Gemeinsamer Bundesausschuss

Justification

for 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
Teprotumumab (thyroid eye disease)

From 20 August 2026

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) 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 G-BA 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,

3rd additional medical benefit in relation to the appropriate comparator therapy,

4th number of patients and patient groups for whom there is a therapeutically significant additional benefit,

5th treatment costs for the statutory health insurance funds,

6th 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 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 teprotumumab on 1 March 2026 in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure of the G-BA (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 Chapter 5, Section 8, paragraph 1, number 1 of the Rules of Procedure (VerfO), the pharmaceutical company submitted the final dossier to the G-BA on 27 February 2026.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 1 June 2026 on the G-BA website at (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 teprotumumab 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 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 teprotumumab.

In the light of the above, and taking into account the statements received and the oral hearing, the G-BA 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 teprotumumab (Tepezza) in accordance with the product information

TEPEZZA is indicated in adults for the treatment of moderate to severe thyroid eye disease (TED).

Therapeutic indication of the resolution (resolution of 20.08.2026):

See the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

a) Adults with moderate to severe thyroid eye disease in its acute stage; first-line therapy

Appropriate comparator therapy for teprotumumab:

- Individualised therapy with selection of
  - Methylprednisolone
  - Methylprednisolone in combination with mycophenolate mofetil

b) Adults with moderate to severe thyroid eye disease in its acute stage who are eligible for second-line therapy

Appropriate comparator therapy for teprotumumab:

- Individualised therapy with selection of
  - Methylprednisolone
  - Glucocorticoids in combination with orbital radiotherapy, cyclosporine or azathioprine
  - Rituximab (monotherapy)

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

c) Adults with moderate to severe thyroid eye disease in its chronic stage

Appropriate comparator therapy:

- Monitoring wait-and-see approach

Criteria according to Chapter 5 Section 6 of the Rules of Procedure of the G-BA 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 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 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 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 addition to teprotumumab, glucocorticoids (methylprednisolone, prednisolone, prednisone) are approved for this therapeutic indication.

On 2. Non-medicinal treatments that are considered in this therapeutic indication include, among others, retrobulbar radiotherapy, orbital decompression, eyelid correction in cases of changes to the eyelid configuration, or eye muscle surgery for diplopia.

On 3. There are no G-BA resolutions relating to the indication under assessment.

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.

In general, the available evidence in this therapeutic indication should be regarded as limited. Consequently, in the absence of higher-quality evidence, the EUGOGO guideline[2] was presented additionally even though it does not fully meet the methodological requirements. No Cochrane reviews or systematic reviews were identified in this therapeutic indication.

According to the mentioned guideline, treatment decisions are made, in particular, depending on disease activity and disease severity. This leads to specific therapy recommendations, on the basis of which it is considered appropriate to determine the appropriate comparator therapy by dividing the patients with moderate to severe thyroid eye disease into groups, depending on their eligibility for first-line therapy or second-line therapy. Furthermore, in line with the guideline recommendations, a distinction is made between the acute and chronic stages of the disease.

This results in the following patient groups:

a) Adults with moderate to severe thyroid eye disease in its acute stage; first-line therapy

b) Adults with moderate to severe thyroid eye disease in its acute stage who are eligible for second-line therapy

c) Adults with moderate to severe thyroid eye disease in its chronic stage

[2] Bartalena L, Kahaly GJ, Baldeschi L et al. The 2021 European Group on Graves' orbitopathy (EUGOGO) clinical practice guidelines for the medical management of Graves' orbitopathy. Eur J Endocrinol 2021; 185(4): G43-G67. https://doi.org/10.1530/EJE-21-0479

For all patient groups, it is assumed that any underlying conditions that may be present (e.g. Graves' disease) are being treated in accordance with current state of medical knowledge.

On patient population a)

Only glucocorticoids are approved for the first-line therapy of adults with moderate to severe thyroid eye disease in its acute stage. The therapy recommendations in the guideline generally list intravenous methylprednisolone, either alone or in combination with mycophenolate mofetil, as first-line therapies. The combination therapy of methylprednisolone and mycophenolate mofetil is therapeutically superior to methylprednisolone monotherapy. This recommendation is based on a randomised controlled trial[3]. It is also clear from the written statement issued by the scientific-medical societies that the combination therapy of methylprednisolone and mycophenolate mofetil is used as first-line therapy.

For some patients, high-dose methylprednisolone monotherapy is indicated. For the vast majority of patients, however, the combination therapy of methylprednisolone and mycophenolate mofetil is recommended as first-line therapy. Pursuant to Section 6, paragraph 2, sentence 3, number 3 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), it is therefore appropriate to determinate the off-label use of methylprednisolone in combination with mycophenolate mofetil as part of the appropriate comparator therapy for this clearly definable patient population.

In the overall assessment of the available evidence and medical treatment practice, an individualised therapy with the selection of methylprednisolone, alone or in combination with mycophenolate mofetil, is determined as the appropriate comparator therapy for the first-line therapy of adults with moderate to severe thyroid eye disease in its acute stage.

