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
Sotatercept (new therapeutic indication: pulmonary arterial hypertension, WHO Functional Class IV)

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

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

According to Section 35a paragraph 3 SGB V, the G-BA 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 sotatercept (Winrevair) was listed for the first time on 15 September 2024 in the "LAUER-TAXE®", the extensive German registry of available medicinal products and their prices.

On 19 January 2026, sotatercept 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 16 February 2026, 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 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 sotatercept with the new therapeutic indication "Winrevair, in combination with other pulmonary arterial hypertension (PAH) therapies, is indicated for the treatment of PAH in adult patients with WHO Functional Class (FC) IV".

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 15 May 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 sotatercept 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, and the statements submitted in the written statement and oral hearing procedure, as well of the addendum drawn up by the IQWiG on the benefit assessment. 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 sotatercept.

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 sotatercept (Winrevair) in accordance with the product information

Winrevair, in combination with other pulmonary arterial hypertension (PAH) therapies, is indicated for the treatment of PAH in adult patients with WHO Functional Class (FC) II, III, and IV.

Therapeutic indication of the resolution (resolution of 06.08.2026):

Winrevair, in combination with other pulmonary arterial hypertension (PAH) therapies, is indicated for the treatment of PAH in adult patients with WHO Functional Class (FC) IV.

[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 pulmonary arterial hypertension (PAH) of WHO Functional Class (WHO FC) IV

Appropriate comparator therapy for sotatercept in combination with other PAH therapies:

Individualised therapy with selection of the following triple therapies:

- Parenteral PCA[2] (epoprostenol, treprostinil) + ERA[3] (ambrisentan, bosentan, macitentan) + PDE5[4]inhibitor (sildenafil, tadalafil)
- Parenteral PCA (epoprostenol, treprostinil) + ERA (ambrisentan, bosentan, macitentan) + sGC stimulator[5] (riociguat)

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

[2] Prostacyclin analogue (PCA)
[3] Endothelin receptor antagonist (ERA)
[4] Phosphodiesterase type 5 inhibitor
[5] Soluble guanylate cyclase (sGC) stimulator

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.

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

On 1. Apart from the active ingredient sotatercept to be assessed, epoprostenol is the only active ingredient approved for the therapeutic indication of PAH of WHO Functional Class IV.

On 2. A lung transplant or heart-lung transplant is, in principle, a therapy option for patients with FC IV PAH. Lung transplant cannot be assumed to be a regular therapy option for patients in the present therapeutic indication as the feasibility of lung transplant is largely determined by patient-individual criteria, including comorbidities, as well as the limited availability of suitable donor organs.

On 3. With regard to pulmonary arterial hypertension, there are resolutions of the G-BA on the benefit assessment of medicinal products with new active ingredients in accordance with Section 35a SGB V:

- sotatercept (resolution of 6 March 2025)
- riociguat (resolution of 3 September 2020, resolution of 21 December 2023)
- macitentan (resolution of 6 April 2017)
- selexipag (resolution of 15 December 2016)

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 indication according to Section 35a paragraph 7 SGB V (see “Information on Appropriate Comparator Therapy”).

Apart from the prostacyclin analogue (PCA) epoprostenol, no other active ingredients are approved for the treatment of patients with WHO FC IV PAH. Overall, it should be emphasised that the available evidence in this therapeutic indication is very limited. The only current guideline available containing treatment recommendations for subjects with PAH is the 2022 ESC/ERS guideline[6]. Although the guideline has methodological limitations and the therapy recommendations it contains do not sufficiently meet international standards of evidence-based medicine, this guideline is used to determine the appropriate comparator therapy in the absence of higher-quality evidence.

