Erdafitinib (urothelial carcinoma)

Benefit assessment according to §35a SGB V[1]

EXTRACT

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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.

Patient and family involvement

The questionnaire on the disease and its treatment was answered by Alfred Marenbach.

IQWiG thanks the respondent and the Selbsthilfe-Bund Blasenkrebs e.V. for participating in the written exchange about how they experienced the disease and its treatment and about the treatment goals. The respondent and the Selbsthilfe-Bund Blasenkrebs e.V. were not involved in the actual preparation of the dossier assessment.

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Part I: Benefit assessment

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I List of tables[2]

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

I List of abbreviations

Abbreviation	Meaning
ACT	appropriate comparator therapy
EAU	European Association of Urology
ECOG PS	Eastern Cooperative Oncology Group Performance Status
FGFR3	fibroblast growth factor receptor 3
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
PD-1	programmed cell death protein 1
PD-L1	programmed cell death ligand 1
RCT	**randomized** controlled trial
SGB	Sozialgesetzbuch (Social Code Book)
SPC	Summary of Product Characteristics

I 1 Executive summary of the benefit assessment

Background

In accordance with § 35a Social Code Book V, the Federal Joint Committee (G-BA) has commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to assess the benefit of the drug erdafitinib. The assessment is based on a dossier compiled by the pharmaceutical company (hereinafter referred to as the "company"). The dossier was sent to IQWiG on 02 January 2025.

Research question

Table 2: Research questions of the benefit assessment of erdafitinib

Research question	Therapeutic indication	Appropriate comparator therapy (ACT)[a, b]
Adults with unresectable or metastatic urothelial carcinoma and certain fibroblast growth factor receptor 3 (FGFR3) genetic alterations after prior therapy with a PD-1 or PD-L1 inhibitor in the unresectable or metastatic stage		
A1	And for whom cisplatin-containing chemotherapy is suitable and who have not yet received such therapy; second-line treatment	Cisplatin in combination with gemcitabine
A2	And for whom cisplatin-containing chemotherapy is unsuitable; second-line treatment	▪ Vinflunine[e, d] or ▪ docetaxel[c, d] or ▪ paclitaxel[c, d]
B	And after prior platinum-containing chemotherapy, and for whom chemotherapy is suitable; third-line treatment	Enfortumab vedotin

a. Presented is the respective ACT specified by the G-BA.
b. The approval and dosing information of the drug's Summary of Product Characteristics (SPC) must be adhered to, and any deviations must be justified separately.
c. According to the G-BA, the added benefit can be proven in comparison with one of the cited treatment options; this can typically be achieved in the context of a single-comparator study.
d. The current guidelines recommend the drugs vinflunine, docetaxel and paclitaxel after prior treatment with a PD-1 or PD-L1 inhibitor for patients with advanced urothelial carcinoma for whom cisplatin-containing chemotherapy is not suitable. The drug vinflunine is approved after failure of platinum-containing treatment. The drugs paclitaxel and docetaxel are not approved in the named therapeutic indication. Accordingly, the use of vinflunine, paclitaxel and docetaxel represents an off-label use for patient group A2). For patient group A2) in the present therapeutic indication, the off-label use is generally preferable to the drugs currently approved in the therapeutic indication, according to the generally recognized state of medical knowledge, §6 (2), sentence 3, number 3, AM-NutzenV. In accordance with the G-BA, it is therefore appropriate to determine the above-mentioned drugs as ACT for this patient group when used off-label.

ACT: appropriate comparator therapy; FGFR3: fibroblast growth factor receptor 3; G-BA: Federal Joint Committee; PD-1: programmed cell death protein-1; PD-L1: programmed cell death ligand 1

The company deviated from the G-BA's specification for distinguishing between the different research questions and for the respective ACT. Instead, it specified an individualized treatment as ACT for all patients in the therapeutic indication, taking into account the approval status, the type of prior therapy and the suitability for cisplatin-based therapy, choosing from cisplatin in combination with gemcitabine, vinflunine, docetaxel, paclitaxel and enfortumab vedotin. The company's justification for deviating from the G-BA's ACT is not plausible. In line with the G-BA's specification, the present assessment is conducted in comparison with the respective ACT specified by the G-BA.

