Gemeinsamer Bundesausschuss

Justification

to 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
Omaveloxolone (reassessment of an orphan drug after exceeding the EUR 30 million turnover limit (Friedreich's ataxia, ≥ 16 years)

of 18 December 2025

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,
7. number of study participants who participated in the clinical studies at study sites within the scope of SGB V, and total number of study participants.

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 pass a resolution 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 omaveloxolone (Skyclarys) was listed for the first time on 15 March 2024 in the “LAUER-TAXE®”, the extensive German registry of available drugs and their prices. Skyclarys for the treatment of Friedreich's ataxia in adults and adolescents aged 16 years and older is approved as a medicinal product for the treatment of rare diseases in accordance with Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999.

At their session on 19 September 2024, the G-BA decided on the benefit assessment of omaveloxolone in the therapeutic indication "Treatment of Friedreich’s ataxia in adults and adolescents aged 16 years and older" according to Section 35a SGB V.

If the sales of the orphan drug through the statutory health insurance at pharmacy sales prices and outside the scope of SHI-accredited medical care, including value-added tax, exceed an amount of € 30 million in the last twelve calendar months, the pharmaceutical company must submit evidence in accordance with Chapter 5 Section 5, paragraphs 1 to 6 Rules of Procedure (VerfO) within three months of being requested to do so by the Federal Joint Committee, and must demonstrate the additional benefit compared to the appropriate comparator therapy in this evidence.

By letter dated 19 March 2025, the pharmaceutical company was requested to submit a dossier for benefit assessment according to Section 35a SGB V by 1 July 2025 due to exceeding the EUR 30 million turnover limit within the period from 15 March 2024 (market launch) up to and including 20 February 2025 (receipt of feedback on the G-BA's request for sales disclosure). The pharmaceutical company has submitted the final dossier to the G-BA in due time in accordance with Section 4, paragraph 3, number 4 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 8, paragraph 1, number 6 VerfO on 30 June 2025.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 1 October 2025 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 omaveloxolone 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. 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 omaveloxolone.

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 Omaveloxolone (Skyclarys) in accordance with the product information

Skyclarys is indicated for the treatment of Friedreich’s ataxia in adults and adolescents aged 16 years and older.

Therapeutic indication of the resolution (resolution of 18.12.2025):

See the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

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

Adults and adolescents aged 16 years and older with Friedreich's ataxia

Appropriate comparator therapy for omaveloxolone:

Best supportive care

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

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

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

According to Section 6, paragraph 2, sentence 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the determination of the appropriate comparator therapy must be based on the actual medical treatment situation as it would be without the medicinal product to be assessed. According to Section 6, paragraph 2, sentence 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the G-BA may exceptionally determine the off-label use of medicinal products as an appropriate comparator therapy or as part of the appropriate comparator therapy if 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. Besides omaveloxolone, there are no approved medicinal products for the therapeutic indication of Friedreich's ataxia.

On 2. Non-medicinal measures are generally measures in accordance with the Remedies Directive or the catalogue of remedies, e.g. physiotherapy, occupational therapy, voice, speech, language and swallowing therapy.

On 3. No previous resolutions on the benefit assessment according to Section 35a SGB V are available.

On 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as systematic reviews of clinical studies in the present indication.

Overall, the evidence in the therapeutic indication of Friedreich's ataxia is limited. The S1 guideline on ataxias of adulthood[2] is considered relevant in the German healthcare context.

Besides omaveloxolone, there are no approved active ingredients available for the treatment of Friedreich's ataxia. According to the available evidence, no pharmacological treatments are recommended as standard therapy for Friedreich's ataxia.

Against this background, Best Supportive Care is determined in the overall assessment of the above-mentioned criteria as the appropriate comparator therapy for omaveloxolone for the treatment of adults and adolescents aged 16 years and older with Friedreich's ataxia. Best supportive care is defined as the therapy that provides the best possible, patient-individual, optimised supportive treatment to alleviate symptoms and improve quality of life.

