Gemeinsamer Bundesausschuss

Justification

of 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: Odevixibat (progressive familial intrahepatic cholestasis)

of 3 March 2022

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assesses the benefit of reimbursable medicinal products with new active ingredients.

For medicinal products for the treatment of a rare disease (orphan drugs) that are approved according to Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999, the additional medical benefit is considered to be proven through the grant of the marketing authorisation according to Section 35a paragraph 1, sentence 11, 1st half of the sentence German Social Code, Book Five (SGB V), the additional medical benefit is considered to be proven through the grant of the marketing authorisation. Evidence of the medical benefit and the additional medical benefit in relation to the appropriate comparator therapy do not have to be submitted (Section 35a, paragraph 1, sentence 11, 2nd half of the sentence SGB V). Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V thus guarantees an additional benefit for an approved orphan drug, although an assessment of the orphan drug in accordance with the principles laid down in Section 35a paragraph 1, sentence 3, No. 2 and 3 SGB V in conjunction with Chapter 5 Sections 5 et seq. of the Rules of Procedure (VerfO) of the G-BA has not been carried out. In accordance with Section 5, paragraph 8 AM-NutzenV, only the extent of the additional benefit is to be quantified indicating the significance of the evidence.

However, the restrictions on the benefit assessment of orphan drugs resulting from the statutory obligation to the marketing authorisation do not apply if the turnover of the medicinal product with the SHI at pharmacy sales prices and outside the scope of SHI-accredited medical care, including VAT exceeds € 50 million in the last 12 calendar months. According to Section 35a paragraph 1, sentence 12 SGB V, the pharmaceutical company must then, within three months of being requested to do so by the G-BA, submit evidence according to Chapter 5, Section 5, subsection 1–6 VerfO, in particular regarding the additional medical benefit in relation to the appropriate comparator therapy as defined by the G-BA according to Chapter 5 Section 6 VerfO and prove the additional benefit in comparison with the appropriate comparator therapy.

In accordance with Section 35a paragraph 2 SGB V, the G-BA decides whether to carry out the benefit assessment itself or to commission the Institute for Quality and Efficiency in Health Care (IQWiG). Based on the legal requirement in Section 35a paragraph 1 sentence 11 SGB V that the additional benefit of an orphan drug is considered to be proven through the grant of the marketing authorisation the G-BA modified the procedure for the benefit assessment of orphan drugs at its session on 15 March 2012 to the effect that, for orphan drugs, the G-BA initially no longer independently determines an appropriate comparator therapy as the basis for the solely legally permissible assessment of the extent of an additional benefit to be assumed by law. Rather, the extent of the additional benefit is assessed exclusively on the basis of the marketing authorisation studies by the G-BA indicating the significance of the evidence.

Accordingly, at its session on 15 March 2012, the G-BA amended the mandate issued to the IQWiG by the resolution of 1 August 2011 for the benefit assessment of medicinal products with new active ingredients in accordance with Section 35a paragraph 2 SGB V to that effect that, in the case of orphan drugs, the IQWiG is only commissioned to carry out a benefit assessment in the case of a previously defined comparator therapy when the sales volume of the medicinal product concerned has exceeded the legal limit of € 50 million and is therefore subject to an unrestricted benefit assessment (cf. Section 35a paragraph 1, sentence 12 SGB V). According to Section 35a paragraph 2 SGB V, the assessment by the G-BA 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 decides on the benefit assessment within three months of its publication. The resolution is to be published on the internet and is part of the Pharmaceuticals Directive.

2. Key points of the resolution

The relevant date for the first placing on the (German) market of the active ingredient odevixibat in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure of the G-BA (VerfO) is 15 September 2021. The pharmaceutical company submitted the final dossier to the G-BA in accordance with Section 4, paragraph 3, number 1 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM- NutzenV) in conjunction with Chapter 5, Section 8, paragraph 1, number 1 VerfO on 13 September 2021.

Odevixibat indicated for the treatment of progressive familial intrahepatic cholestasis is approved as a medicinal product for the treatment of rare diseases under Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999.

