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: Vosoritide (achondroplasia, ≥ 2 years)

of 18 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). 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 vosoritide in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure of the G-BA (VerfO) is 1 October 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 1 October 2021.

Vosoritide indicated for the treatment of achondroplasia in patients 2 years of age and older whose epiphyses are not closed is authorised as a medicinal product for the treatment of rare diseases under Regulation (EC) No. 141/2000 of the European Parliament and of 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 3 January 2022 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 G21-29) and the statements made in the written statement and oral hearing procedure, as well of the amendments 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 vosoritide.

[1] General Methods, version 6.1 from 24.01.2022. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

## 2.1 Additional benefit of the medicinal product

### 2.1.1 Approved therapeutic indication of Vosoritide (Voxzogo) according to product information

Voxzogo is indicated for the treatment of achondroplasia in patients 2 years of age and older whose epiphyses are not closed. The diagnosis of achondroplasia should be confirmed by appropriate genetic testing.

**Therapeutic indication of the resolution (resolution of 18 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 vosoritide is assessed as follows:

Patients 2 years of age and older with achondroplasia and whose epiphyses are not closed

Hint for a non-quantifiable additional benefit since the scientific data does not allow quantification.

**Justification:**
For the benefit assessment of vosoritide, the pharmaceutical company uses the BMN 111-301 and 302 (extension study of study 301), BMN 111-202 and 205 (extension study of study 202) studies and the results of 4 sentinel patients from the study BMN 111-206 in the dossier.

The uncontrolled phase II dose escalation study BMN 111-202 and its extension study 205 investigated the administration of vosoritide in children and adolescents aged 5 to < 15 years. Since a comparator study with vosoritide is available, the single-arm study 202 and the associated extension study 205 are not used for the benefit assessment.

The submitted results of the 4 sentinel patients from the BMN 111-206 study in the age group up to 5 years are considered additionally for the benefit assessment. In view of the fact that only a small number of patients are involved and no comparator data are available, it is not possible to draw any conclusions about the additional benefit of vosoritide on the basis of the results.

**The BMN 111-301 (301) study and the BMN 111-302 (302) extension study**
The double-blind, controlled, multicentre phase 3 study 301, investigated the administration of either vosoritide or placebo in children and adolescents aged 5 to 17 years, who had proven achondroplasia (ACH) after genetic testing. Another prerequisite for enrolment in the study was the prior participation of the children and adolescents in the BMN 111-901 observational study for at least 6 months.

After a 30-day screening phase, 121 patients were allocated to the treatment arms 15 µg/kg vosoritide and placebo each administered in the form of a daily subcutaneous injection for 52 weeks, stratified for the characteristic's "gender" (male or female) and "pubertal development" (Tanner stage I or stage > I). This was followed by a 4-week follow-up phase, unless the children and adolescents were transferred to the BMN 111-302 extension study or participated for more than 4 weeks (after the last dose of the study medication).

In the study 301, the median age of patients at the start of the study was 7.8 years in the vosoritide arm and 9.3 years in the control arm. The youngest subject was 5 years old and the oldest just under 15. The median height of the children and adolescents was approx. 99 cm in the vosoritide arm and approx. 105 cm in the control arm. Overall, patient characteristics were comparable in the study arms. Almost all children and adolescents received concomitant medication (over 90%; including vitamins, anti-inflammatory and antirheumatic drugs, analgesics and systemic antibiotics). Except for two patients in the vosoritide arm who dropped out of the study, all children and adolescents were treated for one year.

The risk of bias at the study level is estimated to be low overall. The primary endpoint investigated in study 301 was the annualized growth velocity. In addition, patient-relevant endpoints on mortality, morbidity, quality of life and side effects are available.