For the treatment of pulmonary arterial hypertension, the ESC/ERS guideline recommends a stepwise regimen that is based, among other factors, on individual risk stratification according to estimated one-year mortality. For subjects without concomitant cardiopulmonary conditions who are at low or intermediate risk, combination therapy comprising endothelin receptor antagonists (ERA) and phosphodiesterase type 5 inhibitors (PDE5I) is recommended as the initial pharmacotherapy (Class of Recommendation [CoR] I, Level of Evidence [LoE] B). This combination therapy should be adjusted in the further course of treatment, depending on the specific risk. For subjects with an intermediate-to-low one-year mortality risk despite ERA/PDE5I therapy, combination therapy comprising ERA and PDE5I may be supplemented with a prostacyclin receptor agonist (selexipag) (CoR IIa, LoE B) or the PDE5I component may be replaced by soluble guanylate cyclase stimulators (riociguat) (CoR IIb, LoE B). In subjects with an intermediate-to-high or high one-year mortality risk, ERA/PDE5I combination therapy should be supplemented with parenteral PCA (CoR IIa, LoE C). For subjects with a high one-year mortality risk at the time of diagnosis, triple therapy comprising a PDE5I, an ERA and a parenteral PCA should be considered for initial pharmacotherapy (CoR IIa, LoE C).

Patients have a high one-year mortality risk in the therapeutic indication - WHO FC IV PAH - under assessment. For this patient group, escalation of the existing treatment is indicated where possible. Based both on the guideline recommendation and on feedback from clinical experts, the addition of a parenteral PCA (epoprostenol, treprostinil) is the primary option for therapy escalation. It should be noted that the active ingredient treprostinil is not approved for the treatment of WHO FC IV PAH. However, clinicians emphasised that, within the German healthcare context, the active ingredient treprostinil plays a key role in the treatment of WHO FC IV PAH. In particular, for patients who are already receiving the active ingredient treprostinil, a switch to the approved epoprostenol is not indicated upon transition to WHO FC IV. Given the current medical treatment situation, it is understandable that patients in WHO FC IV may also receive a treprostinil-based triple therapy in addition to epoprostenol-based triple therapy.

Furthermore, in accordance with the ESC/ERS guideline, switching from a PDE5 inhibitor to an sGC stimulator (riociguat) is also an option for subjects with a low-to-intermediate one-year mortality risk as part of their previous course of treatment. Treatment with an sGC stimulator, like treatment with ERAs and PDE5 inhibitors, is approved for WHO FC II and III, but not for WHO FC IV. Nevertheless, even when patients progress to WHO FC IV, it is medical treatment practice for them to continue their current treatment chosen from the therapy options approved for less severe WHO

[6] Humbert M et al. 2022, ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Heart J 2022;43(38):3618-3731, https://doi.org/10.1183/13993003.00879-2022

functional classes. A further switch from an sGC stimulator to a PDE5 inhibitor is therefore not indicated in this treatment setting.

PAH, as classified by WHO FC IV, is a serious, potentially fatal condition. Given the rarity of the condition, there are no large, randomised studies in this therapeutic indication that would be necessary to establish stronger evidence. The only active ingredient explicitly approved for the treatment of WHO Class IV PAH is epoprostenol. Each of the active ingredients in the product classes - ERAs, PDE5 inhibitors and sGC stimulators - has a marketing authorisation restricted to WHO FC II and III. However, in accordance with the generally recognised state of medical knowledge, it must be noted that the off-label use of these therapy options for continuing treatment upon transition to WHO FC IV is medically essential. It is clear both from the available evidence[6] and from the clinicians' comments that continuing treatment with ERAs (ambrisentan, bosentan, macitentan), PDE5 inhibitors (sildenafil, tadalafil) or sGC stimulators (riociguat) in the therapeutic indication under assessment is considered part of the therapy standard and is generally preferable to discontinuing these active ingredients (Section 6, paragraph 2, sentence 3, number 2 AM-NutzenV). With reference to the above comments on the active ingredient treprostinil, it should also be noted that, within the framework of the recommended triple therapy comprising parenteral PCA + ERA + PDE5 inhibitor or sGC stimulator, not all patients with WHO Class IV PAH are eligible for the approved active ingredient epoprostenol. In accordance with the generally recognised state of medical knowledge, it must be established in the overall assessment that the off-label use of treprostinil for the triple therapy of relevant patient groups is considered the therapy standard in the therapeutic indication to be assessed and is generally preferable to the epoprostenol approved in the therapeutic indication (Section 6, paragraph 2, sentence 3, number 3 AM-NutzenV).

In the overall assessment, an Individualised therapy with selection of the triple therapies "parenteral PCA (epoprostenol, treprostinil) + ERA (ambrisentan, bosentan, macitentan) + PDE5 inhibitor (sildenafil, tadalafil)" and "parenteral PCA (epoprostenol, treprostinil) + ERA (ambrisentan, bosentan, macitentan) + sGC stimulator (riociguat)" constitutes the appropriate comparator therapy for sotatercept in combination with other PAH therapies for the treatment of adults with WHO Class IV PAH. Individualised therapy is based on the assumption that several treatment options, which allow an individualised medical treatment decision, are available.

