IQWiG Reports – Commission No. A16-31

Eribulin (liposarcoma) –

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

Extract

[1] Translation of Sections 2.1 to 2.6 of the dossier assessment *Eribulin (Liposarkom) – Nutzenbewertung gemäß § 35a SGB V* (Version 1.0; Status: 29 August 2016). 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.

Publishing details

Publisher:
Institute for Quality and Efficiency in Health Care

Topic:
Eribulin (liposarcoma) – Benefit assessment according to §35a Social Code Book V

Commissioning agency:
Federal Joint Committee

Commission awarded on:
1 June 2016

Internal Commission No.:
A16-31

Address of publisher:
Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
Im Mediapark 8
50670 Köln
Germany

Phone: +49 221 35685-0
Fax: +49 221 35685-1
E-mail: berichte@iqwig.de
Internet: www.iqwig.de

Medical and scientific advice:

- Dr. Jochem Potenberg, Waldkrankenhaus Protestant Hospital, Berlin, Germany

IQWiG thanks the medical and scientific advisor for his contribution to the dossier assessment. However, the advisor was not involved in the actual preparation of the dossier assessment. The responsibility for the contents of the dossier assessment lies solely with IQWiG.

IQWiG employees involved in the dossier assessment[2]:

- Ana Liberman
- Moritz Felsch
- Wolfram Groß
- Marco Knelangen
- Cornelia Rüdig
- Corinna ten Thoren
- Beate Wieseler

Keywords: eribulin, liposarcoma, benefit assessment

[2] Due to legal data protection regulations, employees have the right not to be named.

Table of contents

List of tables[3]

Page

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

List of figures

Page

List of abbreviations

Abbreviation	Meaning
ACT	appropriate comparator therapy
AE	adverse event
CTCAE	Common Terminology Criteria for Adverse Events
EMA	European Medicines Agency
FDA	Food and Drug Administration
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
RCT	randomized controlled trial
SAE	serious adverse event
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 eribulin. 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 2016.

Research question

The aim of the present report was the assessment of the added benefit of eribulin in comparison with the appropriate comparator therapy (ACT) in adult patients with unresectable liposarcoma who have received prior anthracycline-containing therapy (unless unsuitable) for advanced or metastatic disease.

The present benefit assessment was conducted in comparison with the ACT specified by the G-BA for the research question presented in Table 2.

Table 2: Research question of the benefit assessment of eribulin

Therapeutic indication	**Appropriate comparator therapy**[a]
Adult patients with unresectable liposarcoma who have received prior anthracycline-containing therapy (unless unsuitable) for advanced or metastatic disease	Antineoplastic drug treatment specified by the physician and under consideration of the approval status of the drug and the pretreatment(s) administered
a: Presentation of the appropriate comparator therapy specified by the G-BA. G-BA: Federal Joint Committee	

The company interpreted the ACT specified by the G-BA as all antineoplastic drugs that are principally approved for the treatment of patients in the therapeutic indication. As required by the G-BA, the company considered the prior therapies of the patients in the therapeutic indication by excluding those drugs that should be used as first-line treatment, particularly anthracyclines.

The assessment was conducted based on patient-relevant outcomes and on the data provided by the company in the dossier.

Results

The data presented by the company were unsuitable to draw conclusions on the added benefit of eribulin in comparison with the ACT. This concerned both the study of direct comparison and the indirect comparison presented.

Direct comparison

The company identified one randomized controlled trial (RCT) for the assessment of the added benefit of eribulin: study E7389-G000-309 (hereinafter referred to as "study 309") with the comparator therapy dacarbazine.

Study 309 was a multicentre, randomized, controlled, unblinded study on the comparison of eribulin versus dacarbazine.

Other than described in the Summary of Product Characteristics (SPC), dacarbazine was given in the study as monotherapy at a dosage of 850 mg/m^2, 1000 mg/m^2, or 1200 mg/m^2 body surface area as an intravenous infusion over 15 to 30 minutes on day 1 of every 21-day cycle.

According to the SPC, in soft tissue sarcoma dacarbazine is given in daily doses of 250 mg/m^2 body surface area intravenously (days 1 to 5) in combination with doxorubicin every 3 weeks, however. Hence the use of dacarbazine in study 309 deviated substantially from the approval.

