GBA
Gemeinsamer
Bundesausschuss

Justification

for the Resolution of the Federal Joint Committee (GBA) on an Amendment of the Pharmaceuticals Directive:
Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V
Elinzanetant (vasomotor symptoms associated with menopause)

of 1 October 2026

Contents

1. Legal basis 2

2. Key points of the resolution 2

2.1 Additional benefit of the medicinal product in relation to the appropriate comparator therapy 3

2.1.1 Approved therapeutic indication of Elinzanetant (Lynkuet) in accordance with the product information 3

2.1.2 Appropriate comparator therapy 3

2.1.3 Extent and probability of the additional benefit 7

2.1.4 Summary of the assessment 13

2.2 Number of patients or demarcation of patient groups eligible for treatment 14

2.3 Requirements for a quality-assured application 14

2.4 Treatment costs 14

3. Bureaucratic costs calculation 18

4. Process sequence 18

Courtesy translation – only the German version is legally binding.

1. Legal basis

According to Section 35a, paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (GBA) assess the benefit of all 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 GBA electronically, including all clinical studies the pharmaceutical company have 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 GBA 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 GBA decide 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 relevant date for the start of the benefit assessment procedure was the first placing on the (German) market of the active ingredient elinzanetant on 1 April 2026 in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure of the GBA (VerfO). Pursuant to Section 4, paragraph 3, number 1 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5, Section 8, paragraph 1, number 1 of the Rules of Procedure (VerfO), the pharmaceutical company submitted the final dossier to the GBA on 26 March 2026.

The GBA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 1 July 2026 on the GBA website (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The GBA came to a resolution on whether an additional benefit of elinzanetant compared with the appropriate comparator therapy could be determined on the basis of the dossier of the

Courtesy translation – only the German version is legally binding.

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 GBA have 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 elinzanetant.

In the light of the above, and taking into account the statements received and the oral hearing, the GBA have made 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 Elinzanetant (Lynkuet) in accordance with the product information

Lynkuet is indicated for the treatment of moderate to severe vasomotor symptoms (VMS):

- associated with menopause.

Therapeutic indication of the resolution (resolution of 01.10.2026):

See the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

a) Patients with moderate to severe vasomotor symptoms associated with menopause who are eligible for hormone replacement therapy and have decided in favour of hormone replacement therapy after individual risk-benefit assessment

Appropriate comparator therapy for elinzanetant:

- Individualised therapy with selection of
  - Oestrogens
  - Oestrogen/progestogen combinations

b) Patients with moderate to severe vasomotor symptoms associated with menopause who are ineligible for hormone replacement therapy or have decided against hormone replacement therapy after individual risk-benefit assessment

Appropriate comparator therapy for elinzanetant:

- Monitoring wait-and-see approach

[1] General Methods, version 8.0 from 19.12.2025. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

Courtesy translation – only the German version is legally binding.

Criteria according to Chapter 5, Section 6 of the Rules of Procedure of the GBA and Section 6, paragraph 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV):

The appropriate comparator therapy must be an appropriate therapy in the therapeutic indication according to 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 GBA 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 GBA may exceptionally determine the off-label use of medicinal products as an appropriate comparator therapy or as part of the appropriate comparator therapy if they determine 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 for 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 for the therapeutic indication.

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

Courtesy translation – only the German version is legally binding.

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 addition to elinzanetant, the active ingredient fezolinetant is approved for this therapeutic indication, as are oestrogens for the systemic treatment of oestrogen deficiency symptoms in postmenopausal women. Women with an intact uterus are treated with oestrogen in combination with a progestogen. In addition, medicinal products containing dry extracts of black cohosh rhizome are approved for the relief of psychological and autonomic conditions associated with the menopause, such as hot flushes, night sweats and sleep disorders.

On 2. Non-medicinal treatment that can be provided within the statutory health insurance (SHI) framework is not an option in this therapeutic indication.

On 3. A resolution of 1 August 2024 on fezolinetant is available.

On 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as systematic 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 therapeutic indication according to Section 35a, paragraph 7 SGB V. However, no written feedback has been received.

As part of the evidence search carried out, a guideline from the National Institute for Health and Care Excellence (NICE) was identified for this therapeutic indication. Although the German S3 guideline "Peri- and postmenopause – Diagnostics and interventions"[2] has expired, it is nevertheless taken into account here due to its significance for the German healthcare context and the lack of other guidelines.

