IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

IQWiG Reports – Commission No. A17-25

Etelcalcetide (secondary hyperparathyroidism) –

Benefit assessment according to §35a Social Code Book V[1]

Extract

[1] Translation of Sections 2.1 to 2.6 of the dossier assessment *Etelcalcetid (sekundärer Hyperparathyreoidismus) – Nutzenbewertung gemäß § 35a SGB V* (Version 1.0; Status: 30 August 2017). Please note: This translation is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

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[3] Table numbers start with “2” as numbering follows that of the full dossier assessment.

List of abbreviations

Abbreviation	Meaning
ACT	appropriate comparator therapy
AE	adverse event
cCA	corrected calcium
EMA	European Medicines Agency
EPAR	European Public Assessment Report
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
iPTH	intact parathyroid hormone
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
RCT	randomized controlled trial
SGB	Sozialgesetzbuch (Social Code Book)
SPC	Summary of Product Characteristics

2 Benefit assessment

2.1 Executive summary of the benefit assessment

Background

In accordance with §35a Social Code Book (SGB) V, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to assess the benefit of the drug etelcalcetide. The assessment was based on a dossier compiled by the pharmaceutical company (hereinafter referred to as "the company"). The dossier was sent to IQWiG on 1 June 2017.

Research question

The aim of the present report was to assess the added benefit of etelcalcetide in comparison with cinacalcet as appropriate comparator therapy (ACT) for the treatment of secondary hyperparathyroidism in adult patients with chronic kidney disease on haemodialysis therapy.

This resulted in 1 research question for the benefit assessment, for which the G-BA specified the ACT presented in Table 2.

Table 2: Research question of the benefit assessment of etelcalcetide

Research question	Therapeutic indication	ACT[a]
1	Treatment of secondary hyperparathyroidism in adult patients with chronic kidney disease on haemodialysis therapy[c]	Cinacalcet[b]

a: Presentation of the ACT specified by the G-BA.
b: Cinacalcet may be used as part of a therapeutic regimen including phosphate binders and/or vitamin D (and analogues), as appropriate.
c: It is assumed for the present therapeutic indication that parathyroidectomy is not indicated when the patients are included in the study.
ACT: appropriate comparator therapy; G-BA: Federal Joint Committee

The company followed the G-BA's specification of the ACT.

The assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. Randomized controlled trials (RCTs) with a minimum duration of 52 weeks were used for the derivation of the added benefit.

Results

The company presented the study 20120360 for the assessment of the added benefit of etelcalcetide in comparison with the ACT for the treatment of secondary hyperparathyroidism in adult patients with chronic kidney disease on haemodialysis therapy.

The company's assessment regarding the relevance of study 20120360 for the present benefit assessment was not followed. This is justified below.

Study description

Study 20120360 was a double-blind (double-dummy) randomized parallel-group study in adult patients with secondary hyperparathyroidism (intact parathyroid hormone [iPTH] > 500 pg/mL) and chronic kidney disease on haemodialysis therapy. A total of 683 patients were randomly allocated in a ratio of 1:1 to treatment with etelcalcetide (N = 340) or cinacalcet (N = 343). Patients in both study arms could receive concomitant phosphate binders and/or vitamin D (or analogues), as appropriate.

The duration of study 20120360 was 26 weeks plus 30 days treatment-free follow-up observation. The treatment phase consisted of a 20-week titration phase and a 6-week maintenance phase.

During the titration phase (weeks 0–20), the dose of the study medication may have been increased in both study arms to achieve target iPTH levels of ≤ 300 pg/mL. At the same time, further specifications for titration were defined in the study protocol to prevent decrease of corrected calcium (cCa) levels below 8.3 mg/dL and adverse events (AEs) (including symptomatic hypocalcaemia). The starting dose of the study medication was 5 mg for etelcalcetide and 30 mg for cinacalcet; the maximum dose was 15 mg for etelcalcetide and 180 mg for cinacalcet. The dose of etelcalcetide was increased in 2.5 mg or 5 mg steps. The dose of cinacalcet was increased in 30 mg steps and, in the last escalation step, from 120 to 180 mg (i.e. by 60 mg). During the titration phase, doses may have been increased at 4-week intervals, i.e. at weeks 5, 9, 13 and 17.

During the maintenance phase (weeks 20–26), the dose of the study medications administered at the end of the titration phase was to be maintained – dose reductions (e.g. due to low cCa levels or AEs) were possible, however.

