Gemeinsamer Bundesausschuss

Justification

of the Resolution of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive: Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a (SGB V) Sacituzumab govitecan (new therapeutic indication: breast cancer, HR+, HER2-, at least 3 prior therapies)

of 15 February 2024

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assesses the benefit of reimbursable medicinal products with new active ingredients. This includes in particular the assessment of the additional benefit and its therapeutic significance. The benefit assessment is carried out on the basis of evidence provided by the pharmaceutical company, which must be submitted to the G-BA electronically, including all clinical trials the pharmaceutical company has conducted or commissioned, at the latest at the time of the first placing on the market as well as the marketing authorisation of new therapeutic indications of the medicinal product, and which must contain the following information in particular:

1. approved therapeutic indications,
2. medical benefit,
3. additional medical benefit in relation to the appropriate comparator therapy,
4. number of patients and patient groups for whom there is a therapeutically significant additional benefit,
5. treatment costs for the statutory health insurance funds,
6. requirements for a quality-assured application.

The G-BA may commission the Institute for Quality and Efficiency in Health Care (IQWiG) to carry out the benefit assessment. According to Section 35a, paragraph 2 SGB V, the assessment must be completed within three months of the relevant date for submission of the evidence and published on the internet.

According to Section 35a paragraph 3 SGB V, the G-BA decides on the benefit assessment within three months of its publication. The resolution is to be published on the internet and is part of the Pharmaceuticals Directive.

2. Key points of the resolution

The active ingredient sacituzumab govitecan (Trodelvy) was listed for the first time on 1 December 2021 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

On 26 July 2023, sacituzumab govitecan received marketing authorisation for a new therapeutic indication to be classified as a major type 2 variation as defined according to Annex 2, number 2, letter a to Regulation (EC) No. 1234/2008 of the Commission of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334 from 12.12.2008, sentence 7).

On 14 August 2023, i.e. at the latest within four weeks after the notification of the pharmaceutical company of the approval of a new therapeutic indication, the pharmaceutical company has submitted a dossier in due time in accordance with Section 4, paragraph 3,

number 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5, Section 8, paragraph 1, number 2 of the Rules of Procedure (VerfO) of the G-BA on the active ingredient sacituzumab govitecan with the new therapeutic indication "breast cancer, HR+, HER2-, at least 3 prior therapies". The G-BA commissioned the IQWiG to carry out the dossier assessment. The benefit assessment was published on 15 November 2023 on the G-BA website (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA came to a resolution on whether an additional benefit of sacituzumab govitecan compared with the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG, the statements submitted in the written statement and oral hearing procedure, and the addendum to the benefit assessment prepared by IQWiG. In order to determine the extent of the additional benefit, the G-BA has evaluated the data justifying the finding of an additional benefit on the basis of their therapeutic relevance (qualitative), in accordance with the criteria laid down in Chapter 5 Section 5, paragraph 7 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of sacituzumab govitecan.

In the light of the above, and taking into account the statements received and the oral hearing, the G-BA has come to the following assessment:

2.1 Additional benefit of the medicinal product in relation to the appropriate comparator therapy

2.1.1 Approved therapeutic indication of Sacituzumab govitecan (Trodelvy) in accordance with the product information

Trodelvy as monotherapy is indicated for the treatment of adult patients with unresectable or metastatic hormone receptor (HR)-positive, HER2-negative breast cancer who have received endocrine-based therapy, and at least two additional systemic therapies in the advanced setting.

Therapeutic indication of the resolution (resolution of 15.02.2024):

see the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adults with unresectable or metastatic hormone receptor (HR)-positive, HER2-negative breast cancer who have received endocrine-based therapy, and at least two additional systemic therapies in the advanced setting

Appropriate comparator therapy:

- Capecitabine

1 General Methods, version 7.0 from 19.09.2023. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

or

- Eribulin

  or

- Vinorelbine

  or

- an anthracycline or taxane-containing therapy (only for patients who have not yet received anthracycline and taxane-containing therapy or are eligible for renewed anthracycline or taxane-containing treatment).

Criteria according to Chapter 5 Section 6 of the Rules of Procedure of the G-BA and Section 6 para. 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV):

The appropriate comparator therapy must be an appropriate therapy in the therapeutic indication in accordance with the generally recognised state of medical knowledge (Section 12 SGB V), preferably a therapy for which endpoint studies are available and which has proven its worth in practical application unless contradicted by the guidelines under Section 92, paragraph 1 SGB V or the principle of economic efficiency.

In determining the appropriate comparator therapy, the following criteria, in particular, must be taken into account as specified in Chapter 5 Section 6, paragraph 3 VerfO:

1. To be considered as a comparator therapy, the medicinal product must, principally, have a marketing authorisation for the therapeutic indication.
2. If a non-medicinal treatment is considered as a comparator therapy, this must be available within the framework of the SHI system.
3. As comparator therapy, medicinal products or non-medicinal treatments for which the patient-relevant benefit has already been determined by the G-BA shall be preferred.
4. According to the generally recognised state of medical knowledge, the comparator therapy should be part of the appropriate therapy in the therapeutic indication.

According to Section 6, paragraph 2, sentence 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the determination of the appropriate comparator therapy must be based on the actual medical treatment situation as it would be without the medicinal product to be assessed. According to Section 6, paragraph 2, sentence 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the G-BA may exceptionally determine the off-label use of medicinal products as an appropriate comparator therapy or as part of the appropriate comparator therapy if it determines by resolution on the benefit assessment according to Section 7, paragraph 4 that, according to the generally recognised state of medical knowledge, this is considered a therapy standard in the therapeutic indication to be assessed or as part of the therapy standard in the medical treatment situation to be taken into account according to sentence 2, and

1. for the first time, a medicinal product approved in the therapeutic indication is available with the medicinal product to be assessed,

2. according to the generally recognised state of medical knowledge, the off-label use is generally preferable to the medicinal products previously approved in the therapeutic indication, or
3. according to the generally recognised state of medical knowledge, the off-label use for relevant patient groups or indication areas is generally preferable to the medicinal products previously approved in the therapeutic indication.

An appropriate comparator therapy may also be non-medicinal therapy, the best possible add-on therapy including symptomatic or palliative treatment, or monitoring wait-and-see approach.

