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
Tezepelumab (new therapeutic indication: chronic rhinosinusitis with nasal polyps (CRSwNP))

dated 7 May 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,
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. requirement 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 active ingredient tezepelumab (Tezspire) was listed for the first time on 15 November 2022 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

On 20 October 2025, tezepelumab received marketing authorisation for a new therapeutic indication to be classified as a major type 2 variation as defined according to Annex 2, number 2, letter a to Regulation (EC) No. 1234/2008 of the Commission of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334 from 12.12.2008, sentence 7).

On 9 October 2025, i.e. at the latest within four weeks of informing the pharmaceutical company about the approval for a new therapeutic indication, the pharmaceutical company submitted a dossier in due time in accordance with Section 4, paragraph 3, number 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with

Chapter 5 Section 8, paragraph 1, number 2 of the Rules of Procedure (VerfO) of the G-BA on the active ingredient tezepelumab with the new therapeutic indication "Tezspire is indicated as an add-on therapy with intranasal corticosteroids for the treatment of adult patients with severe CRSwNP for whom therapy with systemic corticosteroids, and/or surgery do not provide adequate disease control".

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 16 February 2026 on the G-BA website (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA came to a resolution on whether an additional benefit of tezepelumab 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 the 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 tezepelumab.

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 Tezepelumab (Tezspire) in accordance with the product information

Tezspire is indicated as an add-on therapy with intranasal corticosteroids for the treatment of adult patients with severe CRSwNP for whom therapy with systemic corticosteroids, and/or surgery do not provide adequate disease control.

Therapeutic indication of the resolution (resolution of 07.05.2026):

See the approved therapeutic indication

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

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adults with severe chronic rhinosinusitis with nasal polyps (CRSwNP) for whom therapy with systemic corticosteroids, and/or surgery do not provide adequate disease control

Appropriate comparator therapy for tezepelumab as an add-on therapy to intranasal corticosteroids:

- Dupilumab or mepolizumab or omalizumab, each in combination with intranasal corticosteroids (budesonide or mometasone furoate)

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

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

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

On 1. In the therapeutic indication for the treatment of CRSwNP, corticosteroids are approved: the active ingredients budesonide and mometasone furoate as intranasal (topical) corticosteroids (INCS) as well as (oral) corticosteroids (OCS). For short-term intervention on demand, antibiotics and analgesics are covered by the marketing authorisation. In addition, besides tezepelumab, the biologic agents depemokimab, dupilumab, mepolizumab and omalizumab are approved for the treatment of CRSwNP following an inadequate response to systemic corticosteroids and/or surgical intervention.

On 2. Non-medicinal treatment alone is not considered in the therapeutic indication. Surgical measures represent an intervention on demand.

On 3. With regard to chronic rhinosinusitis with nasal polyposis (CRSwNP), there are resolutions of the G-BA on the benefit assessment of medicinal products with new active ingredients - according to Section 35a SGB V - of 14 May 2020 for the active ingredient dupilumab and of 19 May 2022 for the active ingredient mepolizumab.

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.

According to the available aggregated evidence, use of the biologic agents dupilumab, mepolizumab or omalizumab as an add-on therapy to INCS maintenance treatment is recommended for adults with chronic rhinosinusitis with nasal polyps for whom therapy with systemic corticosteroids, and/or surgery do not provide adequate control of the CRSwNP disease. The active ingredient depemokimab is a new treatment option in the present therapeutic indication. The active ingredient was only recently approved (marketing authorisation on 12 February 2026). According to the generally recognised state of medical knowledge, depemokimab is not determined to be an appropriate comparator therapy for the present resolution.

Furthermore, the use of saline nasal rinses is recommended on the basis of evidence. According to the recommendations, invasive treatment methods may also be an option in individual cases.

Oral corticosteroids (OCS) are approved in the present therapeutic indication, but the evidence for the long-term use of OCS for standard or maintenance treatment of nasal polyps - especially beyond flare therapy - is to be regarded as rather low; consistently positive recommendations for long-term OCS use are not available on the basis of the aggregated evidence. Antibiotics as well as analgesics are not considered as standard or maintenance treatment, as these are only indicated for short-term treatment on demand (in case of complications, infections). Based on these considerations, the G-BA assume that patients in both arms receive further supportive measures (e.g. nasal rinses) as well as an appropriate, on-label therapy for complications (if applicable, short-term antibiotics, short-term systemic corticosteroids as part of a flare therapy).