Overall, it appears that hormone replacement therapy with oestrogens (and, if applicable, progestogens to protect the endometrium) is the most effective way of alleviating vasomotor symptoms. However, it should be borne in mind that the placebo response rate is also relatively high. The guidelines therefore recommend hormone replacement therapy (oestrogen/progestogen combination in women with an intact uterus or only oestrogen in women without a uterus) not without a clear indication and only after clarification of the individual risk-benefit profile, also due to possible and known side effects. Against this background, a distinction is made between two patient groups in this therapeutic indication.

Patients with moderate to severe vasomotor symptoms associated with the menopause who

a) are eligible for hormone replacement therapy and have decided in favour of hormone replacement therapy after individual risk-benefit assessment

b) are ineligible for hormone replacement therapy or have decided against hormone replacement therapy after individual risk-benefit assessment.

[2] Guideline programme of the DGGG, OEGGG and SGGG. Peri- and postmenopause – Diagnostics and interventions; S3 guideline: 2020. Version 1.1 [accessed 10.08.2026] URL: https://register.awmf.org/assets/guidelines/015-062l_S3_HT_Peri-Postmenopause-Diagnostik-Interventionen_2021-01.pdf

Courtesy translation – only the German version is legally binding.

For group a) patients with moderate to severe vasomotor symptoms associated with menopause who are eligible for hormone replacement therapy and have decided in favour of hormone replacement therapy after individual risk-benefit assessment, an individualised therapy with the selection of oestrogens and oestrogen/progestogen combinations is determined as the appropriate comparator therapy. Whether the patients still have a uterus must be considered when making the treatment decision. Therapy with oestrogens alone is indicated only for women who have undergone a hysterectomy. For women with a uterus, combination therapy with oestrogen and progestogen is indicated. Individualised therapy is based on the assumption that several treatment options, which allow an individualised medical treatment decision, are available.

For group b), the active ingredient fezolinetant and medicinal products containing dry extracts of black cohosh rhizome are considered as approved therapy options.

By the resolution of 1 August 2024, a minor additional benefit of fezolinetant was identified for menopausal women with moderate to severe vasomotor symptoms who are ineligible for hormone therapy or have decided against therapy after individual risk-benefit assessment. Furthermore, a Direct Healthcare Professional Communication ("Rote-Hand-Brief")[3] concerning fezolinetant was published on 13 January 2025, warning of the risk of drug-induced liver damage. As fezolinetant is indicated for the treatment of symptoms in otherwise healthy women, the risk of serious liver damage may significantly affect the benefit-risk ratio. Furthermore, the guidelines contain no recommendations on the use of the active ingredient fezolinetant. In the overall assessment, it cannot therefore be concluded that the active ingredient fezolinetant is an appropriate therapy option in this therapeutic indication.

Medicines containing Cimicifuga racemosa extracts are approved for the relief of psychological and autonomic symptoms associated with the menopause, such as hot flushes, night sweats and sleep disorders. However, according to the UK NICE[4] guideline, there is only limited evidence of its effectiveness in reducing vasomotor symptoms associated with menopause. The German S3 guideline "Peri- and postmenopause – Diagnostics and interventions" issued a non-binding recommendation on the use of medicinal products containing Cimicifuga racemosa extracts. Overall, Cimicifuga extracts therefore do not represent an appropriate therapy option in this therapeutic indication either.

For patients with moderate to severe vasomotor symptoms associated with menopause who are ineligible for hormone replacement therapy and have decided against hormone replacement therapy after individual risk-benefit assessment, the monitoring wait-and-see approach is therefore determined as the appropriate comparator therapy for elinzanetant.

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

---

[3] Direct Healthcare Professional Communication ("Rote-Hand-Brief") concerning Veoza (fezolinetant): risk of drug-induced liver damage and new recommendations on monitoring liver function before and during treatment; dated 13.01.2025 [accessed 31.01.2025] https://www.bfarm.de/SharedDocs/Risikoinformationen/Pharmakovigilanz/DE/RHB/2025/rhb-fezolinetant.html

[4] National Institute for Health and Care Excellence (NICE). Menopause: identification and management [online]. 07.11.2024. London (GBR): NICE; 2015. [accessed: 11.12.2024]. (NICE guideline; Band NG23). URL: https://www.nice.org.uk/guidance/ng101/resources/early-and-locally-advancedbreast-cancer-diagnosis-and-management-pdf-66141532913605.