Justification based on the criteria set out in Chapter 5 Section 6, paragraph 3 VerfO and Section 6, paragraph 2 AM-NutzenV:

on 1. In terms of authorisation status, the active ingredients available are the cytostatic agents 5-fluorouracil, capecitabine, cyclophosphamide, docetaxel, doxorubicin, liposomal doxorubicin, epirubicin, eribulin, ifosfamide, methotrexate, mitomycin, mitoxantrone, nab-paclitaxel, vinblastine, vincristine and vinorelbine as well as the PARP inhibitors olaparib and talazoparib.

Medicinal products with explicit marketing authorisation for HER2-positive breast cancer are not considered.

on 2. A non-medicinal treatment cannot be considered in the present therapeutic indication. This does not affect the implementation of radiotherapy as a palliative patient-individual therapy option for symptom control.

on 3. Resolutions on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V:

- Eribulin: Resolution of 22 January 2015
- Olaparib: Resolution of 16 January 2020
- Talazoparib: Resolution of 20 November 2020

Medicinal products with explicit marketing authorisation for HER2-positive breast cancer are not considered.

Guidelines:

Annex VI to Section K of the Pharmaceuticals Directive – Active ingredients that cannot be prescribed for off-label use:

- Gemcitabine in monotherapy for breast cancer in women

Guideline on examination and treatment methods in the hospital (guideline on inpatient treatment methods), entered into force on 20 March 2019

- Proton therapy for brain metastases
- Proton therapy for breast cancer

on 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as reviews of clinical studies in the present indication and is presented in the "Research and synopsis of the evidence to determine the appropriate comparator therapy according to Section 35a SGB V".

The scientific-medical societies and the Drugs Commission of the German Medical Association (AkdÄ) were also involved in writing on questions relating to the comparator therapy in the present indication according to Section 35a, paragraph 7 SGB V (see "Information on Appropriate Comparator Therapy").

According to the therapeutic indication, sacituzumab govitecan should be used in patients with at least 2 previous systemic chemotherapy regimens in the metastatic stage. (Neo)adjuvant chemotherapy is counted as one of the previous chemotherapy regimens if unresectable, locally advanced or metastatic disease develops within 12 months.

It is also assumed that patients have generally received taxane and/or anthracycline-based chemotherapy as part of their previous treatment and that there is no indication for (secondary) resection or radiotherapy with a curative objective.

In addition, at this time, it is assumed that patients with genomic BRCA1/2 mutations will not be eligible for BRCA-specific therapy at the time of treatment with sacituzumab govitecan.

Among the approved active ingredients listed under 1., only certain active ingredients named below will be included in the appropriate comparator therapy, taking into account the evidence on therapeutic benefit, the guideline recommendations and the reality of care.

According to current guidelines and the explanations by the scientific-medical societies, for patients who were pretreated with an anthracycline and taxane-based chemotherapy, further cytotoxic chemotherapy is the current treatment standard in case of disease progression or relapse.

Primary monotherapies are recommended, polychemotherapy is considered indicated only in cases of severe symptoms, rapid tumour growth and aggressive tumour behaviour. Anthracyclines and taxanes can also be considered as re-therapy for these patients, depending on their individual circumstances. Of the active ingredients primarily mentioned in various guidelines, besides taxanes and anthracyclines, capecitabine, vinorelbine and eribulin are approved for use as monotherapy in the therapeutic indication.

According to guideline recommendations, combination therapy should be considered for patients prone to high remission due to severe symptoms or rapid tumour growth.

For the treatment of patients who have experienced further progression after at least one course of chemotherapy for the treatment of advanced breast cancer, the G-BA identified a hint for a considerable additional benefit of eribulin compared to monotherapy with capecitabine or vinorelbine for patients who can no longer be treated with taxanes or anthracyclines (resolution of 22 January 2015).

Taking into account the importance of eribulin in the current guideline recommendations in relation to other treatment options and in view of the restriction of the identified additional benefit only to a part of the approved therapeutic indication, eribulin is considered to be an equally appropriate treatment option alongside capecitabine and vinorelbine.

However, no direct comparator evidence is available for vinorelbine and capecitabine.

Gemcitabine is approved in combination with paclitaxel for the treatment of patients with inoperable, locally recurrent or metastatic breast cancer with recurrence following adjuvant/ neoadjuvant chemotherapy. Accordingly, gemcitabine monotherapy is not covered by the marketing authorisation for this therapeutic indication. In addition, Annex VI to Section K of the Pharmaceuticals Directive stipulates that gemcitabine cannot be prescribed in monotherapy for breast cancer in women in off-label use.

For those patients who have not undergone chemotherapy with an anthracycline and a taxane, the guidelines recommend chemotherapy containing an anthracycline and/or a taxane. Both monochemotherapy with an anthracycline or a taxane and combination therapy are established treatment options. Combination therapy mainly consists of combining different chemotherapies, including an anthracycline or a taxane, or both in combination. Patients who are not prone to high remission should receive sequential chemotherapy. Polychemotherapy is considered indicated only in cases of severe symptoms, rapid tumour growth and aggressive tumour behaviour.

In addition to women, the therapeutic indication also includes men with breast cancer. The evidence on treatment options for men with breast cancer is extremely limited. According to the guidelines, the recommendations for the treatment of men are predominantly based on the recommendations for the treatment of women.

In summary, capecitabine or eribulin or vinorelbine or anthracycline or taxane-containing therapy (only for patients who have not yet received anthracycline and/or taxane-containing therapy or who are eligible for renewed anthracycline or taxane-containing treatment) is considered as the appropriate comparator therapy.

The additional benefit can be proven compared to one of the therapy options mentioned; usually, this can be done within the framework of a single-comparator study.

The marketing authorisation and dosage specifications in the product information of the active ingredients must be considered; deviations must be justified separately.

The findings in Annex XII do not restrict the scope of treatment required to fulfil the medical treatment mandate.

A change in the appropriate comparator therapy requires a resolution by the G-BA linked to the prior review of the criteria according to Chapter 5 Section 6, paragraph 3 Rules of Procedure.

2.1.3 Extent and probability of the additional benefit

In summary, the additional benefit of sacituzumab govitecan is assessed as follows:

- Indication of a considerable additional benefit

Justification:

<u>About the TROPiCS-02 study</u>

For the benefit assessment, the pharmaceutical company presents results from the open-label, randomised, multicentre phase III TROPiCS-02 study.