In the overall assessment, the G-BA conclude that the biologic agents dupilumab or mepolizumab or omalizumab, each in combination with intranasal corticosteroids (budesonide or mometasone furoate), are considered appropriate for tezepelumab as add-on therapy to intranasal corticosteroids in adults with severe chronic rhinosinusitis with nasal polyps (CRSwNP) for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control. The appropriate comparator therapy determined here includes several therapeutic alternatives. The above-mentioned options dupilumab, mepolizumab and omalizumab are considered equally appropriate for the add-on therapy; within the intranasal corticosteroids, budesonide and mometasone furoate are equally appropriate therapeutic alternatives. The additional benefit over one of the biologic agents mentioned, each in combination with intranasal corticosteroids (budesonide or mometasone furoate) can be proven.

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 tezepelumab is assessed as follows:

There is a hint for a non-quantifiable additional benefit of tezepelumab as an add-on therapy to intranasal corticosteroids for adults with severe chronic rhinosinusitis with nasal polyps (CRSwNP) for whom therapy with systemic corticosteroids, and/or surgery do not provide adequate disease control.

Justification:

In the absence of direct comparator studies of tezepelumab versus the appropriate comparator therapy, the pharmaceutical company presented an adjusted indirect comparison according to the procedure by Bucher et al. for the proof of an additional benefit. For the indirect comparison via the bridge comparator of placebo + intranasal corticosteroids (INCS), the pharmaceutical company included the WAYPOINT study, comparing tezepelumab + INCS versus placebo + INCS, and the SYNAPSE study, comparing mepolizumab + INCS versus placebo + INCS.

Both studies are randomised, double-blind, controlled, multicentre phase III studies.

WAYPOINT study

Adult patients, who were suffering from CRSwNP diagnosed at least 12 months prior to the start of the study despite prior documented treatment with systemic corticosteroids (SCS) and/or surgery for nasal polyps, were enrolled in the WAYPOINT study. At the time of screening, the following four criteria had to be met: a nasal polyp score (NPS) ≥ 5 on a scale of 0 to 8 (≥ 2 for each nostril); a nasal congestion score (NCS) ≥ 2 on a scale of 0 to 3; CRSwNP symptoms such as nasal discharge or reduced sense of smell persisting for ≥ 8 weeks; a total score on the 22-item Sinonasal Outcome Test (SNOT-22) ≥ 30.

Treatment with tezepelumab was according to the product information. During the treatment phase, administration of INCS at a stable dose was continued in both study arms. Overall, patients were randomised in a 1:1 ratio to receive treatment with tezepelumab (N = 204) or placebo (N = 206).

For the adjusted indirect comparison, the pharmaceutical company presented the results for a sub-population of patients whose medical history already includes at least one documented surgery for nasal polyps. This sub-population comprised 144 subjects in the intervention arm and 147 subjects in the comparator arm.

The primary endpoints were the change in the NPS at week 52 and the change in the NCS averaged over the previous 14 days at week 52. In addition, other patient-relevant endpoints in the endpoint categories of morbidity, health-related quality of life and side effects were collected.

SYNAPSE study

Adult patients, who show at least two symptoms of chronic rhinosinusitis persisting for ≥ 12 weeks with recurrent bilateral nasal polyps and have undergone at least one nasal polyp surgery within the last 10 years prior to the time of enrolment, were enrolled in the SYNAPSE study. Patients also had to have undergone at least 8 weeks of treatment with INCS prior to screening. Patients were randomised to the treatment arms if, in addition to meeting the inclusion criteria for screening, they had a NPS score ≥ 5 (≥ 2 for each nostril) on a scale of 0 to 8 and had a VAS score > 7 for total symptoms and > 5 for nasal obstruction in the symptom diary over the 7 days prior to randomisation.

Treatment with mepolizumab was according to the product information. During the treatment phase, administration of intranasal mometasone furoate at a stable dose was continued in both study arms. Overall, 407 patients were randomised in a 1:1 ratio to receive treatment with mepolizumab (N = 206) or placebo (N = 201).