Assessment of the study presented by the company

Treatment duration too short

The treatment duration in study 20120360 (26 weeks) was too short. Etelcalcetide is used as long-term treatment of a chronic disease, which is mainly associated with cardiovascular and bone problems. It can be assumed that these outcomes can only be recorded in studies that are conducted over a longer period of time (i.e. at least 1 year). Guidelines on related topics, such as the European Medicines Agency (EMA) *Guideline on the evaluation of medicinal products for cardiovascular disease prevention* and the EMA *Guideline on the evaluation of medicinal products in the treatment of primary osteoporosis* also recommend a study duration of at least 1 year. In the European Public Assessment Report (EPAR), EMA also describes a minimum study duration of 1 year as mandatory for the assessment of clinical safety given the long-term treatment.

Therefore, study 20120360 with a study duration of only 26 weeks is unsuitable for the assessment of the added benefit of etelcalcetide in comparison with the ACT.

Dose titration

Except for 2 main points of criticism, the specifications for titration in study 20120360 concur with the information provided in the Summaries of Product Characteristics (SPCs) of etelcalcetide and cinacalcet. The 2 main points of criticism are explained below.

Titration was not permanently oriented to achieve target levels, but temporarily limited

According to the SPCs of etelcalcetide and cinacalcet, the study medication should be titrated in order to reach an iPTH target level of 150 to 300 pg/mL (etelcalcetide) or 100 to 300 pg/mL (cinacalcet) for the PTH, which is pathologically increased in secondary hyperparathyroidism. In study 20120360, however, dose increases were not possible after week 20, irrespective of whether or not patients had already reached the iPTH target level (iPTH ≤ 300 pg/mL). After that (i.e. in the maintenance phase), only dose reductions were possible.

On the one hand, this approach, which is not permanently oriented towards achieving PTH target levels, is unjustified, irrespective of the time point for transition to the maintenance phase.

On the other, the time point for transition to the maintenance phase was chosen in a way that, in combination with the dose increase regimens of the study medications, patients in the cinacalcet arm could receive their first maximum dose on the last date for dose increases (week 17). Patients in the etelcalcetide arm, however, may have already received the maximum dose of their study medication for 8 weeks at this time point. This alone could have favoured the etelcalcetide arm regarding the primary goal of the study, i.e. the lowering of iPTH levels (see below).

Neither the approach that was not permanently oriented towards achieving PTH target levels nor the choice of the time point for transition to the maintenance phase were justified by the study results.

On the contrary, the study results indicate that not all options had been exhausted at week 20: When transitioning to the maintenance phase (week 20), the majority of patients had not yet achieved the iPTH target level of ≤ 300 pg/mL (etelcalcetide: 62%; cinacalcet: 74%). The average iPTH value at week 20 was 572 pg/mL (median: 322 pg/mL) in the etelcalcetide arm and 718 pg/mL (median: 479 pg/mL) in the cinacalcet arm. The vast majority of the patients had not yet reached the maximum dose in the period between the last opportunity for dose increase and transition to the maintenance phase (average of weeks 17–20) (etelcalcetide: 79%; cinacalcet: 90% [Institute's calculation]). Explaining the low average dose levels of the study medications solely with the presence of (permanent) AEs or low cCA values is not plausible. In both study arms, the average cCA values at week 20 were above the threshold value (8.3 mg/dL), below which further dose increase would have been excluded. Symptomatic hypocalcaemia was also rare overall (etelcalcetide: 5%; cinacalcet: 2%). Similarly, only few patients had to interrupt treatment in the period between the last

opportunity for dose increase and transition to the maintenance phase (average of weeks 17–20) (etelcalcetide: 17% [Institute's calculation]; cinacalcet: 6% maximum).

In addition, the study results overall support the assumption that the etelcalcetide arm was favoured by the study design, particularly because of the more aggressive titration that was possible until transition to the maintenance phase. Regarding the differences between the treatment groups, it can be seen that the proportion of patients who had not yet reached the possible maximum dose in the period between the last opportunity for dose increase and transition to the maintenance phase (average of weeks 17–20) was higher in the cinacalcet arm. Correspondingly, patients in the etelcalcetide arm on average received a higher proportion of the weekly maximum dose per week during the maintenance phase (weeks 20–26) than patients in the cinacalcet arm. Explaining this difference in dose levels received between the treatment groups solely with the presence of (permanent) AEs or low cCA values is not plausible. The study results suggest that, particularly in the cinacalcet arm, not all options had been exhausted. It is therefore likely that the group difference in the average iPTH levels, at least proportionately, was due to the more aggressive titration possible for etelcalcetide in comparison with cinacalcet in combination with the time point chosen for transition to the maintenance phase.