Non-medicinal measures in accordance with the Remedies Directive or catalogue of remedies (physiotherapy, occupational therapy, voice, speech, language and swallowing therapy) can help to alleviate symptoms. This also applies to the pharmacological treatment of concomitant symptoms and comorbidities. These include diabetes mellitus (treatment e.g. with insulin), cardiomyopathies (treatment e.g. with beta-receptor blockers, angiotensin-converting enzyme [ACE] inhibitors, angiotensin II receptor type 2 [AT2 receptor] antagonists) and scoliosis (treatment by surgical correction if applicable).

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

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

[2] Klockgether T. et al, Ataxias of adulthood, S1 guideline, 2023, in: German Society of Neurology (ed.), Guidelines for Diagnostics and Therapy in Neurology. Online: www.dgn.org/leitlinien

2.1.3 Extent and probability of the additional benefit

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

An additional benefit is not proven.

Justification:

For the benefit assessment, the pharmaceutical company submitted evaluations from the phase II MOXIe study.

Part 2 of the MOXIe study is a multicentre, randomised, controlled, double-blind study phase to investigate the safety and efficacy of omaveloxolone compared to placebo.

Patients aged ≥ 16 and ≤ 40 years with genetically confirmed Friedreich's ataxia and a modified Friedreich's Ataxia Rating Scale (mFARS) score (in a 99-point version) ≥ 20 and ≤ 80 were enrolled.

There was a 1:1 randomisation to treatment with 150 mg omaveloxolone/day or placebo (each administered orally), stratified according to the presence of foot deformity in the form of pes cavus. The treatment was administered over a period of 48 weeks, followed by a 4-week safety follow-up.

In addition, the existing training programme was to be continued unchanged throughout the study period. The treatment of concomitant diseases should be continued at a stable dosage. The use of antispasmodics was not permitted during the study.

The pharmaceutical company submitted evaluations of a study sub-population comprising patients without severe pes cavus as primary analyses. The present therapeutic indication does not include any limitation in terms of foot deformity. The evaluations relating to the total number of randomised patients (= intention-to-treat [ITT] population) in part 2 of the MOXIe study are thus considered relevant for the benefit assessment: A total of 51 patients were assigned to the omaveloxolone arm and 52 patients to the placebo arm.

In addition, the pharmaceutical company presented evaluations of two patient populations, differentiated according to the retention of independent walking ability. In the present case, the entire target population covered by the therapeutic indication is relevant for the research question of the benefit assessment; consequently, the evaluations of the total study population are used.

On the implementation of best supportive care in the MOXIe study part 2

According to the information provided, the patients in both study arms continued an individual training programme during the course of the study.

In addition, the patients received individualised treatment for the cardiomyopathy, which included regular monitoring of heart function and medicinal treatments. Pain medication and antidepressants were also used in the study. The use of antispasmodics was not permitted in the study. In this respect, the use of baclofen in 3 patients in the intervention arm amounts to a protocol deviation.

Recommendations for the treatment of the symptoms of Friedreich's ataxia emphasise the primary significance of non-medical measures. Against this background, the appropriate comparator therapy of best supportive care is considered to be adequately implemented in the overall assessment despite the restriction with regard to the use of antispasmodic agents.

On further evaluations presented in the dossier

The pharmaceutical company presented further evaluations in the dossier as supportive evidence. This includes a comparison of omaveloxolone early start vs omaveloxolone delayed start as well as an indirect comparison of omaveloxolone and "best supportive care" (without bridge comparator) using data from the open-label extension phase of the MOXIe study and a natural history cohort from the Friedreich Ataxia Clinical Outcome Measures Study (FA-COMS).

The early-start vs delayed-start analysis does not allow a comparison of omaveloxolone versus best supportive care and is therefore not used in this benefit assessment. The evaluations based on the indirect comparison with a natural history cohort are not used due to methodological limitations, particularly with regard to confounder identification.

Extent and probability of the additional benefit

Mortality

Deaths were surveyed as part of the safety assessment. No deaths occurred.