The treatment of subjects with PAH of Functional Class IV therefore focuses on a patient-individual triple therapy comprising a parenteral PCA combined with an ERA and either a PDE5 inhibitor or an sGC stimulator.

The available evidence contains recommendations for non-medicinal physiotherapy measures to improve symptomatology and physical performance. Physiotherapy interventions as defined in the Remedies Directive (physical therapy, e.g. remedial gymnastics, exercise therapy, respiratory therapy) may be suitable for all patients and, where indicated, should be made available in addition to medicinal therapy in both arms of the study.

Change in the appropriate comparator therapy:

The appropriate comparator therapy originally specified for patients with WHO FC IV PAH was a triple therapy comprising epoprostenol in combination with an ERA (ambrisentan, bosentan, macitentan) and a PDE5 inhibitor (sildenafil, tadalafil).

However, clinicians explained in the written statement procedure that the specific appropriate comparator therapy did not adequately reflect the medical treatment situation in Germany. The G-BA take this as an opportunity to review the appropriate comparator therapy within the scope of the benefit assessment procedure, taking into account the statements of clinical experts and the criteria set out in Chapter 5, Section 6, paragraph 3 VerfO.

Data from the COMPERA registry was used to review the standard of care. These indicate that, amongst parenteral PCAs, treprostinil is the preferred choice in Europe.[7] In the written statement procedure, clinicians confirmed the high significance of the active ingredient treprostinil in the treatment of PAH and its preferred use amongst parenteral PCAs within the German healthcare context. In particular, for patients who are already receiving the active ingredient treprostinil, a switch to the approved epoprostenol is not indicated upon transition to WHO FC IV solely due to the authorisation status.

Furthermore, in accordance with the guideline recommendation in the context of earlier treatment, the PDE5 inhibitor component may be replaced by the sGC stimulator, riociguat, in subjects with an intermediate-to-low one-year mortality risk, despite existing ERA/PDE5 inhibitor therapy. A switch back to PDE5 inhibitors is not indicated in the further course of treatment, meaning that the sGC stimulator, riociguat, may represent a suitable alternative to PDE5 inhibitors for patients with WHO FC IV PAH.

Taking into account the vulnerable patient population, the limited evidence, and German standards of care, it can be concluded overall that the off-label use of treprostinil and riociguat may also be necessary in addition to the off-label use of ERAs and PDE5 inhibitors. In the overall assessment, the G-BA therefore consider it appropriate to change the standard comparator therapy at this point in time.

Consequently, an individualised therapy with selection of the triple therapies "parenteral PCA (epoprostenol, treprostinil) + ERA (ambrisentan, bosentan, macitentan) + PDE5 inhibitor (sildenafil, tadalafil)" and "parenteral PCA (epoprostenol, treprostinil) + ERA (ambrisentan, bosentan, macitentan) + sGC stimulator (riociguat)" is determined to be the appropriate comparator therapy for sotatercept in combination with other PAH therapies for the treatment of adults with WHO FC IV PAH.

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 sotatercept is assessed as follows:

Adults with pulmonary arterial hypertension (PAH) of WHO Functional Class (WHO FC) IV

[7] Tello et al.: Add-on therapy with Parenteral Prostacyclin Analogues. Journal of Heart and Lung Transplantation 2025

Hint of non-quantifiable additional benefit.

Justification:

For the assessment of the additional benefit of sotatercept, the pharmaceutical company presented the results of the randomised, double-blind, placebo-controlled phase III ZENITH study. This study investigated adult patients with symptomatic WHO Functional Class III or IV PAH who were clinically stable but at high mortality risk (Registry to Evaluate Early and Long-Term PAH Disease Management [REVEAL] Lite 2 risk score ≥ 9).

A total of 173 patients were enrolled in the study and randomly allocated in a 1:1 ratio to receive either sotatercept or placebo in addition to their PAH background therapy. Randomisation was stratified by the REVEAL Lite 2.0 risk score (9 to 10 vs ≥ 11) and PAH subtype (with associated connective tissue disease vs without associated connective tissue disease). A total of 44 patients had WHO Functional Class IV PAH (intervention arm: N = 20, placebo arm: N = 24).