In accordance with Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V, the additional benefit is considered to be proven through the grant of the marketing authorisation. The extent of the additional benefit and the significance of the evidence are assessed on the basis of the marketing authorisation studies by the G-BA.

The G-BA carried out the benefit assessment and commissioned the IQWiG to evaluate the information provided by the pharmaceutical company in Module 3 of the dossier on treatment costs and patient numbers. The benefit assessment was published on 15 December 2021 together with the IQWiG assessment on the website of the G-BA (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA made its resolution on the basis of the pharmaceutical company's dossier, the dossier assessment carried out by the G-BA, the IQWiG assessment of treatment costs and patient numbers (IQWiG G21-28) and the statements made in the written statement and oral hearing procedure, as well of the amendment drawn up by the G-BA on the benefit assessment.

In order to determine the extent of the additional benefit, the G-BA has assessed the studies relevant for the marketing authorisation considering their therapeutic relevance (qualitative) in accordance with the criteria laid down in Chapter 5, Section 5, paragraph 7, sentence 1, numbers 1 – 4 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of odevixibat.

2.1 Additional benefit of the medicinal product

2.1.1 Approved therapeutic indication of Odevixibat (Bylvay®) according to product information

Bylvay® is indicated for the treatment of progressive familial intrahepatic cholestasis (PFIC) in patients aged 6 months or older.

[1] General Methods, version 6.0 from 05.11.2020. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

Therapeutic indication of the resolution (resolution of 3 March 2022):

see the approved therapeutic indication

2.1.2 Extent of the additional benefit and significance of the evidence

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

For children, adolescents and adults aged 6 months or older with progressive familial intrahepatic cholestasis, there is a hint for a minor additional benefit.

Justification:

For the assessment of the additional benefit, the pharmaceutical company submits the results of RCT PEDFIC 1 study as well as the PEDFIC 2 extension study both of which justify the marketing authorisation.

The PEDFIC1 study is a multicentre, double-blind, randomised, placebo-controlled phase III study to investigate the efficacy and safety of odevixibat in children and adolescents aged ≥ 6 months to ≤ 18 years with a genetically confirmed diagnosis of PFIC1 and PFIC2 subtypes.

In the study, a total of 62 patients were randomised in a 1:1:1 ratio into the three study arms with odevixibat at doses of 40 µg/kg/day and 120 µg/kg/day or placebo, stratified by PFIC subtype as well as age group (6 months to 5 years, 6 to 12 years and 13 to ≤ 18 years).

The dosage of 120 µg/kg/day does not correspond to the initial dosage compliant with the marketing authorisation, but is a recommended dose escalation if no adequate clinical response is achieved after 3 months of continuous therapy.

According to the inclusion and exclusion criteria, patients with elevated serum bile acid (sBA) levels and significant pruritus were included and patients with pathological variants of the ABCB11 gene, indicating complete absence of the BSEP protein, and acute or history of other types of liver disease were excluded.

The primary endpoint of the study was reduction in fasting sBA levels (EU and RoW) or improvement in pruritus (USA). The primary endpoint was defined as a secondary endpoint in the other region.

The double-blinded study phase included a treatment phase of 24 weeks in total and a 4-week follow-up. After completion of the treatment phase, the study participants could continue treatment in the PEDFIC 2 open-label extension study.

The PEDFIC2 study is an open-label, single-arm, multicentre phase III extension study with a treatment duration of 72 weeks to investigate the long-term efficacy and safety of odevixibat only at a dose of 120 µg/kg/day in patients with PFIC. In the study, cohort 1 includes children with PFIC1 and PFIC2 who have already participated in the PEDFIC1 study and cohort 2 includes patients with PFIC of any type and age who have elevated sBA levels and cholestatic pruritus and have not participated in the PEDFIC1 study.

The PEDFIC 2 extension study is not taken into account in the benefit assessment since only two study participants completed the study in the data cut-off submitted.

The results of the evaluable patient-relevant endpoints of the PEDFIC 1 study are discussed below.

Mortality

Deaths were recorded in the PEDFIC1 study as part of the safety assessment. No deaths occurred.