Courtesy translation – only the German version is legally binding.

Any change to the appropriate comparator therapy requires a decision by the GBA based on a prior review of the criteria set out in Chapter 5, Section 6, paragraph 3 VerfO.

2.1.3 Extent and probability of the additional benefit

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

a) An additional benefit is not proven for patients with moderate to severe vasomotor symptoms associated with menopause who are eligible for hormone replacement therapy and have decided in favour of hormone replacement therapy after individual risk-benefit assessment

b) An additional benefit is not proven for patients with moderate to severe vasomotor symptoms associated with menopause who are ineligible for hormone replacement therapy or have decided against hormone replacement therapy after individual risk-benefit assessment.

Justification:

a) Patients with moderate to severe vasomotor symptoms associated with menopause who are eligible for hormone replacement therapy and have decided in favour of hormone replacement therapy after individual risk-benefit assessment

No data are available for the assessment of the additional benefit of elinzanetant over the appropriate comparator therapy in patients with moderate to severe vasomotor symptoms associated with menopause who are eligible for hormone replacement therapy and have decided in favour of hormone replacement therapy after individual risk-benefit assessment. An additional benefit is therefore not proven.

b) Patients with moderate to severe vasomotor symptoms associated with menopause who are ineligible for hormone replacement therapy or have decided against hormone replacement therapy after individual risk-benefit assessment

The pharmaceutical company presented data from the SWITCH-1, OASIS-1, OASIS-2, OASIS-3 and NIRVANA studies for patients with moderate to severe vasomotor symptoms associated with menopause who are ineligible for hormone replacement therapy or have decided against hormone replacement therapy after individual risk-benefit assessment.

Courtesy translation – only the German version is legally binding.

OASIS-1 and OASIS-2 studies

The OASIS-1 and OASIS-2 studies are both label-enabling, double-blind, randomised controlled trials comparing elinzanetant with placebo. Postmenopausal women aged 40 to 65 years with moderate to severe vasomotor symptoms associated with menopause were enrolled. According to the inclusion criteria, the patients must have experienced ≥ 50 moderate or severe hot flushes in the 7 days prior to the start of the study. Patients could be enrolled in the studies regardless of whether hormone replacement therapy was suitable for them.

A total of 396 patients were enrolled in the OASIS-1 study and 400 in the OASIS-2 study, and were randomly allocated in a 1:1 ratio to treatment with elinzanetant or placebo. The treatment phase of both studies was divided into a 12-week placebo-controlled phase and a subsequent 14-week uncontrolled treatment phase, during which patients in the control arm switched to treatment with elinzanetant.

The primary endpoint of the studies was the mean change in the frequency of moderate to severe vasomotor symptoms from the start of treatment to week 4 and week 12. Other endpoints were assessed in the categories of morbidity, health-related quality of life and side effects.

OASIS-3 study

The OASIS-3 study is a double-blind, randomised controlled trial comparing elinzanetant with placebo over 52 weeks. Postmenopausal women aged 40 to 65 years with moderate to severe vasomotor symptoms associated with menopause were enrolled. A minimum number of vasomotor symptoms prior to the start of the study was not defined as an inclusion criterion.

A total of 628 patients were enrolled in the OASIS-3 study and were randomly allocated in a 1:1 ratio to treatment with elinzanetant or placebo.

The primary endpoint of the study was the mean change in the frequency of moderate to severe vasomotor symptoms from the start of treatment to week 12. Other endpoints were assessed in the categories of morbidity, health-related quality of life and side effects.

SWITCH-1 study

The SWITCH-1 study is a double-blind, randomised controlled trial comparing elinzanetant with placebo over 12 weeks. Postmenopausal women aged 40 to 65 years with moderate to severe vasomotor symptoms associated with menopause were enrolled. According to the inclusion criteria, the patients had to have experienced an average of ≥ 7 moderate or severe hot flushes per day prior to the start of the study. Patients could be enrolled in the study regardless of whether hormone replacement therapy was suitable for them.