The assessment is conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. Randomized controlled trials (RCTs) are used to derive the added benefit. This concurs with the company's inclusion criteria.

Results

Evidence presented by the company: THOR study

The THOR study is an open-label, randomized, multicentre study with 2 cohorts comparing erdafitinib with chemotherapy (vinflunine or docetaxel) (Cohort 1) or pembrolizumab (Cohort 2). Cohort 1 included patients who had received 1 or 2 prior systemic therapies, including at least 1 therapy with a programmed cell death protein 1 (PD-1) or programmed cell death ligand 1 (PD-L1) inhibitor. Cohort 2 examined patients whose previous systemic therapy did not include a PD-1 or PD-L1 inhibitor (Cohort 2). Cohort 2 is not relevant for the present benefit assessment, as it is not covered by the approved therapeutic indication of erdafitinib due to the lack of PD-1 or PD-L1 inhibitor pretreatment. Cohort 2 is therefore not described in more detail below.

The patient population of Cohort 1 of the THOR study comprised adult patients with advanced, metastatic or unresectable urothelial carcinoma and certain FGFR changes. Patients had to have an Eastern Cooperative Oncology Group Performance Status (ECOG PS) of ≤ 2 and disease progression after 1 or 2 prior therapies, including at least 1 prior therapy with a PD-1 or PD-L1 inhibitor. Treatment with the PD-1 or PD-L1 inhibitor could have been neoadjuvant, adjuvant or in the metastatic stage.

A total of 266 patients in Cohort 1 were randomly assigned in a 1:1 ratio to the two treatment arms erdafitinib (N = 136) or chemotherapy (N = 130). Treatment of the patients in the intervention arm corresponded to the specifications of the Summary of Product Characteristics (SPC). The study's primary outcome was overall survival. Secondary outcomes included outcomes from the categories of morbidity, health-related quality of life and side effects.

No suitable data on the comparison of erdafitinib with the comparator therapy specified by the G-BA

For the patients in the THOR study who corresponded to research questions A1 and B, there are no suitable data for the comparison of erdafitinib with the comparator therapy specified by the G-BA, as treatment with cisplatin in combination with gemcitabine (research question A1) or treatment with enfortumab vedotin (research question B) were not available as treatment options in the THOR study.

Besides paclitaxel, the drugs vinflunine and docetaxel used in the comparator arm of the THOR study represent the ACT for the patient population of research question A2. However, it is unclear whether or how many patients in the THOR study are covered by research question A2.

The analyses presented by the company are not relevant for the benefit assessment

The company also does not consider all patients in Cohort 1 of the THOR study to be suitable for the benefit assessment. With the aim of forming a population relevant for the benefit assessment, the company presented data for a subpopulation in the dossier, which it refers to as the "analysis population". To form this population, the company excluded 15 patients in the intervention arm and 79 in the comparator arm from Cohort 1 using the following criteria:

1) Patients who had received prior therapy with a PD-1 or PD-L1 inhibitor not in the unresectable or metastatic (but in the neoadjuvant or adjuvant) stage, as these are not covered by the approved therapeutic indication of erdafitinib.
2) Patients who have not previously received platinum-based therapy and for whom therapy with cisplatin would be suitable.
3) from the comparator group: patients with previous platinum-containing therapy who received docetaxel in the THOR study. The company justifies this with the lack of approval of docetaxel after prior platinum-containing therapy, in contrast to vinflunine.