Since dacarbazine in the comparator arm was not administered in compliance with the approval, the effects observed in the study could not be interpreted for the approval-compliant use and therefore for the research question specified. For this reason, study 309 was unsuitable for the derivation of the added benefit of eribulin versus the ACT.

Indirect comparison

The company presented an adjusted indirect comparison with the common comparator dacarbazine for the assessment of the added benefit of eribulin. This indirect comparison was unsuitable to draw conclusions on the added benefit of eribulin versus trabectedin, however.

The company's study pool for the indirect comparison comprised 2 RCTs. On the eribulin side, it included its approval study described above, i.e. study 309. On the trabectedin side, the company included study ET743-SAR-3007 (hereinafter referred to as study 3007).

For the assessment of benefit and harm the company used different patient populations in its indirect comparison.

For the assessment of benefit, the company used the relevant subpopulation (patients with liposarcoma) on both sides of the indirect comparison. No patient characteristics at the start of the study were available on the trabectedin side in study 3007, however. Therefore no final conclusion on the similarity of the subpopulations included for the assessment of overall survival could be drawn. At the same time, the available results on overall survival provided indications that the subpopulations were not sufficiently similar.

For the assessment of harm, the company used the total populations of the studies (patients with either liposarcoma or leiomyosarcoma) on both sides of the indirect comparison. The

proportion of relevant patients with liposarcoma in the total population was just about 34% in study 309 and 27% in study 3007. Hence no sufficient comparability of the total population and of the relevant subpopulation and therefore no transferability of the results could be assumed.

Moreover, the different patient populations on the benefit and harm side cannot be included jointly in the assessment of the added benefit if no comparability can be assumed.

Hence no usable data were available for the derivation of the added benefit of eribulin in comparison with the ACT trabectedin.

Extent and probability of added benefit, patient groups with therapeutically important added benefit[4]

On the basis of the results presented, the extent and probability of the added benefit of the drug eribulin compared with the ACT is assessed as follows:

An added benefit of eribulin is not proven because the company presented no suitable data.

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

Table 3: Eribulin – extent and probability of added benefit

Therapeutic indication	**Appropriate comparator therapy[a]**	**Extent and probability of added benefit**
Adult patients with unresectable liposarcoma who have received prior anthracycline-containing therapy (unless unsuitable) for advanced or metastatic disease	Antineoplastic drug treatment specified by the physician and under consideration of the approval status of the drug and the pretreatment(s) administered	Added benefit not proven
a: Presentation of the appropriate comparator therapy specified by the G-BA. G-BA: Federal Joint Committee		

The G-BA decides on the added benefit.

[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].

2.2 Research question

The aim of the present report was the assessment of the added benefit of eribulin in comparison with the ACT in adult patients with unresectable liposarcoma who have received prior anthracycline-containing therapy (unless unsuitable) for advanced or metastatic disease.

The present benefit assessment was conducted in comparison with the ACT specified by the G-BA for the research question presented in Table 4.

Table 4: Research question of the benefit assessment of eribulin

Therapeutic indication	**Appropriate comparator therapy**[a]
Adult patients with unresectable liposarcoma who have received prior anthracycline-containing therapy (unless unsuitable) for advanced or metastatic disease	Antineoplastic drug treatment specified by the physician and under consideration of the approval status of the drug and the pretreatment(s) administered
a: Presentation of the appropriate comparator therapy specified by the G-BA. G-BA: Federal Joint Committee	

The company interpreted the ACT specified by the G-BA as all antineoplastic drugs that are principally approved for the treatment of patients in the therapeutic indication. As required by the G-BA, the company considered the prior therapies of the patients in the therapeutic indication by excluding those drugs that should be used as first-line treatment, particularly anthracyclines.

From the company's point of view, the following drugs concurred with the ACT:

- dacarbazine,
- trabectedin, and
- ifosfamide.

The company regarded ifosfamide primarily as first-line treatment and therefore derived the added benefit of eribulin versus dacarbazine and trabectedin. The company considered its choice to completely cover the ACT specified by the G-BA. Nonetheless, the company searched for suitable evidence for the comparison of eribulin versus ifosfamide.

This approach was only partly followed.

According to the approval [3], dacarbazine is given in combination with doxorubicin, an anthracycline, for the treatment of liposarcoma. Use of doxorubicin is limited by a maximum cumulative dose, however [4]. Hence in the therapeutic indication, dacarbazine is at most suitable for part of the patients as ACT, namely patients who have not yet received the cumulative total dose.