A total of 199 patients were randomly allocated in a 1:1:1:1:1 ratio to one of the 5 treatment groups (elinzanetant 40 mg/ 80 mg/ 120 mg/ 160 mg or placebo) of the SWITCH-1 study.

The primary endpoints of the study were the mean change in the frequency and severity of moderate to severe vasomotor symptoms from the start of treatment to week 4 and week 12. Other endpoints were assessed in the categories of morbidity, health-related quality of life and side effects.

NIRVANA study

Courtesy translation – only the German version is legally binding.

The NIRVANA study is a double-blind, randomised controlled trial comparing elinzanetant with placebo over 12 weeks. Postmenopausal women aged 40 to 65 years with moderate to severe vasomotor symptoms and sleep disorders associated with menopause were enrolled. Only patients who had undergone a hysterectomy were enrolled. Prior to the start of the study, the patients must have experienced an average of ≥ 20 moderate or severe hot flushes per week. Patients could be enrolled in the study regardless of whether hormone replacement therapy was suitable for them.

A total of 110 patients were enrolled in the NIRVANA study and were randomly allocated in a 1:1 ratio to treatment with elinzanetant or placebo.

The primary endpoint of the study was the mean change in the Wakefulness After Sleep Onset (WASO) score at week 4, as measured by polysomnography. Other endpoints were assessed in the categories of morbidity, health-related quality of life and side effects.

Consideration of the available studies

According to the product information, there is no restriction on the treatment duration with elinzanetant. The GBA assume that elinzanetant will be taken for as long as the vasomotor symptoms persist. Studies show that frequent hot flushes (on more than 6 days in the last 2 weeks) and moderate to severe hot flushes occur[5] on average over a period of 7.4 years and last around 4.5 years from the last menstrual period[6] [7] Taking into account the duration of the existing symptomatology in the present indication, a comparative study duration of 12 weeks is considered too short for the assessment of the additional benefit compared with the appropriate comparator therapy. The data presented from the OASIS-1, OASIS-2, SWITCH-1 and NIRVANA studies are therefore not taken into account for the benefit assessment.

The OASIS-3 study, by contrast, provides direct comparator data over a period of 52 weeks. In the comparator arm of the study, the patients received a placebo. In the present therapeutic indication, this is regarded as a sufficient approximation to the appropriate comparator therapy: monitoring wait-and-see approach.

For the OASIS-3 study, the pharmaceutical company presented data on the total population in the dossier. However, these data are not used for the benefit assessment, as it can be assumed that a significant percentage of the patients enrolled would still have been eligible for hormone replacement therapy and therefore do not belong to patient group b).

As part of the written statement procedure and following the oral hearing, the pharmaceutical company therefore submitted data on two sub-populations with adjusted operationalisations regarding the ineligibility for hormone replacement therapy. These are the modified intention-to-treat (mITT) population and the mITT2 population that is further restricted by the inclusion criteria. Although it cannot be ruled out that these sub-populations include patients who are eligible for hormone replacement therapy, it can be assumed that the classification is, for the most part, appropriate. As the mITT population is considered sufficiently

[5] German Society of Gynaecology and Obstetrics (DGGG), Austrian Society of Gynaecology and Obstetrics (OEGGG), Swiss Society of Gynaecology and Obstetrics (SGGG). Peri- and postmenopause - Diagnostics and interventions; S3 guideline, long version 1.1 [online]. AWMF registry number 015-062. Berlin (GER): Association of the Scientific-Medical Societies (AWMF); 2020.

[6] Avis NE, Crawford SL, Greendale G et al. Duration of menopausal vasomotor symptoms over the menopause transition. JAMA Intern Med 2015; 175(4): 531-539. https://doi.org/10.1001/jamainternmed.2014.8063.

[7] Freeman EW, Sammel MD, Sanders RJ. Risk of long-term hot flashes after natural menopause: evidence from the Penn Ovarian Aging Study cohort. Menopause 2014; 21(9): 924-932. https://doi.org/10.1097/GME.0000000000000196.

Courtesy translation – only the German version is legally binding.

appropriate, and this uncertainty persists even in the more narrowly defined and therefore smaller mITT2 population, the mITT population from the OASIS-3 study is considered here.