Optionally, the children and adolescents could move on to the single-arm extension study 302 after completion of the study 301. All but 2 patients were also transferred to the study 302 and were subsequently treated with vosoritide. At the time of the data cut-off of 2 November 2020 available for the benefit assessment, the median treatment duration of all study participants was 743 days (841 days in the vosoritide/vosoritide group[2] and 481 days in the placebo/vosoritide[3] group).

**Results of the study 301**

Mortality

No deaths occurred in the study 301.

Morbidity

In the dossier, the pharmaceutical company presents the results of the primary endpoint "annualized growth velocity (AGV)", the height (z-score) as well as the endpoints "upper to lower body segment ratio" and "body proportion ratio".

*Height (z-score) and annualized growth velocity*

Height was recorded as height (not length) as well as age and sex-adjusted z-scores were calculated. The z-scores reflect the number of standard deviations (SD) of each score from the normal mean scores, standardised by age and sex. The data were presented as SD values above or below the age-specific reference (≙ 0). As comparator data for the z-scores, a sample of healthy children in the USA with the survey periods 1963 to 1994 was used on the one hand, and representative German growth data from the Robert Koch Institute from 2003 to 2006 on the other, in order to analyse the transferability of the results to the German health care context.

Height (z-score) is classified as patient-relevant in the present therapeutic indication. At baseline of the study 301, the children and adolescents were shorter than the German and American reference populations. After 52 weeks of treatment, the height (z-score) of the children and adolescents in the vosoritide arm increased; the control arm showed a decrease in the z-score. The group difference in the results using the German or the American reference population is comparable: the differences are statistically significant in favour of vosoritide in

[2] Vosoritide/vosoritide group: Children and adolescents who received vosoritide in the study 301 and continued to receive vosoritide in the subsequent extension study 302.
[3] Placebo/vosoritide group: Children and adolescents who received placebo in the study 301 and vosoritide in the subsequent extension study 302.

each case. However, evaluations of clinical relevance are only available for the American reference population. These show that the difference shown is also clinically relevant.

The primary endpoint growth rate describes the annual increase in height [cm/year] and is only presented additionally, as it does not provide any information on growth other than height for the benefit assessment.

At baseline of the study 301, the children and adolescents had a similar annualized growth velocity in both study arms. There was a statistically significant increase in the annualized growth velocity at 1 year to the advantage of vosoritide compared to the control group.

*Ratio of upper to lower body segment and ratio of body proportions*

The endpoints "ratio of upper to lower body segment" and "ratio of body proportions[4]" are not considered relevant to patients *per se*. Changes in body proportions should be reflected in particular in directly patient-relevant endpoints in the morbidity category (e.g. functional limitations and mobility).

Notwithstanding this, the results of the endpoints "ratio of upper to lower body segment" and "ratio of body proportions" are presented additionally: After 52 weeks of treatment, there are no statistically significant differences between the treatment groups.

*Child Behaviour Checklist (CBCL)*

The CBCLs are parent-reported questionnaires to assess behavioural and emotional symptoms in children and adolescents. There are two versions of the CBCL: for children aged 18 months to ≤ 5 years and for children and adolescents aged 6 to ≤ 17 years.

There are only a few baseline values for the CBCL in the study 301. The results can therefore not be taken into account.

Quality of life

The pharmaceutical company presents the results of the measurement instruments PedsQL, QoLISSY and WeeFIM from the study 301 in the dossier for the assessment of the quality of life.

*Paediatric Quality of Life Inventory (PedsQL)*

The PedsQL is a generic instrument for measuring health-related quality of life, which includes 23 items from four dimensions (physical, emotional, social and school functioning). The scores are then transformed on a scale of 0 to 100, higher scores indicating a better quality of life. The age-appropriate as well as self and proxy-reported versions for the age groups 5 to 7 years, 8 to 12 years and 13 to 18 years were used, whereby the version for the age group 5 to 7 years was exclusively self-reported. The proxy report was done by the parents/carers. The reference period is one month.