Overall, the company thus considered 121 vs. 51 patients of the 136 vs. 130 patients (erdafitinib vs. chemotherapy) of Cohort 1. The company’s approach of forming the analysis subpopulation is not appropriate. By applying criterion 3), the company excluded patients for the formation of the analysis population only in the comparator group. As a result, the structural equality of the study arms to be compared, which was the aim of randomization, was broken. Overall, about 5 times as many patients as in the intervention arm were excluded from the analysis in the comparator arm. Irrespective of the fact that the company's approach for forming the analysis population was inadequate, the analysis population does not represent any of the patient populations defined in the 3 research questions of the present benefit assessment.

Assessment of the evidence presented

Treatment of the patients in the THOR study that was identified by the company and used for the benefit assessment largely deviated from the ACT of the G-BA. The exact proportion of patients treated in accordance with the G-BA's ACT cannot be determined on the basis of the data presented. In addition, the company's approach of forming the analysis subpopulation is not appropriate. Overall, the data presented by the company on the THOR study are therefore not suitable for drawing conclusions on the added benefit.

Results on added benefit

Since no suitable data are available for the benefit assessment, there is no hint of an added benefit of erdafitinib in comparison with the ACT; an added benefit is therefore not proven.

Probability and extent of added benefit, patient groups with therapeutically important added benefit[3]

Table 3 shows a summary of probability and extent of the added benefit of erdafitinib.

[3] 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, added benefit not proven, or less benefit). For further details see [1,2].

Table 3: Erdafitinib – probability and extent of added benefit

Research question	Therapeutic indication	ACT[a, b]	Probability and extent of added benefit
Adults with unresectable or metastatic urothelial carcinoma and certain fibroblast growth factor receptor 3 (FGFR3) genetic alterations after prior therapy with a PD-1 or PD-L1 inhibitor in the unresectable or metastatic stage			
A1	And for whom cisplatin-containing chemotherapy is suitable and who have not yet received such therapy; second-line treatment	Cisplatin in combination with gemcitabine	Added benefit not proven
A2	And for whom cisplatin-containing chemotherapy is unsuitable; second-line treatment	▪ Vinflunine[c, d] or ▪ docetaxel[c, d] or ▪ paclitaxel[c, d]	Added benefit not proven
B	And after prior platinum-containing chemotherapy, and for whom chemotherapy is suitable; third-line treatment	Enfortumab vedotin	Added benefit not proven

a. Presented is the respective ACT specified by the G-BA.
b. The approval and dosing information of the drug's SPC must be adhered to, and any deviations must be justified separately.
c. According to the G-BA, the added benefit can be proven in comparison with one of the cited treatment options; this can typically be achieved in the context of a single-comparator study.
d. The current guidelines recommend the drugs vinflunine, docetaxel and paclitaxel after prior treatment with a PD-1 or PD-L1 inhibitor for patients with advanced urothelial carcinoma for whom cisplatin-containing chemotherapy is not suitable. The drug vinflunine is approved after failure of platinum-containing treatment. The drugs paclitaxel and docetaxel are not approved in the named therapeutic indication. Accordingly, the use of vinflunine, paclitaxel and docetaxel represents an off-label use for patient group A2). For patient group A2) in the present therapeutic indication, the off-label use is generally preferable to the drugs currently approved in the therapeutic indication, according to the generally recognized state of medical knowledge, §6 (2), sentence 3, number 2, AM-NutzenV. In accordance with the G-BA, it is therefore appropriate to determine the above-mentioned drugs as ACT for this patient group when used off-label.

ACT: appropriate comparator therapy; FGFR3: fibroblast growth factor receptor 3; G-BA: Federal Joint Committee; PD-1: programmed cell death protein-1; PD-L1: programmed cell death ligand 1

The G-BA decides on the added benefit.

I 2 Research question

The aim of this report is to assess the added benefit of erdafitinib compared with the ACT in adult patients with unresectable or metastatic urothelial carcinoma and certain genetic alterations of the FGFR3, who had previously received at least 1 line of treatment with a programmed cell death protein 1 (PD-1) or programmed cell death ligand 1 (PD-L1) inhibitor in the non-resectable or metastatic stage.