As described above, a required minimum number of moderate to severe vasomotor symptoms was not defined as an inclusion criterion in the OASIS-3 study.

The European Medicines Agency (EMA) recommends an inclusion criterion of at least five hot flushes per day for clinical studies in order to establish an indication for treatment. However, the approved therapeutic indication or the further product information for elinzanetant does not specify a minimum requirement for frequency, but only severity (moderate or severe). Similarly, the guidelines do not address the frequency of vasomotor symptoms as a prerequisite for the therapeutic indication[8] [9]. Particularly given that the inclusion criterion required that study participants should be seeking treatment to alleviate these symptoms, it is assumed that medicinal therapy was indicated for the vast majority of patients in the study.

In the overall assessment, the data on the mITT population are used for the benefit assessment. However, there are uncertainties regarding the percentage of patients who would still have been eligible for hormone replacement therapy or for whom there was no therapeutic indication.

Extent and probability of the additional benefit

Mortality

In the OASIS-3 study, there were no deaths in both study arms.

[8] German Society of Gynaecology and Obstetrics (DGGG), Austrian Society of Gynaecology and Obstetrics (OEGGG), Swiss Society of Gynaecology and Obstetrics (SGGG). Peri- and postmenopause - Diagnostics and interventions; S3 guideline, long version 1.1 [online]. AWMF registry number 015-062. Berlin (GER): Association of the Scientific-Medical Societies (AWMF); 2020.

[9] National Institute for Health and Care Excellence (NICE). Menopause: identification and management [online]. 07.11.2024. London (GBR): NICE; 2015. [accessed: 11.12.2024]. (NICE guideline; Band NG23). URL: https://www.nice.org.uk/guidance/ng101/resources/early-and-locally-advancedbreast-cancer-diagnosis-and-management-pdf-66141532913605.

Courtesy translation – only the German version is legally binding.

Morbidity

Vasomotor symptoms

In the OASIS-3 study, vasomotor symptoms were collected using an electronic diary, in which the number of hot flushes, their severity and the number of night-time wake-up phases were documented. Moderate hot flushes were defined as "sensation of heat with sweating but the ability to continue activity" and severe hot flushes as "sensation of heat with sweating leading to cessation of activity". A night-time hot flush that caused the person to wake up should be classified as severe.

For the currently relevant mITT sub-population, the pharmaceutical company did not provide any responder analyses of the reduction in the frequency of moderate and severe vasomotor symptoms at the end of the study. As part of the oral hearing, the relevance of an analysis of the 100% reduction – that is, the absence of symptoms – was discussed, and the pharmaceutical company was given the opportunity to subsequently submit the responder analyses. Time-to-event analyses of the 100% reduction in moderate and severe vasomotor symptoms were subsequently submitted. The pharmaceutical company did not set out a specific operationalisation of the time-to-event analyses. However, based on the information available, it is assumed that they show the time to first occurrence of the event. The data are unsuitable for the research question of the benefit assessment as patients, whose condition subsequently deteriorates, are still included in the analysis as responders, and the analysis of a sustained effect is relevant in this therapeutic indication.

As no responder analyses were presented at the end of the study, the continuous analyses of the mean change in the frequency of moderate and severe vasomotor symptoms are considered.

For this endpoint, there was a statistically significant difference of -2.4 hot flushes per day between the treatment arms to the advantage of elinzanetant.

Sleep disorders

Sleep disorders were assessed in the OASIS-3 study using the patient-reported questionnaire PROMIS SD SF 8b.

No responder analyses at the end of the study were presented for the mITT population; instead, only time-to-event analyses were provided, which – as described for the "vasomotor symptoms" endpoint – are unsuitable for the present benefit assessment. Consequently, the continuous analyses of the mean change are used for the benefit assessment.

For the endpoint of sleep disorders, there was a statistically significant difference in favour of elinzanetant. It cannot be concluded that the effect is clinically relevant as the 95% confidence interval of the standardised mean difference (SMD) is not completely outside the irrelevance range from - 0.2 to 0.2.

Quality of life

Health-related quality of life was assessed using the Menopause-specific Quality of Life (MENQOL) questionnaire. The questionnaire version used in the OASIS-3 study comprises a total of 29 items distributed across the 4 domains vasomotor, physical, psychosocial and sexual. The items assess the occurrence of menopausal symptoms and their impact on health-related quality of life over the past week.