In the TROPiCS-02 study, sacituzumab govitecan was compared with the doctor's instructions under selection of capecitabine, eribulin, gemcitabine and vinorelbine.

The study enrolled adult patients with metastatic hormone receptor-positive, HER2-negative breast cancer who had already received at least one endocrine-based therapy, at least one therapy with CDK4/6 inhibitors and at least one taxane-containing therapy as well as two to four chemotherapy regimens in the metastatic stage. At the time of enrolment in the study, the patients had to have an ECOG-PS of 0 or 1.

A total of 543 patients were enrolled in the study and randomised in a 1:1 ratio to either treatment with sacituzumab govitecan (N = 272) or therapy according to doctor's instructions (N = 271). Randomisation was stratified according to the number of previous chemotherapy regimens in the metastatic stage (2 vs 3 or 4), visceral metastases (yes vs no) and endocrine-based therapy in the metastatic stage for at least 6 months (yes vs no). Only 1% of the participants in the TROPiCS-02 study were men.

Gemcitabine is not part of the appropriate comparator therapy. For the benefit assessment, the pharmaceutical company presents a relevant sub-population of the TROPiCS-02 study. This sub-population includes 205 vs 213 patients for whom, prior to randomisation, capecitabine, eribulin or vinorelbine was selected as the active ingredient to be administered in case of an allocation to the control arm.

Treatment with sacituzumab govitecan, capecitabine, eribulin or vinorelbine was largely carried out in accordance with the product information.

The study medication should be administered until disease progression, unacceptable toxicity, withdrawal of consent, therapy discontinuation due to the principal investigator's decision or until the end of study. Patients could continue treatment after the first detection of disease progression according to version 1.1 of the RECIST criteria if they benefited from it at the principal investigator's discretion. However, treatment with the study medication had to be discontinued in the event of disease progression and/or loss of clinical benefit in the further course.

The primary endpoint of the study is progression-free survival, secondary endpoints include overall survival as well as endpoints in the categories of morbidity, health-related quality of life and side effects.

The still ongoing study was conducted in 91 study sites across Europe and North America and was initiated in May 2019. No information is available on the end of study.

For the benefit assessment, the results of the data cut-off from 01.12.2022 are used.

About the EVER-132-002 study

The EVER-132-002 study is an ongoing, open-label randomised controlled trial comparing sacituzumab govitecan with a therapy according to doctor's instructions under selection of capecitabine, eribulin, gemcitabine and vinorelbine.

The study enrolled adult patients with metastatic hormone receptor-positive, HER2-negative breast cancer who had already received at least one endocrine-based therapy and at least one taxane-containing therapy as well as two to four chemotherapy regimens in the metastatic stage. At the time of enrolment in the study, the patients had to have an ECOG-PS of 0 or 1.

Overall, 331 patients were randomised in a 1:1 ratio to treatment with sacituzumab govitecan (N = 166) or to therapy according to doctor's instructions (N = 165). Randomisation was

stratified according to the number of previous chemotherapy regimens in the metastatic stage (2 vs 3 or 4), visceral metastases (yes vs no) and previous cyclin-dependent kinase (CDK)4/6 inhibitor therapy in the metastatic stage (yes vs no).

Since gemcitabine is not part of the appropriate comparator therapy, the pharmaceutical company submitted a relevant sub-population of the EVER-132-002 study. This sub-population includes 160 vs 155 patients for whom, prior to randomisation, capecitabine, eribulin or vinorelbine was specified as the active ingredient to be administered in case of an allocation to the control arm. The patients were almost exclusively female. Only 2 study participants in the control arm were men.

The study medication should be administered until disease progression, unacceptable toxicity, withdrawal of consent, therapy discontinuation due to the principal investigator's decision or until the end of study.

The primary endpoint of the study is progression-free survival. Patient-relevant secondary endpoints are overall survival and endpoints in the categories of morbidity, health-related quality of life and side effects.

The still ongoing study was conducted in 41 study sites in China, South Korea and Taiwan and was initiated in November 2020. No information is available on the end of study.

For the benefit assessment, the results of the data cut-off from 30.04.2023 are used.

About the meta-analysis

In addition to the results of the TROPiCS-02 and EVER-132-002 studies, the results of an individual patient data (IPD) meta-analysis based on the relevant sub-populations of the EVER-132-002 and TROPiCS-02 studies are available for this benefit assessment. The two studies have an identical design.

There are differences between the studies with regard to the inclusion criterion of prior therapy with (at least) one CDK4/6 inhibitor. This prior therapy was only required in the TROPiCS-02 study prior to enrolment in the study. Furthermore, the TROPiCS-02 study was conducted in study sites across North America and Europe, while the EVER-132-002 study only enrolled patients of Asian descent. Furthermore, the sub-population of the EVER-132-002 study was on average 4 years younger than the sub-population of the TROPiCS-02 study, the percentage with ECOG-PS 1 was approx. 78%, which is around 24 percentage points higher, and the average time between the detection of metastasis and randomisation was shorter (43 months vs 53 months).

For the benefit assessment, prior to use or calculation of the meta-analysis for the individual endpoints, heterogeneity tests were used to show that the two studies are sufficiently homogeneous for a statistical summary.

Extent and probability of the additional benefit

Mortality

Overall survival was defined in both the TROPiCS-02 and EVER-132-002 studies as the time between randomisation and death, regardless of the underlying cause of death.

For the overall survival endpoint, the meta-analysis of the studies shows a statistically significant difference to the advantage of sacituzumab govitecan compared to capecitabine or eribulin or vinorelbine.

Morbidity

Progression-free survival (PFS)

PFS was the primary endpoint in both studies and it was operationalised as the time from randomisation to the first observation of objective tumour progression or death, whichever occurs first.

Tumour response was assessed using radiological images according to RECIST version 1.1.

There is a statistically significant prolonged PFS to the advantage of sacituzumab govitecan compared to the appropriate comparator therapy.

The PFS endpoint is a composite endpoint composed of endpoints of the mortality and morbidity categories. The endpoint component "mortality" was already assessed as an independent endpoint in the present study via the endpoint "overall survival". The morbidity component assessment was not done in a symptom-related manner but exclusively by means of imaging (disease progression assessed by radiology according to the RECIST 1.1 criteria). Taking into account the aspects mentioned above, there are different opinions within the G-BA regarding the patient-relevance of the endpoint PFS. The overall statement on the extent of the additional benefit remains unaffected.