Individualised therapy is based on the assumption that several treatment options, which allow an individualised medical treatment decision, are available.

On patient population b)

The therapy recommendations in the guideline list glucocorticoids, either alone or in combination with orbital radiotherapy, cyclosporine or azathioprine, and rituximab monotherapy, as therapy options for adults with moderate to severe thyroid eye disease in the acute phase of the disease who are eligible for second-line therapy.

[3] Kahaly GJ, Riedl M, König J et al. Mycophenolate plus methylprednisolone versus methylprednisolone alone in active, moderate-to-severe Graves' orbitopathy (MINGO): a randomised, observer-masked, multicentre trial. Lancet Diabetes Endocrinol 2018; 6(4): 287-298. https://doi.org/10.1016/S2213-8587(18)30020-2

These recommendations are based on randomised controlled trials[4,5,6,7,8]. However, the active ingredients cyclosporine, azathioprine and rituximab are not approved for this therapeutic indication.

The guideline and the written statement issued by the scientific-medical societies recommend the use of second-line therapies if first-line therapy is ineffective or patients are no longer eligible for first-line therapy. Intravenously administered methylprednisolone and the orally available glucocorticoids prednisolone and prednisone are considered in the context of second-line therapy. In this case, prednisolone and prednisone are recommended particularly in combination with orbital radiotherapy or the immunosuppressants cyclosporine or azathioprine. For patients with eye movement disorders, the preferred treatment is methylprednisolone in combination with orbital radiotherapy.

For some patients, neither glucocorticoid therapy alone nor glucocorticoid therapy in combination with radiotherapy is an option. There are therefore no other approved therapy options available for these patients. Off-label use is medically necessary for these patients, particularly given that inadequately treated moderate to severe thyroid eye disease may progress to vision-threatening optic nerve compression.

Pursuant to Section 6, paragraph 2, sentence 3, number 3 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), it is therefore appropriate to determine the off-label use of cyclosporine or azathioprine (each in combination with glucocorticoids) or rituximab monotherapy as part of the appropriate comparator therapy for this clearly definable patient population.

In the overall assessment of the available evidence and medical treatment practice, an individualised therapy with the selection of methylprednisolone, glucocorticoids in combination with orbital radiotherapy, cyclosporine or azathioprine, and rituximab monotherapy is therefore determined as the appropriate comparator therapy for adults with moderate to severe thyroid eye disease in its acute stage who are eligible for second-line therapy.

Individualised therapy is based on the assumption that several treatment options, which allow an individualised medical treatment decision, are available.

[4] Kahaly G, Schrezenmeir J, Krause U et al. Ciclosporin and prednisone v. prednisone in treatment of Graves' ophthalmopathy: a controlled, randomised and prospective study. Eur J Clin Invest 1986; 16(5): 415-422. https://doi.org/10.1111/j.1365-2362.1986.tb01016.x

[5] Prummel MF, Mourits MP, Berghout A et al. Prednisone and cyclosporine in the treatment of severe Graves' ophthalmopathy. N Engl J Med 1989; 321(20): 1353-1359. https://doi.org/10.1056/NEJM198911163212002

[6] Rajendram R, Taylor PN, Wilson VJ et al. Combined immunosuppression and radiotherapy in thyroid eye disease (CIRTED): a multicentre, 2 × 2 factorial, double-blind, randomised controlled trial. Lancet Diabetes Endocrinol 2018; 6(4): 299-309. https://doi.org/10.1016/S2213-8587(18)30021-4

[7] Stan MN, Garrity JA, Carranza Leon BG et al. Randomised controlled trial of rituximab in patients with Graves' orbitopathy. J Clin Endocrinol Metab 2015; 100(2): 432-441. https://doi.org/10.1210/jc.2014-2572

[8] Salvi M, Vannucchi G, Currò N et al. Efficacy of B-cell targeted therapy with rituximab in patients with active moderate to severe Graves' orbitopathy: a randomised controlled study. J Clin Endocrinol Metab 2015; 100(2): 422-431. https://doi.org/10.1210/jc.2014-3014

On patient population c)

There are currently no approved medicinal products for the treatment of moderate to severe thyroid eye disease in its chronic stage, and no therapy recommendations can be derived from the guideline. In the overall assessment of the available evidence and medical treatment practice, the monitoring wait-and-see approach is therefore determined as the appropriate comparator therapy for adults with moderate to severe thyroid eye disease in its chronic stage.

It is assumed that patients in the chronic stage of the disease in both study arms will be offered rehabilitative surgery, such as orbital decompression, correction of eye misalignment or eyelid correction, as required.