Courtesy translation – only the German version is legally binding.

No responder analyses at the end of the study were presented for the mITT population; instead, only time-to-event analyses were provided, which – as described for the "vasomotor symptoms" endpoint – are unsuitable for the present benefit assessment. Consequently, the continuous analyses of the mean change are used for the benefit assessment.

In the psychosocial, physical and sexual domains, there was no statistically significant difference between the treatment arms. In the vasomotor domain, there was a statistically significant difference in favour of elinzanetant. It cannot be concluded that the effect is clinically relevant as the 95% confidence interval of the standardised mean difference (SMD) is not completely outside the irrelevance range from - 0.2 to 0.2.

Side effects

Adverse events may have been incompletely captured in the OASIS-3 study. In accordance with the study protocol, progression, signs or symptoms of the investigated disease were not assessed as adverse events, unless these were more severe than would have been expected given the study participants' condition. As no criteria have been defined for this assessment, it is unclear which events were assessed as side effects in the OASIS-3 study and which were not. In the present therapeutic indication, where symptoms are burdensome but predominantly not serious, it is nevertheless assumed that there was no significant under-reporting of the endpoints "serious adverse events" and "discontinuation due to adverse events", meaning that the results can be relied upon.

For the endpoint "serious adverse events", there was no statistically significant difference between the treatment arms.

For the endpoint "discontinuation due to adverse events", there was a statistically significant difference to the disadvantage of elinzanetant.

No data on the specific adverse event "liver-related examinations, clinical signs and symptoms" are available for the relevant sub-population.

Overall assessment

For the assessment of the additional benefit of elinzanetant in the treatment of patients with moderate to severe vasomotor symptoms associated with menopause who are ineligible for hormone replacement therapy or have decided against hormone replacement therapy after individual risk-benefit assessment, the results of the randomised, controlled OASIS-3 study are used for the sub-population of study participants who are ineligible for hormone replacement therapy (mITT).

No deaths occurred in the study.

For the endpoint of vasomotor symptoms - operationalised as a change in the daily number of moderate or severe vasomotor symptoms - in the endpoint category of morbidity, there was a statistically significant advantage of elinzanetant over placebo. For the sleep quality endpoint and for the vasomotor symptoms domain of the MENQOL within the endpoint category of health-related quality of life, there was a statistically significant difference in favour of elinzanetant in each case; however, it cannot be concluded that the effect is clinically relevant. For the other domains of the MENQOL, there were no statistically significant differences between the treatment arms.

For the endpoint "serious adverse events" in the endpoint category of side effects, there was no statistically significant difference between the treatment arms. For the endpoint

Courtesy translation – only the German version is legally binding.

"discontinuation due to adverse events", there was a statistically significant disadvantage of elinzanetant compared with placebo.

For the endpoint "vasomotor symptoms", there was an advantage of elinzanetant overall. This is offset by a disadvantage in the endpoint "therapy discontinuation due to adverse events". Furthermore, the advantage in symptomatology is not reflected in the improvement in health-related quality of life. In the overall benefit-risk assessment, the GBA therefore do not identify any additional benefit of elinzanetant compared with the monitoring wait-and-see approach.

An additional benefit of elinzanetant is therefore not proven for patients with moderate to severe vasomotor symptoms associated with menopause who are ineligible for hormone replacement therapy or have decided against hormone replacement therapy after individual risk-benefit assessment.

2.1.4 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product "Lynkuet" with the active ingredient elinzanetant. Elinzanetant is approved for the treatment of moderate to severe vasomotor symptoms (VMS) associated with menopause.

In the therapeutic indication under consideration, two patient groups were distinguished based on their eligibility for hormone replacement therapy.

a) Patients with moderate to severe vasomotor symptoms associated with menopause who are eligible for hormone replacement therapy and have decided in favour of hormone replacement therapy after individual risk-benefit assessment

The GBA identified an individualised therapy with the selection of oestrogens and oestrogen/progestogen combinations as the appropriate comparator therapy.