The results of the self-reported PedsQL version (children 8 years and older) show no statistically significant differences between the treatment groups in the study 301 up to week 52. The pharmaceutical company does not present separate evaluations of the proxy-reported version for the 5 to 7-year-old children.

[4] Ratio of upper to lower arm length, ratio of thigh length to knee-to-heel length, ratio of thigh length to shin length and ratio of arm span to height.

*Quality of Life in Short Stature Youth Questionnaire (QoLISSY)*

The QoLISSY questionnaire is an instrument for assessing the quality of life of short statured youth, for which there is a version for direct questioning of children and adolescents in the age groups 8 to 12 years and 13 to 18 years and a version for questioning the parents of affected children and adolescents in the age groups 4 to 7 years, 8 to 12 years and 13 to 18 years. The versions contain three main domains (physical, emotional and social) which allow the calculation of a total score, as well as three further domains for coping, beliefs and treatment. The parent version also includes a domain on the child's future and a domain on the effects of the disease on the parents. The scores are then transformed on a scale of 0 to 100, higher scores indicating a better quality of life. The questionnaire was collected during screening and at weeks 26 and 52.

In the study 301, the results of the self-reported quality of life questionnaire QoLISSY (children 8 years and older) show no statistically significant differences between the treatment groups until week 52. The pharmaceutical company does not present separate evaluations of the proxy-reported version for the 5 to 7-year-old children.

*Functional Independence Measure for Children (WeeFIM)*

The WeeFIM instrument was developed to measure functional independence of children aged 6 months to 7 years in a proxy-reported manner. Since a separate evaluation for the age group 5 to 7 years is not available in the dossier and the validity for older children and adolescents is not proven, the WeeFIM is not considered for the benefit assessment.

Side effects

In the study 301, only a few severe or serious adverse events (AEs) or discontinuations of therapy due to AEs occurred. The results of the study 301 are not statistically significantly different between the treatment groups.

*AE of special interest*

AEs of special interest recorded in the study 301 were "Reaction at the injection site", "Hypersensitivity", "Hypotension", "Fractures", "Change in heart rate", "Avascular necrosis or bone necrosis", "Slipped capital femoral epiphysis (SCFE)" and "Algorithmic anaphylaxis". Regarding the endpoint "hypersensitivity", there are statistically significantly more events in the vosoritide arm. For all other AEs of special interest, outcomes were not statistically significantly different between treatment groups, no events occurred or no data are available.

**Results of the study 302**

The results of the single-arm extension study 302[5] are described below additionally: The results show that height (z-score) as well as annualized growth velocity increases in the vosoritide/vosoritide group by week 104 and in the placebo/vosoritide group by week 52, respectively, compared to the baseline. The upper to lower body segment ratio decreases slightly in the vosoritide/vosoritide group by week 104 and in the placebo/vosoritide group by week 52, each compared to the baseline. No data are available for the "ratio of body

[5] Data cut-off of 2 November 2020.

proportions[4]" and for quality of life. Overall, only a few severe or serious AEs or therapy discontinuations due to AEs occurred in the study 302.

Overall assessment

The benefit assessment is based on the results of the double-blind, controlled, multicentre study 301, which investigated the administration of vosoritide versus placebo in children and adolescents with achondroplasia aged 5 to 17 years over 52 weeks. In addition, the results of the single-arm extension study 302 were described. Results from the study 301 are available on patient-relevant endpoints in the categories of mortality, morbidity, quality of life and side effects.

No deaths occurred in the study 301.

In the endpoint category of morbidity, the study 301 shows a statistically significant advantage for the endpoint "height (z-score)" to the advantage of vosoritide.

With regard to quality of life, there were no differences between the treatment groups in the study 301.

In terms of side effects, the study 301 shows a disadvantage in detail for the AE "hypersensitivity", but overall, there are no relevant differences between the treatment groups.

The results of the extension study 302 described additionally show that the "height (z-score)" increases with (further) treatment with vosoritide over 52 weeks compared to the baseline. Since only baseline comparisons were presented after the change in treatment, no statements on the extent of the additional benefit can be derived from the results of this study.

