GA TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	31AUG91	386 (U)	17	13	43 (U)	6.9	2.6	94	64.8	62.1	2.1	8.2	10.1	17.5
28	07OCT91	410 (U)	16	13	38 (U)	5.2	1.6 (L)	107 (U)	62.3	58.6	2.7	9.2	12.4	17.1
56	04NOV91	294	14	13	34	6.9	3.2	106 (U)	62.6	57.3	2.9	9.1	13.7 (U)	17

PATIENT NO.=26 INITIALS=FR TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	31AUG91	298	13	15	20	5.5	1.7 (L)	74	60.8 (L)	62.5	2.9	9.2	9.5	15.9

PATIENT NO.=27 INITIALS=GA TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	31AUG91	440 (U)	16	15	28	11.7	4.7	81	61.1 (L)	61.3	1.2 (L)	11.4	10.1	16
28	07OCT91	392 (U)	15	13	23	8.6	3.9	88	57.3 (L)	56.4	2	13.8 (U)	14 (U)	13.8
56	04NOV91	395 (U)	19	9	17	6.7	0.8 (L)	96	61.8 (L)	52.6 (L)	2.4	14.9 (U)	14.5 (U)	15.6

PATIENT NO.=28 INITIALS=MR TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	31AUG91	600 (U)	46 (U)	27	24	13.3	7.1 (U)	95	64	62.7	2.6	9.6	9.7	15.4
28	07OCT91	536 (U)	25	23	19	13.6	6.8	98	62	63.1	2.7	8.1	9.9	16.2
56	04NOV91	351 (U)	19	17	26	10.8	5.2	95	67	59.9	2.9	8.6	12	16.6

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L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CHEMISTRY (1)

PATIENT NO.=29 INITIALS=TR TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	31AUG91	279	14	10	10	8.9	4.4	79	64.1	60.9	3.2	10.7	9.1	16.1
28	07OCT91	368 (U)	14	6	6	6.2	1 (L)	85	61.2 (L)	62.1	2.1	8.9	11.3	15.6
56	04NOV91	288	11	6	8	5.2	2.9	86	60.7 (L)	57.2	3	9.5	13.8 (U)	16.5

PATIENT NO.=30 INITIALS=PA TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	09SEP91	343 (U)	14	16	13	9.3	4.8	99	61.4 (L)	63.1	2.5	8	9.9	16.5
28	04NOV91	401 (U)	19	13	9	8.8	1.6 (L)	92	58.5 (L)	63.2	2.7	9.8	9.7	14.6
56	02DEC91	377 (U)	14	9	11	12.7	5.1	106 (U)	67	61.3	3.2	8.2	11.7	15.6

PATIENT NO.=31 INITIALS=CC TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	04OCT91	318	16	12	10	5.2	2.8	95	68.5	60.5	2.5	8.7	8.1 (L)	20.2 (U)
28	04NOV91	308	17	15	12	9.4	5.2	98	65.5	57.2	2.6	9.6	9.8	20.8 (U)
56	02DEC91	416 (U)	23	15	8	6.8	1.6 (L)	102 (U)	69.1	55.7	2.7	9.5	10.3	21.8 (U)

PATIENT NO.=32 INITIALS=CE TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	05SEP91	381 (U)	17	19	32	5.8	3	74	63.6	57.8	2.8	12	13.7 (U)	13.7
28	07OCT91	395 (U)	16	16	44 (U)	7.8	4.1	85	68.6	54.8 (L)	2.9	13.3 (U)	16.2 (U)	12.8
56	04NOV91	343 (U)	16	14	32	7	3.7	76	67.8	55.6	2.8	13.5 (U)	15.8 (U)	12.9

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CHEMISTRY (1)

PATIENT NO.=33 INITIALS=VA TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	02OCT91	188	19	27	32	8.5	4.5	91	60.2 (L)	66.4	2.3	10.7	9.8	10.8 (L)
28	04NOV91	154 (L)	12	17	29	10.9	5.5	75	60.9 (L)	64.4	2.5	10.8	10.5	11.8 (L)
56	02DEC91	191	10	16	25	8.3	4.9	86	64.1	57.9	3.5	12.8 (U)	12.8	13

PATIENT NO.=34 INITIALS=BA TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	01OCT91	355 (U)	23	25	20	10.2	5.3	74	70.1	53.8 (L)	2.8	12.2 (U)	13.9 (U)	17.3

PATIENT NO.=35 INITIALS=SB TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	04OCT91	257	13	13	17	7.5	3.9	51	67.1	60.3	2.2	10.4	11.9	15.2
28	04NOV91	218	10	8	16	12.4	5.5	52	59.6 (L)	55.7	2.5	11	14.3 (U)	16.5
56	02DEC91	241	11	11	17	5.5	3.5	49	62.9	56.9	2.5	10.4	13.2 (U)	17

PATIENT NO.=36 INITIALS=SM TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	02OCT91	329 (U)	15	11	14	10.3	3.6	100	69.8	62	2	8.6	10.8	16.6
28	04NOV91	338 (U)	30	58 (U)	33	10.19	2.2	100	66.1	57.9	2.6	9.6	12.7	17.2
56	02DEC91	290	15	17	22	11.1	5.1	88	72.6	54.2 (L)	2.8	8.7	13.1 (U)	21.3 (U)

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CHEMISTRY (1)

PATIENT NO.=37 INITIALS=SE TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	01OCT91	373 (U)	14	13	13	5.9	3.2	91	61.3 (L)	57	3.7	8.6	8.7 (L)	22 (U)
28	04NOV91	322 (U)	14	13	14	4.8	2.6	100	64.5	48.6 (L)	4.6	9.3	9.9	27.6 (U)
56	02DEC91	323 (U)	12	16	16	8.1	4.5	122 (U)	69.7	56.6	3.9	7.2	10.5	21.8 (U)

PATIENT NO.=38 INITIALS=LD TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	01OCT91	353 (U)	16	23	19	4.9	2.9	90	68.3	64.6	1.8	8.5	11	14.1
28	04NOV91	269	14	21	15	6.7	3.2	78	60.7 (L)	62.5	1.7	9.9	11.5	14.4
56	02DEC91	319	15	22	14	5.9	2.5	77	62.8	62	1.9	9.1	11.5	15.5

PATIENT NO.=39 INITIALS=CP TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	08OCT91	349 (U)	22	32	112 (U)	16.8	9.1 (U)	84	71.1	62.9	2.2	8.1	10	16.8
28	04NOV91	285	18	22	107 (U)	12	6.7	90	60.9 (L)	59	4.2	8.3	11	16.8

PATIENT NO.=40 INITIALS=PD TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	02NOV91	483 (U)	17	15	22	19 (U)	9.8 (U)	85	68	49.5 (L)	3.4	10.1	13.2 (U)	24 (U)
28	06DEC91	336 (U)	15	12	13	23.2 (U)	11.6 (U)	88	69.4	52.6 (L)	2.7	10.3	11.8	22.6 (U)
56	03JAN92	318	21	15	19	10	5.8	114 (U)	72.7	47.9 (L)	3.2	12.4 (U)	12.4	24.1 (U)

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CHEMISTRY (1)

PATIENT NO.=41 INITIALS=FE TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	31OCT91	473 (U)	18	33	49 (U)	7.9	2	142 (U)	65.6	56.7	3	8	11.6	20.7 (U)
28	06DEC91	235	13	17	37 (U)	5.3	3.2	132 (U)	67.7	56.4	2.4	8.5	11.4	21.3 (U)
56	03JAN92	207	17	40 (U)	137 (U)	4.4	2.4	163 (U)	66	58.3	2.4	8.4	11.4	19.5

PATIENT NO.=42 INITIALS=LI TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	31OCT91	246	9	9	14	8.2	3.9	108 (U)	66.2	62.9	2.5	9.1	11	14.5
28	06DEC91	262	10	8	12	7.8	4.2	96	70.2	62.5	2.4	9.3	10.5	15.3
56	03JAN92	207	12	11	13	5.7	2.9	92	63.6	60.9	2.2	9.6	10.4	16.9

PATIENT NO.=43 INITIALS=PA TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	30OCT91	340 (U)	18	18	14	8.4	4.4	75	67.4	56.2	2.4	10.1	12.2	19.1
24	03DEC91	355 (U)	20	19	16	9.5	5.3	91	74.8	57.6	2.4	9.6	12.4	18

PATIENT NO.=44 INITIALS=MZ TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	02NOV91	399 (U)	27	39 (U)	39	7	4.2	85	71	47.3 (L)	3.2	8.9	9.4	31.2 (U)
28	06DEC91	326 (U)	36 (U)	35	38	6.2	3.9	115 (U)	79.4	46 (L)	2.9	8.8	8.7 (L)	33.6 (U)
56	03JAN92	259	34 (U)	37 (U)	38	5.3	2.3	110 (U)	67.8	49.1 (L)	2.3	8.1	8.9 (L)	31.6 (U)

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CHEMISTRY (1)

PATIENT NO.=45 INITIALS=PG TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	06NOV91	451 (U)	15	13	18	9.5	5.6	86	69.9	55.1	2.3	11.2	11.4	20
28	06DEC91	283	17	15	17	7	4.2	96	68	54.4 (L)	2.5	10.4	12.5	20.2 (U)

PATIENT NO.=46 INITIALS=AD TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	06NOV91	338 (U)	14	6	17	7.3	3.4	108 (U)	74.2	50.4 (L)	2.3	9.9	14 (U)	23.4 (U)
28	06DEC91	338 (U)	14	9	17	6.2	3.4	121 (U)	81.2 (U)	47.1 (L)	2.5	9.5	15.5 (U)	25.4 (U)

PATIENT NO.=47 INITIALS=SG TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	06NOV91	311	14	10	14	7.5	3.4	67	61.7 (L)	57.5	3.1	9.4	11.9	18.1
28	06DEC91	293	10	8	16	6.9	3.9	82	67.3	52.6 (L)	3.8	10.4	13.7 (U)	19.5
56	03JAN92	312	14	8	25	8.2	4.5	103 (U)	66.1	51.2 (L)	3.8	11.9	12.6	20.5 (U)

PATIENT NO.=48 INITIALS=FA TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	30OCT91	252	18	16	24	9	3.7	107 (U)	59.2 (L)	59.8	2.8	9.4	13.4 (U)	14.6
23	30NOV91	269	21	25	23	7.5	4.9	103 (U)	57.5 (L)	60	3	8.3	13.6 (U)	15.1

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 29124/032

CHEMISTRY (1)

PATIENT NO.=49 INITIALS=SA TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	30OCT91	286	12	9	19	6.1	3.6	89	71.7	54.1 (L)	2.7	9.7	12.9	20.6 (U)
28	06DEC91	251	14	13	22	4.1	2.3	88	71.2	55.7	1.9	8.6	12.7	21.1 (U)
56	03JAN92	259	17	13	25	4.3	2.2	98	67.9	56.8	2.1	9.3	12.3	20.5 (U)

PATIENT NO.=50 INITIALS=ZZ TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	LDH (UI/l)	SGOT (UI/l)	SGPT (UI/l)	GAMMA-GT (UI/l)	TOTAL BILIRUBIN (mcmol/l)	DIRECT BILIRUBIN (mcmol/l)	ALKALINE PHOSPHATASE (UI/l)	TOTAL PROTEIN (g/l)	BLOOD ALBUMIN (%)	GLOBULINS ALFA1 (%)	GLOBULINS ALFA 2 (%)	GLOBULINS BETA (%)	GLOBULINS GAMMA (%)
-1	28NOV91	332 (U)	17	24	62 (U)	7.1	3.5	143 (U)	65.3	58.4	3.6	9.3	13.1 (U)	15.6
28	06DEC91	295	26	<8 (U)	104 (U)	5.2	3.4	163 (U)	65	57.7	3.5	9.5	11.9	17.4

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L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CHEMISTRY (2)

PATIENT NO.=1 INITIALS=TR TREATMENT=REBOXETINE

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	20MAY91	5.9	4.8	85.3	25 (L)	0.3	144	4.1	105	1	2.2	6.3 (U)	2.1	7.6	0.8
28	02JUL91	5.9	7.2	87		0.2	142	4.1	100	1.1	2.3	4.5 (L)	1.8		
56	30JUL91	5.6	7.5	83.1		0.3	140	3.7	101	1	2.4	5.2	1.7		

PATIENT NO.=2 INITIALS=FB TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	25MAY91	4	6.6	70.7	84.2 (L)	0.1 (L)	141	4.2	107	0.8	1.9 (L)	3.3 (L)	1	7.5	1
28	02JUL91	4.5	7.4	70.1		0.1 (L)	144	4.4	107	1	2.3	3.9 (L)	1.2		
56	30JUL91	4.1	8.4 (U)	74.2		0.1 (L)	144	4	109	0.8	1.9 (L)	3.6 (L)	1.1		

PATIENT NO.=3 INITIALS=BI TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	25MAY91	4.4	7.2	76.1	52.4 (L)	0.3	139	4.1	104	1	2.4	6.5 (U)	1	8.7	2.3
28	02JUL91	4.2	8.8 (U)	81.4		0.3	141	3.8	101	1	2.4	6.3 (U)	2.2		
56	30JUL91	4.1	9.3 (U)	79.4		0.3	141	4.2	102	1	2.4	7.1 (U)	1.4		

PATIENT NO.=4 INITIALS=PC TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	25MAY91	4.4	7.7	84.4	65.7 (L)	0.4 (U)	135	3.8	96	1.1	2.1 (L)	5.1 (L)	1.3	7.2	1.1
28	02JUL91	4.7	7.5	90.6		0.4 (U)	138	4.5	97	1	2.4	5.2	1		
56	30JUL91	4.2	5.5	106.4 (U)		0.4 (U)	135	4.4	97	0.9	2.5	5.6	1.8		

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ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CHEMISTRY (2)

PATIENT NO.=5 INITIALS=BL TREATMENT=REBOXETINE

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	25MAY91	4.7	7.9	71	52.2 (L)	0.3	141	4.3	105	1.4	2.1 (L)	5.7	1.3	10.1	0.7
28	02JUL91	6.3 (U)	8.2	86.8		0.3	141	4.6	102	1.2	2.4	5.4	2		
56	30JUL91	6.7 (U)	6.3	64.3		0.3	143	3.3 (L)	104	1.8 (U)	2.3	5.9	1.9		