The specified PAH background therapy in the ZENITH study was a dual or triple combination therapy, according to the principal investigator's decision, consisting of at least 2 active ingredients from different product classes of ERAs, PDE5 inhibitors, sGC stimulators, prostacyclin receptor agonists (PRAs) and/or PCAs. Patients were required to have been receiving a stable dose of this PAH background therapy – at the maximum individually tolerated dose as specified by the principal investigator – for at least 30 days prior to screening, and this therapy was to be continued throughout the study, although a dose adjustment of up to 10% was permitted for parenteral PCAs.

The primary endpoint of the ZENITH study was the time to first event within a composite endpoint comprising hospitalisation ≥ 24 hours due to PAH deterioration, lung transplant or death from any cause. Additional patient-relevant endpoints were assessed in the categories of mortality, morbidity and side effects.

While the ZENITH study had no fixed duration, data cut-offs were to be specified based on the number of events occurring in the primary endpoint. A final analysis was originally planned for the point at which approximately 118 events had occurred in the primary endpoint (after approximately 40 months). This pre-specified final analysis was not carried out as the study was terminated prematurely by an external Data Monitoring Committee following the results of the interim analysis.

This assessment is based on the results of the final data cut-off from 6 June 2025. The median and mean treatment duration and duration of observation of patients in the intervention arm of the relevant sub-population were significantly longer than those in the comparator arm since the end of treatment was event-driven by the primary endpoint of disease progression and follow-up ended shortly after the end of treatment. As of the final data cut-off, the median treatment duration was 64.5 weeks in the intervention arm and 37.4 weeks in the comparator arm.

Implementation of the appropriate comparator therapy

As part of the written statement procedure, the pharmaceutical company also submitted information on the combinations of active ingredients used in the ZENITH study, as well as the reasons for not using a triple therapy.

The placebo arm comprised a total of 24 subjects. Seventeen of these patients (approx. 71%) received a triple therapy, of whom 11 (approx. 46%) received a triple therapy comprising parenteral PCA + ERA + PDE5 inhibitor/ sGC stimulator. A further 6 subjects (25%) received a

triple therapy comprising an inhaled or oral PCA or a prostacyclin receptor agonist (PRA). No reasons were documented as to why these patients did not receive parenteral PCA. It is therefore unclear whether therapy escalation would still have been possible for these patients using a parenteral PCA.

In addition, 7 patients (approx. 29%) in the placebo arm received dual therapy. There were valid reasons for dual therapy for 4 of these patients (approx. 17%), so it can be assumed that further therapy escalation was no longer possible for them. It was also evident from the explanations made by clinicians in the written statement procedure that some patients are not eligible for triple therapy with a parenteral PCA despite being in the severe stage of the disease (WHO FC IV).

Taken together, significant uncertainties regarding the implementation of the appropriate comparator therapy therefore remain. It is unclear why a significant percentage of the study participants did not receive therapy escalation in line with the specified appropriate comparator therapy, or whether therapy escalation was, in fact, no longer possible for them. Given the specific data basis available, the ZENITH study is used for the benefit assessment despite these uncertainties.

Extent and probability of the additional benefit

Mortality

Two analyses of overall survival were presented:

The primary analysis takes into account death from any cause, with the exception of events that occurred following lung transplant or entry into the SOTERIA extension study. The sensitivity analysis takes into account death from any cause, including events that occurred following lung transplant or entry into the SOTERIA extension study; however, patients in the comparator arm of the ZENITH study who received sotatercept in the SOTERIA extension study will continue to be treated as patients in the placebo arm.

For the endpoint of overall survival, there was no statistically significant difference between the treatment groups, either in the primary analysis or in the sensitivity analysis.

Morbidity

Disease progression

The endpoint of disease progression is a composite endpoint, operationalised as death from any cause, lung transplant or hospitalisation ≥ 24 hours due to PAH deterioration (adjudicated by a blinded committee). All 3 individual components are considered patient-relevant, and the endpoint of disease progression is used for the benefit assessment.