According to the approval [5], ifosfamide is used after failed surgery and radiotherapy. Hence second- or third-line treatment is not excluded.

The assessment was conducted based on patient-relevant outcomes and on the data provided by the company in the dossier.

2.3 Information retrieval and study pool

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 eribulin (status: 4 May 2016)
- bibliographical literature search on eribulin (last search on 29 March 2016)
- search in trial registries for studies on eribulin (last search on 24 May 2016)
- bibliographical literature search on the ACT (last search on 29 March 2016)
- search in trial registries for studies on the ACT (last search on 24 May 2016)

To check the completeness of the study pool:

- search in trial registries for studies on eribulin (last search on 10 June 2016)
- bibliographical literature search on dacarbazine (last search on 15 June 2016)
- search in trial registries for studies on dacarbazine(last search on 15 June 2016)

No additional relevant study was identified from the check.

On the one hand, the company presented a study of direct comparison of eribulin versus dacarbazine. On the other, it presented an adjusted indirect comparison of eribulin versus trabectedin. The company presented no relevant study for a comparison of eribulin versus ifosfamide.

However, the studies identified by the company from the steps of information retrieval mentioned were unsuitable for the derivation of conclusions on the added benefit of eribulin versus the ACT. This concerned both the identified study of direct comparison and the indirect comparison presented. The study pool of the company is described below, and the reasons why the respective data were unsuitable for the derivation of the added benefit are explained.

Direct comparison

The company identified one RCT for the assessment of the added benefit of eribulin: study 309 [6] with the comparator therapy dacarbazine.

Study 309

Study 309 was a multicentre, randomized, controlled, unblinded study. Patients aged 18 years or older with unresectable advanced liposarcoma or leiomyosarcoma were included in this study on the comparison of eribulin versus dacarbazine. A further criterion required for inclusion in the study was pretreatment with at least 2 standard systemic regimens for advanced soft tissue sarcoma, including an anthracycline (unless contraindicated).

Eribulin was given in compliance with the approval at a dosage of 1.23 mg/m² body surface area as an intravenous infusion over 2 to 5 minutes on day 1 and day 8 of every 21-day cycle. Any antitumour treatments other than the study treatment were not allowed in the study.

Further information on the design of study 309 can be found in Table 11 and Table 12 in Appendix A of the full dossier assessment.

Use of dacarbazine in the comparator arm not in compliance with the approval

Other than described in the SPC, dacarbazine was given in study 309 as monotherapy at a dosage of 850 mg/m^2, 1000 mg/m^2, or 1200 mg/m^2 body surface area as an intravenous infusion over 15 to 30 minutes on day 1 of every 21-day cycle.

According to the SPC [3], in soft tissue sarcoma dacarbazine is given in daily doses of 250 mg/m^2 body surface area intravenously (days 1 to 5) in combination with doxorubicin every 3 weeks, however. Hence the use of dacarbazine in study 309 deviated substantially from the approval.

There were no data on the comparison of the approval-compliant combination therapy of dacarbazine and doxorubicin versus the regimen given in study 309. It could therefore not be estimated whether these 2 treatment regimens were comparable regarding their benefit and harm.

The regulatory authority also confirmed that the use of dacarbazine as monotherapy for the treatment of liposarcoma is not in compliance with the approval. Since dacarbazine in the comparator arm was not administered in compliance with the approval, the effects observed in the study could not be interpreted for the approval-compliant use and therefore for the research question specified. For this reason, study 309 was unsuitable for the derivation of the added benefit of eribulin versus the ACT.

In Module 3 B (Section 3.3.1) of its dossier, the company stated that the SPC of dacarbazine provided no treatment regimen for the monotherapy for advanced soft tissue sarcoma, but that the use of dacarbazine monotherapy as comparator therapy of the pivotal study 309 was agreed upon with the European Medicines Agency (EMA) and the Food and Drug Administration (FDA) in the framework of the approval. The company presented no further justification of the use of a treatment regimen of dacarbazine that was not in compliance with the approval.

The company's justification was not followed. The regulatory authorities have different requirements for a comparator therapy than in the case of the assessment of the added benefit.

Additional analyses for the benefit assessment

In accordance with the approval of eribulin [7], only the subpopulation of patients with liposarcoma was relevant for the present benefit assessment. The company presented the results of this subpopulation in Module 4 B and derived the added benefit of eribulin from them.