The research questions presented in Table 4 result from the ACT specified by the G-BA.

Table 4: Research questions of the benefit assessment of erdafitinib

Research question	Therapeutic indication	ACT[a, b]
Adults with unresectable or metastatic urothelial carcinoma and certain fibroblast growth factor receptor 3 (FGFR3) genetic alterations after prior therapy with a PD-1 or PD-L1 inhibitor in the unresectable or metastatic stage		
A1	And for whom cisplatin-containing chemotherapy is suitable and who have not yet received such therapy; second-line treatment	Cisplatin in combination with gemcitabine
A2	And for whom cisplatin-containing chemotherapy is unsuitable; second-line treatment	▪ Vinflunine[c, d] or ▪ docetaxel[c, d] or ▪ paclitaxel[c, d]
B	And after prior platinum-containing chemotherapy, and for whom chemotherapy is suitable; third-line treatment	Enfortumab vedotin

a. Presented is the respective ACT specified by the G-BA.
b. The approval and dosing information of the drug's SPC must be adhered to, and any deviations must be justified separately.
c. According to the G-BA, the added benefit can be proven in comparison with one of the cited treatment options; this can typically be achieved in the context of a single-comparator study.
d. The current guidelines recommend the drugs vinflunine, docetaxel and paclitaxel after prior treatment with a PD-1 or PD-L1 inhibitor for patients with advanced urothelial carcinoma for whom cisplatin-containing chemotherapy is not suitable. The drug vinflunine is approved after failure of platinum-containing treatment. The drugs paclitaxel and docetaxel are not approved in the named therapeutic indication. Accordingly, the use of vinflunine, paclitaxel and docetaxel represents an off-label use for patient group A2). For patient group A2) in the present therapeutic indication, the off-label use is generally preferable to the drugs currently approved in the therapeutic indication, according to the generally recognized state of medical knowledge, §6 (2), sentence 3, number 3, AM-NutzenV. In accordance with the G-BA, it is therefore appropriate to determine the above-mentioned drugs as ACT for this patient group when used off-label.

ACT: appropriate comparator therapy; FGFR3: fibroblast growth factor receptor 3; G-BA: Federal Joint Committee; PD-1: programmed cell death protein-1; PD-L1: programmed cell death ligand 1

The company deviated from the G-BA's specification for differentiating between the different research questions and for the respective ACT. Instead, it specified an individualized treatment patient-specific therapy as ACT for all patients in the therapeutic indication, taking

into account the approval status, the type of prior therapy and the suitability for cisplatin-based therapy, choosing from cisplatin in combination with gemcitabine, vinflunine, docetaxel, paclitaxel and enfortumab vedotin. The company's justification for deviating from the G-BA's ACT is not plausible. This is explained in the following Section.

Deviation of the company from the G-BA's ACT

Although the company agrees with the G-BA that the comparator therapy should be determined depending on the type of prior therapy and the suitability for cisplatin-based therapy, it did not derive any necessity for the definition of distinct subpopulations from this. It also points out that none of the previous standard therapies had been explicitly investigated in FGFR-positive patients and a preference for a specific therapy could therefore not be derived. The company also criticises the fact that enfortumab vedotin was defined as the sole ACT for patients who have already received a platinum-containing therapy in addition to a PD-1/PD-L1 inhibitor. With reference to the current guideline of the European Association of Urology (EAU) from 2024 [3], the company states that for patients with FGFR mutation after platinum-containing therapy with or without PD-1/PD-L1 inhibitor, vinflunine or taxanes are mentioned as recommended therapies in addition to erdafitinib. The named guideline only recommends enfortumab vedotin for the patient population not selected for FGFR mutation.

Contrary to the company's assessment, the G-BA divides the therapeutic indication into distinct subpopulations and specifies different ACTs for these. The current guidelines for the treatment of advanced/metastatic urothelial carcinoma provides treatment recommendations depending on the prior therapies and suitability for platinum-based chemotherapies [3-8]. This is reflected in the patient groups defined by the G-BA.