Morbidity

Physical functioning using the modified Friedreich Ataxia Rating Scale (mFARS)

The modified Friedreich Ataxia Rating Scale (mFARS) is used to survey physical functioning in patients with Friedreich's ataxia and comprises four domains (bulbar function, upper limb coordination, lower limb coordination and upright stability). A higher score indicates a more severe physical impairment.

The evaluations presented in the dossier based on the validated 93-point version of the mFARS are used for the benefit assessment. In addition to evaluations of the mean change at week 48, data on responder analyses based on the definition of clinical improvement or deterioration by a decrease of ≤ 1.9 or an increase of ≥ 1.9 points on the mFARS are also available. The relevance threshold selected does not correspond to the relevance threshold of 15% of the scale range considered appropriate for the benefit assessment.

With regard to the evaluations of the mean change in the mFARS total score at week 48, there was a statistically significant difference between the treatment arms in favour of omaveloxolone. The 95% confidence interval of the Hedges' g effect size is however not completely outside the irrelevance range from - 0.2 to 0.2, so that it cannot be concluded that the effect is clinically relevant.

Activities of daily living using Friedreich Ataxia-Activities of Daily Living (FA-ADL)

The FA-ADL is used for patient-reported assessment of limitations in activities of daily living.

Using 9 disease-specific items on a scale from 0 (no limitation) to 4 points (unable to perform the activity), patients provide information on limitations in activities, functions and activities of daily living (speech, swallowing, eating food and handling utensils, dressing, personal hygiene, falls, walking, quality of sitting position and bladder function). The total score is the sum of the item values and can range from 0 (no limitation) to 36 points (maximum limitation).

Evaluations of the change at week 48 based on the FA-ADL were presented in the dossier. These showed no statistically significant difference between the treatment arms.

Frequency of falls

The pharmaceutical company presented evaluations on the frequency of falls in the dossier. The dossier contains the information that the data was collected in patient-reported form using a hardcopy fall diary.

All falls between screening and the end of treatment should be documented, including the date and time of each fall, the activity preceding the fall, the perceived cause of the fall, and any injuries after the fall.

The evaluation was based on the total number of falls from the start to the end of treatment, with incidence rates calculated. There was no statistically significant difference between the treatment arms.

General health status using Patient Global Impression of Change (PGI-C)

The PGI-C is used for patient-reported assessment of the change in health status compared to the start of treatment. The question on the change in health status since the start of treatment is answered using a 7-point scale of "very much improved" (= 1), "much improved" (= 2), "minimally improved" (= 3), "no change" (= 4), "minimally worse" (= 5), "much worse" (= 6) and "very much worse" (= 7).

The evaluations of responder analyses presented in the dossier based on the definition of an improvement (< 4 points) or deterioration (> 4 points) in the PGI-C are used here.

There were no statistically significant differences between the treatment arms for either deterioration or improvement at week 48.

Fine motor skills of the upper extremities using the 9-Hole Peg Test (9-HPT)

The 9-Hole Peg Test (9-HPT) is used to assess the fine motor function of the arms and hands. The time a patient takes to remove 9 pegs individually from a container, insert them into holes in a board and put them back into the container is measured. Longer test times reflect a greater impairment of the function of the upper extremities.

Fine motor function is fundamentally patient-relevant in this therapeutic indication. Data on the execution speed (pegs/second) are presented in the dossier. Evaluations of the time in seconds required to complete the task, which are considered relevant for a meaningful and comprehensible interpretation of the assessment of change in fine motor skills of the upper limbs, are not available.

Functionality of the lower extremities using the Timed 25 Foot Walk Test (T25-FWT)

The Timed 25 Foot Walk Test (T25-FWT) is used to assess walking ability. The time a patient takes to cover a distance of 25 feet (7.6 metres) is measured. Longer test times reflect a greater impairment of walking ability.

The walking ability is fundamentally patient-relevant in this therapeutic indication. The dossier shows data on walking speed. Evaluations of the time in seconds required to complete the task, which are considered relevant for a meaningful and comprehensible interpretation of the assessment of change in walking ability, are not available.