For the endpoint of disease progression, operationalised as death from any cause, lung transplant or hospitalisation ≥ 24 hours due to PAH deterioration, there was a statistically significant difference to the advantage of sotatercept compared with the comparator arm.

Walking ability (6MWT)

Walking ability and physical resilience were assessed using the 6-minute walk test. For the 6-minute walk test (6MWT) endpoint, the pre-specified analysis of the median difference between the treatment arms at week 24 is presented. There was no statistically significant difference between the treatment groups.

Dyspnoea

For the endpoint of dyspnoea, assessed using the Borg-CR10 scale, there was no statistically significant difference between the treatment groups. However, there was an effect modification by the characteristic "Registry to Evaluate Early and Long-Term PAH Disease Management (REVEAL) Lite 2.0 risk score": For patients with a REVEAL Lite 2.0 risk score ≥ 11 at the start of the study, there was a statistically significant advantage of sotatercept compared with the comparator arm (HR 6.69 [1.38; 32.38]; p value 0.018). By contrast, no statistically significant difference was observed for patients with a REVEAL Lite 2.0 risk score between 9 and 10 at the start of the study.

Health status (EQ-5D VAS)

The health status was assessed using the visual analogue scale (VAS) of the EQ-5D questionnaire. There was no statistically significant difference between the treatment groups as of the final data cut-off.

Quality of life

No data on health-related quality of life were collected in the ZENITH study.

Side effects

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

Overall assessment

ZENITH study results for the endpoint categories of mortality, morbidity and side effects are available for the assessment of the additional benefit of sotatercept in combination with other PAH treatments in adults with WHO FC IV PAH. The study compared sotatercept with placebo, with all study participants also receiving PAH background therapy. Overall, there are uncertainties regarding the implementation of the appropriate comparator therapy, as it is unclear for what percentage of the study participants therapy escalation, as defined by the specified appropriate comparator therapy, was in fact no longer possible. Given the specific data basis available, the ZENITH study is used for the benefit assessment despite these uncertainties.

For overall survival, there is no statistically significant difference between the treatment arms.

Results are available for the endpoints of disease progression, walking ability, dyspnoea and health status in the endpoint category of morbidity.

For the endpoint of disease progression, operationalised as death from any cause, lung transplant or hospitalisation ≥ 24 hours due to PAH deterioration, there was a clear advantage of sotatercept compared with the comparator arm.

For the endpoint of dyspnoea, assessed using the Borg-CR10 scale, there was no statistically significant difference between the treatment groups in the total population. However, analysis of an effect modification showed an advantage of sotatercept over the comparator arm in subjects with a REVEAL Lite 2.0 risk score ≥ 11 at the start of the study.

For the endpoints of walking ability (6MWT) and health status (EQ-5D VAS), there was no statistically significant difference between the treatment groups in either case.

No data were collected for the endpoint category of health-related quality of life.

For the endpoints of SAEs or discontinuation due to AEs in the endpoint category of side effects, there was no statistically significant difference between the treatment groups in either case.

The overall assessment showed an additional benefit of sotatercept in combination with other PAH treatments in adults with WHO FC IV PAH, largely due to the demonstrated significant advantage in the endpoint of disease progression; however, the extent of this additional benefit cannot be quantified due to uncertainties regarding the implementation of the appropriate comparator therapy.

Reliability of data (probability of additional benefit)

The present assessment is based on the results of the randomised, double-blind, placebo-controlled phase III ZENITH study.

The risk of bias at study level and in relation to the endpoints of disease progression and discontinuation due to AEs is considered to be low.

For the endpoints of overall survival (primary analysis), walking ability (6MWT), dyspnoea (Borg-CR10 scale) and health status (EQ-5D VAS), the risk of bias due to incomplete observations is assessed as high. There is also a high risk of bias in the sensitivity analysis of overall survival, as patients in the comparator arm who had entered the extension study were also treated with sotatercept but continued to be assigned to the placebo arm. For the endpoint of SAEs, there is a high risk of endpoint-specific bias, as the data provided suggest that a high percentage of potentially disease-related events are included in the analyses presented.

There are also uncertainties regarding the implementation of the appropriate comparator therapy as it is unclear whether further therapy escalation would have been possible for a significant percentage of the study participants. Consequently, only a low reliability of data can be attributed to any of the results.

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 sotatercept.