Symptomatology

Symptomatology was assessed in both the TROPiCS-02 and EVER-132-002 studies using the symptom scales of the cancer-specific EORTC QLQ-C30 questionnaire.

The assessment of symptomatology was operationalised as time to first deterioration. Here, an increase in the score by ≥ 10 points compared to the start of the study was considered a clinically relevant deterioration.

In terms of the endpoints of appetite loss, insomnia and constipation, there is no statistically significant difference between the treatment arms.

For the endpoints of fatigue, pain and dyspnoea, there is a statistically significant difference to the advantage of sacituzumab govitecan compared to the appropriate comparator therapy.

With regard to the endpoints of nausea and vomiting and diarrhoea, there is a statistically significant difference to the disadvantage of sacituzumab govitecan compared to capecitabine, eribulin and vinorelbine. With regard to the assessment of the results, in particular for the endpoints nausea and vomiting and diarrhoea, there are uncertainties both for morbidity endpoints and for safety endpoints against the background of a possible double collection of these events.

Health status

Health status was collected in both studies using the EQ-5D visual analogue scale (VAS) up to 30 days after the end of treatment.

The pharmaceutical company submits responder analyses for the "time to first deterioration" defined as a decrease in the score by ≥ 15 points compared to the baseline value.

For this evaluation, a statistically significant difference to the advantage of sacituzumab govitecan compared to capecitabine, eribulin or vinorelbine could be identified.

The positive effects predominate the overall assessment of the results in the endpoint category of morbidity, so that an advantage of sacituzumab govitecan compared to the appropriate comparator therapy is derived overall with regard to morbidity.

Quality of life

Health-related quality of life was collected in both studies using the functional scales of the cancer-specific questionnaire EORTC QLQ-C30.

The assessment of quality of life was operationalised as time to first deterioration. Here, a decrease in the score by ≥ 10 points compared to the start of the study was considered a clinically relevant deterioration.

There is no statistically significant difference between the treatment arms for the endpoint of social functioning.

With regard to the endpoints of global health status, physical functioning, cognitive functioning, role functioning and emotional functioning, there is a statistically significant difference to the advantage of sacituzumab govitecan compared to capecitabine, eribulin and vinorelbine.

Overall, there are only positive effects of sacituzumab govitecan with regard to quality of life.

Side effects

Adverse events (AEs) in total

In both studies, adverse events occurred in all study arms in almost all patients enrolled. The results were only presented additionally.

Severe adverse events (CTCAE grade ≥ 3)

For the endpoint of severe AE, there is a statistically significant difference to the disadvantage of sacituzumab govitecan compared to the appropriate comparator therapy.

Serious adverse events (SAEs) and discontinuation due to adverse events

With regard to the endpoints of SAEs and discontinuation due to AEs, there is no statistically significant difference between the treatment arms in the meta-analysis.

Specific adverse events

For the specific adverse events, both advantages and disadvantages are shown in detail.

With regard to the endpoints of hand-foot syndrome (AEs), there is a statistically significant difference to the advantage of sacituzumab govitecan compared to capecitabine, eribulin or vinorelbine.

For the endpoints of gastrointestinal toxicity (severe AEs) and neutropenia (severe AEs), there is a statistically significant difference to the disadvantage of sacituzumab govitecan compared to the control arm.

For the endpoint category of side effects, sacituzumab govitecan was found to be at an overall disadvantage compared to capecitabine, eribulin or vinorelbine.

Overall assessment

For the assessment of the additional benefit of sacituzumab govitecan for the treatment of unresectable or metastatic hormone receptor (HR)-positive, HER2-negative breast cancer in adults who have received endocrine-based therapy and at least two additional systemic therapies for advanced settings, results are available from a meta-analysis on the relevant sub-population for the endpoint categories of mortality, morbidity, health-related quality of life and side effects. The meta-analysis includes the randomised, controlled, open-label TROPiCS-02 and EVER-132-002 studies. The relevant sub-population includes patients for whom, prior to randomisation, capecitabine, vinorelbine or eribulin was selected as the active ingredient to be administered in case of allocation to the control arm.

For the overall survival endpoint, the meta-analysis of the studies shows a statistically significant difference to the advantage of sacituzumab govitecan compared to capecitabine or eribulin or vinorelbine.

With regard to morbidity, symptomatology was collected in the meta-analysis using the EORTC-QLQ-C30 and the general health status using the EQ-5D visual analogue scale. The results show a statistically significant difference to the advantage of sacituzumab govitecan compared to capecitabine, eribulin or vinorelbine for the general health status. In terms of symptomatology, there are more positive than negative effects. The positive effects predominate the overall assessment of the results in the endpoint category of morbidity, so that an advantage of sacituzumab govitecan compared to the appropriate comparator therapy is derived overall with regard to morbidity.

With regard to quality of life, the EORTC QLQ-C30 shows only positive effects of sacituzumab govitecan compared to the appropriate comparator therapy. Statements on quality of life are particularly important in the present palliative treatment setting.

For the endpoint category of side effects, a disadvantage of sacituzumab govitecan over capecitabine, eribulin or vinorelbine can be identified for severe AEs, as well as advantages and disadvantages for specific AEs in detail. In the overall assessment of the endpoint of side effects, the negative effects of sacituzumab govitecan predominate.

Overall, a clear and consistent improvement in health-related quality of life was observed for sacituzumab govitecan compared with the appropriate comparator therapy, particularly against the background of the unfavourable prognosis of patients who are already in a late, palliative treatment setting in this therapeutic indication. There are also advantages in overall survival and morbidity. On the contrary, there are disadvantages in terms of side effects. As a result, a considerable additional benefit was identified for sacituzumab govitecan compared to capecitabine or eribulin or vinorelbine.

Reliability of data (probability of additional benefit)

The assessment of the additional benefit in the TROPiCS-02 and EVER-132-002 studies is based on two randomised, open-label, still ongoing and direct comparator phase III studies.

The risk of bias at the study level and at the endpoint level for overall survival is assessed as low.