The primary endpoints were the change in the mean VAS score for nasal obstruction between weeks 49 and 52 and the change in the NPS score at week 52. In addition, other patient-

relevant endpoints in the endpoint categories of morbidity, health-related quality of life and side effects were collected.

On the adjusted indirect comparison according to Bucher

Overall, there are partial differences in study and patient characteristics between the WAYPOINT and SYNAPSE studies, none of which, however, fundamentally calls into question the sufficient similarity to conduct an adjusted indirect comparison via the bridge comparator of placebo, taking into account both the WAYPOINT and SYNAPSE studies.

However, for the WAYPOINT study, the endpoint-specific risk of bias is estimated to be high for all endpoint categories due to a significant percentage of missing values that differs between treatment arms. This is especially due to the fact that any surgery undergone for nasal polyps immediately led to premature therapy discontinuation, with the majority of such surgeries having taken place in the comparator arm. As patients in the SYNAPSE study continued to be monitored even after undergoing surgery for nasal polyps, the observation periods vary in length for the two studies, particularly for the comparator arm. Consequently, for all relevant endpoints, no suitable data with sufficient reliability of data were available to allow for a significant adjusted indirect comparison of the WAYPOINT and SYNAPSE studies.

However, as part of the written statement procedure, the pharmaceutical company subsequently submitted extensive data from the WAYPOINT study on return rates as well as two sensitivity analyses regarding the imputation of missing values for the endpoints in the categories of morbidity and health-related quality of life. These data show that data on the patient-reported endpoints in these two endpoint categories were largely collected at week 52 even for patients who discontinued therapy prematurely during the course of the study. The sensitivity analyses submitted subsequently suggest that the observed effects of the patient-reported endpoints are sufficiently reliable, and remain consistent even when missing values are handled differently. Consequently, it can be assumed on the basis of the subsequently submitted sensitivity analyses that the results derived from an adjusted indirect comparison for the endpoints in the categories of morbidity and health-related quality of life are sufficiently reliable despite the continued high risk of bias at the endpoint level on the intervention side.

The analysis strategy 2 with combined LOCF (last observation carried forward) and responder imputation is used for the present analysis of the endpoint categories of morbidity and health-related quality of life. This analysis strategy appears to be most appropriate for characterising the treatment setting to be assessed, as it incorporates the values observed following surgery for nasal polyps and imputes missing values for patients who have not undergone surgery for nasal polyps using the LOCF method, combined with responder imputation for patients with missing values following surgery for nasal polyps.

Extent and probability of the additional benefit

Mortality

Mortality was assessed in both studies as part of the AEs. In the WAYPOINT study, 1 death was recorded in the placebo arm until week 52.

The reliability of data requirement for carrying out an adjusted indirect comparison for the mortality endpoint is not met. No assessable data on the endpoint category of mortality are thus available for the benefit assessment.

Morbidity

Symptomatology (nasal congestion / obstruction, reduction / loss of sense of smell, nasal discharge, post-nasal drip, facial pain)

In both studies, patients reported the severity of their symptoms in a symptom diary once daily, based on the previous 24 hours. In the WAYPOINT study, patients rated their symptoms in the Nasal Polyposis Symptom Diary (NPSD) on a scale ranging from 0 (no symptoms) to 3 (severe symptoms). A visual analogue scale (VAS) (scale range from 0 to 100) was used in the SYNAPSE study. The VAS scores were divided by 10 and therefore ranged from 0 (no symptoms) to 10 (”worst imaginable symptoms”).

For the symptomatology endpoints, the pharmaceutical company presented responder analyses for week 52 compared with baseline, whereby a response criterion of a 15% scale range was selected, which corresponds to an improvement by ≥ 0.45 points on a scale of 0 to 3 in the WAYPOINT study and an improvement by ≥ 1.5 points on a scale of 0 to 10 in the SYNAPSE study.

Nasal congestion / obstruction

For the endpoint of nasal congestion / obstruction, the adjusted indirect comparison showed a statistically significant advantage of tezepelumab + INCS over mepolizumab + INCS.

Reduction / loss of sense of smell

For the endpoint of reduction / loss of sense of smell, the adjusted indirect comparison showed a statistically significant advantage of tezepelumab + INCS over mepolizumab + INCS.

Nasal discharge

For the endpoint of nasal discharge, the adjusted indirect comparison showed a statistically significant advantage of tezepelumab + INCS over mepolizumab + INCS.