PATIENT NO.=6 INITIALS=SM TREATMENT=REBOXETINE

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	29MAY91	6.6 (U)	6.3	78	46.4 (L)	0.3	142	3.6	104	0.9	2.3	6.3 (U)	0.7	10	0.05 (L)
28	02JUL91	3.1 (L)	12.2 (U)	100.5		0.4 (U)	137	4.8	98	1	2.5	6.6 (U)	1.2		
56	30JUL91	5.5	6.8	98.7		0.4 (U)	139	4.5	102	1	2.4	7.3 (U)	1.6		

PATIENT NO.=7 INITIALS=DA TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	04JUN91	4.3	7.9	89.7	30.4 (L)	0.1 (L)	143	4.6	108	1	2 (L)	5.2	0.7	6.3	0.6
28	02JUL91	4.9	9.4 (U)	83.2		0.2	139	3.3 (L)	97	0.9	2.2	5.6	0.9		
56	30JUL91	5.2	8.9 (U)	85		0.3	137	3.3 (L)	97	0.7 (L)	2.3	5.8	0.9		

PATIENT NO.=8 INITIALS=SC TREATMENT=REBOXETINE

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	25MAY91	4.8	8.8 (U)	98.8	54.2 (L)	0.3	139	4.6	99	1.2	1.9 (L)	3.4 (L)	1.1	16.2 (U)	2.5
28	02JUL91	4.9	5.9	93.7		0.3	140	3.9	100	1.1	2.2	3.9 (L)	1.2		
56	30JUL91	4.7	6.5	88.7		0.2	138	4	100	1.1	2.4	3.9 (L)	1.5		

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CHEMISTRY (2)

PATIENT NO.=9 INITIALS=PA TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	25MAY91	4.2	6.2	95	78.7 (L)	0.2	143	4.4	106	1.2	2.1 (L)	4.4 (L)	1.9	9.2	1.4
28	02JUL91	4.1	7.1	97.4		0.4	141	4.8	105	1	2.4	3.9 (L)	1.3		
56	30JUL91	3.9	7.8	100.8		0.4	139	4.3	105	0.9	2.6	3.8 (L)	1.4		

PATIENT NO.=10 INITIALS=PE TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	30MAY91	6.6 (U)	4.8	107	135	0.3	142	4.3	99	1	2.3	4.3 (L)	1	8.5	0.25 (L)
28	02JUL91	6	5.2	100.6		0.2	140	4.6	101	0.9	2.4	4.2 (L)	1.1		
56	12JUL91	9.3 (U)	5.3	98.1		0.2	140	4.5	101	0.8	2.1 (L)	4.3 (L)	1.2		

PATIENT NO.=11 INITIALS=CL TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	04JUN91	4.4	12.8 (U)	123 (U)	38.1 (L)	0.6 (U)	143	3.4 (L)	93 (L)	1.1	2 (L)	4.7 (L)	1.2	1.1 (L)	1.8
28	02JUL91	4.2	12.9 (U)	115.7 (U)		0.3	143	4.6	104	1.2	2.4	4.7 (L)	1.5		
56	30JUL91	3.3 (L)	9.6 (U)	118.5 (U)		0.2	140	4.7	106	0.9	2.3	4 (L)	1.7		

PATIENT NO.=12 INITIALS=ML TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	01JUL91	5.8	7.2	71.5	49.3 (L)	0.3	142	5.2	102	1.2	2.4	5.4	1.3	4.9	1.6
28	05AUG91	5.6	6.9	64.6		0.2	143	4.5	107	0.9	2.3	5.2	1.1		
56	02SEP91	5.6	7.6	71		0.2	144	4.5	107	0.9	2.1 (L)	5.1 (L)	0.9		

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CHEMISTRY (2)

PATIENT NO.=13 INITIALS=DSC TREATMENT=REBOXETINE

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	03JUL91	5.1	6.5	75.4	75 (L)	0.2	139	4.2	103	1	2.4	5.1 (L)	1.3	11.4	2.9
28	05AUG91	5.1	8.4 (U)	75.4		0.2	147	4.3	108	0.9	2.5	4.3 (L)	0.9		
56	02SEP91	5.1	6.3	70.6		0.2	145	4	104	0.9	2.4	4.9 (L)	1.4		

PATIENT NO.=14 INITIALS=BM TREATMENT=REBOXETINE

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	01JUL91	7.1 (U)	7.6	98	40 (L)	0.2	139	5.1	96	1	2.3	3.1 (L)	1.7	8.7	0.7
28	05AUG91	3.9	11 (U)	117 (U)		0.3	138	5	100	1.2	2.6	4.3 (L)	1.4		
56	02SEP91	5	9.4 (U)	116.9 (U)		0.3	140	5.4 (U)	102	1.1	2.4	5 (L)	1.7		

PATIENT NO.=15 INITIALS=GI TREATMENT=REBOXETINE

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	04JUL91	3.9	4.2	103.7	41.2 (L)	0.4 (U)	144	4.1	104	1.3	2.4	5.4	1.5	4.8	0.7
8	16JUL91	5	4.4	61.1		0.2	101 (L)	3.3 (L)	61 (L)	0.7 (L)	2.1 (L)	(ND)	(ND)		

PATIENT NO.=16 INITIALS=PJ TREATMENT=REBOXETINE

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	03JUL91	5.4	5.9	68.2	59 (L)	0.2	143	3.6	107	1	2.2	5.8	1	6.2	1.2
28	05AUG91	4.8	4.7	79.9		0.2	142	3.8	99	1.2	2.4	4.5 (L)	0.8		
56	02SEP91	4.8	6	76.9		0.2	143	3.7	102	1.1	2.1 (L)	5.3	0.7		

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CHEMISTRY (2)

PATIENT NO.=17 INITIALS=MM TREATMENT=REBOXETINE

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	04JUL91	4.1	0.2 (L)	71.7	25 (L)	0.2	144	4	105	0.8	2.4	4.6 (L)	1.3	6.5	1.3
28	05AUG91	3.8	11.3 (U)	69.4		0.2	144	4	105	0.9	2.5	4.8 (L)	1.6		
56	02SEP91	3.6	10 (U)	74.5		0.2	144	4.8	107	0.9	2.1 (L)	4.3 (L)	1		

PATIENT NO.=18 INITIALS=VM TREATMENT=REBOXETINE

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	02JUL91	4.3	6.3	110.9	59 (L)	0.3	142	4.7	103	0.8	2.3	4.7 (L)	1.5	6.5	0.03 (L)
28	05AUG91	4.5	6.8	111.3		0.3	144	4.4	105	0.7 (L)	2.3	4.5 (L)	1.8		
56	02SEP91	4.8	5.9	108.2		0.2	145	4.7	108	0.6 (L)	2.2	4.5 (L)	2		

PATIENT NO.=19 INITIALS=NI TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	05JUL91	4.1	5.1	94.9	40 (L)	0.3	147	3.3 (L)	105	1	2.3	4.2 (L)	0.6	2.2 (L)	0.6
28	05AUG91	4.1	5.8	91.7		0.3	144	3.9	105	0.9	2.3	4.6 (L)	0.5 (L)		
56	02SEP91	4.3	5.7	93.4		0.3	148	4.2	106	0.8	2.1 (L)	4.6 (L)	0.7		

PATIENT NO.=20 INITIALS=BE TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	04JUL91	5.88	8.7 (U)	147 (U)	40 (L)	0.5 (U)	141	4.7	95 (L)	0.6 (L)	2.7 (U)	5.5	1.9	4.7	1.3
28	05AUG91	5	9.2 (U)	153.7 (U)		0.4	141	4.5	101	0.6 (L)	2.6	4.5 (L)	1.2		
56	13AUG91	4.7	9.6 (U)	135.6 (U)		0.4	139	4.8	99	0.6 (L)	2.7 (U)	4.4 (L)	1.2		

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CHEMISTRY (2)

PATIENT NO.=21 INITIALS=SE TREATMENT=REBOXETINE

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	06JUL91	4	6	91.7	62 (L)	0.4 (U)	144	3.6	102	1	1.9 (L)	5.4	1.1	1.1 (L)	0.03 (L)
28	05AUG91	4.3	4.5	101.5		0.3	134 (L)	4.3	93 (L)	1	2.4	5.3	0.9		

PATIENT NO.=22 INITIALS=BA TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	31AUG91	4.2	6.4	70.5	71 (L)	0.2	144	3.7	108	0.8	2.3	5.4	1.8	7.9	0.8
28	07OCT91	4.2	7.1	70.1		0.2	141	4.1	105	0.6 (L)	2.2	5.1 (L)	1.2		
56	04NOV91	4.1	6.3	66.8		0.1 (L)	146	3.6	107	0.7 (L)	2.1 (L)	4.9 (L)	1		

PATIENT NO.=23 INITIALS=UT TREATMENT=REBOXETINE

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	13AUG91	4.4	8.2	108.8 (U)	30.7 (L)	0.4 (U)	144	4.6	110	1	2.5	6.2 (U)	1.7	6.6	0.7
28	07OCT91	5.4	9.7 (U)	111.6 (U)		0.4 (U)	137	5	100	0.8	2.5	6	2.2		
56	04NOV91	5.4	8.8 (U)	110.4 (U)		0.4 (U)	141	4.8	100	0.9	2.4	5.8	2.4		

PATIENT NO.=24 INITIALS=BEA TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	31AUG91	3.8	11.6 (U)	114.8 (U)	21 (L)	0.4 (U)	142	4.6	100	0.8	1.6 (L)	4.7 (L)	1.2	7.5	0.4 (L)
28	07OCT91	4	6.7	104.4		0.4 (U)	120 (L)	5.1	102	0.8	2.3	4.8 (L)	1.2		
56	04NOV91	4.1	7	95.1		0.4 (U)	145	4.3	107	0.7 (L)	2.2	4.5 (L)	1.2		

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/052

CHEMISTRY (2)

PATIENT NO.=25 INITIALS=GA TREATMENT=REBOXETINE

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	31AUG91	4.9	6.4	80.2	27 (L)	0.2	143	4.4	102	1.2	2.4	6.9 (U)	2.8	7.8	0.9
28	07OCT91	4.8	7	77.3		0.2	137	5.1	98	1.1	2.3	5.9	2		
56	04NOV91	4.6	8.1	73		0.2	135	4.4	98	1	2.2	5.7	1.9		

PATIENT NO.=26 INITIALS=PR TREATMENT=REBOXETINE

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	31AUG91	5	4.6	75.5	61 (L)	0.3	142	4.5	99	1.1	2.3	4.7 (L)	0.8	8.9	1.2

PATIENT NO.=27 INITIALS=GA TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	31AUG91	3.7	9.5 (U)	110.7 (U)	38.6 (L)	0.3	142	4.5	101	2.5 (U)	1.9 (L)	6.3 (U)	2.1	5.8	0.8
28	07OCT91	5	10.9 (U)	112.6 (U)		0.3	137	4.3	97	0.8	2.3	5.7	2.6		
56	04NOV91	4.8	7.8	101.5		0.3	140	4.2	98	0.7 (L)	2.2	5.8	1.7		

PATIENT NO.=28 INITIALS=MR TREATMENT=REBOXETINE

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	31AUG91	5.1	7.3	103.9	45.5 (L)	0.4 (U)	152 (U)	2.9 (L)	108	1.8 (U)	2.3	3.5 (L)	1.2	6	3.4
28	07OCT91	4.8	5.8	93		0.4 (U)	140	4.4	102	0.9	1.9 (L)	4.8 (L)	2.1		
56	04NOV91	5	8.1	101.2		0.4 (U)	143	4.9	101	1	2.2	5.5	2.2		

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CHEMISTRY (2)

PATIENT NO.=29 INITIALS=TR TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	31AUG91	4	4.6	78.6	57 (L)	0.1 (L)	140	5.3	102	1.2	1.6 (L)	4.4 (L)	0.8	8.3	1.5
28	07OCT91	4.3	5.6	90.8		0.2	142	5.2	98	1	2.3	5.3	1.1		
56	04NOV91	4.6	6.7	94		0.2	143	5.1	101	1	2.2	4.6 (L)	0.8		

PATIENT NO.=30 INITIALS=PA TREATMENT=REBOXETINE

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	30SEP91	4.7	8.6 (U)	85.8	31 (L)	0.3	141	4.5	102	1.1	2.3	4.2 (L)	1.1	9.93	0.24 (L)
28	04NOV91	4.6	7.1	86.6		0.3	137	4.5	96	0.9	2.1 (L)	3.6 (L)	0.9		
56	02DEC91	5.9	7.4	84.4		0.3	139	4	97	1	2.5	4.6 (L)	0.9		

PATIENT NO.=31 INITIALS=CC TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	04OCT91	5.4	7.6	72.4	22 (L)	0.2	138	4	96	1.03	2.5	5.8	0.8	6.46	0.65
28	04NOV91	5.4	5.8	62.1		0.2	133 (L)	3.9	88 (L)	1	2.3	5.4	0.7		
56	02DEC91	6.3 (U)	6.4	71		0.3	129 (L)	3.8	84 (L)	0.9	2.4	6	0.5 (L)		

PATIENT NO.=32 INITIALS=CE TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	05SEP91	5.6	6.2	65.2	52.4 (L)	0.3	145	3.7	100	0.9	2.2	5.1 (L)	2.4	9.3	1.3
28	07OCT91	6.1	3.8	75.7		0.4 (U)	134 (L)	3.9	90 (L)	1	2.4	4.8 (L)	2.3		
56	04NOV91	5.6	3.6	68.7		0.3	140	3.7	98	1.1	2.4	6.2 (U)	3.2 (U)		

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CHEMISTRY (2)

PATIENT NO.=33 INITIALS=VA TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	02OCT91	7.8 (U)	3.7	87.9	106	0.3	138	4.5	96	1	2.5	5 (L)	1.5	7.6	1.13
28	04NOV91	7 (U)	4.5	82		0.3	140	4.7	95 (L)	0.8	2.2	4.4 (L)	1.7		
56	02DEC91	8.1 (U)	6	87.6		0.3	139	4.6	93 (L)	0.9	2.5	4.2 (L)	1.3		