Winrevair was approved as an orphan drug. A standard assessment of the new therapeutic indication is carried out as the EUR 30 million turnover limit has been exceeded.

The therapeutic indication assessed here is as follows: Sotatercept, in combination with other pulmonary arterial hypertension (PAH) therapies, is indicated for the treatment of PAH in adult patients with WHO Functional Class (FC) IV.

The G-BA determined the appropriate comparator therapy to be an individualised therapy with selection of the following triple therapies: "parenteral PCA (epoprostenol, treprostinil) + ERA (ambrisentan, bosentan, macitentan) + PDE5 inhibitor (sildenafil, tadalafil)" and "parenteral PCA (epoprostenol, treprostinil) + ERA (ambrisentan, bosentan, macitentan) + sGC stimulator (riociguat)".

For the assessment of the additional benefit of sotatercept, the pharmaceutical company presented the results of the randomised, double-blind, placebo-controlled phase III ZENITH study for the sub-population with WHO FC IV PAH. All study participants received PAH background therapy. Overall, there are uncertainties regarding the implementation of the appropriate comparator therapy. Given the specific data basis available, the ZENITH study is used for the benefit assessment despite these uncertainties.

For the endpoint of overall mortality, there was no statistically significant difference between the treatment groups.

For the endpoint of disease progression in the endpoint category of morbidity, there was a clear advantage of sotatercept over the comparator arm. For the endpoint of dyspnoea, there was no statistically significant difference between the treatment groups in the total population. However, analysis of an effect modification showed an advantage of sotatercept over the comparator arm in subjects with a REVEAL Lite 2.0 risk score ≥ 11 at the start of the study. For the endpoints of walking ability and health status, there was no statistically significant difference between the treatment groups in either case.

No data were collected for the endpoint category of health-related quality of life.

In the endpoint category of side effects, there was no statistically significant difference between the treatment groups.

Overall, an additional benefit was identified largely due to the demonstrated significant advantage in the endpoint of disease progression; however, the extent of this additional benefit cannot be quantified due to uncertainties regarding the implementation of the appropriate comparator therapy.

The significance of the evidence is classified in the hint category. In addition to a high risk of bias at the level of some endpoints, the uncertainties regarding the implementation of the appropriate comparator therapy mean that only a low reliability of data can be attributed to any of the results.

In summary, a hint of non-quantifiable additional benefit of sotatercept over the appropriate comparator therapy was identified.

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

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

The resolution is based on information provided by the pharmaceutical company in the dossier on the benefit assessment. It may well be an underestimate. This is largely due to the fact that only patients documented in the COMPERA registry were taken into account. Furthermore, uncertainties remain as the details of the COMPERA registry search cannot be verified in full.

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 Winrevair (active ingredient: sotatercept) at the following publicly accessible link (last access: 22 June 2026):

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

Treatment with sotatercept should only be initiated and monitored by specialists experienced in the therapy of pulmonary arterial hypertension.

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 June 2026).

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

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

The prostacyclin analogues epoprostenol and treprostinil (OLU) are administered as a long-term continuous infusion via a central venous catheter. It is not possible to present the treatment costs due to the dosages that are different from patient to patient.

The endothelin receptor antagonists (ambrisentan, bosentan, macitentan), the phosphodiesterase type 5 inhibitors (sildenafil, tadalafil), and the sGC stimulator (riociguat) are approved for the treatment of PAH, but not in WHO FC IV. For the calculation of treatment costs, the requirements in the product information on the treatment of PAH in the other WHO functional classes are used.

Treatment period:

Adults with pulmonary arterial hypertension (PAH) of WHO Functional Class (WHO FC) IV

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Sotatercept in combination with other PAH therapies				