Drug applications for which - in addition to other criteria - the added benefit has already been established by the G-BA are preferred as comparator therapies. In the procedure on enfortumab vedotin [9], the G-BA identified a hint of considerable added benefit of enfortumab vedotin versus chemotherapy of physician’s choice choosing from vinflunine, paclitaxel and docetaxel each as monotherapy in adults with locally advanced or metastatic urothelial carcinoma who have previously received platinum-containing chemotherapy and a PD-1 or PD-L1 inhibitor and for whom chemotherapy is suitable. In addition, the current guidelines recommend enfortumab vedotin as the therapy with the strongest level of recommendation or with the highest-quality underlying evidence, regardless of FGFR mutation status, for patients who have previously received platinum-containing chemotherapy and a PD-1 or PD-L1 inhibitor [3,5].

In line with the G-BA’s specification, the present assessment is conducted in comparison with the respective ACT specified by the G-BA.

The assessment is conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. RCTs are used to derive the added benefit. This concurs with the company's inclusion criteria.

Since no suitable data are available for either of the research questions designated by the G-BA, the assessment below is performed in a joint section of the report.

I 3 Information retrieval and study pool

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

Sources used by the company in the dossier:

- Study list on erdafitinib (status: 07 November 2024)
- Bibliographical literature search on erdafitinib (last search on 02 October 2024)
- Search of trial registries/trial results databases for studies on erdafitinib (last search on 07 November 2024)
- Search on the G-BA website for erdafitinib (last search on 07 November 2024)

To check the completeness of the study pool:

- Search in trial registries for studies on erdafitinib (last search on 16 January 2025); for search strategies, see I Appendix A of the full dossier assessment

The company identified study 42756493BLC3001 (hereinafter referred to as the THOR study) [10-12] on the direct comparison of erdafitinib versus chemotherapy (vinflunine or docetaxel; Cohort 1) or pembrolizumab (Cohort 2). However, the data presented by the company on the THOR study are not suitable for drawing conclusions on the added benefit. Below, the THOR study is first described and then the lack of suitability of the data presented for the benefit assessment is justified.

I 3.1 Evidence provided by the company

For a characterization THOR study presented by the company and described below, see also Table 6 and Table 7 in I Appendix B of the full dossier assessment.

THOR study

The THOR study is an open-label, randomized, multicentre study with 2 cohorts comparing erdafitinib with chemotherapy (vinflunine or docetaxel) (Cohort 1) or pembrolizumab (Cohort 2). Cohort 1 included patients who had received 1 or 2 prior systemic therapies, including at least 1 therapy with a PD-1 or PD-L1 inhibitor. Cohort 2 examined patients whose previous systemic therapy did not include a PD-1 or PD-L1 inhibitor (Cohort 2). Cohort 2 is not relevant for the present benefit assessment, as it is not covered by the approved therapeutic indication of erdafitinib due to the lack of PD-1 or PD-L1 inhibitor pretreatment. Cohort 2 is therefore not described in more detail below.

The patient population of Cohort 1 of the THOR study comprised adult patients with advanced, metastatic or unresectable urothelial carcinoma and certain FGFR alterations (see Table 6 of the full dossier assessment). Patients had to have an ECOG PS of ≤ 2 and disease progression

after 1 or 2 prior therapies, including at least 1 prior therapy with a PD-1 or PD-L1 inhibitor. Treatment with the PD-1 or PD-L1 inhibitor could have been neoadjuvant, adjuvant or in the metastatic stage.

A total of 266 patients in Cohort 1 were randomly assigned in a 1:1 ratio to the two treatment arms erdafitinib (N = 136) and chemotherapy (N = 130). Stratification factors were region (North America vs. Europe vs. rest of the world), ECOG PS (0 or 1 vs. 2) and disease distribution (presence vs. absence of visceral metastases in lung, liver or bone).