Assessment-relevant uncertainties arise for the results of the endpoints of symptomatology, health status and health-related quality of life due to the high percentage of patients not included in the evaluation and due to the lack of blinding in the subjective endpoint collection.

Furthermore, there is a limitation in the representativeness of the meta-analysis for the patient population according to the approved therapeutic indication, as no data are available for patients with ECOG-PS > 1.

These uncertainties justify downgrading the reliability of data for the overall assessment, which could be classified in the "proof" category in the presence of two randomised and direct comparator phase III studies, particularly in view of the importance of the quality of life results for the additional benefit in the current treatment setting. Thus, the reliability of data for the additional benefit determined is classified in the category "indication".

2.1.4 Summary of the assessment

The present assessment is the benefit assessment of a new therapeutic indication for the active ingredient sacituzumab govitecan. The therapeutic indication assessed here is as follows:

"Trodelvy as monotherapy is indicated for the treatment of adult patients with unresectable or metastatic hormone receptor (HR)-positive, HER2-negative breast cancer who have received endocrine-based therapy, and at least two additional systemic therapies in the advanced setting"

The appropriate comparator therapy was determined by the G-BA as follows:

- Capecitabine

  or

- Eribulin

  or

- Vinorelbine

  or

- an anthracycline or taxane-containing therapy (only for patients who have not yet received anthracycline and taxane-containing therapy or are eligible for renewed anthracycline or taxane-containing treatment).

For the assessment of the additional benefit of sacituzumab govitecan for the treatment of unresectable or metastatic hormone receptor (HR)-positive, HER2-negative breast cancer in adult patients who have received endocrine-based therapy and at least two additional systemic therapies for advanced settings, results are available from a meta-analysis on the endpoint categories of mortality, morbidity, health-related quality of life and side effects compared with capecitabine or eribulin or vinorelbine. The meta-analysis includes the randomised, controlled, open-label TROPiCS-02 and EVER-132-002 studies.

For the overall survival endpoint, the meta-analysis of the studies shows a statistically significant difference to the advantage of sacituzumab govitecan compared to capecitabine or eribulin or vinorelbine.

The positive effects predominate the overall assessment of the results in the endpoint category of morbidity, so that an advantage of sacituzumab govitecan compared to the appropriate comparator therapy is derived overall with regard to morbidity.

With regard to quality of life, the EORTC QLQ-C30 shows only positive effects of sacituzumab govitecan compared to the appropriate comparator therapy. Statements on quality of life are particularly important in the present palliative treatment setting.

For the endpoint category of side effects, sacituzumab govitecan was found to be at a disadvantage compared to capecitabine, eribulin or vinorelbine.

Overall, a clear and consistent improvement in health-related quality of life was observed for sacituzumab govitecan compared with the appropriate comparator therapy, particularly against the background of the unfavourable prognosis of patients who are already in a late, palliative treatment setting in this therapeutic indication. There are also advantages in overall survival and morbidity. On the contrary, there are disadvantages in terms of side effects. As a result, a considerable additional benefit was identified for sacituzumab govitecan compared to capecitabine or eribulin or vinorelbine.

The reliability of data of the additional benefit identified is classified in the "indication" category.

In the overall assessment, an indication of a considerable additional benefit of sacituzumab govitecan compared to the appropriate comparator therapy is identified.

2.2 Number of patients or demarcation of patient groups eligible for treatment

The information on the number of patients is based on the target population in statutory health insurance (SHI).

The G-BA bases its resolution on the information from the dossier of the pharmaceutical company. However, the following uncertainties arise:

On the one hand, patients with a survival from metastasis > 3 years are not considered. On the other, the transferability of the percentage values for the receipt of a third or fourth-line therapy from the evaluation of the Tumour Registry for Breast Cancer (TMK) to the baseline calculated by the pharmaceutical company is unclear due to the now different medical treatment situation and the potentially different duration of observation.

2.3 Requirements for a quality-assured application

The requirements in the product information are to be taken into account. The European Medicines Agency (EMA) provides the contents of the product information (summary of product characteristics, SmPC) for Trodelvy (active ingredient: sacituzumab govitecan) at the following publicly accessible link (last access: 1 November 2023):

https://www.ema.europa.eu/en/documents/product-information/trodelvy-epar-product-information_en.pdf

Treatment with sacituzumab govitecan should only be initiated and monitored by specialists in internal medicine, haematology, and oncology who are experienced in the treatment of patients with breast cancer, as well as specialists in obstetrics and gynaecology, and other specialists participating in the Oncology Agreement.

2.4 Treatment costs

The treatment costs are based on the requirements in the product information and the information listed in the LAUER-TAXE® (last revised: 15 January 2024).

The annual treatment costs shown refer to the first year of treatment.

If no maximum treatment duration is specified in the product information, the treatment duration is assumed to be one year (365 days), even if the actual treatment duration varies from patient to patient and/or is shorter on average. The time unit "days" is used to calculate the "number of treatments/ patient/ year", time intervals between individual treatments and for the maximum treatment duration, if specified in the product information.

Treatment period:

Adults with unresectable or metastatic hormone receptor (HR)-positive, HER2-negative breast cancer who have received endocrine-based therapy, and at least two additional systemic therapies in the advanced setting

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Sacituzumab govitecan	2 x per 21-day cycle (Day 1 and 8)	17.4	2	34.8
Appropriate comparator therapy				
Capecitabine	2 x on day 1-14 of a 21-day cycle	17.4	14	243.6
Eribulin	2 x per 21-day cycle (Day 1 and 8)	17.4	2	34.8
Vinorelbine	1 x weekly	52.1	1	52.1
Anthracycline or taxane-containing treatment regimens				
Docetaxel	1 x per 21-day cycle	17.4	1	17.4
Paclitaxel	1 x per 21-day cycle	17.4	1	17.4
nab-paclitaxel	1 x per 21-day cycle	17.4	1	17.4

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Doxorubicin	1 x per 21-day cycle	5 - 11 [2]	1	5.0 – 11.0
Pegylated liposomal doxorubicin	1 x per 28-day cycle	13.0	1	13.0
Eprirubicin	1 x per 21-day cycle	10 - 16 [3]	1	10.0 – 16.0

Consumption:

Adults with unresectable or metastatic hormone receptor (HR)-positive, HER2-negative breast cancer who have received endocrine-based therapy, and at least two additional systemic therapies in the advanced setting

For the cost representation, only the dosages of the general case are considered. Patient-individual dose adjustments (e.g. because of side effects or comorbidities) are not taken into account when calculating the annual treatment costs.