In the study 301, there was only one statistically significant advantage for the endpoint "height (z-score)" to the advantage of vosoritide. However, there is no improvement with regard to the endpoints of disproportionality of body proportions presented additionally. Although these endpoints are not considered to be patient-relevant *per se*, they are used to assess growth progression, according to the clinical experts. The disproportionality of body proportions resulting from achondroplasia also leads to functional limitations in patients, especially in later life.

No other patient-relevant endpoints of the morbidity category (e.g. functional limitations and mobility) were assessed in the study 301. In the overall analyses, the interpretability of the positive result with regard to increasing height (z-score) is therefore difficult.

Taken together, the assessment of the magnitude of the additional benefit of vosoritide based on the positive effects on height alone is not possible. Furthermore, it is uncertain whether the magnitude of the positive effects shown by vosoritide in terms of growth will be maintained over a longer period of time. Against this background, the G-BA states a non-quantifiable additional benefit since the scientific data basis does not allow quantification.

Significance of the evidence

The present therapeutic indication includes patients 2 years of age and older with achondroplasia and whose epiphyses are not closed. However, only children and adolescents aged between 5 and 17 years were enrolled in the study 301. The marketing authorisation for the younger children (2 to 5 years) is also based on preliminary results of 4 sentinel patients from the BMN 111-206 study of the age group up to 5 years (data cut-off of 12 September

2019). The EPAR[6] states that due to the underlying genetic alteration of achondroplasia, which affects all patients regardless of age, it is also assumed that effects can be expected for children aged 2 to 5 years similar to those for older children. In addition, the EMA assumes that even stronger effects can be achieved through early treatment with vosoritide. However, the pharmaceutical company is instructed by the EMA to submit the complete data of the study 206 and the associated extension study 208 after completion.

Data are available from the study 301 on 52 weeks of treatment with vosoritide and from the additionally described extension study 302 on 24 months of treatment with vosoritide. In view of the fact that children and adolescents need to be treated for several years, it is not possible to make a conclusive statement about the sustainability of the effects and the safety profile on the basis of these data.

In addition, no data are available for children aged 2 to 5 years that would allow a conclusion to be drawn about the additional benefit of vosoritide in children aged 2 to 5 years. The data from the 4 sentinel patients from the BMN 111-206 study in this age group are only a small number of patients and no comparator data are available. The full results of the study 206 and the associated extension study 208 are still pending.

Against the background of these uncertainties, the reliability of data is therefore classified as "hint".

### 2.1.3 Summary of the assessment

In the present benefit assessment of the new medicinal product Voxzogo with the active ingredient vosoritide, the therapeutic indication assessed here is "patients aged 2 years and older with achondroplasia and whose epiphyses are not closed". Voxzogo was approved as an orphan drug.

For the benefit assessment of vosoritide, the double-blind, placebo-controlled, multicentre study 301 and, in addition, the single-arm extension study 302 are considered.

No deaths occurred in the study 301.

In the endpoint category of morbidity, the study 301 shows a statistically significant advantage for the endpoint "height (z-score)" to the advantage of vosoritide.

With regard to quality of life, there were no differences between the treatment groups in the study 301.

In terms of side effects, the study 301 shows a disadvantage in detail for the AE "hypersensitivity", but overall, there are no relevant differences between the treatment groups.

The results of the extension study 302 described additionally show that the "height (z-score)" increases with (further) treatment with vosoritide over 52 weeks compared to the baseline. Since only baseline comparisons were presented after the change in treatment, no statements on the extent of the additional benefit can be derived from the results of this study.

No data are available for children aged 2 to 5 years. Overall, uncertainties remain as to whether the data of children and adolescents over 5 years of age can be transferred to children aged 2 to 5 years.