Treatment of the patients in the intervention arm was in compliance with the specifications of the SPC [13]. It must be noted that the drugs vinflunine and docetaxel, which the G-BA specified as ACT in addition to paclitaxel for the A2 patient population, both represent a cross-approval application for the A2 patient group (see Table 4). Docetaxel is generally not approved for the therapeutic indication and vinflunine is only approved for this patient group after failure of platinum-containing therapy. Irrespective of this, the dosage regimens of both drugs used in the THOR study largely correspond to the specifications in the approved therapeutic indications of these drugs [14,15].

The study's primary outcome was overall survival. According to the information in Module 4 A, secondary outcomes comprised outcomes of the categories of morbidity, health-related quality of life and side effects.

I 3.2 No suitable data on the comparison of erdafitinib with the comparator therapy specified by the G-BA

For the patients in the THOR study who corresponded to research questions A1 and B (see Table 4), there are no suitable data for the comparison of erdafitinib with the comparator therapy specified by the G-BA, as treatment with cisplatin in combination with gemcitabine (research question A1) or treatment with enfortumab vedotin (research question B) were not available as treatment options in the THOR study.

The drugs vinflunine and docetaxel used in the comparator arm of the THOR study represent the ACT besides paclitaxel solely for the patient population of research question A2 (patients pretreated with a PD-1 or PD-L1 inhibitor for whom cisplatin-containing chemotherapy is not suitable). However, it is unclear whether or how many patients in the THOR study are covered by research question A2. This is explained in more detail below.

Around 88% of patients in Cohort 1 of the THOR study received prior platinum-containing chemotherapy in addition to a PD-1 or PD-L1 inhibitor. Enfortumab vedotin would have been the preferred treatment option for them. The remaining 12% of patients, 14 patients in the intervention and 19 patients in the comparator arm, did not receive any prior platinum-based therapy. However, the available documents do not show for how many of these 14 or 19

patients cisplatin-containing chemotherapy was not suitable (see research question A2). It should generally be noted that for Cohort 1 and correspondingly also for the small group of patients without prior platinum-based therapy, it is unclear how many patients received prior treatment with a PD-1 or PD-L1 inhibitor not in the unresectable or metastatic stage, but as neoadjuvant or adjuvant therapy (see study description in Section I 3.1) and would therefore not be covered by the approval.

I 3.3 The analyses presented by the company are not relevant for the benefit assessment

The company also does not consider all patients in Cohort 1 of the THOR study to be suitable for the benefit assessment. With the aim of forming a population relevant for the benefit assessment, the company presented data for a subpopulation in the dossier, which it refers to as the "analysis population". To form this population, the company excluded 15 patients in the intervention arm and 79 in the comparator arm from Cohort 1 using the following criteria:

1) Patients who had received prior therapy with a PD-1 or PD-L1 inhibitor not in the unresectable or metastatic (but in the neoadjuvant or adjuvant) stage, as these are not covered by the approved therapeutic indication of erdafitinib
2) Patients who have not previously received platinum-based therapy and for whom therapy with cisplatin would be suitable
3) from the comparator group: patients with previous platinum-containing therapy who received docetaxel in the THOR study. The company justifies this with the lack of approval of docetaxel after prior platinum-containing therapy, in contrast to vinflunine.

Information on how many patients were excluded from the analysis according to the respective justification is not available. Overall, the company thus considered 121 vs. 51 patients of the 136 vs. 130 patients (erdafitinib vs. chemotherapy) of Cohort 1.

The company’s approach of forming the analysis subpopulation is not appropriate. By applying criterion 3), the company excluded patients for the formation of the analysis population only in the comparator group. As a result, the structural equality of the study arms to be compared, which was the aim of randomization, was broken. Overall, about 5 times as many patients as in the intervention arm were excluded from the analysis in the comparator arm. Irrespective of the fact that the company's approach for forming the analysis population was inadequate, the analysis population does not represent any of the patient populations defined in the 3 research questions of the present benefit assessment. Similar to the total population of Cohort 1 (see Section I 3.2), the analysis population presented here largely comprised patients for whom enfortumab vedotin would have been the indicated treatment option in the comparator arm according to the ACT.