In general, initial induction regimens are not taken into account for the cost representation, since the present indication is a chronic disease with a continuous need for therapy and, as a rule, no new titration or dose adjustment is required after initial titration.

The information on dosages refers to applications in women, as breast cancer is relatively rare in men. The average body measurements of adult females were applied for dosages, depending on body weight (BW) or body surface area (BSA) (average body height: 1.66 m; average body weight: 69.2 kg). This results in a body surface area of 1.77 m² (calculated according to Du Bois 1916).[4]

For doxorubicin and epirubicin, the total cumulative dose was considered (450 - 550 mg/m² for doxorubicin or 900 - 1,000 mg/m² for epirubicin). Product information with different dosage recommendations is available for doxorubicin and epirubicin (doxorubicin: 50 - 80 mg/m² and 60 - 75 mg/m²; epirubicin: 75 - 90 mg/m² and 60 - 90 mg/m². The dosage recommendations with the largest range were used for the cost calculation: Doxorubicin 50 - 80 mg/m² and epirubicin: 60 - 90 mg/m². In the table "Consumption", only the dosage regimens that result in the range of annual treatment costs when calculated are shown.

[2] The maximum total doxorubicin dose of 450-550 mg/m² body surface area should not be exceeded to avoid cardiac toxicity.

[3] The total cumulative epirubicin dose of 900 - 1000 mg/m² should not be exceeded to avoid cardiac toxicity.

[4] Federal Health Reporting. Average body measurements of the population (2021, female sex, 15 years and older), www.gbe-bund.de

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Sacituzumab govitecan	10 mg/kg = 692.0 mg	692.0 mg	4 x 200 mg	34.8	139.2 x 200 mg
Appropriate comparator therapy					
Capecitabine	2150 mg	2 x 2150 mg	8 x 500 mg + 2 x 150 mg	243.6	1948.8 x 500 mg + 487.2 x 150 mg
Eribulin	1.23 mg/m^2 = 2.18 mg	2.18 mg	3 x 0.88 mg	34.8	104.4 x 0.88 mg
Vinorelbine	25 mg/m^2 - 30 mg/m^2 = 44.3 mg - 53.1 mg	44.3 mg - 53.1 mg	1 x 50 mg – 1 x 50 mg + 1 x 10 mg	52.1	52.1 x 50 mg – 52.1 x 50 mg + 52.1 x 10 mg
Anthracycline or taxane-containing treatment regimens					
Docetaxel	100 mg/m^2 = 177 mg	177 mg	1 x 160 mg + 1 x 20 mg	17.4	17.4 x 160 mg + 17.4 x 20 mg
Paclitaxel	175 mg/m^2 = 309.8 mg	309.8 mg	1 x 300 mg + 1 x 30 mg	17.4	17.4 x 300 mg + 17.4 x 30 mg
nab-paclitaxel	260 mg/m^2 = 460.2 mg	460.2 mg	5 x 100 mg	17.4	87 x 100 mg
Doxorubicin	50 mg/m^2 80 mg/m^2 = 88.5 mg - 141.6 mg	88.5 mg - 141.6 mg	1 x 100 mg - 1 x 150 mg	5.0 - 11.0	11 x 100 mg – 5 x 150 mg
Pegylated liposomal doxorubicin	50 mg/m^2 = 88.5 mg	88.5 mg	1 x 50 mg + 2 x 20 mg	13.0	13.0 x 50 mg + 26.0 x 20 mg
Eprirubicin	60 mg/m^2 - 90 mg/m^2 = 106.2 - 159.3 mg	106.2 - 159.3 mg	1 x 100 mg + 1 x 10 mg - 1 x 100 mg + 1 x 50 mg + 1 x 10 mg	10.0 - 16.0	16 x 100 mg + 16 x 10 mg - 10 x 100 mg + 10 x 50 mg + 10 x 10 mg

Costs:
Adults with unresectable or metastatic hormone receptor (HR)-positive, HER2-negative breast cancer who have received endocrine-based therapy, and at least two additional systemic therapies in the advanced

setting

In order to improve comparability, the costs of the medicinal products were approximated both on the basis of the pharmacy sales price level and also deducting the statutory rebates in accordance with Section 130 and Section 130a SGB V. To calculate the annual treatment costs, the required number of packs of a particular potency was first determined on the basis of consumption. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated on the basis of the costs per pack after deduction of the statutory rebates.

Any fixed reimbursement rates shown in the cost representation may not represent the cheapest available alternative.

Costs of the medicinal products:

Designation of the therapy		Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Medicinal product to be assessed						
Sacituzumab govitecan	200 mg	1 PCI	€ 1,246.56	€ 2.00	€ 68.39	€ 1,176.17
Appropriate comparator therapy						
Capecitabine [5]	500 mg	120 FCT	€ 151.84	€ 2.00	€ 11.12	€ 138.72
Capecitabine [5]	150 mg	120 FCT	€ 54.15	€ 2.00	€ 3.39	€ 48.76
Eribulin	0.88 mg	6 SFI	€ 2,429.97	€ 2.00	€ 135.48	€ 2,292.49
Vinorelbine	50 mg	10 CIS	€ 1,424.56	€ 2.00	€ 67.07	€ 1,355.49
Vinorelbine	10 mg	10 CIS	€ 294.01	€ 2.00	€ 13.42	€ 278.59
Docetaxel	160 mg	1 CIS	€ 820.48	€ 2.00	€ 38.40	€ 780.08
	20 mg	1 CIS	€ 112.47	€ 2.00	€ 4.80	€ 105.67
Paclitaxel	300 mg	1 CIS	€ 845.77	€ 2.00	€ 39.60	€ 804.17
	30 mg	1 CIS	€ 94.76	€ 2.00	€ 3.96	€ 88.80
nab-paclitaxel	100 mg	1 PIS	429.36	€ 2.00	€ 19.84	€ 407.52
Doxorubicin [5]	100 mg	1 CIS	€ 285.79	€ 2.00	€ 15.77	€ 262.08
	150 mg	1 SFI	€ 418.36	€ 2.00	€ 32.19	€ 384.17
Pegylated liposomal doxorubicin	20 mg	1 CIS	€ 721.49	€ 2.00	€ 89.87	€ 629.62
	50 mg	1 CIS	€ 1778.90	€ 2.00	€ 224.69	€ 1552.21
Eprirubicin	100 mg	1 CIS	€ 300.84	€ 2.00	€ 13.74	€ 285.10
	50 mg	1 CIS	€ 155.45	€ 2.00	€ 6.84	€ 146.61