PATIENT NO.=34 INITIALS=BA TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	01OCT91	6.4 (U)	12.3 (U)	85.1	33 (L)	0.3	148	4.6	102	1.3	2.4	4.5 (L)	1.1	6.2	0.6

PATIENT NO.=35 INITIALS=SB TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	04OCT91	4.4	6.4	89.7	72.2 (L)	0.2	143	4.7	98	1.1	2.2	5.1	1.1	6.4	0.9
28	04NOV91	4.2	5.5	98.6		0.2	141	4.5	98	1	2.1 (L)	5.7	1.3		
56	02DEC91	5.1	7.6	88		0.2	141	4.3	102	1	2.4	5.1	1		

PATIENT NO.=36 INITIALS=SM TREATMENT=REBOXETINE

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	02OCT91	4.8	6.5	76	66.9 (L)	0.3	142	4.7	100	1.2	2.6	6.6 (U)	2.4	8.3	1
28	04NOV91	4.2	6.75	76		0.3	142	4.6	98	1.18	2.3	7.7 (U)	2.8		
56	02DEC91	5	8	92.4		0.3	144	4.2	99	1.1	2.4	6.4 (U)	1.9		

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CHEMISTRY (2)

PATIENT NO.=37 INITIALS=SE TREATMENT=REBOXETINE

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	01OCT91	4.4	4.4	63.7	92.4 (L)	0.2	139	4.5	102	1	2.3	3.1 (L)	1	6.4	0.09 (L)
28	04NOV91	4	3.8	59.4		0.2	143	4.1	101	1.1	2.2	3.3 (L)	1.2		
56	02DEC91	5.4	4.8	69.9		0.2	141	3.4 (L)	100	1	2.5	3.9 (L)	1.7		

PATIENT NO.=38 INITIALS=LO TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	01OCT91	7.4 (U)	5.4	78.9	75.3 (L)	0.2	139	4.9	100	0.9	2 (L)	5.1 (L)	1.2	6.6	0.79
28	04NOV91	5.9	4.8	77.8		0.2	146	4.6	100	1.1	2.2	4.8 (L)	1.2		
56	02DEC91	6.1	4.4	77.4		0.2	140	4.2	100	1	2.1 (L)	4.7 (L)	1.2		

PATIENT NO.=39 INITIALS=CP TREATMENT=REBOXETINE

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	06OCT91	5.8	5.2	129	51 (L)	0.2	138	5.7	95 (L)	0.9	2.1 (L)	4.2 (L)	1	5.8	1.13
28	04NOV91	5.8	5.8	105.5		0.2	139	3.8	100	0.8	2.1 (L)	3.6 (L)	0.8		

PATIENT NO.=40 INITIALS=PD TREATMENT=REBOXETINE

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	02NOV91	4.5	6.3	89.7	60 (L)	0.3	147	4.3	102	0.9	2.6	4.9 (L)	1.2	6	0.9
28	06DEC91	4.4	6.5	106.7		0.3	141	4.1	101	0.9	2.5	4.2 (L)	0.9		
56	03JAN92	5.4	6.5	98		0.3	141	4.2	99	1.1	2.4	4.7 (L)	1.2		

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CHEMISTRY (2)

PATIENT NO.=41 INITIALS=FE TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	31OCT91	4.7	6.5	89	45 (L)	0.3	141	4.5	102	1	2.4	4.9 (L)	1.4	7.7	0.7
28	06DEC91	2.6 (L)	6.9	94.3		0.2	141	4.7	101	1.1	2.6	5.5	1.6		
56	03JAN92	7.8 (U)	7.5	79		0.1 (L)	142	4.1	101	1.1	2.4	6	2		

PATIENT NO.=42 INITIALS=LI TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	31OCT91	8.4 (U)	5.8	66.7	18 (L)	0.2	144	4.5	104	0.8	2.6	4.7 (L)	1.4	9.6	0.8
28	06DEC91	7.3 (U)	8.1	73.8		0.3	141	4.1	98	0.6 (L)	2.8 (U)	4.4 (L)	1.4		
56	03JAN92	7.9 (U)	15.2 (U)	103		0.3	142	4.6	98	0.7 (L)	2.7 (U)	4.8 (L)	1.6		

PATIENT NO.=43 INITIALS=PA TREATMENT=REBOXETINE

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	30OCT91	5.4	7.4	109 (U)	48 (L)	0.3	145	4.6	106	0.7 (L)	2.6	5 (L)	1.9	6.4	1.4
24	03DEC91	6	8.7 (U)	115.9 (U)		0.3	144	4.7	102	0.9	2.9 (U)	7 (U)	1.2		

PATIENT NO.=44 INITIALS=MZ TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	02NOV91	4.2	15.3 (U)	190.4 (U)	29 (L)	0.4	141	5.3	108	1.3	2.5	3.4 (L)	0.7	8.2	2.5
28	06DEC91	4.2	14.3 (U)	181 (U)		0.4	140	5.2	103	0.8	2.6	3.7 (L)	1.1		
56	03JAN92	4.6	19.8 (U)	194 (U)		0.4	141	5.5 (U)	105	1	2.4	3.7 (L)	1		

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

CHEMISTRY (2)

PATIENT NO.=45 INITIALS=PG TREATMENT=REBOXETINE

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	05NOV91	5	11.2 (U)	131 (U)	16 (L)	0.4 (U)	139	5	102	1.3	2.1 (L)	3.9 (L)	1	6.7	1.7
28	06DEC91	5.2	12.5 (U)	136.6 (U)		0.3	138	5.2	99	0.9	2.4	4.3 (L)	0.9		

PATIENT NO.=46 INITIALS=AD TREATMENT=REBOXETINE

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	06NOV91	4.5	9.1 (U)	93.7	34 (L)	0.5 (U)	141	5.3	99	1	2.3	6.1	1.2	7.8	1.3
28	06DEC91	4.7	14.2 (U)	124.5		0.5 (U)	141	5	99	1	2.5	6.1	0.9		

PATIENT NO.=47 INITIALS=SG TREATMENT=REBOXETINE

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	06NOV91	4.3	6.3	79.9	25 (L)	0.2	141	4.2	100	1	2.3	5 (L)	0.6	6.5	0.03 (L)
28	06DEC91	4.5	7.1	89		0.3	142	4.4	101	0.9	2.5	5.1 (L)	0.8		
56	03JAN92	6.1	7.8	95		0.3	142	3.7	99	1.1	2.3	5.7	1.1		

PATIENT NO.=48 INITIALS=FA TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	30OCT91	4.8	4.3	73.9	46 (L)	0.2	143	4	101	1.1	2.2	5.1 (L)	1.9	9	4
28	30NOV91	5	4.1	77.5		0.3	146	3.6	102	1.2	2.3	5.1 (L)	1.5		

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

PHARMACIA CMS R&D

REBOXETINE - PROTOCOL 20126/032

CHEMISTRY (2)

PATIENT NO.=49 INITIALS=SA TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/m)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	30OCT91	5.3	9.3 (U)	90.5	42 (L)	0.2	141	4.3	102	1.1	2.3	5.5	1.4	8.2	1.1
28	06DEC91	4.6	9.7 (U)	102.6		0.3	138	5.1	109	1.2	2.6	6.1	1.4		
56	03JAN92	5.3	9.8 (U)	105		0.3	140	5.5 (U)	102	1.2	2.5	6.5 (U)	2		

PATIENT NO.=50 INITIALS=ZZ TREATMENT=PLACEBO

VISIT NO.	LAB. DATE	BLOOD SUGAR (mmol/l)	BUN (mcmol/l)	CREATININE (mcmol/l)	CREAT. CLEARANCE (ml/ml)	URIC ACID (mmol/l)	NA+ (mmol/l)	K+ (mmol/l)	CL- (mmol/l)	PO4 (mmol/l)	CA++ (mmol/l)	CHOLESTE-ROL (mmol/l)	TRIGLY-CERIDES (mmol/l)	T4 (mcg/dl)	TSH (mcUI/ml
-1	08NOV91	4.4	8.6 (U)	103.6	36.8 (L)	0.2	141	4.9	100	1.1	2.5	5.2	1	9.6	1.6
28	06DEC91	4.8	8.6 (U)	98.7		0.2	146	4.4	105	1	2.4	5.1 (L)	0.9		

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

HEMATOLOGY

PATIENT NO.=1 INITIALS=TR TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	20MAY91	12.5	37.6	4.04 (L)	6.6	47.9	34.9	7.1	6.7	0.6	222
28	02JUL91	13	39.9	4.42	8.13	47.1	34.9	7	8.3 (U)	0.7	249
56	30JUL91	12.8	39.2	4.38	9.01	47.7	39.7	6.2	4.9	0.4	264

PATIENT NO.=2 INITIALS=FB TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	25MAY91	12.6	35.6 (L)	4.14 (L)	5.06	56.9	31.9	7.3	2	0.6	187
28	02JUL91	13	39.7	4.33	4.55 (L)	56.1	32.2	7.5	2	0.5	197
56	30JUL91	12.6	38.8	4.29	5.03	54.3	36.1	5.8	1.8	0.5	193

PATIENT NO.=3 INITIALS=BI TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	25MAY91	12.3	37.9	4.38	4.08 (L)	44.5	41.4	8.1	2.6	0.5	348
28	02JUL91	12	35.5 (L)	3.95 (L)	4.16 (L)	41.2	45.9	7.7	2.2	0.8	333
56	30JUL91	12.7	38.4	4.24	4.68 (L)	40.5	48.4 (U)	7.8	2.3	0.6	308

PATIENT NO.=4 INITIALS=PC TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	25MAY91	12.8	36.7 (L)	4.19 (L)	7.06	50.1	32.5	9.9 (U)	4.4	1.1	317
28	02JUL91	13.2	39.2	4.23	6.93	52.8	30.4	9.3 (U)	3.6	1.4	280
56	30JUL91	12.4	38.4	4.22	8.53	53	31.1	9.2 (U)	3.8	0.8	331

PATIENT NO.=5 INITIALS=BL TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	HB (g/cl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	25MAY91	11.3 (L)	33.9 (L)	4.55	5.65	64.4	27.3	6.3	0.1	0.4	425 (U)
28	02JUL91	13	40.2	5.05	6.35	62	27.5	7.8	0.1	0.4	408 (U)

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

HEMATOLOGY

PATIENT NO.=5 INITIALS=BL TREATMENT=REBOXETINE (continued)

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
56	30JUL91	12.3	39.1	4.8	5.33	61.6	27	8.5	0.5	0.4	354

PATIENT NO.=6 INITIALS=SM TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	29MAY91	10.6 (L)	30.9 (L)	3.19 (L)	8.6	70.8	17.5 (L)	8.4	1.5	0.5	250
28	02JUL91	12.8	37.7	4.02 (L)	8.32	59.6	27.7	7.3	3.7	0.5	332
56	30JUL91	12	36.4 (L)	3.85 (L)	9.51	62.5	24	8.2	3.6	0.6	311

PATIENT NO.=7 INITIALS=DA TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	04JUN91	9.4 (L)	28.9 (L)	3.17 (L)	5.43	58.2	26.2	8.6	4.1	0.6	419 (U)
28	02JUL91	12.8	39.6	4.56	6.23	56.4	30.7	8.4	1.6	0.6	313
56	30JUL91	12.8	38.3	4.56	6.49	56.7	31.2	8.7	1.2	0.6	279

PATIENT NO.=8 INITIALS=SC TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	25MAY91	11.6 (L)	34 (L)	3.96 (L)	9.78	70.9	19.6	5.6	1.9	0.4	388
28	02JUL91	11.6 (L)	35.8 (L)	4 (L)	6.38	58.1	32.2	4.8	3	0.4	296
56	30JUL91	11.9 (L)	36.3 (L)	4.1 (L)	5.23	47.3	39.9	7.5	3.3	0.7	284

PATIENT NO.=9 INITIALS=PA TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	25MAY91	11.3 (L)	34.9 (L)	4.27 (L)	7.5	50.7	37	5.7	4.5	0.7	192
28	02JUL91	12.8 (L)	40.9 (L)	5.11	7.89	50.3	34.7	8	4	0.9	228
56	30JUL91	13.7 (L)	42.6	5.26	7.8	55.5	30.5	7.7	3.6	0.9	204

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

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HEMATOLOGY

PATIENT NO.=10 INITIALS=PE TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	30MAY91	11.3 (L)	34.1 (L)	3.87 (L)	11.2 (U)	63.1	23.4	8.7	3.1	0.1	333
28	02JUL91	11.7 (L)	36.1 (L)	3.85 (L)	11.03 (U)	70.3	19.5	6.7	1.9	0.4	300
56	12JUL91	11.2 (L)	36 (L)	3.84 (L)	10.37	68.8	21	6.9	1.9	0.5	378

PATIENT NO.=11 INITIALS=CL TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	04JUN91	8.3 (L)	27.2 (L)	3.58 (L)	8.6	71.9	16.8 (L)	8.2	1.4	0.2	284
28	02JUL91	8.2 (L)	27.6 (L)	3.52 (L)	8.51	64.6	24	7.5	1.7	0.4	357
56	30JUL91	7.8 (L)	26.6 (L)	3.36 (L)	8.36	62.3	27.1	7.5	1.7	0.2	284

PATIENT NO.=12 INITIALS=ML TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	01JUL91	13.6	44	4.73	5.76	57.7	28.7	7.7	3.8	0.6	205
28	05AUG91	12.1	36.4 (L)	4.17 (L)	6.55	56	27.9	9.9 (U)	4	0.6	187
56	02SEP91	12.1	41.4	4.5	6.99	59.4	27.8	6.7	3.9	0.9	208

PATIENT NO.=13 INITIALS=DSC TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	03JUL91	14.5	42.6	5	5.51	39.1 (L)	47.5	7.4	2.1	0.8	208
28	05AUG91	14.8	42.4	5	6.75	40	47	7.1	1.6	0.8	204
56	02SEP91	14.9	47.1 (U)	5.41 (U)	6.26	42.6	45.5	5.2	1.2	1.1	200