Assessment of the evidence presented

As described above, the company did not follow the G-BA's ACT. Treatment of the patients in the THOR study that was identified by the company and used for the benefit assessment largely deviated from the ACT of the G-BA. The exact proportion of patients treated in accordance with the G-BA's ACT cannot be determined on the basis of the data presented. In addition, the company's approach of forming the analysis subpopulation is not appropriate. Overall, the data presented by the company on the THOR study are therefore not suitable for drawing conclusions on the added benefit for all 3 research questions.

I 4 Results on added benefit

No suitable data are available for the assessment of the added benefit of erdafitinib compared with the ACT in adult patients with unresectable or metastatic urothelial carcinoma and certain genetic FGFR3 alterations who have previously received at least one line of therapy with a PD-1 or PD-L1 inhibitor in the unresectable or metastatic stage. There is thus no hint of added benefit of erdafitinib in comparison with the ACT for either of the research questions; an added benefit is therefore not proven in any case.

I 5 Probability and extent of added benefit

I 5.1 Overall conclusion on added benefit

The result of the assessment of the added benefit of erdafitinib in comparison with the ACT is summarized in Table 5.

Table 5: Erdafitinib – probability and extent of added benefit

Research question	Therapeutic indication	ACT[a, b]	Probability and extent of added benefit
Adults with unresectable or metastatic urothelial carcinoma and certain FGFR3 genetic alterations after prior therapy with a PD-1 or PD-L1 inhibitor in the unresectable or metastatic stage			
A1	And for whom cisplatin-containing chemotherapy is suitable and who have not yet received such therapy; second-line treatment	Cisplatin in combination with gemcitabine	Added benefit not proven
A2	And for whom cisplatin-containing chemotherapy is unsuitable; second-line treatment	▪ Vinflunine[c, d] or ▪ docetaxel[c, d] or ▪ paclitaxel[c, d]	Added benefit not proven
B	And after prior platinum-containing chemotherapy, and for whom chemotherapy is suitable; third-line treatment	Enfortumab vedotin	Added benefit not proven

a. Presented is the respective ACT specified by the G-BA.
b. The approval and the dosing information of the drugs' SPC must be adhered to, and any deviations must be justified separately.
c. According to the G-BA, the added benefit can be proven in comparison with one of the cited treatment options; this can typically be achieved in the context of a single-comparator study.
d. The current guidelines recommend the drugs vinflunine, docetaxel and paclitaxel after prior treatment with a PD-1 or PD-L1 inhibitor for patients with advanced urothelial carcinoma for whom cisplatin-containing chemotherapy is not suitable. The drug vinflunine is approved after failure of platinum-containing treatment. The drugs paclitaxel and docetaxel are not approved in the named therapeutic indication. Accordingly, the use of vinflunine, paclitaxel and docetaxel represents an off-label use for patient group A2). For patient group A2) in the present therapeutic indication, the off-label use is generally preferable to the drugs currently approved in the therapeutic indication, according to the generally recognized state of medical knowledge, §6 (2), sentence 3, number 2, AM-NutzenV. In accordance with the G-BA, it is therefore appropriate to determine the above-mentioned drugs as ACT for this patient group when used off-label.

ACT: appropriate comparator therapy; FGFR3: fibroblast growth factor receptor 3; G-BA: Federal Joint Committee; PD-1: programmed cell death protein-1; PD-L1: programmed cell death ligand 1

The assessment described above deviates from that by the company. Based on the analysis population presented in the dossier, the company sees an indication of a considerable added benefit of erdafitinib.

The G-BA decides on the added benefit.

I 6 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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