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Sotatercept	Continuously, every 21 days	17.4	1	17.4
Individual components of PAH background therapy:				
ERA				
Ambrisentan	Continuously, 1 x daily	365.0	1	365.0
Bosentan	Continuously, 2 x daily	365.0	1	365.0
Macitentan	Continuously, 1 x daily	365.0	1	365.0
PDE5I				
Sildenafil	Continuously, 3 x daily	365.0	1	365.0
Tadalafil	Continuously, 1 x daily	365.0	1	365.0
sGC stimulator				
Riociguat	Continuously, 3 x daily	365.0	1	365.0
Parenteral PCA				
Epoprostenol	Different from patient to patient			
Treprostinil	Different from patient to patient			
Appropriate comparator therapy: Individualised therapy with selection of the following triple therapies: parenteral PCA (epoprostenol, treprostinil) + ERA (ambrisentan, bosentan, macitentan) + PDE5 inhibitor (sildenafil, tadalafil) or parenteral PCA (epoprostenol, treprostinil) + ERA (ambrisentan, bosentan, macitentan) + sGC stimulator (riociguat)				
Individual components of the PAH triple therapy:				
ERA				
Ambrisentan	Continuously, 1 x daily	365.0	1	365.0
Bosentan	Continuously, 2 x daily	365.0	1	365.0
Macitentan	Continuously, 1 x daily	365.0	1	365.0
PDE5I				

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Sildenafil	Continuously, 3 x daily	365.0	1	365.0
Tadalafil	Continuously, 1 x daily	365.0	1	365.0
sGC stimulator				
Riociguat	Continuously, 3 x daily	365.0	1	365.0
Parenteral PCA				
Epoprostenol	Different from patient to patient			
Treprostinil	Different from patient to patient			

Consumption:

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.

For dosages depending on body weight (BW), the average body measurements from the official representative statistics "2025 Microcensus – body measurements of the population"[8] were applied (average body weight of subjects 18 years of age and older: 78.3 kg).

Adults with pulmonary arterial hypertension (PAH) of WHO Functional Class (WHO FC) IV

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					
Sotatercept in combination with other PAH therapies					
Sotatercept	0.7 mg/kg BW = 54.81 mg	1.1 ml	1 x 60 mg	17.4	17.4 x 60 mg

[8] 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
Individual components of PAH background therapy:					
ERA					
Ambrisentan	5 mg – 10 mg	5 mg – 10 mg	1 x 5 mg – 1 x 10 mg	365.0	365 x 5 mg – 365 x 10 mg
Bosentan	125 mg	250 mg	2 x 125 mg	365.0	730 x 125 mg
Macitentan	10 mg	10 mg	1 x 10 mg	365.0	365 x 10 mg
PDE5I					
Sildenafil	20 mg	60 mg	3 x 20 mg	365.0	1,095 x 20 mg
Tadalafil	40 mg	40 mg	2 x 20 mg	365.0	730 x 20 mg
sGC stimulator					
Riociguat	1 mg - 2.5 mg	3 mg - 7.5 mg	3 x 1 mg - 3 x 2.5 mg	365.0	1,095 x 1 mg - 1,095 x 2.5 mg
Parenteral PCA					
Epoprostenol	Different from patient to patient				
Treprostinil	Different from patient to patient				
Appropriate comparator therapy					
Individual components of the PAH triple therapy:					
Endothelin receptor antagonists					
Ambrisentan	5 mg – 10 mg	5 mg – 10 mg	1 x 5 mg – 1 x 10 mg	365.0	365 x 5 mg – 365 x 10 mg
Bosentan	125 mg	250 mg	2 x 125 mg	365.0	730 x 125 mg
Macitentan	10 mg	10 mg	1 x 10 mg	365.0	365 x 10 mg
Phosphodiesterase type 5 inhibitors					
Sildenafil	20 mg	60 mg	3 x 20 mg	365.0	1,095 x 20 mg
Tadalafil	40 mg	40 mg	2 x 20 mg	365.0	730 x 20 mg
sGC stimulator					
Riociguat	1 mg -	3 mg -	3 x 1 mg -	365.0	1,095 x 1 mg -
	2.5 mg	7.5 mg	3 x 2.5 mg		1,095 x 2.5 mg
Prostacyclin analogues					

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Epoprostenol	Different from patient to patient				
Treprostinil	Different from patient to patient				

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:

Adults with pulmonary arterial hypertension (PAH) of WHO Functional Class (WHO FC) IV