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

Any change to the appropriate comparator therapy requires a decision by the G-BA 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 teprotumumab is assessed as follows:

a) Adults with moderate to severe thyroid eye disease in its acute stage; first-line therapy

The additional benefit is not proven for adults with moderate to severe thyroid eye disease in its acute stage who are eligible for first-line therapy.

b) Adults with moderate to severe thyroid eye disease in its acute stage who are eligible for second-line therapy

The additional benefit is not proven for adults with moderate to severe thyroid eye disease in its acute stage who are eligible for second-line therapy.

c) Adults with moderate to severe thyroid eye disease in its chronic stage

The additional benefit is not proven for adults with moderate to severe thyroid eye disease in its chronic stage.

Justification:

Patient populations a) and b)

For the benefit assessment, the pharmaceutical company presented the label-enabling TED01RV and HZNP-TEP-301 studies across all patient groups for the treatment of the acute phase of the disease, as well as the HZNP-TEP-403 study for the treatment of the chronic phase of the disease.

The TED01RV study is a multicentre, randomised, double-blind, placebo-controlled phase II study for the assessment of the efficacy and safety of teprotumumab in adults with moderate to severe thyroid eye disease in its acute phase. A total of 87 patients were randomised in a 1:1 ratio to the treatment arms: teprotumumab (n = 42) versus placebo (n = 45). The treatment was administered over a period of 24 weeks in the form of 8 infusions, each given at 3-week intervals. The primary endpoint was the percentage of subjects showing a combined response at week 24, defined as a reduction in proptosis by ≥ 2 mm and a reduction in the Clinical Activity Score (CAS) by ≥ 2 points in the eye under study, without simultaneous deterioration in the other eye.

The HZNP-TEP-301 study is a multicentre, randomised, double-blind, placebo-controlled phase III study. 83 patients, who were randomised in a 1:1 ratio to the treatment arms: teprotumumab (n = 41) versus placebo (n = 42), were enrolled in the study. The study participants likewise received 8 infusions at a 3-week interval over a period of 24 weeks. The primary endpoint of the study was the percentage of subjects showing a proptosis response at week 24, defined as a reduction in proptosis by ≥ 2 mm in the eye under study without simultaneous deterioration or increase by ≥ 2 mm in the other eye.

As the TED01RV and HZNP-TEP-301 studies are placebo-controlled studies in which none of the first- or second-line therapy options specified in the appropriate comparator therapy were used, the data submitted by the pharmaceutical company are unsuitable for drawing conclusions on the additional benefit of teprotumumab compared with the appropriate comparator therapy in adults with thyroid eye disease in its acute stage.

Patient population c)

The pharmaceutical company presented the HNZP-TEP-403 study for the assessment of patient population c). This study is a double-blind RCT comparing teprotumumab with placebo. The comparative treatment period spans 24 weeks. Adults with chronic (inactive) thyroid eye disease were enrolled in the study. For enrolment in the study, patients had to show an increase in proptosis by ≥ 3 mm compared with the value prior to the diagnosis of thyroid eye disease and/or proptosis of ≥ 3 mm above the normal value for their descent and sex. In addition, either a Clinical Activity Score (CAS) ≤ 1 in both eyes for ≥ 1 year prior to screening, or the following 3 criteria for ≥ 1 year prior to screening, had to be met: no deterioration of proptosis, no deterioration of diplopia (if present) and no new signs of inflammation. Furthermore, there must have been no indication for immediate surgery, nor must any reconstructive surgery and/or orbital radiotherapy have been planned. 62 patients were enrolled and randomly allocated in a 2:1 ratio to receive treatment with teprotumumab (N = 42) or a placebo (N = 20). On day 1, the eye that was more severely affected at the start of the study (with a greater degree of proptosis) was defined as the eye under study in the randomised patients. Following completion of the double-blind phase (24 weeks), patients from both groups who had not shown a clinical response (i.e. with a reduction in proptosis by < 2 mm compared with the start of the study) were able to continue treatment with teprotumumab during the open-label treatment phase. Treatment with teprotumumab was

administered during the double-blind phase according to the requirements in the product information.

The primary endpoint of the HNZP-TEP-403 study was the change in proptosis at week 24 compared with the start of the study. Patient-relevant secondary endpoints comprised endpoints in the categories of morbidity, health-related quality of life and side effects.

Whilst the chronic stage of the disease is reflected in the inclusion criteria for the HZNP-TEP-403 study, the study population was not restricted to patients with moderate to severe thyroid eye disease on the basis of these inclusion criteria. In contrast to the label-enabling HZNP-TEP-301 study for the acute stage of the disease, in which the presence of moderate to severe disease was an inclusion criterion as defined by the 2008 EUGOGO Consensus Statement, the HZNP-TEP-403 study does not have a comparable inclusion criterion. It was therefore at the discretion of the principal investigators to also enrol patients with mild thyroid eye disease in the HZNP-TEP-403 study. There is no evidence to suggest that the study was designed to enrol patients with moderate to severe thyroid eye disease. The EUGOGO criteria, which are cited in both the 2008 Consensus Statement and the 2021 guideline on severity grading of the disease, were not fully assessed at the start of the HZNP-TEP-403 study.