In summary, the study design – also under consideration of the study results – has the following 2 main limitations:

- It cannot be estimated, whether and to what extent patients who had not yet achieved an iPTH value of ≤ 300 pg/mL when transitioning to the maintenance phase (week 20) could have benefited from further dose increases or whether these would have been harmful to them.
- The more aggressive titration possible for etelcalcetide until transition to the maintenance phase in comparison with cinacalcet (which may have resulted in reaching the maximum dose at an earlier time point) makes it likely that etelcalcetide was favoured with respect to the primary goal of the study, i.e. the lowering of iPTH levels.

Opportunities for dose increase of cinacalcet were too rare

There were too few opportunities for dose increase in study 20120360 for patients under cinacalcet. According to the SPC, it should be possible to increase the dose of cinacalcet every 2 to 4 weeks. In study 20120360, however, the dose could only be increased every 4 weeks, which corresponds to the requirements of the SPC for etelcalcetide. Since patients under cinacalcet did not have the opportunity to increase their dose every 2 weeks, etelcalcetide was possibly favoured with respect to the primary goal of the study, i.e. the lowering of iPTH levels.

Hence, no relevant data were available for the benefit assessment.

Probability and extent of added benefit, patient groups with therapeutically important added benefit[4]

Table 3 presents a summary of the probability and extent of the added benefit of etelcalcetide.

Table 3: Etelcalcetide – probability and extent of added benefit

Therapeutic indication	ACT[a]	Probability and extent of added benefit
Treatment of secondary hyperparathyroidism in adult patients with chronic kidney disease on haemodialysis therapy[c]	Cinacalcet[b]	Added benefit not proven

a: Presentation of the ACT specified by the G-BA.
b: Cinacalcet may be used as part of a therapeutic regimen including phosphate binders and/or vitamin D (and analogues), as appropriate.
c: It is assumed for the present therapeutic indication that parathyroidectomy is not indicated when the patients are included in the study.
ACT: appropriate comparator therapy; G-BA: Federal Joint Committee

The G-BA decides on the added benefit.

2.2 Research question

The aim of the present report was to assess the added benefit of etelcalcetide in comparison with cinacalcet as ACT for the treatment of secondary hyperparathyroidism in adult patients with chronic kidney disease on haemodialysis therapy.

This resulted in 1 research question for the benefit assessment, for which the G-BA specified the ACT presented in Table 4.

[4] On the basis of the scientific data analysed, IQWiG draws conclusions on the (added) benefit or harm of an intervention for each patient-relevant outcome. Depending on the number of studies analysed, the certainty of their results, and the direction and statistical significance of treatment effects, conclusions on the probability of (added) benefit or harm are graded into 4 categories: (1) "proof", (2) "indication", (3) "hint", or (4) none of the first 3 categories applies (i.e., no data available or conclusions 1 to 3 cannot be drawn from the available data). The extent of added benefit or harm is graded into 3 categories: (1) major, (2) considerable, (3) minor (in addition, 3 further categories may apply: non-quantifiable extent of added benefit, no added benefit, or less benefit). For further details see [1,2].

Table 4: Research question of the benefit assessment of etelcalcetide

Research question	Therapeutic indication	ACT[a]
1	Treatment of secondary hyperparathyroidism in adult patients with chronic kidney disease on haemodialysis therapy[c]	Cinacalcet[b]

a: Presentation of the ACT specified by the G-BA.
b: Cinacalcet may be used as part of a therapeutic regimen including phosphate binders and/or vitamin D (and analogues), as appropriate.
c: It is assumed for the present therapeutic indication that parathyroidectomy is not indicated when the patients are included in the study.
ACT: appropriate comparator therapy; G-BA: Federal Joint Committee

The company followed the G-BA's specification of the ACT.

The assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. RCTs with a minimum duration of 52 weeks were used for the derivation of the added benefit. This deviates from the approach of the company, which used studies with a minimum duration of 24 weeks.