[5] Fixed reimbursement rate

Designation of the therapy		Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
	10 mg	1 CIS	€ 39.51	€ 2.00	€ 1.34	€ 36.17
Abbreviations: FCT = film-coated tablets; CIS = concentrate for the preparation of an infusion solution; SFI = solution for injection; PIS = powder for the preparation of an infusion suspension; PCI= powder for a concentrate for the preparation of an infusion solution						

LAUER-TAXE® last revised: 15 January 2024

Costs for additionally required SHI services:

Only costs directly related to the use of the medicinal product are taken into account. If there are regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, the costs incurred for this must be taken into account as costs for additionally required SHI services.

Medical treatment costs, medical fee services, and costs incurred for routine examinations (e.g. regular laboratory services such as blood count tests) that do not exceed the standard expenditure in the course of the treatment are not shown.

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates	Treatment days/ year	Costs/ patient/ year
Appropriate comparator therapy							
Paclitaxel							
Dexamethasone[5] 2 x 20 mg	50 TAB x 20 mg	€ 118.88	€ 2.00	€ 0.00	€ 116.88	17.4	€ 81.35
Dimetindene IV 1 mg/10 kg = 6.92 mg	5 x 4 mg SFI	€ 23.72	€ 2.00	€ 5.29	€ 16.43	17.4	€ 114.35
Cimetidine IV 300 mg	10 AMP each 200 mg	€ 19.80	€ 2.00	€ 0.40	€ 17.40	17.4	€ 60.55
Abbreviations: AMP = ampoules; SFI = solution for injection; TAB = tablets							

Other SHI services:

The special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe) (Sections 4 and 5 of the Pharmaceutical Price Ordinance) from 01.10.2009 is not fully used to calculate costs. Alternatively, the pharmacy sales price publicly accessible in the directory services according to Section 131, paragraph 4 SGB V is a suitable basis for a standardised calculation.

According to the currently valid version of the special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe), surcharges for the production of parenteral preparations containing cytostatic drugs a maximum amount of € 100 per ready-to-use preparation, and for the production of parenteral solutions containing monoclonal antibodies a maximum of € 100 per ready-to-use unit are to be payable. These additional other costs do not add to the pharmacy sales price but follow the rules for calculation in the special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe). The cost representation is based on the pharmacy retail price and the maximum surcharge for the preparation and is only an approximation of the treatment costs. This presentation does not take into account, for example, the rebates on the pharmacy purchase price of the active ingredient, the invoicing of discards, the calculation of application containers, and carrier solutions in accordance with the regulations in Annex 3 of the special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe).

2.5 Designation of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V that can be used in a combination therapy with the assessed medicinal product

According to Section 35a, paragraph 3, sentence 4, the G-BA designates all medicinal products with new active ingredients that can be used in a combination therapy with the assessed medicinal product for the therapeutic indication to be assessed on the basis of the marketing authorisation under Medicinal Products Act.

Basic principles of the assessed medicinal product

A designation in accordance with Section 35a, paragraph 3, sentence 4 SGB V requires that it is examined based on the product information for the assessed medicinal product whether it can be used in a combination therapy with other medicinal products in the assessed therapeutic indication. In the first step, the examination is carried out on the basis of all sections of the currently valid product information for the assessed medicinal product.

If the assessed medicinal product contains an active ingredient or a fixed combination of active ingredients in the therapeutic indication of the resolution (assessed therapeutic indication) and is approved exclusively for use in monotherapy, a combination therapy is not considered due to the marketing authorisation under Medicinal Products Act, which is why no designation is made.

A designation is also not considered if the G-BA has decided on an exemption as a reserve antibiotic for the assessed medicinal product in accordance with Section 35a, paragraph 1c, sentence 1 SGB V. The additional benefit is deemed to be proven if the G-BA has decided on an exemption for a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V; the extent of the additional benefit and its therapeutic significance are not to be assessed by the G-BA. Due to the lack of an assessment mandate by the G-BA following the resolution on an exemption according to Section 35a, paragraph 1c, sentence 1 SGB V with regard to the extent of the additional benefit and the therapeutic significance of the reserve antibiotic to be assessed, there is a limitation due to the procedural privileging of the pharmaceutical companies to the effect that neither the proof of an existing nor an expected at least considerable additional benefit is possible for exempted reserve antibiotics in the procedures according to Section 35a paragraph 1 or 6 SGB V and Section 35a paragraph 1d SGB V. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V must therefore also be taken into account at the level of

designation according to Section 35a, paragraph 3, sentence 4 SGB V in order to avoid valuation contradictions.

With regard to the further examination steps, a differentiation is made between a "determined" or "undetermined" combination, which may also be the basis for a designation.

A "determined combination" exists if one or more individual active ingredients which can be used in combination with the assessed medicinal product in the assessed therapeutic indication are specifically named.

An "undetermined combination" exists if there is information on a combination therapy, but no specific active ingredients are named. An undetermined combination may be present if the information on a combination therapy:

- names a product class or group from which some active ingredients not specified in detail can be used in combination therapy with the assessed medicinal product, or
- does not name any active ingredients, product classes or groups, but the assessed medicinal product is used in addition to a therapeutic indication described in more detail in the relevant product information, which, however, does not include information on active ingredients within the scope of this therapeutic indication.

Concomitant active ingredient:

The concomitant active ingredient is a medicinal product with new active ingredients that can be used in combination therapy with the assessed medicinal product for the therapeutic indication to be assessed.

For a medicinal product to be considered as a concomitant active ingredient, it must be classified as a medicinal product with new active ingredients according to Section 2 paragraph 1 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with the corresponding regulations in Chapter 5 of the Rules of Procedure of the G-BA as of the date of the present resolution. In addition, the medicinal product must be approved in the assessed therapeutic indication, whereby a marketing authorisation is sufficient only for a sub-area of the assessed therapeutic indication.