The 2021 EUGOGO guideline defines moderate to severe thyroid eye disease in adults as a non-vision-threatening condition that has a sufficient impact on daily living to justify the risks associated with immunosuppression (active disease) or surgical intervention (inactive disease). In this case, two or more of the following criteria are usually met:

- Eyelid retraction by ≥ 2 mm
- Moderate to severe soft-tissue involvement
- Proptosis of ≥ 3 mm above the normal value for the patient's descent and sex
- Intermittent or constant diplopia

Given that proptosis (as described above) was an inclusion criterion for the HZNP-TEP-403 study, it is assumed that the proptosis criterion was met by the majority of patients enrolled in the study. By contrast, soft-tissue involvement was not included in the study. It therefore remains unclear to what extent the criterion of moderate to severe soft-tissue involvement was met in the patients enrolled in the study. Constant or intermittent diplopia was present in only 16% of the patients enrolled in the study, whilst eyelid retraction was documented in the medical history of only one subject in the HZNP-TEP-403 study.

Both the EUGOGO guideline and the oral hearing emphasised that the impact of the disease on daily living must be taken into account in the severity grading. In the HZNP-TEP-403 study, health-related quality of life was assessed using the Graves' Ophthalmopathy Quality of Life (GO-QoL) questionnaire, which covers the domains of "visual function" and "appearance". Analysis of the data relating to the "visual function" domain showed that the patients enrolled had only minor impairments at the start of the study. It is unclear to what extent the data on impairments of psychosocial well-being - as reflected in the "appearance" domain - indicate relevant impacts on daily living.

Overall, the data provided are insufficient to examine and conclusively assess the severity of the condition in the patients of the presented study.

During the oral hearing, the clinicians involved emphasised that, in clinical practice, significant proptosis does not generally occur in isolation, but is usually associated with other EUGOGO criteria (in particular, soft-tissue involvement). Against this background, the G-BA consider the HZNP-TEP-403 study to be a suitable body of evidence, albeit with limitations, for the assessment of teprotumumab in patients with chronic thyroid eye disease, despite the remaining uncertainties arising from the failure to assess the EUGOGO criteria.

Consequently, the results of the HZNP-TEP-403 study are used for the benefit assessment.

Extent and probability of the additional benefit

Mortality

There were no deaths in either treatment group up to week 24.

Morbidity

Absence of diplopia

For the "absence of diplopia" endpoint, there was no statistically significant difference between the treatment groups at week 24.

Orbital pain (VAS)

For the endpoint of orbital pain, assessed using a 10-cm VAS, there was no statistically significant difference between the treatment groups up to week 24.

Quality of life

Graves' Ophthalmopathy Quality of Life (GO-QoL) questionnaire

The GO-QoL is a validated questionnaire used to assess health-related quality of life in patients with thyroid eye disease. The questionnaire with a total of 16 questions comprises the domains of visual function and appearance. For each domain, 8 questions (1-week assessment period) are answered on a 3-point Likert scale. To calculate the domain scores, the scores for questions 1 to 8 (visual function) and questions 9 to 16 (appearance) are added together and then converted to a scale of 0 to 100. In this context, a higher domain score indicates a better health-related quality of life. The calculation of a total score across all 16 questions has not been validated.

The pharmaceutical company shall provide the dossier with post-hoc responder analyses for both domains, covering both improvement and deterioration by at least 15 points (corresponding to 15% of the scale range) at week 24. In addition, pre-specified continuous analyses using MMRM are available for the mean change from the start of the study to week 24. Due to relevant ceiling effects, the continuous analyses of both domains are used for this assessment.

For the visual function domain, there was a statistically significant difference in favour of teprotumumab compared with placebo up to week 24. The 95% confidence interval of the standardised mean difference (SMD) is however not completely outside the irrelevance range from - 0.2 to 0.2, so that it cannot be concluded that the effect is clinically relevant.

For the appearance domain, there was no statistically significant difference between the treatment groups up to week 24.

Side effects

SAEs, severe AEs (CTCAE grade ≥ 3) and discontinuation due to AEs

For the endpoints of SAEs, severe AEs and discontinuation due to AEs, there was no statistically significant difference between the treatment groups at week 24.

Specific AEs

Hearing disorder (SMQ, HLT, AEs)

For the endpoint of hearing disorder, there was no statistically significant difference between the treatment groups at week 24.

Overall assessment

For adults with moderate to severe thyroid eye disease in its chronic stage, data on the endpoints of mortality, morbidity, health-related quality of life and side effects are available from the HZNP-TEP-403 study comparing teprotumumab with placebo.

With regard to the patient-relevant endpoints in the endpoint categories of mortality, morbidity and side effects, there were neither advantages nor disadvantages of teprotumumab compared to placebo.