Morbidity

Disease symptomatology via patient diary (Albireo PRO/ObsRO)

The endpoints for pruritus, scratching and sleep parameters were assessed in the PEDFIC1 study via an electronic patient diary (eDiary), which was filled out every day in the morning and evening to record the severity of pruritus and scratching, aspects of sleep disturbances and tiredness upon waking or during the day using a 5-point Likert scale. An improvement of one point was defined as a clinically relevant change. The self-reported version Albireo PRO and a third-party-reported version Albireo ObsRO of the eDiary were used, whereby patients under 8 years of age responded only to the Albireo ObsRO while patients from 8 to 18 years of age responded to both the Albireo PRO and the Albireo ObsRO.

The patient-reported recording of pruritus as a distressing symptom in the clinical picture of PFIC is considered to be patient-relevant. A parent/caregiver-reported assessment of externally visible scratching may also be considered patient-relevant for younger or cognitively impaired children who are unable to complete the questionnaire themselves.

The ObsRO data are subject to uncertainty as the results of the PEDFIC1 study were simultaneously used to develop and validate the instrument.

In the evaluations of the improvement of the pruritus symptom using the eDiary (Albireo ObsRO), there was a statistically significant advantage of odevixibat in both doses for the operationalisation "percentage of positive pruritus assessments" and a statistically significant advantage of odevixibat at the dose 40 µg/kg/day in the operationalisation "subjects with ≥ 50% positive pruritus assessment".

The patient relevance of the symptoms of fatigue or sleep behaviour of the test subjects, which are also recorded with the eDiary, is unclear and the effects of sleep deprivation and fatigue on everyday activities or the behaviour of test subjects are not properly recorded with the items of the eDiary. In this respect, the burden on patients resulting from daytime fatigue cannot be assessed in the present operationalisation for the benefit assessment. For this reason, the symptoms of fatigue or sleep behaviour recorded with the eDiary are not taken into account.

Global impression of symptom change and severity (GIC/GIS)

Symptoms of itching and scratching as well as sleep were assessed in the PEDFIC1 study with the global impression of symptom change (GIC) and the global impression of symptom severity (GIS) in addition to the eDiary. These are 12 individual items each, which were answered either by all test subjects ≥ 8 years, the caregivers or the medical investigators.

No valid statistical analyses are available for the endpoint GIC/GIS due to inadequate responder criteria, no reference to the baseline value for symptom severity and low return rates. This is therefore not taken into account in the benefit assessment.

Surgical interventions

In the PEDFIC1 study, no patient-relevant surgical interventions such as surgical biliary diversions and liver transplants were performed.

Growth deficit

Anthropometric parameters can be assessed as patient-relevant morbidity parameters, especially in children with characteristic, disease-related growth disorders. Data adjusted for age and gender are preferred to absolute values.

In the PEDFIC1 study, z values of height, weight and body mass index (BMI) were recorded at weeks 12 and 24 compared to baseline using standardised growth curves.

At baseline, all treatment groups showed growth deficits in height and weight. However, there was no statistically significant advantage or disadvantage of the anthropometric parameters under treatment with odevixibat at week 12 or at week 24.

Reduction of serum bile acid concentration

In the present therapeutic indication, the serum bile acid concentration is a clinically relevant parameter which is used for diagnosis and therapy management.

The endpoint of serum bile acid concentration is presented additionally in the benefit assessment.

The reduction of bile acids is considered a therapy goal in order to reduce the risk of secondary damage to the liver. The increased serum bile acid concentration is a direct manifestation of PFIC and, as a disease toxin, is causative for the disease symptomatology. However, the symptomatology of patients with PFIC is different from patient to patient.

No valid data could be identified to show what effect a specific change in serum bile acid concentration has on patient-individual symptomatology or on the risk of liver damage.

In the PEDFIC 1 study, the primary endpoint was a 70% reduction in sBA level from baseline to the end of treatment or the achievement of an sBA level of < 70 µmol/l after a treatment period of 24 weeks.

There is a statistically Significant advantage of odevixibat for the endpoint "reduction of serum bile acid concentration".