PATIENT NO.=14 INITIALS=BM TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	01JUL91	12.1	37.6	4.16 (L)	10.3	65.1	23.2	7.8	1.2	0.6	284
28	05AUG91	11.9 (L)	36.6 (L)	4.18 (L)	9.64	68.2	38.7	8.8	1.7	0.6	298

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

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HEMATOLOGY

PATIENT NO.=14 INITIALS=BM TREATMENT=REBOXETINE
(continued)

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
56	02SEP91	13.2	44.7	4.96	9.35	39.8 (L)	47.2	7.6	1.9	0.8	283

PATIENT NO.=15 INITIALS=GI TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	04JUL91	15.1	44.3	4.74	4 (L)	43.2	42.6	7.5	3.7	0.8	175
8	16JUL91	17.1 (U)	45.4	5.27	10.2	91.1 (U)	3.4 (L)	4.9	0.1	0.2	229

PATIENT NO.=16 INITIALS=PJ TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	03JUL91	12.4	37.4	3.83 (L)	6.34	46.5	38.6	5.7	6.6	0.6	196
28	05AUG91	12.7	37.5	4.07 (L)	8.27	54.4	30.3	6.6	6.4	0.7	255
56	02SEP91	12.5	41.5	4.41	6.72	50.6	32.5	7.6	6.5	0.8	253

PATIENT NO.=17 INITIALS=MM TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	04JUL91	12.2	36.9 (L)	3.97 (L)	4.58 (L)	64	27	6	2	1	242
28	05AUG91	13.1	39.2	4.3	5.86	52.7	36.2	6.9	2	0.5	237
56	02SEP91	12.4	40.7	4.34	4.95	54.4	31.2	9.2 (U)	2.7	0.7	219

PATIENT NO.=18 INITIALS=VM TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	02JUL91	12.3 (L)	35.1 (L)	4.09 (L)	7.86	66.9	21.3	7.8	1.9	0.4	185
28	05AUG91	12.3 (L)	35 (L)	4.19 (L)	7.26	67.4	19.7	6.7	2	0.4	187
56	02SEP91	12 (L)	38.4 (L)	4.48 (L)	7.96	69.3	19.1	6.5	2.2	0.5	191

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

HEMATOLOGY

PATIENT NO.=19 INITIALS=NI TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	05JUL91	11.5 (L)	36.4 (L)	4.05 (L)	3.19 (L)	43	44	9	3	1	134
28	05AUG91	10.9 (L)	32.6 (L)	3.64 (L)	3.17 (L)	50.2	39	5.2	3.4	0.5	122 (L)
56	02SEP91	11.4 (L)	39.6	4.24	3.19 (L)	57.6	32.7	5.9	1.3	0.7	144

PATIENT NO.=20 INITIALS=BE TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	04JUL91	15.2	49.5	5.08	6.55	61.2	24.2	4.9	3.6	0.9	187
28	05AUG91	14.1	42.8	4.61 (L)	7.02	59.7	28.9	5.8	3.2	0.5	154
56	13AUG91	14.1	45.6	4.73	6.53	55.9	32.4	5.9	2.8	0.7	173

PATIENT NO.=21 INITIALS=SE TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	06JUL91	12	36.8 (L)	4.14 (L)	5.3	55.6	30.9	9	2	0.4	129 (L)
28	05AUG91	12.6	35.9 (L)	4.22	7.58	46	40.7	8.3	1.6	0.3	159

PATIENT NO.=22 INITIALS=BA TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	31AUG91	13.3	42.4	4.46	4.2 (L)	59.4	22.4	10.5 (U)	5.2	0.7	171
28	07OCT91	12.5	39.1	4.15 (L)	4.41 (L)	60	20.4	10.8 (U)	4.3	1.3	166
56	04NOV91	11.8 (L)	36 (L)	3.84 (L)	4.98	60.6	24.4	9.6 (U)	2.2	1	164

PATIENT NO.=23 INITIALS=UT TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	13AUG91	12.2	38.1	4.18 (L)	4.95	52.9	30.7	7.8	6.2	0.6	231
28	07OCT91	12.5	38.9	4.31	6.32	58	27	6.3	5.4	0.6	266
56	04NOV91	12.7	37.9	4.17 (L)	7.58	55.2	27.9	8.1	4.7	1	262

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/052

HEMATOLOGY

PATIENT NO.=24 INITIALS=BEA TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	31AUG91	13	41.3	4.14 (L)	6.66	68	19.9	7.4	1.7	0.8	208
28	07OCT91	11.7 (L)	37.3	3.71 (L)	5.05	59.6	28.2	5.7	3	0.8	216
56	04NOV91	11 (L)	33.8 (L)	3.47 (L)	5.75	64.5	20.9	6.9	3.9	1	193

PATIENT NO.=25 INITIALS=GA TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	31AUG91	13.2	42.6	4.35	4.91	54.7	33.1	6.3	2	1	165
28	07OCT91	12.7	40.2	4 (L)	4.73 (L)	56.4	31.3	6.3	2.6	1.4	185
56	04NOV91	12.7	38.3	3.87 (L)	6.3	58.2	28.9	6.3	2	1.1	192

PATIENT NO.=26 INITIALS=PR TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	31AUG91	12.6 (L)	40.3 (L)	4.41 (L)	9.38	66.5	20.2	6.4	4.4	0.7	267

PATIENT NO.=27 INITIALS=GA TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	31AUG91	11.1 (L)	37.2	4.07 (L)	9.12	68.2	22.1	6.9	0.7	0.5	233
28	07OCT91	11.1 (L)	35.6 (L)	3.86 (L)	5.51	67.2	18.8 (L)	10.4 (U)	1	0.5	232
56	04NOV91	11.3 (L)	35.5 (L)	3.83 (L)	6.25	63.5	20.1	10.7 (U)	2.1	0.6	285

PATIENT NO.=28 INITIALS=MR TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	31AUG91	12.4	39.4	4.25	5.12	81.9 (U)	11.9 (L)	3.4	1.7	0.5	123 (L)
28	07OCT91	10.2 (L)	32.3 (L)	3.51 (L)	4.31 (L)	76.6 (U)	14 (L)	4.4	2.5	0.5	122 (L)
56	04NOV91	11.6 (L)	33.6 (L)	3.58 (L)	5.25	74.8 (U)	14.9 (L)	5.3	2.6	0.5	140

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

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HEMATOLOGY

PATIENT NO.=29 INITIALS=TR TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	31AUG91	12.3 (L)	40.5 (L)	4.63 (L)	6.37	49.8	35.7	7.2	5.2	0.5	218
28	07OCT91	13.1 (L)	42.3	4.7	6.88	46.5	40.2	6	5.7	0.6	205
56	04NOV91	13.4 (L)	40.7 (L)	4.57 (L)	7.68	48.6	37.6	5	4.5	0.8	211

PATIENT NO.=30 INITIALS=PA TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	30SEP91	13.5	42.5	4.75	7.92	59.2	25.7	7	6	0.8	254
28	04NOV91	14.4	44.4	5.12	9.07	67.4	21.2	6.1	2.9	0.7	197
56	02DEC91	15.2	43.7	5.09	9.16	61	24.9	7.5	3.2	1.4	209

PATIENT NO.=31 INITIALS=CC TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	04OCT91	11.7 (L)	36.8 (L)	4 (L)	5.42	64	21.3	8.7	3.2	1.3	269
28	04NOV91	10.9 (L)	33.8 (L)	3.7 (L)	7.42	66.3	18.8 (L)	9	2.4	1	267
56	02DEC91	12	34.2 (L)	3.83 (L)	7.18	62.5	20.6	9	3.7	1.5	300

PATIENT NO.=32 INITIALS=CE TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	05SEP91	12.6	38.9	4.41	6.67	60.9	23.3	9.9 (U)	2.4	0.6	275
28	07OCT91	13.9	43	4.88	8.72	50.1	34.8	8.4	3.7	0.9	346
56	04NOV91	13.8	40.7	4.64	9.79	45.6	39.4	6	4.4	1.1	293

PATIENT NO.=33 INITIALS=VA TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	02OCT91	14.6	43.3	4.68 (L)	9.71	63.6	17.9 (L)	7.9	8.5	0.6	204
28	04NOV91	15	44.4	4.8	10.98 (U)	65.7	18.5 (L)	7.8	7.3 (U)	1.1	214

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

HEMATOLOGY

PATIENT NO.=33 INITIALS=VA TREATMENT=PLACEBO
(continued)

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
56	02DEC91	13.9 (L)	38.8 (L)	4.28 (L)	13.58 (U)	72.8	12.4 (L)	7.8	3.1	0.7	270

PATIENT NO.=34 INITIALS=BA TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	01OCT91	11.7 (L)	37.9	4.21	5.1	45.7	38.7	6.6	4.8	1.1	236

PATIENT NO.=35 INITIALS=SB TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	04OCT91	12.4	37.7	4.14 (L)	6.8	52.1	31.3	7.5	5.1	0.7	171
28	04NOV91	12.8	39.6	4.32	9.28	62.6	23	8.5	3.4	0.4	187
56	02DEC91	11.7 (L)	35 (L)	3.85 (L)	8.87	45.9	36.9	7.1	6.7	0.8	198

PATIENT NO.=36 INITIALS=SM TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	02OCT91	13.5	41.8	4.64	7.6	61.1	28.3	5.3	1.9	1	297
28	04NOV91	13	40.3	4.37	9.99	54.1	30.6	7	4.2	1.1	256
56	02DEC91	12.7	36.4 (L)	4.04 (L)	10.83 (U)	58.5	29.4	6.6	2.1	0.9	255

PATIENT NO.=37 INITIALS=SE TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	01OCT91	11.7 (L)	37.2	4.29	8.38	66.1	22.9	7.7	1.1	0.4	250
28	04NOV91	10.7 (L)	35 (L)	4.15 (L)	9.47	64.2	26.1	6.3	1.4	0.3	305
56	02DEC91	13.2	39.8	4.72	16.47 (U)	64.5	26.9	5.9	0.8	0.5	261

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

HEMATOLOGY

PATIENT NO.=38 INITIALS=LO TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	01OCT91	13.5	41.9	4.75	9.71	60.4	29.1	6.1	1.9	0.9	298
28	04NOV91	12.8	39.5	4.45	10.05	52.4	35.4	5.6	3	0.9	283
56	02DEC91	12.9	37.7	4.34	10.31	52.5	35.9	6.2	2.2	1	192

PATIENT NO.=39 INITIALS=CP TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	06OCT91	14.6	41.6 (L)	4.76	6.54	61.5	24.4	8.4	2.9	1	225
28	04NOV91	12.7 (L)	37.4 (L)	4.26 (L)	6.29	59.5	22.3	9.1 (U)	5.1	0.9	211

PATIENT NO.=40 INITIALS=PO TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	02NOV91	10.9 (L)	33.8 (L)	3.38 (L)	6.64	57.5	27.2	9.2 (U)	2.3	0.8	170
28	06DEC91	11.5 (L)	35.8 (L)	3.64 (L)	7.93	57.2	25.7	10.7 (U)	2.2	0.7	189
56	03JAN92	12.4 (L)	38.9 (L)	4.17 (L)	9.02	62.1	23.5	9.3 (U)	1.6	0.7	223

PATIENT NO.=41 INITIALS=FE TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	31OCT91	10.6 (L)	35 (L)	4.08 (L)	9.9	50.6	36.1	4.8	3.7	1.6 (U)	412 (U)
28	06DEC91	12.2	37.5	4.36	10.69	53.9	34.4	4.4	2.8	1.2	286
56	03JAN92	12.4	37.1	4.51	9.86	55.5	33.8	4	3.1	0.9	292

PATIENT NO.=42 INITIALS=LI TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	31OCT91	13	41.6	4.28	7.34	65.5	27	5.2	1.1	0.8	190
28	06DEC91	12.9	39.9	4.3	13.99 (U)	79 (U)	13.5 (L)	4.7	1	0.4	181
56	03JAN92	13.3	39.5	4.41	9.07	69.7	22	5.2	0.8	0.5	183

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

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REBOXETINE - PROTOCOL 20124/032

HEMATOLOGY

PATIENT NO.=43 INITIALS=PA TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	30OCT91	11.9 (L)	36.9 (L)	3.89 (L)	5.3	48.6	39.1	5.9	3.1	0.7	176
24	03DEC91	13.5	40.8	4.34	6.78	47.6	40.6	5.9	2	0.6	211

PATIENT NO.=44 INITIALS=MZ TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	02NOV91	11 (L)	35 (L)	3.51 (L)	7.48	56.7	26.1	7.1	6.1	0.6	207
28	06DEC91	11.4 (L)	35 (L)	3.57 (L)	8.71	63.8	21.5	5.2	6.2	0.4	184
56	03JAN92	10.6 (L)	32 (L)	3.35 (L)	6.03	56.2	27.5	5.4	7.2 (U)	0.6	153

PATIENT NO.=45 INITIALS=PG TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	06NOV91	13.4	41.1	4.28	7.37	45.8	37.9	5.8	7.7 (U)	0.7	197
28	06DEC91	12.1	36.7 (L)	3.84 (L)	6.92	41.6	45.3	6.4	2.9	0.5	135

PATIENT NO.=46 INITIALS=AD TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	06NOV91	12.3 (L)	37.2 (L)	3.87 (L)	7.42	58.5	29	6.9	2.1	1	295
28	06DEC91	12.5 (L)	38.8 (L)	4.17 (L)	8.69	56.8	30.4	7.4	1.4	0.8	332

PATIENT NO.=47 INITIALS=SG TREATMENT=REBOXETINE

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	06NOV91	11.5 (L)	36.3 (L)	4.15 (L)	7.69	59.6	24	6.9	5.6	0.9	212
28	06DEC91	12.2	37.6	4.37	8.62	68.1	18.2 (L)	6.9	4	0.8	218
56	03JAN92	13.9	41.6	5	9.58	74.4 (U)	15.6 (L)	6.4	1.2	0.5	226

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

HEMATOLOGY

PATIENT NO.=48 INITIALS=FA TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	30OCT91	12.3	38.4	4.54	10.03	54	36	4	2.4	1	252
23	30NOV91	12.5	38	4.24	10.21	55.3	34.5	4.3	2.1	0.7	226