Indirect comparison

The company presented an adjusted indirect comparison for the assessment of the added benefit of eribulin versus trabectedin. Trabectedin was one of the drugs identified by the company on the basis of its interpretation of the ACT. The common comparator in the indirect comparison was dacarbazine (see Figure 1).

The company's study pool for the indirect comparison comprised 2 RCTs. On the eribulin side, it included its approval study described above, i.e. study 309. Complete patient and study data for this study were available to the company.

Since study 309 was the only study of direct comparison with eribulin in the therapeutic indication and dacarbazine was used as comparator therapy in this study, dacarbazine constituted the only possible common comparator for an indirect comparison.

On the trabectedin side, the company included study 3007 [8].

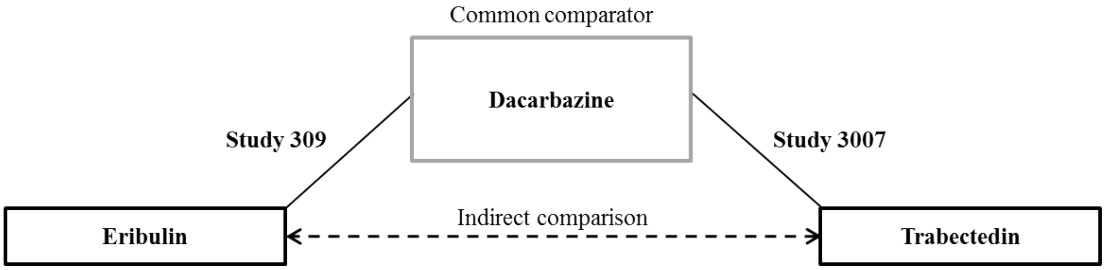

Figure 1: Study pool of the company for the indirect comparison between eribulin and trabectedin

Study 3007

Study 3007 was a multicentre, randomized, controlled, unblinded study on the comparison of trabectedin versus dacarbazine. Patients aged 15 years and older with unresectable, locally advanced or metastatic liposarcoma or leiomyosarcoma were included in the study. In addition, they had to have been pretreated with an anthracycline- and an ifosfamide-containing regimen or with an anthracycline-containing regimen and additional chemotherapy.

Whereas in study 3007, trabectedin was given in compliance with the approval [9], dacarbazine, as in study 309, was given in a treatment regimen deviating from the approval: as monotherapy, 1000 mg/m^2 body surface area as intravenous infusion on day 1 of every 21-day cycle.

Since study 3007 was conducted by a different sponsor, the company did not have the complete study data.

Data cut-offs and patient populations included

The available data source for the first data cut-off of study 3007 was a full publication presenting the patient characteristics and the results of the total population [8].

The company used this total population for the assessment of harm. The company included the total population (patients with either liposarcoma or leiomyosarcoma) also on the eribulin side (study 309).

For a second data cut-off of study 3007, 2 congress presentations containing data on the outcome "overall survival" for the relevant subpopulation (patients with liposarcoma) in the framework of subgroup analyses were additionally publicly available [10,11].

The company used these data of the relevant subpopulation for the assessment of overall survival on the trabectedin side. The company included the relevant subpopulation also on the eribulin side for this outcome.

The indirect comparison presented by the company was unsuitable to draw conclusions on the added benefit of eribulin versus trabectedin, however. This is justified below.

Lack of similarity of the populations included for the assessment of overall survival

For the assessment of overall survival, the company used the relevant subpopulation (patients with liposarcoma) on both sides of its indirect comparison. As described above, the data on the trabectedin side were from congress presentations. However, these sources contained no patient characteristics at the start of the study for the subpopulation used. Therefore no final conclusion on the similarity of the subpopulations included for the assessment of overall survival could be drawn.

The marked differences in overall survival in the respective comparator arms indicate that there was in fact no similarity of the patient populations included. Median survival time in the dacarbazine arm of study 309 was 8.4 months, whereas it was 13.1 months in the dacarbazine arm of study 3007 (see Table 5).