No data are available for the assessment of the additional benefit of elinzanetant over the appropriate comparator therapy in patients with moderate to severe vasomotor symptoms associated with menopause who are eligible for hormone replacement therapy and have decided in favour of hormone replacement therapy after individual risk-benefit assessment. An additional benefit is therefore not proven.

b) Patients with moderate to severe vasomotor symptoms associated with menopause who are ineligible for hormone replacement therapy or have decided against hormone replacement therapy after individual risk-benefit assessment

The GBA determined the monitoring wait-and-see approach as the appropriate comparator therapy.

Data from the 52-week, randomised, controlled OASIS-3 study for the sub-population of study participants who are ineligible for hormone replacement therapy (modified intention-to-treat population) are used for the benefit assessment.

No deaths occurred in the study. For the endpoint "vasomotor symptoms" - operationalised as a change in the daily number of moderate or severe vasomotor symptoms - in the endpoint category of morbidity, there was a statistically significant advantage of elinzanetant over placebo. For the "sleep quality" endpoint and for the "vasomotor symptoms" domain of the menopause-specific quality of life (MENQOL) questionnaire within the endpoint category of health-related quality of life, there was a statistically significant difference in favour of elinzanetant in each case; however, it cannot be concluded that the effect is clinically relevant.

Courtesy translation – only the German version is legally binding.

For the other domains of the MENQOL, there were no statistically significant differences between the treatment arms.

For the endpoint "serious adverse events" in the endpoint category of side effects, there was no statistically significant difference between the treatment arms. For the endpoint "discontinuation due to adverse events", there was a statistically significant disadvantage of elinzanetant compared with placebo.

For the endpoint "vasomotor symptoms", there was an advantage of elinzanetant overall. This is offset by a disadvantage in the endpoint "therapy discontinuation due to adverse events". Furthermore, the advantage in symptomatology is not reflected in the improvement in health-related quality of life. In the overall benefit-risk assessment, the GBA therefore do not identify any additional benefit over the monitoring wait-and-see approach.

An additional benefit of elinzanetant is therefore not proven.

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

The information on the number of patients is based on the SHI target population.

For patient group b), the resolution is based on the information provided by the pharmaceutical company in the benefit assessment dossier. Overall, the figures are uncertain and the lower limit may be underestimated.

When determining the number of postmenopausal women with moderate to severe vasomotor symptoms, there are uncertainties particularly regarding the publications cited as it remains unclear whether the patients are already postmenopausal or how the moderate to severe vasomotor symptoms were operationalised. Furthermore, there are uncertainties regarding the percentages of those patients who are eligible for hormone replacement therapy.

The lower limit may be underestimated, as some patients with successfully treated vasomotor symptoms, as well as those who had received hormone replacement therapy, were excluded.

For patient group a), the pharmaceutical company has not provided any information on the number of patients in the SHI target population. The resolution is therefore based on the IQWiG's calculations, which were carried out using data provided by the pharmaceutical company. The uncertainties described for patient group b), as well as the potentially underestimated aspects (in relation to the lower limit), remain. In particular, the distinction between the two patient groups is uncertain.

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 Lynkuet (active ingredient: elinzanetant) at the following publicly accessible link (last access: 26 May 2026):

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

Courtesy translation – only the German version is legally binding.

2.4 Treatment costs

The treatment costs are based on the contents of the product information and the information listed in the LAUER-TAXE® (last revised: 15 July 2026). The calculation of treatment costs is generally based on the last revised LAUER-TAXE® version following the publication of the benefit assessment.

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.

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 is different 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.

Oestrogens and oestrogen/progestogen combinations are each assigned to reference price groups. For this reason, one representative is selected in each case as an example to illustrate how the costs are derived.

a) Patients with moderate to severe vasomotor symptoms associated with menopause who are eligible for hormone replacement therapy and have decided in favour of hormone replacement therapy after individual risk-benefit assessment

Treatment period:

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Elinzanetant	Continuously, 1 x daily	365.0	1	365.0
Appropriate comparator therapy				
Individualised therapy with the selection of oestrogens and oestrogen/progestogen combinations				
Oestrogens				
Estradiol	Continuously, 1 x daily	365.0	1	365.0
Oestrogen/progestogen combination				
Estradiol + drospirenone	Continuously, 1 x daily	365.0	1	365.0

Courtesy translation – only the German version is legally binding.