Based on an "undetermined combination", the concomitant active ingredient must be attributable to the information on the product class or group or the therapeutic indication according to the product information of the assessed medicinal product in the assessed therapeutic indication, whereby the definition of a product class or group is based on the corresponding information in the product information of the assessed medicinal product.

In addition, there must be no reasons for exclusion of the concomitant active ingredient from a combination therapy with the assessed medicinal product, in particular no exclusive marketing authorisation as monotherapy.

In addition, all sections of the currently valid product information of the eligible concomitant active ingredient are checked to see whether there is any information that excludes its use in combination therapy with the assessed medicinal product in the assessed therapeutic indication under marketing authorisation regulations. Corresponding information can be, for example, dosage information or warnings. In the event that the medicinal product is used as part of a determined or undetermined combination which does not include the assessed medicinal product, a combination with the assessed medicinal product shall be excluded.

Furthermore, the product information of the assessed medicinal product must not contain any specific information that excludes its use in combination therapy with the eligible

concomitant active ingredient in the assessed therapeutic indication under marketing authorisation regulations.

Medicinal products with new active ingredients for which the G-BA has decided on an exemption as a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V are ineligible as concomitant active ingredients. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V also applies accordingly to the medicinal product eligible as a concomitant active ingredient.

Designation

The medicinal products which have been determined as concomitant active ingredients in accordance with the above points of examination are named by indicating the relevant active ingredient and the invented name. The designation may include several active ingredients, provided that several medicinal products with new active ingredients may be used in the same combination therapy with the assessed medicinal product or different combinations with different medicinal products with new active ingredients form the basis of the designation.

If the present resolution on the assessed medicinal product in the assessed therapeutic indication contains several patient groups, the designation of concomitant active ingredients shall be made separately for each of the patient groups.

Exception to the designation

The designation excludes combination therapies for which - patient group-related - a considerable or major additional benefit has been determined by resolution according to Section 35a, paragraph 3, sentence 1 SGB V or it has been determined according to Section 35a, paragraph 1d, sentence 1 SGB V that at least considerable additional benefit of the combination can be expected. In this context, the combination therapy that is excluded from the designation must, as a rule, be identical to the combination therapy on which the preceding findings were based.

In the case of designations based on undetermined combinations, only those concomitant active ingredients - based on a resolution according to Section 35a, paragraph 3, sentence 1 SGB V on the assessed medicinal product in which a considerable or major additional benefit had been determined - which were approved at the time of this resolution are excluded from the designation.

Legal effects of the designation

The designation of combinations is carried out in accordance with the legal requirements according to Section 35a, paragraph 3, sentence 4 and is used exclusively to implement the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. The designation is not associated with a statement as to the extent to which a therapy with the assessed medicinal products in combination with the designated medicinal products corresponds to the generally recognised state of medical knowledge. The examination was carried out exclusively on the basis of the possibility under Medicinal Products Act to use the medicinal products in combination therapy in the assessed therapeutic indication based on the product information; the generally recognised state of medical knowledge or the use of the medicinal products in the reality of care were not the subject of the examination due to the lack of an assessment mandate of the G-BA within the framework of Section 35a, paragraph 3, sentence 4 SGB V.

The findings made neither restrict the scope of treatment required to fulfil the medical treatment mandate, nor do they make statements about expediency or economic feasibility.

Justification for the findings on designation in the present resolution:

Adults with unresectable or metastatic hormone receptor (HR)-positive, HER2-negative breast cancer who have received endocrine-based therapy, and at least two additional systemic therapies in the advanced setting

No designation of medicinal products with new active ingredients that can be used in combination therapy pursuant to Section 35a, paragraph 3, sentence 4 SGB V, as the active ingredient to be assessed is an active ingredient authorised in monotherapy.

References:

Product information for sacituzumab govitecan (Trodelvy); product information for Trodelvy; last revised: July 2023

3. Bureaucratic costs calculation

The proposed resolution does not create any new or amended information obligations for care providers within the meaning of Annex II to Chapter 1 VerfO and, accordingly, no bureaucratic costs.

4. Process sequence

At its session on 22 June 2021, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

A review of the appropriate comparator therapy took place once the positive opinion was granted. At its session on 2 August 2023, the Subcommittee on Medicinal Products adjusted the appropriate comparator therapy.

On 14 August 2023, the pharmaceutical company submitted a dossier for the benefit assessment of sacituzumab govitecan to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 2 VerfO.

By letter dated 14 August 2023 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefits of medicinal products with new active ingredients in accordance with Section 35a SGB V, the G-BA commissioned the IQWiG to assess the dossier concerning the active ingredient sacituzumab govitecan.

The dossier assessment by the IQWiG was submitted to the G-BA on 13 November 2023, and the written statement procedure was initiated with publication on the G-BA website on 15 November 2023. The deadline for submitting statements was 6 December 2023.

The oral hearing was held on 8 January 2024.

By letter dated 9 January 2024, the IQWiG was commissioned with a supplementary assessment. The addendum prepared by IQWiG was submitted to the G-BA on 02 February 2024.

In order to prepare a recommendation for a resolution, the Subcommittee on Medicinal Products commissioned a working group (Section 35a) consisting of the members nominated

by the leading organisations of the care providers, the members nominated by the SHI umbrella organisation, and representatives of the patient organisations. Representatives of the IQWiG also participate in the sessions.

The evaluation of the written statements received and the oral hearing was discussed at the session of the subcommittee on 6 February 2024, and the proposed resolution was approved.

At its session on 15 February 2024, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	22 June 2021	Determination of the appropriate comparator therapy
Subcommittee Medicinal products	2 August 2023	Implementation of the appropriate comparator therapy
Working group Section 35a	20 December 2023	Information on written statements received, preparation of the oral hearing
Subcommittee Medicinal products	8 January 2024	Conduct of the oral hearing, Commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	17 January 2024 31 January 2024	Consultation on the dossier assessment by the IQWiG, evaluation of the written statement procedure
Subcommittee Medicinal products	8 February 2024	Concluding discussion of the draft resolution
Plenum	15 February 2024	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 15 February 2024

Federal Joint Committee (G-BA)
in accordance with Section 91 SGB V
The Chair

Prof. Hecken