Table 5: Median survival time in studies 309 and 3007

Study **Population** **Treatment arm**	**N**	**Median survival time in months [95% CI]**
309		
Relevant subpopulation[a]		
Eribulin	71	15.6 [10.2; 18.6]
Dacarbazine[b]	72	8.4 [5.2; 10.1]
3007		
Relevant subpopulation[a]		
Trabectedin	102	12.6 [9.3; 17.8]
Dacarbazine[c]	52	13.1 [7.0; 25.6]

a: The relevant subpopulation comprises patients with liposarcoma.
b: 850 mg/m^2, 1000 mg/m^2, or 1200 mg/m^2. According to information provided by the company in Module 4 of the dossier, a dose of 1000 mg/m^2 was mandated for 46 of 72 patients (63.9%) in the relevant subpopulation. In the total population of the study, a dose of 850 mg/m^2 was mandated for 47 of 224 patients (21.0%), a dose of 1000 mg/m^2 for 141 of 224 patients (62.9%), and a dose of 1200 mg/m^2 for 36 of 224 patients (16.1%). Median overall survival in the total population was 12.3 months (850 mg/m^2), 11.6 months (1000 mg/m^2), and 10.3 months (1200 mg/m^2). Hence there were no important differences between the 3 dosages in the total population. No data were available for the relevant subpopulation.
c: 1000 mg/m^2
CI: confidence interval; N: number of patients treated

Hence sufficient similarity of these studies could not be assumed. The studies 309 and 3007 were not usable for an indirect comparison.

Irrespective of the missing similarity of the studies 309 and 3007, the results of the indirect comparison were not interpretable for further reasons detailed below.

The total populations included for the assessment of harm did not cover the research question of the present assessment

In contrast to study 309, only data for the total population but not for the relevant subpopulation were available for study 3007 for the assessment of harm. The company therefore used the respective total population on both sides of the indirect comparison.

The proportion of relevant patients with liposarcoma in the total population was just about 34% in study 309 and 27% in study 3007.

Sufficient comparability of the total population and the relevant subpopulation and therefore transferability of the results is generally only assumed if more than 80% of the patients included fulfil the inclusion criteria of the present assessment [1]. This was not the case in both total populations included. The assessment of harm conducted by the company therefore did not cover the research question of this assessment and was not relevant for the assessment of the added benefit.

In addition, differences in the patient characteristics at the start of the study between the total population and the relevant subpopulation in study 309 suggested that the mixed total population and the relevant subpopulation were not comparable (see Table 6). In particular, there were differences between the populations regarding the distribution of sexes and tumour grades.

Table 6: Differences in patient characteristics at the start of the study in study 309

Study **Characteristics** **Category**	**Eribulin**		**Dacarbazine**	
	Total population[a]	**Relevant subpopulation[b]**	**Total population[a]**	**Relevant subpopulation[b]**
309	N = 228	N = 71	N = 224	N = 72
Sex [F/M], %	71/29	46/54	63/37	29/71
Tumour grade, n (%)				
High	150 (65.8)	38 (53.5)	152 (67.9)	39 (54.2)
Intermediate	77 (33.8)	32 (45.1)	69 (30.8)	32 (44.4)
Not conducted	1 (0.4)	1 (1.4)	3 (1.3)	1 (1.4)

a: The total population comprises patients with liposarcoma and patients with leiomyosarcoma.
b: The relevant subpopulation only comprises patients with liposarcoma.
F: female; M: male; n: number of patients in the category; N: number of randomized patients

Moreover, the different patient populations used by the company on the benefit and harm side cannot be included jointly in the assessment of the added benefit if no comparability can be assumed.

Outcomes

In the category “side effects”, the company only presented analyses for the total populations of the studies on individual severe adverse events (AEs) of Common Terminology Criteria for Adverse Events (CTCAE) grade 3 or 4. There were no analyses of the overall rates of serious AEs (SAEs) and severe AEs according to CTCAE as well as of discontinuations due to AEs. There were also no data on patient-relevant outcomes also on outcomes of the categories “morbidity” and “health-related quality of life”.

Summary

Due to the lack of similarity of the studies and the lack of relevance of the total populations included for the assessment of harm for the present research question and the missing outcomes, the indirect comparison presented by the company was not used for the present benefit assessment. Hence no usable data were available for the derivation of the added benefit of eribulin in comparison with the ACT trabectedin.

2.4 Results

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

2.5 Extent and probability of added benefit

The result of the assessment of the added benefit of eribulin in comparison with the ACT is shown in Table 7.