In the endpoint category of health-related quality of life, the GO-QoL visual function domain showed a statistically significant difference in favour of teprotumumab compared with placebo up to week 24. The 95% confidence interval of the standardised mean difference (SMD) is however not completely outside the irrelevance range from - 0.2 to 0.2, so that it cannot be concluded that the effect is clinically relevant.

The fact that it cannot be conclusively determined whether the HZNP-TEP-403 study adequately reflects moderate to severe disease severity leads to further uncertainties in the assessment of the study.

Overall, without prejudice to the question of whether the HZNP-TEP-403 study adequately reflects moderate to severe disease severity, no additional benefit of teprotumumab can be inferred from the results presented.

2.1.4 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product TEPEZZA with the active ingredient teprotumumab.

Teprotumumab is approved for the treatment of moderate to severe thyroid eye disease. The following patient populations were distinguished for the benefit assessment:

a) Adults with moderate to severe thyroid eye disease in its acute stage; first-line therapy

b) Adults with moderate to severe thyroid eye disease in its acute stage who are eligible for second-line therapy

c) Adults with moderate to severe thyroid eye disease in its chronic stage

Patient population a)

An individualised therapy with the selection of methylprednisolone, alone or in combination with mycophenolate mofetil, was determined as the appropriate comparator therapy.

In the dossier, the pharmaceutical company presented data from the TED01RV and HZNP-TEP-301 studies, which compared teprotumumab with placebo. Due to the lack of comparison with the appropriate comparator therapy, the data presented are therefore unsuitable for deriving an additional benefit.

Accordingly, an additional benefit of teprotumumab compared with the appropriate comparator therapy is not proven for adults with moderate to severe thyroid eye disease in its acute stage who are eligible for first-line therapy.

Patient population b)

An individualised therapy with the selection of methylprednisolone, glucocorticoids in combination with orbital radiotherapy, cyclosporine or azathioprine, and rituximab monotherapy, was determined as the appropriate comparator therapy.

For this patient population as well, the pharmaceutical company presented the dossier with data from the TED01RV and HZNP-TEP-301 studies, which compared teprotumumab with placebo. Due to the lack of comparison with the appropriate comparator therapy, the data presented are therefore unsuitable for deriving an additional benefit.

Accordingly, an additional benefit of teprotumumab compared with the appropriate comparator therapy is not proven for adults with moderate to severe thyroid eye disease in its acute stage who are eligible for second-line therapy.

Patient population c)

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

In the dossier, the pharmaceutical company presented data from the HZNP-TEP-403 study, which compared teprotumumab with placebo.

With regard to the patient-relevant endpoints in the endpoint categories of mortality, morbidity and side effects, there were neither advantages nor disadvantages of teprotumumab compared to placebo.

In the endpoint category of health-related quality of life, the GO-QoL visual function domain showed a statistically significant difference in favour of teprotumumab. The 95% confidence interval is however not completely outside the irrelevance range, so that it cannot be concluded that the effect is clinically relevant.

The fact that it cannot be conclusively determined whether the HZNP-TEP-403 study adequately reflects moderate to severe disease severity leads to further uncertainties in the assessment of the study.

Overall, without prejudice to the question of whether the HZNP-TEP-403 study adequately reflects moderate to severe disease severity, no additional benefit of teprotumumab can be inferred from the results presented.

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 resolution is based on the information provided by the pharmaceutical company in the benefit assessment dossier. Overall, the percentage of patients with moderate to severe

thyroid eye disease is considered to be overestimated; furthermore, the data are subject to uncertainty. One of the reasons for these uncertainties is that the figures are based on outdated data. The criteria used for severity grading of the disease are also based on outdated data sources, meaning that the category of moderate to severe disease burden is defined more broadly, which leads to an overestimation of the target population. In addition, the calculation was based on the prevalence of the disease, which leads to a further overestimation of the target population.

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 Tepezza (active ingredient: teprotumumab) at the following publicly accessible link (last access: 3 June 2026):

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

Treatment with teprotumumab should only be initiated and monitored by specialists who are experienced in the treatment of patients with thyroid eye disease.

A clinical response is expected after 8 treatment doses. If no response is achieved with this treatment regimen, no further doses should be administered.

In accordance with the EMA requirements regarding additional risk minimisation measures, the pharmaceutical company must provide training material that contains information for medical professionals and patients (including patient guideline). The training material contains, in particular, information and warnings regarding hearing disorders and for women of reproductive age.

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 June 2026). The calculation of treatment costs is generally based on the last revised LAUER-TAXE® version following the publication of the benefit assessment.

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

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.

The active ingredients mycophenolate mofetil, cyclosporine, azathioprine and rituximab, which form part of the appropriate comparator therapy, are not approved for this therapeutic indication. The marketing authorisation applies exclusively to treatment with glucocorticoids. However, the product information contains neither a specific treatment regimen nor clear dosage information. The costs of the approved and off-label therapy options for the appropriate comparator therapy were therefore represented on the basis of the sources cited in each case.