Quality of life

Short Form (36)-health survey (SF-36)

SF-36 is a generic instrument for measuring health-related quality of life, consisting of eight domains and a total of 36 questions. In addition, the 8 domains are summarised into a physical component summary (PCS) score and a mental component summary (MCS) score. For the domain and summary scores, higher values mean a better health-related quality of life.

For the benefit assessment, evaluations of responder analyses with a definition of deterioration as a change from baseline to week 48 by ≤ -9.4 points in the physical component summary score and ≤ -9.6 points in the mental component summary score (corresponding to 15% of the scale range in each case) are presented.

There were no statistically significant differences between the treatment arms for the physical and mental component summary scores of the SF-36.

Side effects

There were no statistically significant differences between the treatment arms for the overall rates of serious adverse events (SAEs) and adverse events that led to discontinuation of the study medication. No evaluations of severe adverse events, defined as grade 3 or 4 according to the Common Terminology Criteria for Adverse Events (CTCAE), were available.
In detail, for the endpoint of gastrointestinal disorders, there was a statistically significant difference to the disadvantage of omaveloxolone. This is an endpoint based on non-severe and non-serious adverse events (AEs) at the system organ class (SOC) level.

Overall assessment

Results of the randomised, double-blind MOXIe study part 2 which compared omaveloxolone with placebo are available for the benefit assessment of omaveloxolone for the treatment of Friedreich's ataxia in adults and adolescents aged 16 years and older. The data allow comparative statements to be made versus the appropriate comparator therapy of best supportive care.

With regard to mortality, no deaths occurred in either treatment arm of the study.

In the morbidity category, there was a statistically significant advantage in favour of omaveloxolone in the endpoint of physical functioning. Based on Hedges' g, it cannot be concluded in this regard that the effect is clinically relevant. There was no statistically significant difference for the endpoints of activities of daily living, general health status and frequency of falls respectively.

With regard to quality of life, the available data show no statistically significant differences in either the physical or mental component summary score of the SF-36.

In the category of side effects, there were no statistically significant differences in the overall rates of serious adverse events and treatment discontinuation due to adverse events. In detail, for the endpoint of gastrointestinal disorders (SOC, AE), there was a disadvantage of omaveloxolone. Overall, there were no relevant differences for the benefit assessment in the category of side effects.

In the overall assessment, based on the MOXIe part 2 study, no relevant differences for the benefit assessment were identified for the endpoint categories of mortality, morbidity,

health-related quality of life and side effects. An additional benefit of omaveloxolone for adults and adolescents aged 16 years and older with Friedreich's ataxia is therefore not proven.

2.1.4 Summary of the assessment

This is a new benefit assessment of the active ingredient omaveloxolone due to exceeding the € 30 million turnover limit. Omaveloxolone is approved for the treatment of Friedreich's ataxia in adults and adolescents aged 16 years and older.

The G-BA determined the appropriate comparator therapy for omaveloxolone in the present therapeutic indication to be best supportive care.

The results of the double-blind randomised MOXIe study part 2, which compared omaveloxolone with placebo over a treatment period of 48 weeks, are available for the benefit assessment. The data allow comparative statements to be made versus the appropriate comparator therapy of best supportive care.

With regard to mortality, no deaths occurred in either treatment arm of the study.

In the morbidity category, there was a statistically significant advantage in favour of omaveloxolone in the endpoint of physical functioning. Based on Hedges' g, it cannot be concluded in this regard that the effect is clinically relevant. There were no statistically significant differences for the endpoints of activities of daily living, general health status and frequency of falls.

With regard to quality of life, the available data show no statistically significant differences in either the physical or mental component summary score of the SF-36.

Overall, there were no relevant differences for the benefit assessment in the side effects category.

In the overall assessment, based on the MOXIe part 2 study, no relevant differences for the benefit assessment were identified for the endpoint categories of mortality, morbidity, health-related quality of life and side effects. An additional benefit of omaveloxolone for adults and adolescents aged 16 years and older with Friedreich's ataxia is therefore not proven.

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

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

The resolution is based on the information provided by the pharmaceutical company in the dossier. These were derived on the basis of the same methodology as the data used in the resolution on the benefit assessment according to Section 35a SGB V of 19 September 2024 in the same therapeutic indication.