Consumption:

Designation of the therapy	Dosage/ application	Dosage/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Elinzanetant	120 mg	120 mg	2 x 60 mg	365.0	730.0 x 60 mg
Appropriate comparator therapy					
Individualised therapy with the selection of oestrogens and oestrogen/progestogen combinations					
Oestrogen					
Estradiol	1 mg – 2 mg	1 mg – 2 mg	1 x 1 mg – 1 x 2 mg	365.0	365.0 x 1 mg – 365.0 x 2 mg
Oestrogen/progestogen combination					
Estradiol + drospirenone	1 mg/2 mg	1 mg/2 mg	1 x 1 mg/ 2 mg	365.0	365.0 x 1 mg/2 mg

b) Patients with moderate to severe vasomotor symptoms associated with menopause who are ineligible for hormone replacement therapy or have decided against hormone replacement therapy after individual risk-benefit assessment

Treatment period:

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Elinzanetant	Continuously, 1 x daily	365.0	1	365.0
Appropriate comparator therapy				
Monitoring wait-and-see approach	Not calculable			

Courtesy translation – only the German version is legally binding.

Consumption:

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					
Elinzanetant	120 mg	120 mg	2 x 60 mg	365.0	730.0 x 60 mg
Appropriate comparator therapy					
Monitoring wait-and-see approach	Not calculable				

Patient populations a) and b)

Costs of the medicinal products:

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 reference prices shown in the cost representation may not represent the cheapest available alternative.

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					
Elinzanetant 60 mg	180 SC	€ 296.56	€ 1.77	€ 15.75	€ 279.04
Appropriate comparator therapy					
Estradiol 1 mg/ drospirenone 2 mg[10]	84 FCT	€ 38.19	€ 1.77	€ 2.13	€ 34.29
Estradiol 1 mg10	84 FCT	€ 19.33	€ 1.77	€ 0.00	€ 17.56
Estradiol 2 mg[10]	100 TAB	€ 23.67	€ 1.77	€ 0.00	€ 21.90
Monitoring wait-and-see approach	Not calculable				
Abbreviations: SC = soft capsules; FCT = film-coated tablets; TAB = tablets					

LAUER-TAXE® last revised: 15 July 2026

[10] Fixed reimbursement rate

Courtesy translation – only the German version is legally binding.

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.

Because there are no 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 assessed10 and the appropriate comparator therapy in accordance with the product information, no costs for additionally required SHI services had to be taken into account.

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 their sessions on 22 December 2020 and 11 February 2025, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

A review of the appropriate comparator therapy took place. At their session on 25 November 2025, the Subcommittee on Medicinal Products newly determined the appropriate comparator therapy.

On 26 March 2026, the pharmaceutical company submitted a dossier for the benefit assessment of elinzanetant to the GBA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 VerfO.

By letter dated 26 March 2026 in conjunction with the resolution of the GBA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefit of medicinal products with new active ingredients in accordance with Section 35a SGB V, the GBA commissioned the IQWiG to assess the dossier concerning the active ingredient elinzanetant.

The dossier assessment by the IQWiG was submitted to the GBA on 29 June 2026, and the written statement procedure was initiated with publication on the GBA website on 1 July 2026. The deadline for submitting written statements was 22 July 2026.

The oral hearing was held on 10 August 2026.

By letter of 11 August 2026, the IQWiG was commissioned with a supplementary assessment of data submitted in the written statement procedure. The addendum prepared by the IQWiG was submitted to the GBA on 11 September 2026.

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

Courtesy translation – only the German version is legally binding.

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 were discussed at the Subcommittee's session on 22 September 2026, and deliberation of the draft resolution was concluded.

At their session on 1 October 2026, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	22 December 2020 and 11 February 2025	Determination of the appropriate comparator therapy
Subcommittee on Medicinal Products	25 November 2025	New determination of the appropriate comparator therapy
Working group Section 35a	5 August 2026	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	10 August 2026	Conduct of the oral hearing, commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	19 August 2026 16 September 2026	Consultation on the dossier assessment by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	22 September 2026	Concluding discussion of the draft resolution
Plenum	1 October 2026	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 1 October 2026

Federal Joint Committee
in accordance with Section 91 SGB V
The Chair

Dr Optendrenk

Courtesy translation – only the German version is legally binding.