2.3 Information retrieval and study pool

2.3.1 Information retrieval

The study pool of the assessment was compiled on the basis of the following information:

Sources of the company in the dossier:

- study list on etelcalcetide (status: 1 March 2017)
- bibliographical literature search on etelcalcetide (last search on 1 March 2017)
- search in trial registries for studies on etelcalcetide (last search on 13 March 2017)

To check the completeness of the study pool:

- search in trial registries for studies on etelcalcetide (last search on 14 June 2017)

No relevant study was identified from the check.

2.3.2 Study pool of the company

The company presented the study 20120360 [3] for the assessment of the added benefit of etelcalcetide in comparison with the ACT for the treatment of secondary hyperparathyroidism in adult patients with chronic kidney disease on haemodialysis therapy.

The company's assessment regarding the relevance of study 20120360 for the present benefit assessment was not followed. This is explained in Section 2.3.2.2. At first, a description of the study is provided in the following Section 2.3.2.1.

2.3.2.1 Study description

Study 20120360 was a double-blind (double-dummy) randomized parallel-group study in adult patients with secondary hyperparathyroidism (iPTH > 500 pg/mL) and chronic kidney disease on haemodialysis therapy. A total of 683 patients were randomly allocated in a ratio of 1:1 to treatment with etelcalcetide (N = 340) or cinacalcet (N = 343). Patients in both study arms could receive concomitant phosphate binders and/or vitamin D (or analogues), as appropriate. For further information, see Table 10 in Appendix A of the full dossier assessment.

The duration of study 20120360 was 26 weeks plus 30 days treatment-free follow-up observation. The treatment phase consisted of a 20-week titration phase and a 6-week maintenance phase.

Titration phase (weeks 0–20)

During the titration phase, the dose of the study medication may have been increased in both study arms. The starting dose of the study medication was 5 mg 3 times a week for etelcalcetide and 30 mg daily for cinacalcet; the maximum dose was 15 mg 3 times a week for etelcalcetide and 180 mg daily for cinacalcet. Doses were increased following the regimen presented in Table 5.

Table 5: Dose increase regimen of study 20120360 during the titration phase based on iPTH values (at weeks 5, 9, 13 and 17)

iPTH (pg/mL)	Etelcalcetide (starting dose 5 mg)	Cinacalcet[a] (starting dose 30 mg)
iPTH > 450	Dose increase[b] by 5 mg	Dose increase[b] by 30 mg
300 < iPTH ≤ 450	Dose increase[b] by 2.5 mg	Dose increase[b] by 30 mg
iPTH ≤ 300	Dose maintenance	Dose maintenance
a: In the last titration step, the dose of cinacalcet was increased by 60 mg (from 120 to 180 mg). b: The dose was only increased if the cCA value was at least 8.3 mg/dL. cCa: corrected calcium; iPTH: intact parathyroid hormone		

As shown in Table 5 and according to further titration specifications defined in the protocol, the dose should not be increased, however, if

- the iPTH value was ≤ 300 pg/mL, or
- the cCa level was < 8.3 mg/dL, or
- an AE (including symptomatic hypocalcaemia) indicated otherwise.

A dose increase was also not allowed if the dose had been reduced in the previous 3 weeks or ≥ 3 doses of etelcalcetide had been omitted.

Dose reduction was only possible after treatment interruption. According to the protocol, treatment interruption was only possible if any of the following criteria applied: a) iPTH

value < 100 pg/mL, b) cCa < 7.5 mg/dL, presence of c) symptomatic hypocalcaemia or d) an AE considered by the investigator to require treatment interruption. The dose was then reduced, unless treatment had been interrupted due to an AE that was unrelated to the treatment.

During the titration phase, doses may have been increased at 4-week intervals, i.e. at weeks 5, 9, 13 and 17. Treatment interruptions and dose reductions were possible at any time (e.g. due to an AE). For the study, the iPTH and cCA values were recorded every 2 weeks over the total study duration. The protocol did not exclude additional cCA measurements (unrelated to the study), however.

Maintenance phase (weeks 20–26)

During the maintenance phase, the dose of the study medications administered at the end of the titration phase was to be maintained – dose reductions (e.g. due to low cCa levels or AEs) were possible, however.

For further information on the characteristics of the interventions, see Table 11 in Appendix A of the full dossier assessment.

Blinding

The investigators were blinded to the iPTH values. To maintain blinding, dose adjustments of the study medication were conducted automatically by an interactive voice/web response system. This system always adjusted the doses both for the active and for the placebo drugs (i.e. also for the dummies). Dose adjustments by the investigators were possible. They also had to follow the titration specifications mandated by the protocol and had to be documented.