The results on serum bile acid concentration show that the pathological accumulation of bile acids caused by the genetic defect is reduced under therapy with odevixibat.

<u>Health-related quality of life</u>

Paediatric Quality of Life Inventory (PedsQL)

The PedsQL 4.0 measures the general health-related quality of life in children and adolescents. It consists of four multidimensional scales (Physical Functioning, Emotional functioning, Social functioning, and School functioning) with a total of 23 items and three sum scores: Total score, physical health summary score, psychosocial health summary score. The questionnaire consists of a Likert scale from 1 to 4 (1 = best function [never] to 4 = worst function [always]).

The scores are then transformed into a scale of 1 to 100; higher scores indicate a higher quality of life.

The PedsQL is an established and adequately validated generic instrument for assessing the quality of life in pediatric populations with chronic conditions.

In the PEDFIC1 study, different versions of the PedsQL core module were used to assess health-related quality of life, depending on the age of the test subject: Patient and parent reports for the core modules 5-7 year olds (young children), 8-12 year olds (children) and 13-18 year olds (teens) and a core module for parent reports for toddlers (2-4 years).

In relation to the total population, the study does not achieve the required return rate of at least 70% for either the self-assessments or the external assessments. Overall, no usable data on health-related quality of life are therefore available in the PEDFIC1 study.

In addition to the core module, the PedsQL Family Impact Module was also used for caregivers in the PEDFIC1 study. It consists of 36 items, distributed over a total of 8 domains. This does not measure the quality of life of the test subject, but the impact of the quality of life on the family from the perspective of the parent. Accordingly, the results are classified as not directly patient-relevant and are not taken into account in the benefit assessment.

Side effects

Within the PEDFIC1 study, a post hoc analysis of the differences between the treatment groups was performed. For the adverse events (AEs), only one-sided p values were reported, without this procedure being plausibly justified with a directed hypothesis.

No adequate evaluations were submitted within the framework of the written statement procedure either. Due to the lack of suitable p values, only the relative risk and the confidence intervals are given. The confidence intervals are used for evaluation.

Furthermore, it is unclear which events related to side effects were recorded due to disease progression and should therefore be counted as disease-related events.

In the PEDFIC1 study, at least one AE occurred in each treatment group in just over 80% of the subjects. Severe AEs were defined in the study protocol as those that rendered the patient incapable of acting or performing normal activities. These occurred in 2 subjects each from the 120 µg/kg/day odevixibat treatment group and the placebo group, and in 1 subject from the 40 µg/kg/day odevixibat treatment group. Serious AEs (SAEs) occurred in 3 of 19 (16%) subjects in the 120 µg/kg/day odevixibat treatment arm and in 5 of 20 (25%) people in the placebo arm. In the odevixibat arm (120 µg/kg/day), one AE of the preferred term "diarrhoea" led to discontinuation of study medication in one subject.

The evaluations presented on the overall rates of AE show neither advantages nor disadvantages of odevixibat with regard to side effects on the basis of the confidence intervals.

In addition, further uncertainties also emerged in the EMA's assessment, which led to the requirement to generate further safety data.

Overall, uncertainties remain regarding the assessment of side effects.

Overall assessment

For the benefit assessment of odevixibat for the treatment of children, adolescents and adults aged 6 months or older with progressive familial intrahepatic cholestasis (PFIC), assessable results on mortality, morbidity and side effects are available based on the PEDFIC1 study.

There were no deaths in the PEDFIC1 study.

In the endpoint category of morbidity, the endpoints "pruritus", "sleep quality", "surgical interventions" and "growth deficits" were assessed.

For the endpoint of pruritus, there is a statistically significant advantage of odevixibat both in the operationalisation "percentage of positive pruritus assessment" for both dosages and there is a statistically significant advantage of odevixibat in the operationalisation "subjects with ≥ 50% positive pruritus assessment" at the dose of 40 µg/kg/day.

Surgical interventions did not occur in the study. There is no statistically significant advantage or disadvantage for the endpoint of growth deficits.

No usable data on health-related quality of life are available in the study.

In the case of side effects, neither advantages nor disadvantages can be seen with regard to the overall rates of AEs on the basis of the confidence intervals. Overall, uncertainties remain, even taking into account the EMA requirements.