The (daily) doses recommended in the product information or in the labelled publications were used as the basis for calculation.

A period of one year is assumed for calculating the costs of off-label use of mycophenolate mofetil, cyclosporine, azathioprine and rituximab.

Treatment period:

a) Adults with moderate to severe thyroid eye disease in its acute stage; first-line therapy

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Teprotumumab	1 x per 21-day cycle	8	1	8
Appropriate comparator therapy				
Methylprednisolone (monotherapy)				
Methylprednisolone[2]	1 x every 7 days	12	1	12
Methylprednisolone in combination with mycophenolate mofetil				
Methylprednisolone[2]	1 x every 7 days	12	1	12
Mycophenolate mofetil[2]	2 x daily	365	1	365

b) Adults with moderate to severe thyroid eye disease in its acute stage who are eligible for second-line therapy

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Teprotumumab	1 x per 21-day cycle	8	1	8
Appropriate comparator therapy				
Methylprednisolone (monotherapy)				
Methylprednisolone[2]	1 x every 7 days	12	1	12

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Glucocorticoids in combination with orbital radiotherapy				
Methylprednisolone[9]	1 x every 7 days	6 - 12	1	6 - 12
Methylprednisolone, followed by prednisone[10]	1 x on day 1 – 3, followed by 1 x every 7 days	9	1	9
Glucocorticoid (Prednisone[10,11])	Different from patient to patient[12]			
Orbital radiotherapy2[,10,11]	1 x daily or 1 x every 7 days	10 - 20	1	10 - 20
Glucocorticoids in combination with cyclosporine				
Prednisone[2,4]	1 x daily	70	1	70
Cyclosporine[4]	1 x daily	365	1	365
Glucocorticoids in combination with azathioprine				
Prednisolone[6]	1 x daily	168	1	168
Azathioprine[6]	1 x daily	365	1	365
Rituximab (monotherapy)				
Rituximab[2]	1 x every 365 days	1	1	1

[9] Oeverhaus M, Witteler T, Lax H et al. Combination Therapy of Intravenous Steroids and Orbital Irradiation is More Effective Than Intravenous Steroids Alone in Patients with Graves' Orbitopathy. Horm Metab Res 2017; 49(10): 739-747. https://doi.org/10.1055/s-0043-116945

[10]Kim JW, Han SH, Son BJ, et al. Efficacy of combined orbital radiation and systemic steroids in the management of Graves' orbitopathy. Graefes Arch Clin Exp Ophthalmol. 2016; 254 (5): 991–8. https://doi.org/10.1007/s00417-016-3280-7

[11]Marcocci C, Bartalena L, Bogazzi F, et al. Orbital radiotherapy combined with high dose systemic glucocorticoids for Graves' ophthalmopathy is more effective than radiotherapy alone: results of a prospective randomised study. J Endocrinol Invest. 1991; 14 (10): 853–60. https://doi.org/10.1007/BF03347943

[12]According to the study, the gradual reduction in dosage depends on the activity and severity of thyroid eye disease over a period of 2 to 3 months.

c) Adults with moderate to severe thyroid eye disease in its chronic stage

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Teprotumumab	1 x per 21-day cycle	8	1	8
Appropriate comparator therapy				
Monitoring wait-and-see approach	Non-quantifiable			

Consumption:

For dosages depending on body weight (BW), the average body measurements from the official representative statistics "2025 Microcensus – body measurements of the population" were used as a basis (average body weight 78.3 kg)[13].

As it is not always possible to achieve the exact calculated dose per day with the commercially available dosage strengths, in these cases rounding up or down to the next higher or lower available dose that can be achieved with the commercially available dose strengths as well as the scalability of the respective dosage form.

a) Adults with moderate to severe thyroid eye disease in its acute stage; first-line therapy

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					
Teprotumumab	Initial dose: 10 mg/kg BW = 783 mg Subsequent doses:	Initial dose: 783 mg Subsequent doses: 1,566 mg	2 x 500 mg – 4 x 500 mg	8	30 x 500 mg

[13]Federal Health Reporting. Average body measurements of the population (2025, both sexes), 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
	20 mg/kg BW = 1,566 mg				
Appropriate comparator therapy					
Methylprednisolone (monotherapy)					
Methylprednisolone[2]	Initial doses: 500 mg – 750 mg Subsequent doses: 250 mg – 500 mg	Initial doses: 500 mg – 750 mg Subsequent doses: 250 mg – 500 mg	1 x 250 mg – 1 x 1,000 mg	12	18 x 250 mg – 12 x 250 mg + 6 x 1,000 mg
Methylprednisolone in combination with mycophenolate mofetil					
Methylprednisolone[2,3]	Initial doses: 500 mg Subsequent doses: 250 mg	Initial doses: 500 mg Subsequent doses: 250 mg	2 x 250 mg – 1 x 250 mg	12	18 x 250 mg
Mycophenolate mofetil[2,3]	500 mg	1,000 mg	2 x 500 mg	365	730 x 500 mg

b) Adults with moderate to severe thyroid eye disease in its acute stage who are eligible for second-line therapy