2.3.2.2 Assessment of the study presented by the company

Treatment duration too short

The treatment duration in study 20120360 (26 weeks) was too short. Etelcalcetide is used as long-term treatment of a chronic disease, which is mainly associated with cardiovascular and bone problems. It can be assumed that these outcomes can only be recorded in studies that are conducted over a longer period of time (i.e. at least 1 year). Guidelines on related topics, such as the EMA *Guideline on the evaluation of medicinal products for cardiovascular disease prevention* [4] and the EMA *Guideline on the evaluation of medicinal products in the treatment of primary osteoporosis* [5] also recommend a study duration of at least 1 year. In the EPAR, EMA also describes a minimum study duration of 1 year as mandatory for the assessment of clinical safety given the long-term treatment [6].

Therefore, study 20120360 with a study duration of only 26 weeks is unsuitable for the assessment of the added benefit of etelcalcetide in comparison with the ACT.

Dose titration

Except for 2 main points of criticism, the specifications for titration (including the dose increase regimen) in study 20120360 concur with the information provided in the SPCs of etelcalcetide and cinacalcet [7,8]. The 2 main points of criticism are explained below.

Titration was not permanently oriented to achieve target levels, but temporarily limited

According to the SPCs of etelcalcetide and cinacalcet, the study medication should be titrated in order to reach an iPTH target level of 150 to 300 pg/mL (etelcalcetide) or 100 to 300 pg/mL (cinacalcet) for the PTH, which is pathologically increased in secondary hyperparathyroidism. In study 20120360, however, dose increases were not possible after week 20, irrespective of whether or not patients had already reached the iPTH target level (iPTH ≤ 300 pg/mL). After that (i.e. in the maintenance phase), only dose reductions were possible.

On the one hand, this approach, which is not permanently oriented towards achieving PTH target levels, is unjustified, irrespective of the time point for transition to the maintenance phase. The period of time in which the dose can be increased is not limited in either of both SPCs of the study medications [7,8]. On the contrary, the SPC of etelcalcetide describes that dose adjustment may be necessary at any time during treatment. The 2017 guideline of the Kidney Disease: Improving Global Outcomes (KDIGO) Work Group [9] also recommends aiming at a target PTH level with therapeutic correction of deviations (initiation and adjustment of treatment). A time point at which the effect of one of both drugs typically reaches saturation is also not mentioned in any of the 3 documents. The company also did not provide any evidence that justified the limitation of the phase in which dose increases were possible.

On the other hand, the time point for transition to the maintenance phase was chosen in a way that patients in the cinacalcet arm could receive their first maximum dose on the last date for dose increases (week 17). Patients in the etelcalcetide arm, however, may have already received the maximum dose of their study medication for 8 weeks at this time point. This alone could have favoured the etelcalcetide arm regarding the primary goal of the study, i.e. the lowering of iPTH levels (see below).

Therefore, the transition to the maintenance phase at week 20 in study 20120360 would have been adequate for the present research question only if, at this time point:

1) all patients had already had an iPTH value ≤ 300 pg/mL, or
2) all patients who had not yet had an iPTH value ≤ 300 pg/mL had already received the maximum dose of the study medication, or
3) all patients who had not yet had an iPTH value ≤ 300 pg/mL and who were not already receiving the maximum dose had not been candidates for further dose increases due to – permanent – AEs or low cCa levels.

On the contrary, the study results indicate that not all options had been exhausted at week 20, however:

Re 1) When transitioning to the maintenance phase (week 20), the majority of patients had not yet achieved the iPTH target level of ≤ 300 pg/mL (etelcalcetide: 62%; cinacalcet: 74%)[5]. The average iPTH value at week 20 was 572 pg/mL (median: 322 pg/mL) in the etelcalcetide arm and 718 pg/mL (median: 479 pg/mL) in the cinacalcet arm (see Figure 1 in Appendix B of the full dossier assessment).

Re 2) The vast majority of the patients had not yet reached the maximum dose in the period between the last opportunity for dose increase and transition to the maintenance phase (average of weeks 17–20) (etelcalcetide: 79%; cinacalcet: 90% [Institute's calculation]). Correspondingly, patients in the maintenance phase (weeks 20–26) received an average of 46% (median: 33%) (etelcalcetide) and 32% (median: 29%) (cinacalcet) per week [Institute's calculations] of the weekly maximum doses.