In the overall assessment of the available results, a minor additional benefit of odevixibat is determined due to the advantage in the endpoint of pruritus.

Significance of the evidence

For the PEDFIC1 RCT presented, the risk of bias at study level is assessed as low. However, uncertainties arise from the choice of a fixed dose of odevixibat in the two study arms, especially with regard to the 120 µg/kg/day described as dose escalation according to the product information. Further uncertainties exist with regard to the survey instrument for recording the endpoint of itching (Albireo ObsRO). Overall, the uncertainties mentioned with regard to the significance of the evidence result in a hint for an additional benefit.

2.1.3 Limitation of the period of validity of the resolution

The limitation of the period of validity of the resolution on the benefit assessment of odevixibat finds its legal basis in Section 35a paragraph 3 sentence 4 SGB V. Thereafter, the G-BA may limit the validity of the resolution on the benefit assessment of a medicinal product. In the present case, the limitation is justified by objective reasons consistent with the purpose of the benefit assessment according to Section 35a paragraph 1 SGB V.

The pharmaceutical company is obliged to submit further clinical data on the safety and efficacy of odevixibat to the EMA for review, which may be relevant for the assessment of the additional benefit of the medicinal product pursuant to Section 35a SGB V. The limitation enables the timely inclusion of the evidence to be provided to the regulatory authority with regard to safety and efficacy in the benefit assessment of the medicinal product according to Section 35a SGB V.

Regarding the evidence to be provided, the EMA requires that one register-based efficacy study and one register-based safety study each be conducted to collect further efficacy and safety data. The final report of the register-based safety study is expected by 31 December 2026. The report on the register-based efficacy study is annual and is expected for the first time on 16 July 2022.

Since clinical data on efficacy and safety are expected to be relevant for the assessment of the medicinal product, it is justified to limit the validity of the resolution until further scientific knowledge is available for the assessment of the additional benefit of odevixibat. The limitation enables the expected interim results from the register-based studies to be included in the benefit assessment of the medicinal product in accordance with Section 35a SGB V in a timely manner.

For this purpose, the G-BA considers a limitation for the resolution until 1 June 2027 to be appropriate.

Conditions of the limitation:

For the new benefit assessment after expiry of the deadline, the results on all patient-relevant endpoints used for the evidence of an additional benefit are to be presented in the dossier.

A change in the limitation can generally be granted if it is justified and clearly demonstrated that the limitation is insufficient or too long.

In accordance with Section 3 paragraph 7 AM-NutzenV in conjunction with Chapter 5 Section 1, paragraph 2, number 6 VerfO, the procedure for the benefit assessment of the medicinal product odevixibat recommences when the deadline has expired. For this purpose, the pharmaceutical company must submit a dossier to the G-BA for the quantification of an additional benefit of odevixibat no later than the day of the deadline.

The possibility that a benefit assessment for the medicinal product odevixibat can be carried out at an earlier point in time due to other reasons (cf. Chapter 5, Section 1 paragraph 2, nos. 2 – 4 VerfO) remains unaffected hereof.

2.1.4 Summary of the assessment

The present assessment is the benefit assessment of the new medicinal product Bylvay® with the active ingredient odevixibat, which was approved as an orphan drug under special conditions for the treatment of progressive familial intrahepatic cholestasis (PFIC) in patients aged 6 months and older.

For the patient group of children, adolescents and adults aged 6 months or older with progressive familial intrahepatic cholestasis, the pharmaceutical company presents results from the 24-week, double-blind, randomised, placebo-controlled PEDFIC1 study and the open-label, single-arm extension PEDFIC2 study.

The PEDFIC2 study is not included because only two study participants completed the study in the data cut-off presented.

There were no deaths in the PEDFIC 1 study. In the morbidity category, there was a statistically significant advantage of odevixibat for the endpoint of pruritus. Surgical interventions did not occur in the study. There is no statistically significant advantage or disadvantage for the endpoint of "growth deficits". No usable data are available on health-related quality of life. In the case of side effects, neither advantages nor disadvantages can be seen with regard to the overall rates of AEs on the basis of the confidence intervals. Overall, uncertainties remain, even taking into account the EMA requirements.