Post-nasal drip

For the endpoint of post-nasal drip, the adjusted indirect comparison showed no statistically significant difference between tezepelumab + INCS and mepolizumab + INCS.

Facial pain

For the endpoint of facial pain, the adjusted indirect comparison showed no statistically significant difference between tezepelumab + INCS and mepolizumab + INCS.

SNOT-22 (22-item Sinonasal Outcome Test)

The SNOT-22 is a disease-specific, patient-reported questionnaire with 22 individual questions to assess the severity and frequency of occurrence of symptoms and social/ emotional

consequences of rhinosinusitis. Each question is answered on a scale from 0 (no complaints) to 5 (worst possible complaints) and a total score (0 to 110) is calculated from the individual scores for each question, with lower values corresponding to less impairment. This questionnaire is classified as a morbidity questionnaire as it is primarily designed to assess the impairments caused by symptoms (e.g. a blocked nose, a runny nose, post-nasal drip, and a reduced sense of smell or taste).

For the SNOT-22, the pharmaceutical company presented responder analyses for week 52 compared with baseline for both studies, using a response criterion of 15% scale range which corresponds to a reduction in the SNOT-22 total score by ≥ 16.5 points.

For the SNOT-22 endpoint, the adjusted indirect comparison showed no statistically significant difference between tezepelumab + INCS and mepolizumab + INCS.

Activity impairment (assessed using WPAI question 6)

The Work Productivity and Activity Impairment (WPAI) is used to collect impairments to work productivity and activities. Health economic aspects such as the endpoints of absenteeism and presenteeism collected by the WPAI are not considered patient-relevant and are therefore not taken into account in this benefit assessment. However, activity impairment due to the disease (question 6) addresses a patient-relevant aspect.

However, the reliability of data requirement for carrying out an adjusted indirect comparison for the activity impairment endpoint is not met. Consequently, no assessable data on this endpoint that allow a comparison of tezepelumab with the appropriate comparator therapy are available for the benefit assessment.

Quality of life

Health-related quality of life was assessed in both studies using the SF-36v2. For the SF-36, the physical component summary (PCS) score and the mental component summary (MCS) score are considered individually. For the SF-36, the adjusted indirect comparison showed no statistically significant difference between tezepelumab + INCS and mepolizumab + INCS in the percentage of patients with an improvement in the total score by ≥ 9.4 points (PCS) or ≥ 9.6 points (MCS) (15% of the scale range) at week 52.

Side effects

The reliability of data requirement for carrying out an adjusted indirect comparison for the endpoints of SAEs and discontinuation due to AEs is not met.

Consequently, no assessable data on the endpoint category of side effects that allow a comparison of tezepelumab with the appropriate comparator therapy are available for the benefit assessment.

Overall assessment

Based on an adjusted indirect comparison by Bucher et al., results for the endpoints in the morbidity and quality of life categories are available for the assessment of the additional benefit of tezepelumab in combination with INCS compared with the appropriate comparator therapy of mepolizumab in combination with INCS for the treatment of severe chronic rhinosinusitis with nasal polyps.

For the comparison via the bridge comparator of placebo in combination with INCS, the pharmaceutical company included the WAYPOINT study on the intervention side and the SYNAPSE study on the comparator side. The comparator study duration of both studies was 52 weeks each.

No assessable data on the endpoint category of mortality are available for an adjusted indirect comparison, as the reliability of data requirements for carrying out an adjusted indirect comparison have not been met.

For the endpoints of nasal congestion / obstruction, reduction / loss of sense of smell and nasal discharge in the endpoint category of morbidity, there was a statistically significant advantage in favour of tezepelumab + INCS compared with mepolizumab + INCS in each case. For the endpoints of post-nasal drip, facial pain and SNOT-22, there was no statistically significant difference between tezepelumab + INCS and mepolizumab + INCS in each case. No assessable data on the endpoint of activity impairment are available for an adjusted indirect comparison.

For the physical component summary (PCS) score or the mental component summary (MCS) score in the endpoint category of health-related quality of life, the SF-36v2 did not show any statistically significant difference between tezepelumab + INCS and mepolizumab + INCS.

No assessable data on the endpoint category of side effects are available for an adjusted indirect comparison, as the reliability of data requirements for carrying out an adjusted indirect comparison have not been met. However, given the specific data basis in this context, it is assumed that the results for side effects do not influence the conclusions on the additional benefit.