Re 3) Explaining the low average dose levels of the study medications solely with the presence of (permanent) AEs or low cCA values is not plausible. In both study arms, the average cCA values at week 20 were above the threshold value (8.3 mg/dL), below which further dose increase would have been excluded (see Figure 2 in Appendix B of the full dossier assessment). Symptomatic hypocalcaemia was also rare overall (etelcalcetide: 5%; cinacalcet: 2%). Similarly, only few patients had to interrupt treatment in the period between the last opportunity for dose increase and transition to the maintenance phase (average of weeks 17–20) (etelcalcetide: 17% [Institute's calculation]; cinacalcet: 6% maximum).

In addition, the study results cited above overall support the assumption that the etelcalcetide arm was favoured by the study design, particularly because of the more aggressive titration that was possible until transition to the maintenance phase. Regarding the differences between the treatment groups, it can be seen that the proportion of patients who had not yet reached the possible maximum dose in the period between the last opportunity for dose increase and transition to the maintenance phase (average of weeks 17–20) was higher in the cinacalcet arm. Correspondingly, patients in the etelcalcetide arm on average received a higher proportion of the weekly maximum dose per week during the maintenance phase (weeks 20–26) than patients in the cinacalcet arm. Explaining this difference in dose levels received between the treatment groups solely with the presence of (permanent) AEs or low cCA values is not plausible. The study results suggest that, particularly in the cinacalcet arm, not all options had been exhausted. It is therefore likely that the group difference in the average iPTH levels, at least proportionately, was due to the more aggressive titration possible for etelcalcetide in comparison with cinacalcet in combination with the time point chosen for transition to the maintenance phase.

[5] 12% (etelcalcetide arm) and 10% (cinacalcet arm) were imputed with non-responder imputation.

In summary, the study design – also under consideration of the study results – has the following 2 main limitations:

- It cannot be estimated, whether and to what extent patients who had not yet achieved an iPTH value of ≤ 300 pg/mL when transitioning to the maintenance phase (week 20) could have benefited from further dose increases or whether these would have been harmful to them.
- The more aggressive titration possible for etelcalcetide until transition to the maintenance phase in comparison with cinacalcet (which may have resulted in reaching the maximum dose at an earlier time point) makes it likely that etelcalcetide was favoured with respect to the primary goal of the study, i.e. the lowering of iPTH levels.

Opportunities for dose increase of cinacalcet were too rare

There were too few opportunities for dose increase in study 20120360 for patients under cinacalcet. According to the SPC, it should be possible to increase the dose of cinacalcet every 2 to 4 weeks [7]. In study 20120360, however, the dose could only be increased every 4 weeks, which corresponds to the requirements of the SPC for etelcalcetide [8]. Since patients under cinacalcet did not have the opportunity to increase their dose every 2 weeks, etelcalcetide was possibly favoured with respect to the primary goal of the study, i.e. the lowering of iPTH levels.

Hence, no relevant data were available for the benefit assessment.

2.4 Results on added benefit

In its dossier, the company presented no suitable data for the assessment of the added benefit of etelcalcetide versus the ACT. This resulted in no hint of an added benefit of etelcalcetide in comparison with the ACT; an added benefit is therefore not proven.

2.5 Probability and extent of added benefit

The result of the assessment of the added benefit of etelcalcetide in comparison with the ACT is summarized in Table 6.

Table 6: Etelcalcetide – probability and extent of added benefit

Therapeutic indication	**ACT[a]**	**Probability and extent of added benefit**
Treatment of secondary hyperparathyroidism in adult patients with chronic kidney disease on haemodialysis therapy[c]	Cinacalcet[b]	Added benefit not proven
a: Presentation of the ACT specified by the G-BA. b: Cinacalcet may be used as part of a therapeutic regimen including phosphate binders and/or vitamin D (and analogues), as appropriate. c: It is assumed for the present therapeutic indication that parathyroidectomy is not indicated when the patients are included in the study. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee		

An added benefit of etelcalcetide is not proven because the company did not present any suitable data.

This deviates from the assessment of the company, which derived an indication of a non-quantifiable added benefit of etelcalcetide on the basis of study 20120360.

The G-BA decides on the added benefit.

2.6 List of included studies

Not applicable as the company presented no relevant data for the benefit assessment.

References for English extract

Please see full dossier assessment for full reference list.

The reference list contains citations provided by the company in which bibliographical information may be missing.

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