The deviation in the data compared to the preliminary resolution is due to more recent data on the percentage of patients aged ≥ 16 years based on the population figures from the Federal Statistical Office as at 31.12.2024 and rounding differences.

Overall, the information provided by the pharmaceutical company on the number of patients is subject to uncertainties. These are based on the same limitations as the data in the preliminary resolution. Limitations arise in particular in the estimation of prevalence due to

the unclear completeness of the patient lists and the limited timeliness based on the underlying source, as well as the lack of consideration of a range and the assumption of the percentage of patients aged ≥ 16 years based on the total population.

2.3 Requirements for a quality-assured application

The requirements in the product information are to be taken into account. The European Medicines Agency (EMA) provides the contents of the product information (summary of product characteristics, SmPC) for Skyclarys (active ingredient: omaveloxolone) at the following publicly accessible link (last access: 15 October 2025):

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

Treatment with omaveloxolone should only be initiated and monitored by specialists experienced in treating patients with Friedreich's ataxia.

2.4 Treatment costs

The treatment costs are based on the contents of the product information and the information listed in the LAUER-TAXE® (last revised: 15 October 2025). The calculation of treatment costs is generally based on the last revised LAUER-TAXE® version following the publication of the benefit assessment.

The treatment costs for best supportive care are different from patient to patient. Because best supportive care has been determined as an appropriate comparator therapy, this is also reflected in the medicinal product to be assessed. The type and scope of best supportive care can vary depending on the medicinal product to be assessed and the comparator therapy.

Treatment period:

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.

Adults and adolescents aged 16 years and older with Friedreich's ataxia

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Omaveloxolone	1 x daily	365.0	1	365.0
Best supportive care	Different from patient to patient			

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Appropriate comparator therapy				
Best supportive care	Different from patient to patient			

Consumption:

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

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					
Omaveloxolone	150 mg	150 mg	3 x 50 mg	365.0	1095 x 50 mg
Best supportive care	Different from patient to patient				
Appropriate comparator therapy					
Best supportive care					
Best supportive care	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:

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					
Omaveloxolone 50 mg	270 HC	€ 72,570.03	€ 1.77	€ 4,141.20	€ 68,427.06
Abbreviations: HC = hard capsules					

LAUER-TAXE® last revised: 15 October 2025

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.

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 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 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 and adolescents aged 16 years and older with Friedreich's ataxia

No medicinal product with new active ingredients that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

References:
Product information for omaveloxolone (Skyclarys); Skyclarys™ 50 mg; last revised: February 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 25 October 2022, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 30 June 2025 the pharmaceutical company submitted a dossier for the benefit assessment of omaveloxolone to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 6 VerfO.

By letter dated 1 July 2025 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefits of medicinal products with new active ingredients in accordance with Section 35a SGB V, the G-BA commissioned the IQWiG to assess the dossier concerning the active ingredient omaveloxolone.

The dossier assessment by the IQWiG was submitted to the G-BA on 26 September 2025, and the written statement procedure was initiated with publication on the G-BA website on 1 October 2025. The deadline for submitting statements was 22 October 2025.

The oral hearing was held on 10 November 2025.

In order to prepare a recommendation for a resolution, the Subcommittee on Medicinal Products commissioned a working group (Section 35a) consisting of the members nominated by the leading organisations of the care providers, the members nominated by the SHI umbrella organisation, and representatives of the patient organisations. Representatives of the IQWiG also participate in the sessions.

The evaluation of the written statements received and the oral hearing was discussed at the session of the Subcommittee on 9 December 2025, and the proposed draft resolution was approved.

At their session on 18 December 2025, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	25 October 2022	Determination of the appropriate comparator therapy
Working group Section 35a	4 November 2025	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	10 November 2025	Conduct of the oral hearing
Working group Section 35a	18 November 2025 2 December 2025	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	9 December 2025	Concluding discussion of the draft resolution
Plenum	18 December 2025	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 18 December 2025

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

Prof. Hecken