Table 7: Eribulin – extent and probability of added benefit

Therapeutic indication	**Appropriate comparator therapy**[a]	**Extent and probability of added benefit**
Adult patients with unresectable liposarcoma who have received prior anthracycline-containing therapy (unless unsuitable) for advanced or metastatic disease	Antineoplastic drug treatment specified by the physician and under consideration of the approval status of the drug and the pretreatment(s) administered	Added benefit not proven
a: Presentation of the appropriate comparator therapy specified by the G-BA. G-BA: Federal Joint Committee		

This deviates from the company's approach, which derived an indication of major added benefit of eribulin from the data it presented from the direct comparison of eribulin versus dacarbazine, and a hint of major added benefit of eribulin from the indirect comparison of eribulin versus trabectedin. In the overall consideration, the company derived an indication of major added benefit of eribulin versus the ACT.

The G-BA decides on the added benefit.

2.6 List of included studies

Not applicable as no studies were included in the benefit assessment.

References for English extract

Please see full dossier assessment for full reference list.

1. Institute for Quality and Efficiency in Health Care. General Methods: version 4.2 [online]. 22.04.2015 [Accessed: 01.06.2016]. URL: https://www.iqwig.de/download/IQWiG_General_Methods_Version_%204-2.pdf.

2. Skipka G, Wieseler B, Kaiser T, Thomas S, Bender R, Windeler J et al. Methodological approach to determine minor, considerable, and major treatment effects in the early benefit assessment of new drugs. Biom J 2015; 58(1): 43-58

3. Medac. Detimedac: Fachinformation [online]. 03.2015 [Accessed: 15.07.2016]. URL: http://www.fachinfo.de.

4. TEVA. Doxorubicinhydrochlorid Teva 2 mg/ml Konzentrat zur Herstellung einer Infusionslösung: Fachinformation [online]. 05.2016 [Accessed: 15.07.2016]. URL: http://www.fachinfo.de.

5. Baxter Oncology. Holoxan: Fachinformation [online]. 01.2015 [Accessed: 15.07.2016]. URL: http://www.fachinfo.de.

6. Schöffski P, Chawla S, Maki RG, Italiano A, Gelderblom H, Choy E et al. Eribulin versus dacarbazine in previously treated patients with advanced liposarcoma or leiomyosarcoma: a randomised, open-label, multicentre, phase 3 trial. Lancet 2016; 387(10028): 1629-1637.

7. Eisai. HALAVEN 0,44 mg/ml Injektionslösung: Fachinformation [online]. 05.2016 [Accessed: 15.07.2016]. URL: http://www.fachinfo.de.

8. Demetri GD, Von Mehren M, Jones RL, Hensley ML, Schuetze SM, Staddon A et al. Efficacy and safety of trabectedin or dacarbazine for metastatic liposarcoma or leiomyosarcoma after failure of conventional chemotherapy: results of a phase III randomized multicenter clinical trial. J Clin Oncol 2015; 34(8): 786-793.

9. Pharma Mar S.A. Yondelis 0,25 mg/1 mg Pulver für ein Konzentrat zur Herstellung einer Infusionslösung: Fachinformation [online]. 12.2015 [Accessed: 15.07.2016]. URL: http://www.fachinfo.de.

10. Demetri G, Patel SR, Thomas S, Livingston M, Undevia SD, Richardson G et al. Efficacy and safety of trabectedin (T) or dacarbazine (D) for treatment of patients (pts) with advanced leiomyosarcoma (LMS) or liposarcoma (LPS) after prior chemotherapy. Eur J Cancer 2015; 51(Suppl 3): S700.

11. Patel SR, Von Mehren M, Reed D, Agulnik M, Kaiser P, Charlson J et al. Final overall survival (OS) analysis of the randomized phase-3 study of trabectedin (T) or dacarbazine (D) for the treatment of patient with advanced leiomyosarcoma (LMS) or liposarcoma (LPS) [Präsentationsfolien]. In: 2015 European Cancer Congress; 25.-29.09.2015; Wien, Österreich. URL: http://player.meta-fusion.com/final-overall-survival-os-analysis-of-the-randomized-phase-3-study-of-trabectedin-t-or-dacarbazine-d-for-the-treatment-of-patients-pts-with-advanced-leiomyosarcoma-lms-or-liposarcoma-lps.

The full report (German version) is published under https://www.iqwig.de/en/projects-results/projects/drug-assessment/a16-31-eribulin-new-therapeutic-indication-benefit-assessment-according-to-35a-social-code-book-v.7429.html.