Consequently, the overall assessment showed exclusively positive effects of tezepelumab + INCS compared with mepolizumab + INCS. However, the assessment of the herein statistically significant morbidity endpoints is based on the use of different survey tools. Assessment of the manifestation of symptoms using a 4-point NRS (WAYPOINT) and a VAS (SYNAPSE) allows for estimation of the respective severity of symptomatology with varying levels of detail; consequently, the magnitude of the advantages demonstrated can only be quantified to a limited extent.

Furthermore, based on the adjusted indirect comparison, no assessable results are available for the endpoint categories of mortality and side effects. Due to the non-assessable results for

adverse events, the weighting of the advantages demonstrated in the study against the disadvantages cannot be conclusively made.

Overall, the demonstrated advantages therefore indicate an additional benefit of tezepelumab in adults with severe chronic rhinosinusitis with nasal polyps (CRSwNP) for whom therapy with systemic corticosteroids, and/or surgery do not provide adequate disease control; the extent of this benefit cannot be quantified on the basis of the available data.

Reliability of data (probability of additional benefit)

This assessment is based on the results of an adjusted indirect comparison. There is only one RCT on each side of the adjusted indirect comparison, meaning that the homogeneity and consistency of the results cannot be checked. Overall, the reliability of data is classified as low.

In both studies, there is also uncertainty regarding the need for nasal polyps surgeries, both at the start of the study and in its course. The significance of repeat nasal polyps surgeries following therapy failure compared with other (subsequent) therapy options, such as switching to a different biologic agent is unclear. Furthermore, nasal polyps surgery undergone during the course of the WAYPOINT study led to premature therapy discontinuation, whereas nasal polyps surgery in the SYNAPSE study had no impact on the planned treatment duration with the study medication mepolizumab.

Overall, a "hint" is derived for the reliability of data.

2.1.4 Summary of the assessment

The present assessment is the benefit assessment of a new therapeutic indication for the active ingredient tezepelumab. The therapeutic indication assessed here is: "as an add-on therapy with intranasal corticosteroids for the treatment of adult patients with severe CRSwNP for whom therapy with systemic corticosteroids, and/or surgery do not provide adequate disease control".

The G-BA determined the biologic agents dupilumab or mepolizumab or omalizumab, each in combination with the intranasal corticosteroids (INCS) budesonide or mometasone furoate, as the appropriate comparator therapy.

For the assessment of the additional benefit of tezepelumab, the pharmaceutical company presented an adjusted indirect comparison of tezepelumab in combination with INCS (WAYPOINT study) versus mepolizumab in combination with INCS (SYNAPSE study) via the bridge comparator of placebo in combination with INCS. Despite the high risk of bias at the endpoint level in the WAYPOINT study, it was possible to carry out an adjusted indirect comparison for the patient-reported endpoints in the categories of morbidity and health-related quality of life.

For the endpoints of nasal congestion, sense of smell and nasal discharge in the endpoint category of morbidity, there was a statistically significant advantage in favour of tezepelumab + INCS compared with mepolizumab + INCS. For the endpoints of post-nasal drip, facial pain and SNOT-22, there was no statistically significant difference between tezepelumab + INCS and mepolizumab + INCS in each case.

For the endpoint category of health-related quality of life, there were no statistically significant differences.

Based on the adjusted indirect comparison, no assessable results are available for the endpoint categories of mortality and side effects.

Consequently, the overall assessment showed exclusively positive effects of tezepelumab + INCS compared with mepolizumab + INCS, the extent of which cannot be quantified on the basis of available data. Furthermore, there is uncertainty regarding the need for nasal polyp surgeries, both at the start of the study and in its course, as well as the significance of repeat nasal polyp surgeries following therapy failure compared with other (subsequent) therapy options.

Due to the non-assessable results for adverse events, the weighting of the advantages demonstrated in the study against the disadvantages cannot be conclusively made. Overall, the demonstrated advantages therefore indicate a hint for a non-quantifiable additional benefit of tezepelumab in adults with severe chronic rhinosinusitis with nasal polyps.