PATIENT NO.=49 INITIALS=SA TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	30OCT91	10.8 (L)	34.2 (L)	3.85 (L)	7.8	60.7	25.3	1.8 (L)	8.4 (U)	0.8	392
28	06DEC91	10.8 (L)	33.1 (L)	3.72 (L)	7.49	54.6	27.9	7.6	4	1.2	268
56	03JAN92	11 (L)	32.7 (L)	3.78 (L)	6.77	57.8	24.9	8.8	3.7	0.8	290

PATIENT NO.=50 INITIALS=ZZ TREATMENT=PLACEBO

VISIT NO.	LABORATORY DATE	HB (g/dl)	HCT (%)	RBC (mln/cl)	WBC (/cl)	NEUTROPHILS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	BASOPHILS (%)	PLATELETS (tsd/cl)
-1	08NOV91	12	38.6	4.45	4.63 (L)	55.3	37.5	1.3 (L)	1.9	0.6	213
28	06DEC91	11.1 (L)	35.1 (L)	4.05 (L)	4.56 (L)	55.2	38.2	2.1 (L)	1.9	0.5	173

U = above the upper limit of normal range
L = below the lower limit of normal range
ND = note done

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REBOXETINE - PROTOCOL 20124/032

URINALYSIS

PATIENT NO.	INITIALS	TREATMENT	VISIT NO.	SPECIFIC GRAVITY (ND/N/A)	ALBUMIN (ND/N/A)	SUGAR (ND/N/A)	RBC (ND/N/A)	WBC (ND/N/A)
1	IR	REBOXETINE	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
2	FB	PLACEBO	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
3	BI	PLACEBO	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
4	PC	PLACEBO	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
5	BL	REBOXETINE	-1	ND	ND	ND	ND	ND
			28	N	N	N	N	N
			56	N	N	N	N	N
6	SM	REBOXETINE	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
7	DA	PLACEBO	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
8	SC	REBOXETINE	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
9	PA	PLACEBO	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
10	PE	PLACEBO	-1	N	N	N	N	N
			28	N	N	N	N	N

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

URINALYSIS

PATIENT NO.	INITIALS	TREATMENT	VISIT NO.	SPECIFIC GRAVITY (ND/N/A)	ALBUMIN (ND/N/A)	SUGAR (ND/N/A)	RBC (ND/N/A)	WBC (ND/N/A)
10	PE	PLACEBO	56	N	N	N	N	N
11	CL	PLACEBO	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
12	ML	PLACEBO	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
13	DSC	REBOXETINE	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
14	BM	REBOXETINE	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
15	GI	REBOXETINE	-1	N	N	N	N	N
			8	A	A	N	A	N
16	PJ	REBOXETINE	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
17	MM	REBOXETINE	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
18	VM	REBOXETINE	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
19	NI	PLACEBO	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
20	BE	PLACEBO	-1	N	N	N	N	N

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REBOXETINE - PROTOCOL 2124/052

URINALYSIS

PATIENT NO.	INITIALS	TREATMENT	VISIT NO.	SPECIFIC GRAVITY (ND/N/A)	ALBUMIN (ND/N/A)	SUGAR (ND/N/A)	RBC (ND/N/A)	WBC (ND/N/A)
20	BE	PLACEBO	28	N	N	N	N	N
			56	N	N	N	N	N
21	SE	REBOXETINE	-1	N	N	N	N	N
			28	N	N	N	N	N
22	BA	PLACEBO	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
23	UT	REBOXETINE	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
24	BEA	PLACEBO	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
25	GA	REBOXETINE	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
26	PR	REBOXETINE	-1	N	N	N	N	N
27	GA	PLACEBO	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
28	MR	REBOXETINE	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
29	TR	PLACEBO	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
30	PA	REBOXETINE	-1	N	N	N	N	N
			28	N	N	N	N	N

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REBOXETINE - PROTOCOL 20126/032

URINALYSIS

PATIENT NO.	INITIALS	TREATMENT	VISIT NO.	SPECIFIC GRAVITY (ND/N/A)	ALBUMIN (ND/N/A)	SUGAR (ND/N/A)	RBC (ND/N/A)	WBC (ND/N/A)
30	FA	REBOXETINE	56	N	N	N	N	N
31	CC	PLACEBO	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
32	CE	PLACEBO	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
33	VA	PLACEBO	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
34	BA	PLACEBO	-1	N	N	N	N	N
35	SB	PLACEBO	-1	N	N	N	N	N
			28	N	N	N	N	N
			56					
36	SM	REBOXETINE	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
37	SE	REBOXETINE	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
38	LO	PLACEBO	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
39	CP	REBOXETINE	-1	N	N	N	N	N
			28	N	N	N	N	N
40	PD	REBOXETINE	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 2012A/1032

URINALYSIS

PATIENT NO.	INITIALS	TREATMENT	VISIT NO.	SPECIFIC GRAVITY (ND/N/A)	ALBUMIN (ND/N/A)	SUGAR (ND/N/A)	RBC (ND/N/A)	WBC (ND/N/A)
41	FE	PLACEBO	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
42	LI	PLACEBO	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
43	PA	REBOXETINE	-1	N	N	N	N	N
			24	N	N	N	N	N
44	MZ	PLACEBO	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
45	PG	REBOXETINE	-1	N	N	N	N	N
			28	N	N	N	N	N
46	AD	REBOXETINE	-1	N	N	N	N	N
			28	N	N	N	N	N
47	SG	REBOXETINE	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
48	FA	PLACEBO	-1	N	N	N	N	N
			23	N	N	N	N	N
49	SA	PLACEBO	-1	N	N	N	N	N
			28	N	N	N	N	N
			56	N	N	N	N	N
50	ZZ	PLACEBO	-1	N	N	N	N	N
			28	N	N	N	N	N

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

LISTING OF LABORATORY ABNORMALITIES

TREATMENT	PATIENT NO.	INITIALS	SEX	VISIT	LABORATORY TEST	VALUE	MIN	MAX	% VARIATION ABOVE OR BELOW NORMAL RANGE	
REBOXETINE	6	SM	F	-1	HTC	30.90	37.00	47.00	-	-15
	6	SM	F	-1	RBC	3.19	4.20	5.40	-	-15
	8	SC	F	28	GAMMA-GT	121.00	1.00	35.00	+	100
	8	SC	F	56	SGPT	74.00	1.00	35.00	+	100
	13	DSC	F	56	GAMMA-GT	70.00	1.00	35.00	+	100
	14	BM	F	-1	GAMMA-GT	301.00	1.00	35.00	+	100
	14	BM	F	-1	ALKALINE PHOSPHATASE	314.00	30.00	100.00	+	100
	14	BM	F	28	GAMMA-GT	274.00	1.00	35.00	+	100
	14	BM	F	56	GAMMA-GT	224.00	1.00	35.00	+	100
	15	GI	F	8	LYMPHOCYTES	3.40	19.00	48.00	-	-30
	15	GI	F	8	DIRECT BILIRUBIN	22.30	1.71	6.84	+	100
	15	GI	F	8	NA+	101.00	135.00	150.00	+-	10
	15	GI	F	8	CL-	61.00	96.00	112.00	+-	10
	18	VM	M	-1	HTC	35.10	42.00	52.00	-	-15
	18	VM	M	28	HTC	35.00	42.00	52.00	-	-15
	18	VM	M	56	PO4-	0.60	0.80	1.61	+-	15
	28	MR	F	-1	LYMPHOCYTES	11.90	19.00	48.00	-	-30
	28	MR	F	-1	K+	2.90	3.50	5.30	+-	15
	28	MR	F	28	HTC	30.30	37.00	47.00	-	-15
	28	MR	F	28	RBC	3.31	4.20	5.40	-	-15
	37	SE	F	28	GLOBULINS: GAMMA	27.60	12.00	20.00	+-	30
	39	CP	M	-1	GAMMA-GT	112.00	1.00	50.00	+	100
	39	CP	M	28	GAMMA-GT	107.00	1.00	50.00	+	100
	40	PO	M	-1	HB	10.90	14.00	18.00	-	-15
	40	PO	M	-1	HTC	33.80	42.00	52.00	-	-15
	40	PO	M	-1	RBC	3.38	4.70	6.10	-	-15
	40	PO	M	28	HB	11.50	14.00	18.00	-	-15
	40	PO	M	28	RBC	3.64	4.70	6.10	-	-15
	45	PG	F	28	BUN	12.50	1.66	8.32	+	50
	46	AD	M	-1	RBC	3.87	4.70	6.10	-	-15
	46	AD	M	28	BUN	14.20	1.66	8.32	+	50
PLACEBO	7	DA	F	-1	HB	9.40	12.00	16.00	-	-15
	7	DA	F	-1	HTC	28.90	37.00	47.00	-	-15
	7	DA	F	-1	RBC	3.17	4.20	5.40	-	-15
	9	PA	M	-1	HB	11.30	14.00	18.00	-	-15
	9	PA	M	-1	HTC	34.90	42.00	52.00	-	-15
	10	PE	M	-1	HB	11.30	14.00	18.00	-	-15
	10	PE	M	-1	HTC	34.10	42.00	52.00	-	-15
	10	PE	M	-1	RBC	3.67	4.70	6.10	-	-15
	10	PE	M	28	HB	11.70	14.00	18.00	-	-15
	10	PE	M	28	RBC	3.85	4.70	6.10	-	-15
	10	PE	M	28	GLOBULINS: ALFA2	18.30	7.00	12.00	+-	30
	10	PE	M	56	HB	11.20	14.00	18.00	-	-15

(*) MINUS INDICATES BELOW THE LOWER LIMIT OF NORMAL RANGE, PLUS ABOVE THE UPPER LIMIT OF NORMAL RANGE

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

LISTING OF LABORATORY ABNORMALITIES

TREATMENT	PATIENT NO.	INITIALS	SEX	VISIT	LABORATORY TEST	VALUE	MIN	MAX	% VARIATION ABOVE OR BELOW NORMAL RANGE	
PLACEBO	10	PE	M	56	RBC	3.84	4.70	6.10	-	-15
	10	PE	M	56	GAMMA-GT	114.00	1.00	50.00	+	100
	10	PE	M	56	GLOBULINS: ALFA2	18.40	7.00	12.00	+-	30
	10	PE	M	56	BLOOD SUGAR	9.30	3.33	6.10	+-	30
	11	CL	F	-1	HB	8.30	12.00	16.00	-	-15
	11	CL	F	-1	HTC	27.20	37.00	47.00	-	-15
	11	CL	F	-1	BUN	12.80	1.66	8.32	+	50
	11	CL	F	-1	URIC ACID	0.60	0.14	0.34	+	30
	11	CL	F	-1	ALKALINE PHOSPHATASE	213.00	30.00	100.00	+	100
	11	CL	F	28	HB	8.20	12.00	16.00	-	-15
	11	CL	F	28	HTC	27.60	37.00	47.00	-	-15
	11	CL	F	28	RBC	3.52	4.20	5.40	-	-15
	11	CL	F	28	BUN	12.90	1.66	8.32	+	50
	11	CL	F	28	ALKALINE PHOSPHATASE	222.00	30.00	100.00	+	100
	11	CL	F	56	HB	7.80	12.00	16.00	-	-15
	11	CL	F	56	HTC	26.60	37.00	47.00	-	-15
	11	CL	F	56	RBC	3.36	4.20	5.40	-	-15
	19	NI	F	-1	WBC	3.19	4.80	10.80	-	-30
	19	NI	F	28	WBC	3.17	4.80	10.80	-	-30
	19	NI	F	56	WBC	3.19	4.80	10.80	-	-30
	20	BE	M	-1	PO4-	0.60	0.80	1.61	+-	15
	20	BE	M	28	PO4-	0.60	0.80	1.61	+-	15
	20	BE	M	36	PO4-	0.60	0.80	1.61	+-	15
	22	BA	F	28	PO4-	0.60	0.80	1.61	+-	15
	24	BEA	F	-1	ALKALINE PHOSPHATASE	356.00	30.00	100.00	+	100
	24	BEA	F	-1	CA++	1.60	2.12	2.61	+-	15
	24	BEA	F	28	ALKALINE PHOSPHATASE	316.00	30.00	100.00	+	100
	24	BEA	F	28	NA+	120.00	135.00	150.00	+-	10
	24	BEA	F	56	RBC	3.47	4.20	5.40	-	-15
	24	BEA	F	56	ALKALINE PHOSPHATASE	278.00	30.00	100.00	+	100
	27	GA	F	-1	PO4-	2.50	0.80	1.61	+-	15
	29	TR	M	-1	CA++	1.60	2.12	2.61	+-	15
	31	CC	F	56	CL-	84.00	96.00	112.00	+-	10
	33	VA	M	56	LYMPHOCYTES	12.40	19.00	48.00	-	-30
	33	VA	M	56	BLOOD SUGAR	8.10	3.33	6.10	+-	30
	41	FE	F	56	GAMMA-GT	137.00	1.00	35.00	+	100
	42	LI	F	-1	BLOOD SUGAR	8.40	3.33	6.10	+-	30
	42	LI	F	28	PO4-	0.60	0.80	1.61	+-	15
	42	LI	F	56	BUN	13.20	1.66	8.32	+	50
	44	MZ	M	-1	HB	11.00	14.00	18.00	-	-15
	44	MZ	M	-1	HTC	35.00	42.00	52.00	-	-15
	44	MZ	M	-1	RBC	3.51	4.70	6.10	-	-15
	44	MZ	M	-1	BUN	15.30	1.66	8.32	+	50
	44	MZ	M	-1	GLOBULINS: GAMMA	31.20	12.00	20.00	+-	30