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					
Teprotumumab	Initial dose: 10 mg/kg BW = 783 mg Subsequent doses:	Initial dose: 783 mg Subsequent doses: 1,566 mg	2 x 500 mg – 4 x 500 mg	8	30 x 500 mg

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
	20 mg/kg BW = 1,566 mg				
Appropriate comparator therapy					
Methylprednisolone (monotherapy)					
Methylprednisolone[2]	Initial doses: 500 mg – 750 mg Subsequent doses: 250 mg – 500 mg	Initial doses: 500 mg – 750 mg Subsequent doses: 250 mg – 500 mg	1 - 2 x 250 mg – 1 x 1,000 mg	12	18 x 250 mg – 12 x 250 mg + 6 x 1,000 mg
Glucocorticoids in combination with orbital radiotherapy					
Methylprednisolone[2,9]	Initial doses: 250 mg – 500 mg Subsequent doses: 125 mg – 250 mg	Initial doses: 250 - 500 mg Subsequent doses: 125 mg – 250 mg	1 - 2 x 250 mg – 1 x 125 mg	6 - 12	3 x 250 mg + 3 x 125 mg - 18 x 250 mg
Methylprednisolone, followed by prednisone[10]	Initial doses: 500 mg Subsequent doses: 500 mg	500 mg	2 x 250 mg	9	18 x 250 mg
Glucocorticoid (Prednisone [11])	Different from patient to patient[12]				
Orbital radiotherapy2[,10,11]	2 Gray – 1 Gray	20 Gray	10 × 2 Gray or 20 x 1 Gray	10 - 20	10 × 2 Gray or 20 x 1 Gray
Glucocorticoids in combination with cyclosporine					
Prednisone[2,4]	Week 1: 50 mg – 100 mg Week 2: 45 mg – 90 mg	100 mg – 5 mg	Week 1: 2 x 20 mg + 1 x 10 mg - 5 x 20 mg Week 2: 2 x 20 mg + 1 x 5 mg -	70	70 x 20 mg + 35 x 10 mg + 28 x 5 mg – 161 x 20 mg + 42 x 10 mg

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Prednisone[2,4]			4 x 20 mg + 1 x 10 mg		
	<u>Week 3:</u> 40 mg – 80 mg		<u>Week 3:</u> 2 x 20 mg + - 4 x 20 mg		
	<u>Week 4:</u> 35 mg – 70 mg		<u>Week 4:</u> 1 x 20 mg + 1 x 10 mg + 1 x 5 mg - 3 x 20 mg + 1 x 10 mg		
	<u>Week 5:</u> 30 mg – 60 mg		<u>Week 5:</u> 1 x 20 mg + 1 x 10 mg - 3 x 20 mg +		
	<u>Week 6:</u> 25 mg – 50 mg		<u>Week 6:</u> 1 x 20 mg + 1 x 5 mg – 2 x 20 mg + 1 x 10 mg		
	<u>Week 7:</u> 20 mg – 40 mg		<u>Week 7:</u> 1 x 20 mg – 2 x 20 mg		
	<u>Week 8:</u> 15 mg – 30 mg		<u>Week 8:</u> 1 x 10 mg + 1 x 5 mg – 1 x 20 mg + 1 x 10 mg		
	<u>Week 9:</u> 10 mg – 20 mg		<u>Week 9:</u> 1 x 10 mg – 1 x 20 mg		

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
	Week 10: 5 mg – 10 mg		Week 10: 1 x 5 mg – 1 x 10 mg		
Cyclosporine[4]	Starting dose: 5 mg/kg BW = 391.5 mg – 7.5 mg/kg BW = 587.25 mg Subsequent doses[14]: Different from patient to patient	Starting dose: 391.5 mg – 587.25 mg Subsequent doses[14]: Different from patient to patient	1 x 250 mg + 3 x 50 mg - 2 x 250 mg + 2 x 50 mg	365	Different from patient to patient
Glucocorticoids in combination with azathioprine					
Prednisolone[6]	Week 1-6: 80 mg Week 7-14: 20 mg Week 15-20: 10 mg Week 21-24: 5 mg	80 mg – 5 mg	4 x 20 mg – 1 x 5 mg	168	224 x 20 mg + 42 x 10 mg - 28 x 5 mg
Azathioprine[6]	100 mg – 200 mg	100 mg – 200 mg	1 x 100 mg – 2 x 100 mg	365	365 x 100 mg – 730 x 100 mg
Rituximab (monotherapy)					
Rituximab[2]	100 mg – 500 mg	100 mg – 500 mg	1 x 100 mg – 1 x 500 mg	1	1 x 100 mg – 1 x 500 mg

[14]According to the study, subsequent doses are adjusted depending on the blood levels of ciclosporin (the therapeutic value is in the range between 300 and 700 ng/ml).

c) Adults with moderate to severe thyroid eye disease in its chronic stage

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					
Teprotumumab	Initial dose: 10 mg/kg BW = 783 mg Subsequent doses: 20 mg/kg BW = 1,566 mg	Initial dose: 783 mg Subsequent doses: 1,566 mg	2 x 500 mg – 4 x 500 mg	8	30 x 500 mg
Appropriate comparator therapy					
Monitoring wait-and-see approach	Non-quantifiable				

Costs:

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.