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 data from the G-BA resolution on dupilumab[2] in the therapeutic indication for CRSwNP from 2020 are used as a basis for the information. Here too, the pharmaceutical company base their calculation on the routine data analysis of the benefit assessment procedure for dupilumab; however, unlike the previous calculation, they do not indicate a range but a specific value within the range calculated for dupilumab.

However, the patient numbers given are subject to uncertainty as already stated in the previous resolutions[2,3] regarding the CRSwNP indication, where the calculations are based on routine data analysis. On the one hand, the calculation is limited to an issued prescription for INCS; on the other, it is based on a time interval of four quarters between the last documented diagnosis and a previous sinus surgery. There is an underestimate of the number of patients covered by statutory health insurance in the overall assessment. The indication of a range takes greater account of this uncertainty and is therefore also the basis for this resolution on tezepelumab.

[2] Resolution on dupilumab of 14 May 2020
[3] Resolution on mepolizumab of 19 May 2022

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 Tezspire (active ingredient: tezepelumab) at the following publicly accessible link (last access: 26 February 2026):

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

Treatment with tezepelumab should only be initiated and monitored by specialists experienced in treating patients with CRSwNP.

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: 1 March 2026).

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

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.

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

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.

Adults with severe chronic rhinosinusitis with nasal polyps (CRSwNP) for whom therapy with systemic corticosteroids, and/or surgery do not provide adequate disease control

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:				
Tezepelumab	Continuously, 1 x every 28 days	13.0	1	13.0
In combination with intranasal corticosteroids				
Budesonide	Continuously, 2 x daily	365.0	1	365.0
Mometasone	Continuously, 1 x daily	365.0	1	365.0
Appropriate comparator therapy				
Dupilumab or omalizumab or mepolizumab, each in combination with intranasal corticosteroids (budesonide or mometasone furoate)				
Dupilumab	Continuously, 1 x every 14 days	26.1	1	26.1
Mepolizumab	Continuously, 1 x every 28 days	13.0	1	13.0
Omalizumab	Continuously, 1 x every 14 days - 1 x every 28 days	13.0 - 26.1	1	13.0 - 26.1
In each case, in combination with intranasal corticosteroids				
Budesonide	Continuously, 2 x daily	365.0	1	365.0
Mometasone	Continuously, 1 x daily	365.0	1	365.0

Consumption:

The consumption of omalizumab was calculated on the basis of dosages depending on body weight (BW), using the average body weight taken from the official representative statistics "Microcensus 2021 – body measurements of the population" (average body weight: 77.7 kg)[4].

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

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed:					
Tezepelumab	210 mg	210 mg	1 x 210 mg	13.0	13 x 210 mg
In combination with intranasal corticosteroids					
Budesonide	0.1 mg – 0.2 mg	0.2 mg – 0.4 mg	4 x 0.05 mg – 8 x 0.05 mg	365.0	1,460 puffs 0.05 mg each – 2,920 puffs 0.05 mg each
Mometasone	0.1 mg – 0.4 mg	0.1 mg – 0.4 mg	2 x 0.05 mg – 8 x 0.05 mg	365.0	730 puffs 0.05 mg each – 2,920 puffs 0.05 mg each
Appropriate comparator therapy					
Dupilumab or omalizumab or mepolizumab, each in combination with intranasal corticosteroids (budesonide or mometasone furoate)					
Dupilumab	300 mg	300 mg	1 x 300 mg	26.1	26.1 x 300 mg
Mepolizumab	100 mg	100 mg	1 x 100 mg	13.0	13 x 100 mg
Omalizumab	150 mg – 600 mg	150 mg – 600 mg	1 x 150 mg – 4 x 150 mg	13.0 - 26.1	13 x 150 mg – 104.4 x 150 mg
In each case, in combination with intranasal corticosteroids					
Budesonide	0.1 mg – 0.2 mg	0.2 mg – 0.4 mg	4 x 0.05 mg – 8 x 0.05 mg	365.0	1,460 puffs 0.05 mg each – 2,920 puffs 0.05 mg each
Mometasone	0.1 mg – 0.4 mg	0.1 mg – 0.4 mg	2 x 0.05 mg – 8 x 0.05 mg	365.0	730 puffs 0.05 mg each – 2,920 puffs 0.05 mg each

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:

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:					
Tezepelumab 210 mg	3 PEN	€ 3,384.01	€ 1.77	€ 189.97	€ 3,192.27
Budesonide 0.05 mg[5]	2 NDS	€ 30.87	€ 1.77	€ 1.55	€ 27.55
Mometasone 0.05 mg[5]	2 NAS	€ 26.33	€ 1.77	€ 1.19	€ 23.37
Appropriate comparator therapy					
Dupilumab 300 mg	6 SFI	€ 3,886.33	€ 1.77	€ 218.66	€ 3,665.90
Mepolizumab 100 mg	3 SFI	€ 3,731.92	€ 1.77	€ 0.00	€ 3,730.15
Omalizumab 150 mg	10 SFI	€ 4,172.18	€ 1.77	€ 234.98	€ 3,935.43
Budesonide 0.05 mg[5]	2 NDS	€ 30.87	€ 1.77	€ 1.55	€ 27.55
Mometasone 0.05 mg[5]	2 NAS	€ 26.33	€ 1.77	€ 1.19	€ 23.37
Abbreviations: SFI = solution for injection; NAS = nasal spray; NDS = nasal dosing spray; PEN = solution for injection in a pre-filled pen					

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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.

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 evaluated and the

[5] Fixed reimbursement rate

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

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

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

Basic principles of the assessed medicinal product

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

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

A designation is also not considered if the G-BA have decided on an exemption as a reserve antibiotic for the assessed medicinal product in accordance with Section 35a, paragraph 1c, sentence 1 SGB V. The additional benefit is deemed to be proven if the G-BA have decided on an exemption for a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V; the extent of the additional benefit and its therapeutic significance are not to be assessed by the G-BA. Due to the lack of an assessment mandate by the G-BA following the resolution on an exemption according to Section 35a, paragraph 1c, sentence 1 SGB V with regard to the extent of the additional benefit and the therapeutic significance of the reserve antibiotic to be assessed, there is a limitation due to the procedural privileging of the pharmaceutical companies to the effect that neither the proof of an existing nor an expected at least considerable additional benefit is possible for exempted reserve antibiotics in the procedures according to Section 35a paragraph 1 or 6 SGB V and Section 35a paragraph 1d SGB V. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V must therefore also be taken into account at the level of designation according to Section 35a, paragraph 3, sentence 4 SGB V in order to avoid valuation contradictions.

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

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

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

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

Concomitant active ingredient

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

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

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

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

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

Furthermore, the product information of the assessed medicinal product must not contain any specific information that excludes its use in combination therapy with the eligible concomitant active ingredient in the assessed therapeutic indication under marketing authorisation regulations.

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

Designation

The medicinal products which have been determined as concomitant active ingredients in

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

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

Exception to the designation

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

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

Legal effects of the designation

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

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

Justification for the findings on designation in the present resolution:

Adults with severe chronic rhinosinusitis with nasal polyps (CRSwNP) for whom therapy with systemic corticosteroids, and/or surgery do not provide adequate disease control

No medicinal product with new active ingredients for use in combination therapy in compliance with the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

References:
Product information for tezepelumab (Tezspire); Tezspire 210 mg solution for injection in a pre-filled syringe; Tezspire 210 mg solution for injection in a pre-filled pen; last revised: October 2025

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 11 June 2025, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 9 October 2025, the pharmaceutical company submitted a dossier for the benefit assessment of tezepelumab to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 2, sentence 2 VerfO.

By letter dated 17 November 2025 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 tezepelumab.

The dossier assessment by the IQWiG was submitted to the G-BA on 11 February 2026, and the written statement procedure was initiated with publication on the G-BA website on 16 February 2026. The deadline for submitting statements was 9 March 2026.

The oral hearing was held on 23 March 2026.

By letter dated 24 March 2026, the IQWiG was commissioned with a supplementary assessment of data submitted in the written statement procedure. The addendum prepared by IQWiG was submitted to the G-BA on 17 April 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 conclusively discussed at the Subcommittee's session on 28 April 2026, and the draft resolution was approved.

At their session on 7 May 2026, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	11 June 2025	Determination of the appropriate comparator therapy
Working group Section 35a	17 March 2026.	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	23 March 2026	Conduct of the oral hearing, commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	31 March 2026 21 April 2026	Consultation on the dossier assessment by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	28 April 2026	Concluding discussion of the draft resolution
Plenum	7 May 2026	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 7 May 2026

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

Prof. Hecken