(*) MINUS INDICATES BELOW THE LOWER LIMIT OF NORMAL RANGE, PLUS ABOVE THE UPPER LIMIT OF NORMAL RANGE

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

LISTING OF LABORATORY ABNORMALITIES

TREATMENT	PATIENT NO.	INITIALS	SEX	VISIT	LABORATORY TEST	VALUE	MIN	MAX	% VARIATION ABOVE OR BELOW NORMAL RANGE
PLACEBO	44	M2	M	28	HB	11.40	14.00	18.00	-15
	44	M2	M	28	HTC	35.00	42.00	52.00	-15
	44	M2	M	28	RBC	3.57	4.70	6.10	-15
	44	M2	M	28	BUN	14.30	1.66	8.32	50
	44	M2	M	28	GLOBULINS: GAMMA	33.60	12.00	20.00	30
	44	M2	M	56	HB	10.60	14.00	18.00	-15
	44	M2	M	56	HTC	32.00	42.00	52.00	-15
	44	M2	M	56	RBC	3.35	4.70	6.10	-15
	44	M2	M	56	BUN	19.80	1.66	8.32	50
	44	M2	M	56	GLOBULINS: GAMMA	31.60	12.00	20.00	30
	50	22	F	28	GAMMA-GT	104.00	1.00	35.00	100

(*) MINUS INDICATES BELOW THE LOWER LIMIT OF NORMAL RANGE, PLUS ABOVE THE UPPER LIMIT OF NORMAL RANGE

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

VITAL SIGNS

Pat. No.	Initials	Treatment	Visit No.	Body Temp.	Respiratory Rate (breaths/min)	5m. Lying Sys BP (mmHg)	5m. Lying Dias BP (mmHg)	5m. Lying Heart Rate (beats/min)	2m. Stand Sys BP (mmHg)	2m. Stand Dias BP (mmHg)	2m. Stand Heart Rate (beats/min)	Body Weigth (kg)
1	TR	REBOXETINE	-1	36.5	20	140	80	80	130	80	92	.
			0	37.6	.	140	80	80	130	80	92	75
			7	36.4	.	130	80	80	125	75	92	75
			14	36.6	.	145	80	78	140	80	84	75
			28	36.6	.	145	70	86	135	75	92	74
			56	36.5	.	150	80	96	145	75	106	72
2	FB	PLACEBO	-1	36.5	20	160	80	76	160	80	78	.
			0	36.7	.	110	60	58	135	70	60	65
			7	36.4	.	130	40	64	120	75	68	65
			14	36.7	.	135	70	64	125	70	66	65
			28	36.7	.	140	80	76	135	75	80	67
			56	36.8	.	140	70	70	135	70	78	67
3	BI	PLACEBO	-1	36.6	22	145	70	60	130	70	68	.
			0	36.7	.	145	80	60	140	70	64	52
			7	36.6	.	145	70	60	140	70	68	52
			14	36.6	.	145	70	64	140	70	68	52
			28	36.4	.	150	80	72	145	75	76	51
			56	36.4	.	140	70	74	120	70	80	53
4	PC	PLACEBO	-1	36.8	22	140	70	78	135	70	80	.
			0	36.7	.	140	80	74	135	75	78	56
			7	36.4	.	160	80	70	155	85	74	56
			14	36.4	.	150	80	72	145	75	78	56
			21	36.4	.	180	90	80	170	85	86	55
			28	36.6	.	150	70	82	140	75	86	55
			56	36.6	.	110	60	100	110	65	120	53
5	BL	REBOXETINE	-1	36.8	20	140	70	82	130	70	88	.
			0	36.8	.	130	70	76	125	70	84	52
			7	36.4	.	145	70	88	140	70	92	53
			14	36.7	.	140	70	84	135	75	88	53
			28	36.6	.	180	85	82	175	80	86	52
			56	36.4	.	180	85	92	165	90	104	52
6	SM	REBOXETINE	-1	36.7	22	160	80	80	150	80	84	.
			0	36.8	.	160	80	74	150	75	80	67
			7	36.4	.	110	60	84	100	65	92	67
			14	36.4	.	115	75	76	110	70	84	68
			28	36.8	.	160	90	76	150	85	84	64
			56	36.8	.	110	70	92	110	75	104	63
7	DA	PLACEBO	-1	36.5	20	120	70	84	115	75	88	.
			0	36.5	.	120	70	84	115	75	88	49
			7	36.5	.	120	70	78	115	70	82	49
			14	36.6	.	120	70	84	110	70	88	49
			28	36.6	.	135	70	76	115	70	82	47

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 28124/032

VITAL SIGNS

Pat. No.	Initials	Treatment	Visit No.	Body Temp.	Respiratory Rate (breaths/min)	5m. Lying Sys BP (mmHg)	5m. Lying Dias BP (mmHg)	5m. Lying Heart Rate (beats/min)	2m. Stand Sys BP (mmHg)	2m. Stand Dias BP (mmHg)	2m. Stand Heart Rate (beats/min)	Body Heigth (kg)
7	DA	PLACEBO	56	35.8	.	135	80	74	125	70	80	45
8	SC	REBOXETINE	-1	36.5	24	120	75	74	115	70	80	.
			0	36.4	.	125	75	88	115	70	92	82
			7	36.4	.	120	75	92	115	70	94	82
			14	36.5	.	130	75	88	120	70	96	82
			28	36.8	.	145	100	92	135	100	98	78
			56	36.8	.	130	85	100	120	80	112	75
9	PA	PLACEBO	-1	36.4	20	115	80	88	110	75	92	.
			0	36.7	.	125	80	84	115	75	88	70
			7	36.7	.	125	80	80	115	75	84	70
			14	36.4	.	120	80	84	115	75	88	69
			28	36.8	.	140	90	82	130	85	88	69
			56	35.8	.	140	90	84	135	90	88	70
10	PE	PLACEBO	-1	36.4	20	160	80	66	155	80	70	.
			0	36.6	.	160	80	70	155	85	74	61
			7	36.3	.	160	80	64	155	75	72	61
			14	36.6	.	150	80	68	145	80	74	61
			28	37.0	.	185	90	78	180	95	84	58
			56	36.8	.	175	90	84	170	85	90	.
11	CL	PLACEBO	-1	36.4	22	130	65	80	120	70	84	.
			0	36.5	.	130	70	80	125	70	84	82
			7	36.4	.	130	65	90	120	70	84	82
			14	36.7	.	130	75	78	125	70	82	82
			28	36.6	.	130	70	80	120	70	86	80
			56	36.4	.	140	85	88	120	75	100	80
12	ML	PLACEBO	-1	36.4	24	150	80	100	145	85	108	.
			0	35.8	.	150	80	100	145	80	104	70
			14	36.4	.	180	80	68	185	90	80	69
			28	36.7	.	160	80	80	155	85	86	68
			56	36.5	.	140	80	80	135	75	90	69
13	DSC	REBOXETINE	-1	35.7	18	150	90	70	145	85	76	.
			0	35.7	.	145	90	72	140	90	76	59
			7	36.6	.	155	90	80	130	90	86	59
			14	36.2	.	150	85	76	140	85	84	58
			28	36.7	.	150	80	74	140	70	80	56
			56	36.8	.	130	80	94	130	90	100	56
14	BM	REBOXETINE	-1	35.9	20	140	85	80	135	80	84	.
			0	35.7	.	140	80	82	135	75	86	59
			14	36.8	.	130	85	92	120	80	98	58
			21	36.8	.	140	80	76	130	70	84	58
			28	36.7	.	140	80	76	130	70	84	58

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

VITAL SIGNS

Pat. No.	Initials	Treatment	Visit No.	Body Temp.	Respiratory Rate (breaths/min)	5m. Lying Sys BP (mmHg)	5m. Lying Dias BP (mmHg)	5m. Lying Heart Rate (beats/min)	2m. Stand Sys BP (mmHg)	2m. Stand Dias BP (mmHg)	2m. Stand Heart Rate (beats/min)	Body Weigth (kg)
14	BM	REBOXETINE	56	36.4	.	130	80	78	125	75	84	58
15	GI	REBOXETINE	-1	36.4	20	140	80	76	135	75	80	.
			0	35.8	.	140	80	76	135	75	82	48
			7	36.8	.	160	80	76	140	80	80	48
			8	35.7	.	150	80	96	105	60	110	47
16	PJ	REBOXETINE	-1	36.2	20	140	80	73	135	75	80	.
			0	35.8	.	140	80	78	135	80	82	72
			14	36.4	.	145	70	80	140	80	84	71
			28	36.4	.	140	70	80	130	70	84	69
			56	36.4	.	145	80	72	140	80	86	70
17	MM	REBOXETINE	-1	36.6	16	150	90	88	145	85	94	.
			0	35.8	.	145	90	80	135	85	84	54
			14	36.8	.	170	100	100	145	100	104	51
			28	36.4	.	150	90	92	140	85	104	51
			56	36.8	.	130	80	78	125	80	88	51
18	VM	REBOXETINE	-1	36.4	18	140	80	70	135	75	72	.
			0	35.8	.	140	80	70	135	75	76	78
			14	36.4	.	130	70	80	115	75	100	77
			28	36.4	.	135	70	80	125	75	86	76
			56	36.4	.	140	70	82	140	75	88	75
19	NI	PLACEBO	-1	35.6	18	135	70	72	130	75	76	.
			0	35.8	.	135	70	74	130	75	80	45
			14	36.4	.	160	80	76	140	85	80	44
			28	36.7	.	150	80	80	140	75	96	44
			56	36.4	.	130	70	76	130	75	84	44
20	BE	PLACEBO	-1	35.8	16	145	80	76	140	75	80	.
			0	35.8	.	145	80	74	135	75	78	73
			14	36.6	.	180	100	80	150	90	98	72
			28	36.4	.	160	70	80	145	75	92	72
			36	36.8	.	170	80	94	165	85	104	71
21	SE	REBOXETINE	-1	35.8	18	120	80	74	115	75	80	.
			0	35.7	.	130	70	74	125	70	78	73
			14	36.4	.	120	80	88	110	75	94	73
			28	36.8	.	120	70	86	110	70	92	70
			30	36.8	.	120	70	86	110	75	94	71
22	BA	PLACEBO	-1	36.0	22	120	65	80	115	70	84	.
			0	36.5	.	125	70	70	120	75	74	74
			14	36.4	.	150	80	80	140	75	84	74
			28	36.5	.	160	75	74	150	80	82	73
			56	36.8	.	150	85	76	145	80	84	73

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

VITAL SIGNS

Pat. No.	Initials	Treatment	Visit No.	Body Temp.	Respiratory Rate (breaths/min)	5m. Lying Sys BP (mmHg)	5m. Lying Dias BP (mmHg)	5m. Lying Heart Rate (beats/min)	2m. Stand Sys BP (mmHg)	2m. Stand Dias BP (mmHg)	2m. Stand Heart Rate (beats/min)	Body Weigth (kg)
23	UT	REBOXETINE	-1	36.4	19	160	80	76	155	85	80	.
			0	36.4	.	140	80	68	135	80	74	67
			14	36.7	.	135	70	78	130	75	84	66
			28	36.4	.	140	70	78	140	75	84	65
			56	36.5	.	130	60	76	125	65	82	66
24	BEA	PLACEBO	-1	36.4	24	140	75	84	135	70	90	.
			0	36.8	.	140	70	70	135	75	76	38
			14	36.4	.	135	70	78	125	75	86	38
			28	36.6	.	135	70	76	130	70	80	37
			56	36.5	.	150	70	74	150	80	78	37
25	GA	REBOXETINE	-1	36.5	22	160	80	80	150	75	90	.
			0	36.6	.	150	80	76	145	80	84	83
			14	36.4	.	150	85	76	145	80	84	82
			28	36.4	.	140	80	72	135	75	78	82
			56	36.6	.	130	70	78	125	75	84	83
26	PR	REBOXETINE	-1	36.4	18	120	70	90	115	75	96	.
			0	36.8	.	120	80	78	110	75	90	73
			14	36.7	.	120	70	76	.	.	.	72
27	GA	PLACEBO	-1	36.4	20	170	90	76	165	95	84	.
			0	36.6	.	170	90	78	165	85	86	82
			14	36.8	.	145	80	76	140	80	84	84
			28	36.6	.	160	80	76	150	70	86	85
			56	36.8	.	170	80	80	160	85	86	85
28	MR	REBOXETINE	-1	36.4	22	170	80	84	160	80	92	.
			0	36.4	.	170	90	76	165	85	82	68
			14	36.8	.	210	100	80	200	105	85	67
			28	36.4	.	150	80	98	145	85	110	66
			56	36.6	.	145	80	76	145	75	84	67
29	TR	PLACEBO	-1	36.6	22	125	80	76	120	75	84	.
			0	36.4	.	120	70	72	115	70	76	64
			14	36.6	.	120	70	76	120	75	84	66
			28	36.4	.	130	80	74	125	80	80	68
			56	36.5	.	130	80	78	120	80	86	68
30	PA	REBOXETINE	-1	36.6	22	180	90	80	175	85	84	.
			0	36.6	.	170	85	78	165	85	84	53
			14	36.6	.	180	100	84	175	100	88	52
			28	36.7	.	180	90	78	170	85	84	52
			56	36.4	.	180	90	76	175	80	80	52
31	CC	PLACEBO	-1	36.6	20	170	80	84	160	80	92	.
			0	36.5	.	160	80	76	155	80	84	42