The significance of the evidence is categorised as a hint due to uncertainties arising from the choice of a fixed dosage of odevixibat in the two study arms and with regard to the survey instrument used to assess the endpoint of itching (AlbireoObsRO).

In the overall assessment of the available results, a hint for a minor additional benefit of odevixibat is determined due to the advantage in the endpoint of itching.

The validity of the resolution is limited to 01.06.2027.

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 from the dossier assessment of the IQWiG (mandate G21-28).

The G-BA takes into account the patient numbers stated in the pharmaceutical company's dossier, which, however, are subject to uncertainty overall due to the limited epidemiological data on incidence and prevalence in the therapeutic indication, the exclusion of patients with surgical biliary diversion, the estimation of the average life expectancy and an incomprehensible uncertainty range applied across the board. Overall, these uncertainties do not allow an assessment of the extent to which an underestimation or overestimation of the patient numbers can be assumed.

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 Bylvay® (active ingredient: odevixibat) at the following publicly accessible link (last access: 15 February 2022):
https://www.ema.europa.eu/en/documents/product-information/bylvay-epar-product-information_en.pdf

Treatment with odevixibat should only be initiated and monitored by doctors experienced in treating patients with primary familial intrahepatic cholestasis.

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 February 2022).

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

The treatment duration is assumed to be one year (365 days), even if the actual treatment duration varies 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, the average body measurements from the official representative statistics "Microcensus 2017 – body measurements of the population" were applied (average body weight: 77.0 kg).[2]

Treatment period:

Designation of the therapy	Treatment mode	Number of treatments/ patient /year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Odevixibat	Continuously, 1 x daily	365	1	365

Consumption:

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Odevixibat (40 µg/kg/day)	4 to < 7.5 kg: 160 µg	160 µg	1 x 200 µg	365	365 x 200 µg
	≥ 55 kg: 2200 µg	2200 µg	6 x 400 µg	365	2,190 x 400 µg
Odevixibat (120 µg/kg/day)	4 to < 7.5 kg: 480 µg	480 µg	1 x 400 µg + 1 x 300 µg	365	365 x 400 µg + 365 x 200 µg
	≥ 55 kg: 6600 µg	6600 µg	6 x 1200 µg	365	2,190 x 1200 µg

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.

[2] Federal Statistical Office, Wiesbaden 2018: http://www.gbe-bund.de/

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					
Odevixibat 200 µg	30 HC	€ 4,596.62	€ 1.77	€ 259.22	€ 4,335.63
Odevixibat 400 µg	30 HC	€ 9,135.64	€ 1.77	€ 518.45	€ 8,615.42
Odevixibat 1200 µg	30 HC	€ 27,291.69	€ 1.77	€ 1,555.34	€ 25,734.58
HC = hard capsules					

LAUER-TAXE® last revised: 15.02.2022

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

On 13 September 2021, the pharmaceutical company submitted a dossier for the benefit assessment of odevixibat to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 VerfO.

The benefit assessment of the G-BA was published on 15 December 2021 together with the IQWiG assessment of treatment costs and patient numbers on the website of the G-BA (www.g-ba.de), thus initiating the written statement procedure. The deadline for submitting written statements was 5 January 2022.

The oral hearing was held on 24 January 2022.

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 22 February 2022, and the proposed resolution was approved.

At its session on 3 March 2022, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal product	7 December 2021	Information of the benefit assessment of the G-BA
Working group Section 35a	18 January 2022	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal product	24 January 2022	Conduct of the oral hearing
Working group Section 35a	1 February 2022 15 February 2022	Consultation on the dossier assessment by the G-BA, the assessment of treatment costs and patient numbers by the IQWiG, and the evaluation of the written statement procedure
Subcommittee Medicinal product	22 February 2022	Concluding discussion of the draft resolution
Plenum	3 March 2022	Adoption of the resolution on the amendment of Annex XII AM-RL

Berlin, 3 March 2022

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

Prof. Hecken