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					
Sotatercept 60 mg	2 PSI	€ 11,997.28	€ 1.77	€ 681.87	€ 11,313.64
Ambrisentan 5 mg[9]	60 FCT	€ 3,007.15	€ 1.77	€ 240.64	€ 2,764.74
Ambrisentan 10 mg[9]	60 FCT	€ 3,134.59	€ 1.77	€ 251.04	€ 2,881.78
Bosentan 125 mg[9]	120 FCT	€ 3,134.59	€ 1.77	€ 251.04	€ 2,881.78
Epoprostenol 0.5 mg	1 PIF	€ 146.41	€ 1.77	€ 17.09	€ 127.55
Epoprostenol 1.5 mg	1 PIF	€ 236.04	€ 1.77	€ 28.43	€ 205.84
Macitentan 10 mg[9]	30 FCT	€ 1,573.14	€ 1.77	€ 0.00	€ 1,571.37
Riociguat 1 mg	84 FCT	€ 1,585.47	€ 1.77	€ 87.25	€ 1,496.45
Riociguat 2.5 mg	294 FCT	€ 5,405.04	€ 1.77	€ 305.39	€ 5,097.88
Sildenafil 20 mg[9]	30 FCT	€ 72.23	€ 1.77	€ 4.82	€ 65.64
Tadalafil 20 mg[9]	12 FCT	€ 37.84	€ 1.77	€ 2.10	€ 33.97
Treprostinil 10 mg	1 INF	€ 2,234.71	€ 1.77	€ 298.92	€ 1,934.02

[9] Fixed reimbursement rate

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Treprostinil 200 mg	1 INF	€ 15,555.41	€ 1.77	€ 758.64	€ 14,795.00
Appropriate comparator therapy					
Ambrisentan 5 mg	60 FCT	€ 3,007.15	€ 1.77	€ 240.64	€ 2,764.74
Ambrisentan 10 mg[9]	60 FCT	€ 3,134.59	€ 1.77	€ 251.04	€ 2,881.78
Bosentan 125 mg[9]	120 FCT	€ 3,134.59	€ 1.77	€ 251.04	€ 2,881.78
Epoprostenol 0.5 mg	1 PIF	€ 146.41	€ 1.77	€ 17.09	€ 127.55
Epoprostenol 1.5 mg	1 PIF	€ 236.04	€ 1.77	€ 28.43	€ 205.84
Macitentan 10 mg[9]	30 FCT	€ 1,573.14	€ 1.77	€ 0.00	€ 1,571.37
Riociguat 1 mg	84 FCT	€ 1,585.47	€ 1.77	€ 87.25	€ 1,496.45
Riociguat 2.5 mg	294 FCT	€ 5,405.04	€ 1.77	€ 305.39	€ 5,097.88
Sildenafil 20 mg[9]	30 FCT	€ 72.23	€ 1.77	€ 4.82	€ 65.64
Tadalafil 20 mg[9]	12 FCT	€ 37.84	€ 1.77	€ 2.10	€ 33.97
Treprostinil 10 mg	1 INF	€ 2,103.90	€ 1.77	€ 267.12	€ 1,835.01
Treprostinil 200 mg	1 INF	€ 15,555.41	€ 1.77	€ 758.64	€ 14,795.00
Abbreviations: FCT = film-coated tablets; INF = infusion solution; SON = solution for a nebuliser; PIF = powder for the preparation of an infusion solution; PSI = powder and solvent for solution for injection					

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

3. Bureaucratic costs calculation

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

4. Process sequence

The Subcommittee on Medicinal Products determined the appropriate comparator therapy at their session on 25 November 2025.

On 16 February 2026, the pharmaceutical company submitted a dossier for the benefit assessment of sotatercept to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 2 VerfO.

By letter dated 16 February 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 sotatercept.

The dossier assessment by the IQWiG was submitted to the G-BA on 7 May 2026, and the written statement procedure was initiated with publication on the G-BA website on 15 May 2026. The deadline for submitting written statements was 5 June 2026.

The oral hearing was held on 22 June 2026.

By letter dated 23 June 2026, the IQWiG was commissioned with a supplementary assessment. The addendum prepared by the IQWiG was submitted to the G-BA on 10 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 28 July 2026, and the draft resolution was conclusively discussed.

At their session on 6 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	25 November 2025	Determination of the appropriate comparator therapy
Working group Section 35a	16 June 2026	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	22 June 2026	Conduct of the oral hearing, commissioning of the IQWiG with the supplementary assessment of documents

Working group Section 35a	1 July 2026 15 July 2026	Consultation on the dossier assessment by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	28 July 2026	Concluding discussion of the draft resolution
Plenum	6 August 2026	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 6 August 2026

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

Dr Optendrenk