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

VITAL SIGNS

Pat. No.	Initials	Treatment	Visit No.	Body Temp.	Respiratory Rate (breaths/min)	5m. Lying Sys BP (mmHg)	5m. Lying Dias BP (mmHg)	5m. Lying Heart Rate (beats/min)	2m. Stand Sys BP (mmHg)	2m. Stand Dias BP (mmHg)	2m. Stand Heart Rate (beats/min)	Body Weigth (kg)
31	CC	PLACEBO	14	36.6	.	160	80	78	150	85	84	44
			28	36.7	.	180	80	76	175	85	82	44
			56	35.8	.	135	80	72	130	85	78	45
32	CE	PLACEBO	-1	36.5	18	135	70	70	140	80	76	.
			0	36.6	.	130	70	76	125	75	84	74
			14	36.8	.	160	90	78	155	85	86	74
			28	36.4	.	125	75	74	120	80	80	72
			56	36.4	.	140	70	72	135	75	78	71
33	VA	PLACEBO	-1	36.5	20	150	80	84	145	80	88	.
			0	36.4	.	130	70	76	125	75	82	96
			14	36.5	.	140	70	78	135	75	84	95
			28	36.4	.	150	70	78	150	75	86	94
			56	36.7	.	130	70	76	125	75	84	92
34	BA	PLACEBO	-1	36.5	18	150	80	74	145	80	78	.
			0	36.6	.	150	80	64	140	75	72	64
			7	36.4	.	150	80	72	145	80	78	64
35	SB	PLACEBO	-1	36.4	16	150	80	72	140	75	76	.
			0	36.4	.	140	80	72	135	80	78	76
			14	36.6	.	130	70	72	120	75	78	73
			28	36.7	.	130	75	78	120	75	82	74
			56	36.6	.	130	70	72	125	75	80	73
36	SM	REBOXETINE	-1	36.5	18	140	80	76	135	80	82	.
			0	36.4	.	135	80	74	130	80	82	59
			14	36.4	.	130	70	72	130	70	78	62
			28	36.6	.	140	80	76	130	75	82	63
			56	36.6	.	115	80	76	105	75	84	64
37	SE	REBOXETINE	-1	36.4	20	125	80	76	120	80	84	.
			0	36.4	.	130	70	76	125	75	82	64
			14	36.4	.	120	70	100	115	75	104	64
			28	36.4	.	140	85	76	135	85	82	64
			56	36.4	.	130	80	72	120	75	80	62
38	LO	PLACEBO	-1	36.6	20	140	70	76	135	75	84	.
			0	36.4	.	180	80	76	175	80	84	65
			14	36.4	.	150	70	68	145	70	76	66
			28	36.5	.	140	80	78	130	80	84	65
			56	36.4	.	150	70	72	140	70	78	65
39	CP	REBOXETINE	-1	36.4	18	170	80	72	165	80	78	.
			0	36.4	.	160	80	68	150	80	76	67
			14	36.7	.	160	100	78	155	95	84	67
			28	36.6	.	150	90	76	145	85	84	67

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

VITAL SIGNS

Pat. No.	Initials	Treatment	Visit No.	Body Temp.	Respiratory Rate (breaths/min)	5m. Lying Sys BP (mmHg)	5m. Lying Dias BP (mmHg)	5m. Lying Heart Rate (beats/min)	2m. Stand Sys BP (mmHg)	2m. Stand Dias BP (mmHg)	2m. Stand Heart Rate (beats/min)	Body Heigth (kg)
39	CP	REBOXETINE	33	36.8	.	150	90	72	140	90	78	67
40	PO	REBOXETINE	-1	36.4	22	110	60	74	100	65	80	.
			0	36.5	.	120	80	76	110	80	84	83
			14	36.4	.	115	70	70	110	70	76	82
			28	36.6	.	115	70	76	110	75	84	83
			56	36.6	.	120	70	72	115	75	78	84
41	FE	PLACEBO	-1	36.4	18	135	70	70	130	75	74	.
			0	36.4	.	140	80	70	135	80	74	65
			14	36.6	.	140	80	74	135	75	78	66
			28	36.4	.	155	75	76	150	75	84	65
			56	36.4	.	135	80	74	130	80	80	63
42	LI	PLACEBO	-1	36.7	20	180	90	84	175	85	90	.
			0	36.6	.	190	100	84	185	105	88	48
			14	36.4	.	180	90	76	175	90	82	48
			28	36.5	.	180	95	76	175	90	84	49
			56	36.5	.	160	85	76	150	80	80	46
43	PA	REBOXETINE	-1	36.5	18	180	100	77	175	95	84	.
			0	36.6	.	160	90	76	150	85	82	60
			14	36.5	.	150	80	76	145	80	78	60
			21	36.7	.	170	90	80	160	80	84	60
			24	36.6	.	180	100	80	170	95	84	61
44	MZ	PLACEBO	-1	36.6	22	180	70	76	170	80	82	.
			0	36.4	.	190	80	68	180	85	76	55
			14	36.6	.	125	70	64	115	75	68	60
			28	36.7	.	150	60	78	140	65	86	57
			56	36.5	.	140	65	76	140	70	82	55
45	PG	REBOXETINE	-1	36.4	20	130	80	80	120	75	84	.
			0	36.7	.	140	80	72	135	80	78	90
			14	36.4	.	145	80	74	140	75	78	89
			28	36.7	.	120	70	76	110	75	82	86
46	AD	REBOXETINE	-1	36.8	20	130	80	70	125	85	76	.
			0	36.4	.	140	70	68	135	75	74	58
			14	36.4	.	135	70	72	130	70	76	59
			28	36.4	.	160	85	70	150	80	76	60
47	SG	REBOXETINE	-1	36.6	22	170	80	78	160	85	84	.
			0	36.7	.	160	80	74	150	80	78	45
			14	36.4	.	120	60	74	115	65	80	43
			28	36.7	.	140	80	72	130	75	80	41
			56	36.4	.	125	70	74	120	75	78	40

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

VITAL SIGNS

Pat. No.	Initials	Treatment	Visit No.	Body Temp.	Respiratory Rate (breaths/min)	5m. Lying Sys BP (mmHg)	5m. Lying Dias BP (mmHg)	5m. Lying Heart Rate (beats/min)	2m. Stand Sys BP (mmHg)	2m. Stand Dias BP (mmHg)	2m. Stand Heart Rate (beats/min)	Body Weigth (kg)
48	FA	PLACEBO	-1	36.6	22	145	85	80	140	85	86	.
			0	36.6	.	150	85	78	140	85	84	64
			14	36.6	.	140	80	76	130	80	82	64
			23	36.6	.	160	80	84	150	75	88	62
49	SA	PLACEBO	-1	36.8	18	110	60	72	100	65	76	.
			0	36.8	.	120	70	74	115	75	78	63
			14	36.5	.	145	80	76	140	80	84	62
			28	36.4	.	145	80	72	135	80	84	63
			56	36.6	.	155	80	72	150	80	76	64
50	22	PLACEBO	-1	36.5	20	140	70	78	.	.	.	.
			0	36.5	.	150	70	64	145	75	70	58
			14	36.6	.	145	70	72	140	75	78	54
			28	36.4	.	155	80	78	145	75	84	54

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

ECG
TREATMENT: REBOXETINE

Patient No.	Initials	Visit Day	Heart Rate	Date of ECG	Result (*)	Abnormalities (Specify)	Abnormalities
1	TR	-1	90	20MAY91	A		LEFT VENTRICULAR HYPERTROPHY
1	TR	28	90	02JUL91	A		LEFT VENTRICULAR HYPERTROPHY
1	TR	56	84	30JUL91	N		.
5	BL	-1	78	25MAY91	N		.
5	BL	28	86	02JUL91	N		.
5	BL	56	82	30JUL91	N		.
6	SM	-1	77	04JUN91	A		RIGHT BUNDLE BRANCH BLOCK
6	SM	28	86	02JUL91	A		VENTRICULAR ECTOPIC BEATS - OCCASIONAL RIGHT VENTRICULAR HYPERTROPHY
6	SM	56	90	30JUL91	A		ATRIAL ECTOPIC BEATS - OCCASIONAL VENTRICULAR ECTOPIC BEATS - OCCASIONAL RIGHT BUNDLE BRANCH BLOCK
8	SC	-1	108	25MAY91	A		SINUS TACHYCARDIA (> 100) VENTRICULAR ECTOPIC BEATS - OCCASIONAL LEFT VENTRICULAR HYPERTROPHY LEFT ANTERIOR HEMIBLOCK
8	SC	28	100	02JUL91	A		LEFT VENTRICULAR HYPERTROPHY LEFT ANTERIOR HEMIBLOCK
8	SC	56	107	30JUL91	A		SINUS TACHYCARDIA (> 100) LEFT VENTRICULAR HYPERTROPHY LEFT ANTERIOR HEMIBLOCK
13	DSC	-1	71	03JUL91	N		.
13	DSC	28	77	05AUG91	N		.
13	DSC	56	88	02SEP91	N		.
14	BM	-1	90	01JUL91	N		.
14	BM	28	91	05AUG91	N		.
14	BM	56	92	02SEP91	N		.
15	GI	-1	76	01JUL91	A	COR PULMONALE	OTHER

RESULT: N=NORMAL A=ABNORMAL

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

ECG
TREATMENT: REBOXETINE

Patient No.	Initials	Visit Day	Heart Rate	Date of ECG	Result (*)	Abnormalities (Specify)	Abnormalities
15	GI	8	76	16JUL91	A	COR PULMONALE	OTHER
16	PJ	-1	71	02JUL91	A		LEFT VENTRICULAR HYPERTROPHY LEFT ANTERIOR HEMIBLOCK
16	PJ	28	94	05AUG91	A		LEFT VENTRICULAR HYPERTROPHY LEFT BUNDLE BRANCH BLOCK
16	PJ	56	80	02SEP91	A		LEFT VENTRICULAR HYPERTROPHY LEFT BUNDLE BRANCH BLOCK
17	MM	-1	92	04JUL91	A		LEFT ANTERIOR HEMIBLOCK
17	MM	28	92	05AUG91	A		LEFT ANTERIOR HEMIBLOCK
17	MM	56	110	02SEP91	A		LEFT ANTERIOR HEMIBLOCK
18	VM	-1	78	02JUL91	A		LEFT ANTERIOR HEMIBLOCK
18	VM	28	86	05AUG91	A		LEFT ANTERIOR HEMIBLOCK
18	VM	56	86	02SEP91	A		LEFT ANTERIOR HEMIBLOCK
21	SE	-1	78	02JUL91	A		LEFT ANTERIOR HEMIBLOCK
21	SE	28	86	05AUG91	A		RIGHT BUNDLE BRANCH BLOCK
23	UT	-1	68	13AUG91	A	LEFT VENTRICLE OVERLOADED	ATRIAL ECTOPIC BEATS - OCCASIONAL OTHER
23	UT	28	83	07OCT91	A		OTHER
23	UT	56	86	04NOV91	A	LEFT VENTRICLE OVERLOADED	OTHER
25	GA	-1	70	31AUG91	A		RIGHT BUNDLE BRANCH BLOCK
25	GA	28	76	07OCT91	A		RIGHT BUNDLE BRANCH BLOCK
25	GA	56	77	04NOV91	A		RIGHT BUNDLE BRANCH BLOCK
26	PR	-1	118	31AUG91	A		ATRIAL FIBRILLATION / FLUTTER
28	MR	-1	80	31AUG91	N		
28	MR	28	100	07OCT91	A		VENTRICULAR ECTOPIC BEATS - OCCASIONAL
28	MR	56	100	04NOV91	A		SINUS TACHYCARDIA (> 100)

RESULT: N=NORMAL A=ABNORMAL

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

ECG
TREATMENT: REBOXETINE

Patient No.	Initials	Visit Day	Heart Rate	Date of ECG	Result (*)	Abnormalities (Specify)	Abnormalities
28	MR	56	100	04NOV91	A		ATRIAL ECTOPIC BEATS - OCCASIONAL
30	PA	-1	86	30SEP91	A		ATRIAL FIBRILLATION / FLUTTER
30	PA	28	98	04NOV91	A	LEFT VENTRICLE OVERLOADED	ATRIAL FIBRILLATION / FLUTTER LEFT AXIAL DEVIATION
30	PA	56	103	02DEC91	A	LEFT VENTRICLE OVERLOADED	ATRIAL FIBRILLATION / FLUTTER LEFT AXIAL DEVIATION
36	SM	-1	60	02OCT91	N		.
36	SM	28	79	04NOV91	A		ATRIAL ECTOPIC BEATS - OCCASIONAL
36	SM	56	81	02DEC91	N		.
37	SE	-1	100	01OCT91	A		LEFT ANTERIOR HEMIBLOCK
37	SE	28	98	04NOV91	N		.
37	SE	56	90	02DEC91	N		.
39	CP	-1	76	06OCT91	A		LEFT BUNDLE BRANCH BLOCK
39	CP	28	83	04NOV91	A		LEFT BUNDLE BRANCH BLOCK
40	PO	-1	75	02NOV91	A		ATRIAL FIBRILLATION / FLUTTER
40	PO	28	72	06DEC91	A		ATRIAL FIBRILLATION / FLUTTER
40	PO	56	84	03JAN92	A		ATRIAL FIBRILLATION / FLUTTER
43	PA	-1	60	30OCT91	A	LEFT BUNDLE CONDUCTION DISTUR.	SINUS BRADYCARDIA (< 60) OTHER
43	PA	24	68	03DEC91	A		VENTRICULAR ECTOPIC BEATS - OCCASIONAL RIPOLARIZATION DISTURBANCES
45	PG	-1	72	30OCT91	A	PACEMAKER RHYTHM	OTHER
45	PG	28	72	06DEC91	A	PACEMAKER RHYTHM	OTHER
46	AD	-1	53	06NOV91	A		SINUS BRADYCARDIA (< 60) LEFT VENTRICULAR HYPERTROPHY
46	AD	28	61	06DEC91	A		ATRIAL ECTOPIC BEATS - OCCASIONAL LEFT VENTRICULAR HYPERTROPHY

RESULT: N=NORMAL A=ABNORMAL

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

ECG

TREATMENT: REBOXETINE

Patient No.	Initials	Visit Day	Heart Rate	Date of ECG	Result (*)	Abnormalities (Specify)	Abnormalities
47	SG	-1	64	06NOV91	A		LEFT VENTRICULAR HYPERTROPHY RIGHT BUNDLE BRANCH BLOCK
47	SG	28	75	06DEC91	A		RIGHT BUNDLE BRANCH BLOCK
47	SG	56	89	03JAN92	A		RIGHT BUNDLE BRANCH BLOCK