Costs of the medicinal products:

Patient groups a), b) and c)

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					
Teprotumumab 500 mg	1 PCI	€ 7,415.04	€ 1.77	€ 420.18	€ 6,993.09

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
Appropriate comparator therapy					
Azathioprine 100 mg	100 FCT	€ 58.01	€ 1.77	€ 3.69	€ 52.55
Ciclosporin 50 mg	10 CIS	€ 82.37	€ 1.77	€ 9.39	€ 71.21
Ciclosporin 250 mg	10 CIS	€ 343.68	€ 1.77	€ 43.50	€ 298.41
Methylprednisolone 125 mg	1 PII	€ 24.00	€ 1.77	€ 1.86	€ 20.37
Methylprednisolone 250 mg	5 PII	€ 64.51	€ 1.77	€ 5.89	€ 56.85
Methylprednisolone 1,000 mg	3 PII	€ 166.47	€ 1.77	€ 18.31	€ 146.39
Mycophenolate mofetil 500 mg[15]	250 FCT	€ 409.94	€ 1.77	€ 31.53	€ 376.64
Prednisone 20 mg[15]	100 TAB	€ 29.29	€ 1.77	€ 1.42	€ 26.10
Prednisone 10 mg[15]	50 TAB	€ 16.55	€ 1.77	€ 0.41	€ 14.37
Prednisone 5 mg[15]	50 TAB	€ 14.18	€ 1.77	€ 0.23	€ 12.18
Prednisolone 20 mg[15]	100 TAB	€ 21.62	€ 1.77	€ 0.81	€ 19.04
Prednisolone 10 mg[15]	50 TAB	€ 14.85	€ 1.77	€ 0.28	€ 12.80
Prednisolone 5 mg[15]	30 TAB	€ 12.80	€ 1.77	€ 0.12	€ 10.91
Rituximab 100 mg	1 CIS	€ 387.37	€ 1.77	€ 20.82	364.78
Rituximab 500 mg	1 CIS	€ 1,777.34	€ 1.77	€ 84.18	€ 1,691.39
Radiotherapy using a linear accelerator for benign disease (FSI 25316)	-				€ 56.06[16]
Surcharge where there is more than one target volume in the case of a benign disease (FSI 25317)	-				€ 25.99[17]
Radiotherapy planning I (FSI 25340)	-				€ 15.29[18]
Monitoring wait-and-see approach	Non-quantifiable				
Abbreviations: FCT = film-coated tablets; CIS = concentrate for the preparation of an infusion solution; PII = powder for the preparation of an injection solution; PCI = powder for a concentrate for the preparation of an infusion solution; TAB = tablets					

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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.

[15] Fixed reimbursement rate
[16] Calculable once on the treatment day
[17] Extra charge billable for the 2nd eye
[18] 1 x per treatment case for the same target volume

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.

According to the product information, teprotumumab may cause severe hearing disorders, including hearing loss. The patient's hearing should be assessed using an audiogram prior to treatment, during treatment (for example, before the third or fourth infusion) and after completion of treatment with teprotumumab.

Designation of the therapy	Designation of the service	Number	Costs per unit	Costs/ patient/ year
Teprotumumab	Pure-tone audiometry (FSI 09320)	3	€ 18.60	€ 55.80

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 agents 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-apply unit are to be payable. These additional other costs are not added to the pharmacy sales price but rather follow the rules for calculating in the 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 Hilfstaxe.

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 session on 6 February 2024, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 27 February 2026, the pharmaceutical company submitted a dossier for the benefit assessment of teprotumumab to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 VerfO.

By letter dated 2 March 2026 in conjunction with the resolution of the G-BA 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 G-BA commissioned the IQWiG to assess the dossier concerning the active ingredient teprotumumab.

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

The oral hearing was held on 6 July 2026.

By letter dated 7 July 2026, the IQWiG was commissioned with a supplementary assessment. The addendum prepared by the IQWiG was submitted to the G-BA on 30 July 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 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 11 August 2026, and deliberation of the draft resolution was concluded.

At their session on 20 August 2026, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	6 February 2024	Determination of the appropriate comparator therapy
Working group Section 35a	1 July 2026	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	6 July 2026	Conduct of the oral hearing, commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	15 July 2026 5 August 2026	Consultation on the dossier assessment by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	11 August 2026	Concluding discussion of the draft resolution
Plenum	20 August 2026	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 20 August 2026

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

Dr Optendrenk