[6] European Medicines Agency (EMA): European public assessment report (EPAR) on vosoritide, 24 June 2021 https://www.ema.europa.eu/en/documents/assessment-report/voxzogo-epar-public-assessment-report_en.pdf [accessed online on 22 February 2022]

In the overall analysis, the study 301 shows an advantage for the endpoint " height z-score)" for vosoritide over placebo. Overall, the assessment of the magnitude of the additional benefit of vosoritide based on the positive effects on height alone is not possible. Furthermore, it is uncertain whether the magnitude of the positive effects shown by vosoritide in terms of growth will be maintained over a longer period of time. Against this background, the G-BA identifies a hint for a non-quantifiable additional benefit since the scientific data basis does not allow quantification.

## 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.

The stated range of approx. 340 to 480 patients is subject to uncertainties. The range is considered to be probably overestimated due to uncertainties regarding the birth-related incidence of achondroplasia, determined by the pharmaceutical company and the assumptions made by the same in calculating the number of patients whose epiphyseal joints are not yet closed.

## 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 Voxzogo (active ingredient: vosoritide) at the following publicly accessible link (last access: 9 February 2022):

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

Treatment with vosoritide may only be initiated and monitored by doctors experienced in the treatment of patients with growth disorders or skeletal dysplasias.

## 2.4 Treatment costs

The treatment costs are based on the contents of the product information and the information listed in the LAUER-TAXE® (last revised: 1 March 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.

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.

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 | | | | |
| Vosoritide | Children ≥ 2 years | | | |
| | Continuously, 1 x daily | 365 | 1 | 365 |
| | Patients aged between 17 and < 18 years | | | |
| | Continuously, 1 x daily | 365 | 1 | 365 |

Consumption:

For dosage range 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 of a child aged 2 years = 14.1 kg and patients aged 17 to < 18 years = 67.0 kg,).[7]

| 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 | | | | | |
| Vosoritide | Children ≥ 2 years | | | | |
| | 0.35 ml = 0.28 mg | 0.28 mg | 1 x 0.40 mg | 365 | 365 x 0.40 mg |
| | Patients aged between 17 and < 18 years | | | | |
| | 0.35 ml = 0.70 mg | 0.70 mg | 1 x 1.2 mg | 365 | 365 x 1.2 mg |

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

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

the medicinal products were then calculated on the basis of the costs per pack after deduction of the statutory rebates.

**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 | | | | | |
| Vosoritide 0.4 mg | 10 PSI | € 9,445.80 | € 1.77 | € 536.16 | € 8,907.87 |
| Vosoritide 1.2 mg | 10 PSI | € 9,445.80 | € 1.77 | € 536.16 | € 8,907.87 |
| Abbreviations: PSI = powder and solvent for solution for injection | | | | | |

LAUER-TAXE® last revised: 1 March 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, 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.

No additionally required SHI services are taken into account for the cost representation.

## 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 1 October 2021, the pharmaceutical company submitted a dossier for the benefit assessment of vosoritide to the G-BA in due time in accordance with Chapter 5, Section 8, number 1, sentence 2 VerfO.

The benefit assessment of the G-BA was published on 3 January 2022 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 24 January 2022.

The oral hearing was held on 7 February 2022.

Two amendments to the benefit assessment with supplementary assessments were submitted on 23 February 2022 and 2 March 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 were discussed at the session of the subcommittee on 9 March 2022, and the draft resolution was approved.

At its session on 18 March 2022, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

### Chronological course of consultation

| Session | Date | Subject of consultation |
|---|---|---|
| Subcommittee Medicinal product | 21 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 | 7 February 2022 | Conduct of the oral hearing |
| Working group Section 35a | 15 February 2022<br>1 March 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 | 9 March 2022 | Concluding discussion of the draft resolution |
| Plenum | 18 March 2022 | Adoption of the resolution on the amendment of Annex XII AM-RL |

Berlin, 18 March 2022

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

Prof. Hecken