RESULT: N=NORMAL A=ABNORMAL

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

ECG

TREATMENT: PLACEBO

Patient No.	Initials	Visit Day	Heart Rate	Date of ECG	Result (*)	Abnormalities (Specify)	Abnormalities
2	FB	-1	72	25MAY91	N		
2	FB	28	58	02JUL91	N		
2	FB	56	65	30JUL91	N		
3	BI	-1	49	25MAY91	A		SINUS BRADYCARDIA (< 60) MYOCARDIAL ISCHEMIA LEFT AXIAL DEVIATION
3	BI	28	68	02JUL91	A		MYOCARDIAL ISCHEMIA LEFT AXIAL DEVIATION
3	BI	56	56	30JUL91	A		MYOCARDIAL ISCHEMIA LEFT AXIAL DEVIATION
4	PC	-1	73	25MAY91	A		MYOCARDIAL ISCHEMIA
4	PC	28	88	02JUL91	A		MYOCARDIAL ISCHEMIA
4	PC	56	83	30JUL91	A		VENTRICULAR ECTOPIC BEATS - OCCASIONAL
7	DA	-1	72	04JUN91	A		LEFT AXIAL DEVIATION
7	DA	28	96	02JUL91	A		LEFT AXIAL DEVIATION
7	DA	56	74	30JUL91	A		LEFT AXIAL DEVIATION
9	PA	-1	86	25MAY91	A		ATRIAL ECTOPIC BEATS - OCCASIONAL
9	PA	28	84	02JUL91			
9	PA	56	82	30JUL91	N		
10	PE	-1	79	30MAY91	A		VENTRIC. ECTOPIC BEATS-FREQUENT (>6/MM) LEFT VENTRICULAR HYPERTROPHY
10	PE	28	49	02JUL91	A		SINUS BRADYCARDIA (< 60) VENTRIC. ECTOPIC BEATS - COUPLETS
10	PE	56	70	11JUL91	A		VENTRIC. ECTOPIC BEATS-FREQUENT (>6/MM) LEFT VENTRICULAR HYPERTROPHY
11	CL	-1	85	03JUN91	N		
11	CL	28	85	02JUL91	N		

RESULT: N=NORMAL A=ABNORMAL

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

ECG

TREATMENT: PLACEBO

Patient No.	Initials	Visit Day	Heart Rate	Date of ECG	Result (*)	Abnormalities (Specify)	Abnormalities
11	CL	56	99	30JUL91	N		
12	ML	-1	63	01JUL91	A		LEFT BUNDLE BRANCH BLOCK
12	ML	28	68	05AUG91	A		LEFT BUNDLE BRANCH BLOCK
12	ML	56	84	02SEP91	A		LEFT BUNDLE BRANCH BLOCK
19	NI	-1	77	05JUL91	N		
19	NI	28	70	05AUG91	N		
19	NI	56	74	02SEP91	N		
20	BE	-1	101	04JUL91	A		VENTRIC. ECTOPIC BEATS-FREQUENT (>6/MN)
20	BE	28	90	05AUG91	A		ATRIAL ECTOPIC BEATS - OCCASIONAL VENTRICULAR ECTOPIC BEATS - OCCASIONAL
22	BA	-1	78	31AUG91	A		ATRIAL ECTOPIC BEATS - OCCASIONAL LEFT ANTERIOR HEMIBLOCK
22	BA	28	60	07OCT91	A		LEFT ANTERIOR HEMIBLOCK
22	BA	56	74	04NOV91	A		ATRIAL ECTOPIC BEATS - OCCASIONAL LEFT ANTERIOR HEMIBLOCK
24	BEA	-1	64	31AUG91	A		LEFT VENTRICULAR HYPERTROPHY
24	BEA	28	65	07OCT91	A		LEFT VENTRICULAR HYPERTROPHY LEFT ANTERIOR HEMIBLOCK
24	BEA	56	72	04NOV91	A		LEFT ANTERIOR HEMIBLOCK
27	GA	-1	78	31AUG91	A		ATRIAL ECTOPIC BEATS - OCCASIONAL
27	GA	28	95	07OCT91	N		
27	GA	56	96	04NOV91	A		ATRIAL ECTOPIC BEATS - OCCASIONAL
29	TR	-1	62	31AUG91	A		LEFT VENTRICULAR HYPERTROPHY LEFT ANTERIOR HEMIBLOCK
29	TR	28	54	07OCT91	A		LEFT VENTRICULAR HYPERTROPHY LEFT ANTERIOR HEMIBLOCK
29	TR	56	75	04NOV91	A		LEFT VENTRICULAR HYPERTROPHY

RESULT: N=NORMAL A=ABNORMAL

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

ECG
TREATMENT: PLACEBO

Patient No.	Initials	Visit Day	Heart Rate	Date of ECG	Result (*)	Abnormalities (Specify)	Abnormalities
29	TR	56	75	04NOV91	A		LEFT BUNDLE BRANCH BLOCK
31	CC	-1	64	03OCT91	A		VENTRICULAR ECTOPIC BEATS - OCCASIONAL LEFT VENTRICULAR HYPERTROPHY
31	CC	28	85	04NOV91	A		LEFT VENTRICULAR HYPERTROPHY
31	CC	56	70	02DEC91	A		LEFT VENTRICULAR HYPERTROPHY
32	CE	-1	63	05SEP91	A		LEFT ANTERIOR HEMIBLOCK
32	CE	28	66	07OCT91	A		LEFT ANTERIOR HEMIBLOCK
32	CE	56	72	04NOV91	A		LEFT ANTERIOR HEMIBLOCK
33	VA	-1	80	02OCT91	A		ATRIAL FIBRILLATION / FLUTTER
33	VA	28	84	04NOV91	A		ATRIAL FIBRILLATION / FLUTTER
33	VA	56	98	02DEC91	A		ATRIAL FIBRILLATION / FLUTTER OTHER
34	BA	-1	52	04OCT91	A		SINUS BRADYCARDIA (< 60) RIGHT BUNDLE BRANCH BLOCK LEFT ANTERIOR HEMIBLOCK
35	SB	-1	64	04OCT91	A		MYOCARDIAL ISCHEMIA LEFT ANTERIOR HEMIBLOCK
35	SB	28	64	04NOV91	A		LEFT ANTERIOR HEMIBLOCK
35	SB	56	66	02DEC91	A		MYOCARDIAL ISCHEMIA
38	LO	-1	74	01OCT91	A		LEFT ANTERIOR HEMIBLOCK
38	LO	28	68	04NOV91	A		LEFT ANTERIOR HEMIBLOCK
38	LO	56	77	02DEC91	A		LEFT ANTERIOR HEMIBLOCK
41	FE	-1	70	30OCT91	A		LEFT VENTRICULAR HYPERTROPHY
41	FE	28	63	06DEC91	A		LEFT VENTRICULAR HYPERTROPHY
41	FE	56	63	03JAN92	A		LEFT VENTRICULAR HYPERTROPHY
42	LI	-1	91	31OCT91	A		LEFT VENTRICULAR HYPERTROPHY LEFT AXIAL DEVIATION

RESULT: N=NORMAL A=ABNORMAL

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

ECG

TREATMENT: PLACEBO

Patient No.	Initials	Visit Day	Heart Rate	Date of ECG	Result (*)	Abnormalities (Specify)	Abnormalities
42	LI	28	79	06DEC91	N		
42	LI	56	80	03JAN92	N		
44	MZ	-1	55	30OCT91	A		ATRIAL ECTOPIC BEATS - FREQUENT (> 6/MM) A-V BLOCK 1ST DEGREE PREVIOUS MYOCARDIAL INFARCTION
44	MZ	28	77	06DEC91	A		ATRIAL FIBRILLATION / FLUTTER PREVIOUS MYOCARDIAL INFARCTION OTHER
44	MZ	56	69	03JAN92	A		
48	FA	-1	77	30OCT91	N		
48	FA	23	71	01DEC91	N		
49	SA	-1	79	30OCT91	A		LEFT VENTRICULAR HYPERTROPHY
49	SA	28	63	06DEC91	A		LEFT VENTRICULAR HYPERTROPHY MYOCARDIAL ISCHEMIA
49	SA	56	72	03JAN92	A		ATRIAL ECTOPIC BEATS - OCCASIONAL LEFT VENTRICULAR HYPERTROPHY
50	ZZ	-1	60	07NOV91	A		ATRIAL ECTOPIC BEATS - OCCASIONAL LEFT AXIAL DEVIATION
50	ZZ	28	53	06DEC91	N		

RESULT: N=NORMAL A=ABNORMAL

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

LISTING OF PATIENTS WITH ECG NORMAL AT VISIT -1 CHANGED TO ABNORMAL AT LEAST ONCE DURING THE STUDY

TREATMENT	Patient No.	INITIALS	Visit Day	Abnormality Group	Abnormalities
REBOXETINE	28	MR	-1	NORMAL	
			28	RHYTHM DISORDERS	VENTRICULAR ECTOPIC BEATS - OCCASIONAL
			56	RHYTHM DISORDERS	SINUS TACHYCARDIA (> 100)
			56	RHYTHM DISORDERS	ATRIAL ECTOPIC BEATS - OCCASIONAL
REBOXETINE	36	SM	-1	NORMAL	
			28	RHYTHM DISORDERS	ATRIAL ECTOPIC BEATS - OCCASIONAL
			56	NORMAL	

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

LISTING OF PATIENTS WITH ECG ABNORMAL AT SCREEN, CHANGED TO NORMAL DURING THE STUDY

Treatment	Patient	Initials	Visit Day	Abnormality Group	Abnormalities	Normal at Last ECG
REBOXETINE	1	TR	-1	OTHER DISORDERS	LEFT VENTRICULAR HYPERTROPHY	
			28	OTHER DISORDERS	LEFT VENTRICULAR HYPERTROPHY	
			56			**
REBOXETINE	37	SE	-1	CONDUCTION DISORDERS	LEFT ANTERIOR HEMIBLOCK	
			28			
			56			**
PLACEBO	9	PA	-1	RHYTHM DISORDERS	ATRIAL ECTOPIC BEATS - OCCASIONAL	
			56			**
PLACEBO	27	GA	-1	RHYTHM DISORDERS	ATRIAL ECTOPIC BEATS - OCCASIONAL	
			28			
			56	RHYTHM DISORDERS	ATRIAL ECTOPIC BEATS - OCCASIONAL	
PLACEBO	42	LI	-1	CONDUCTION DISORDERS	LEFT AXIAL DEVIATION	
			-1	OTHER DISORDERS	LEFT VENTRICULAR HYPERTROPHY	
			28			
			56			**
PLACEBO	50	ZZ	-1	RHYTHM DISORDERS	ATRIAL ECTOPIC BEATS - OCCASIONAL	
			-1	CONDUCTION DISORDERS	LEFT AXIAL DEVIATION	
			28			**

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

EEG

Patient No.	Initials	Treatment	Visit No.	Result: Normal	Result: Borderline	Generalized Abnormalities
1	TR	REBOXETINE	-1			MODERATE DIFFUSE AB.
			56			MODERATE DIFFUSE AB.
2	FB	PLACEBO	-1	YES		
			56	YES		
3	BI	PLACEBO	-1	YES		
			56	YES		
4	PC	PLACEBO	-1	YES		
			56	YES		
5	BL	REBOXETINE	-1	YES		
			56	YES		
6	SM	REBOXETINE	-1	YES		
			56	YES		
7	DA	PLACEBO	-1			MILD GENER.SLOWNESS
			56			MILD GENER.SLOWNESS
8	SC	REBOXETINE	-1			MODER.GENER.SLOWNESS
			56			MODER.GENER.SLOWNESS
9	PA	PLACEBO	-1	YES		
			56	YES		
10	PE	PLACEBO	-1	YES		
11	CL	PLACEBO	-1	YES		
			56	YES		
12	ML	PLACEBO	-1	YES		
			56	YES		
13	DSC	REBOXETINE	-1	YES		
			56	YES		
14	BM	REBOXETINE	-1	YES		
			56	YES		
15	GI	REBOXETINE	-1			FAST LOW VOLT.ACTIV.
16	PJ	REBOXETINE	-1	YES		
			56	YES		
17	MM	REBOXETINE	-1	YES		
			56	YES		

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

EEG

Patient No.	Initials	Treatment	Visit No.	Result: Normal	Result: Borderline	Generalized Abnormalities
18	VM	REBOXETINE	-1		YES	
			56	YES		
19	NI	PLACEBO	-1		YES	
			56	YES		
20	BE	PLACEBO	-1	YES		
21	SE	REBOXETINE	-1	YES		
22	BA	PLACEBO	-1	YES		
			56	YES		
23	UT	REBOXETINE	-1		YES	
			56	YES		
24	BEA	PLACEBO	-1	YES		
			56	YES		
25	GA	REBOXETINE	-1	YES		
			56	YES		
26	PR	REBOXETINE	-1		YES	
27	GA	PLACEBO	-1			DIFFUSE ABNORMALITY MOD.GEN.THETA ACTIV.
			56			
28	MR	REBOXETINE	-1	YES		
			56	YES		
29	TR	PLACEBO	-1	YES		
			56	YES		
30	PA	REBOXETINE	-1	YES		
			56	YES		
31	CC	PLACEBO	-1	YES		
			56	YES		
32	CE	PLACEBO	-1	YES		
			56	YES		
33	VA	PLACEBO	-1	YES		
			56	YES		
34	BA	PLACEBO	-1			MODER.GENER.SLOWNESS
35	SB	PLACEBO	-1	YES		

PHARMACIA CNS R&D

REBOXETINE - PROTOCOL 20124/032

EEG

Patient No.	Initials	Treatment	Visit No.	Result: Normal	Result: Borderline	Generalized Abnormalities
35	SB	PLACEBO	56	YES		
36	SM	REBOXETINE	-1			DIFFUSE ABNORMALITY
			56			DIFFUSE ABNORMALITY
37	SE	REBOXETINE	-1	YES		
			56	YES		
38	LO	PLACEBO	-1	YES		
			56	YES		
39	CP	REBOXETINE	-1			DIFFUSE ABNORMALITY
40	PO	REBOXETINE	-1			MILD GENER.SLOWNESS
			56			MILD GENER.SLOWNESS
41	FE	PLACEBO	-1	YES		
			56	YES		
42	LI	PLACEBO	-1	YES		
			56	YES		
43	PA	REBOXETINE	-1	YES		
44	M2	PLACEBO	-1	YES		
			56	YES		
45	PG	REBOXETINE	-1	YES		
46	AD	REBOXETINE	-1	YES		
47	SG	REBOXETINE	-1			DIFFUSE CORTICAL AB.
			56			DIFFUSE CORTICAL AB.
48	FA	PLACEBO	-1	YES		
49	SA	PLACEBO	-1	YES		
			56		YES	
50	ZZ	PLACEBO	-1	YES		

12.2.3 CRFs

Individual Patient CRFs are filed in the Study Master File.