Gemeinsamer Bundesausschuss

Justification

for the Resolution of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive:
Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V
Selumetinib (new therapeutic indication: neurofibromatosis type 1 (≥ 1 to < 3 years))

From 6 August 2026

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assess the benefit of all reimbursable medicinal products with new active ingredients. This includes in particular the assessment of the additional benefit and its therapeutic significance. The benefit assessment is carried out on the basis of evidence provided by the pharmaceutical company, which must be submitted to the G-BA electronically, including all clinical studies the pharmaceutical company have conducted or commissioned, at the latest at the time of the first placing on the market as well as the marketing authorisation of new therapeutic indications of the medicinal product, and which must contain the following information in particular:

1. approved therapeutic indications,

2. medical benefit,

3rd additional medical benefit in relation to the appropriate comparator therapy,

4th number of patients and patient groups for whom there is a therapeutically significant additional benefit,

5th treatment costs for the statutory health insurance funds,

6th requirements for a quality-assured application.

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

According to Section 35a paragraph 3 SGB V, the G-BA decide on the benefit assessment within three months of its publication. The resolution is to be published on the internet and is part of the Pharmaceuticals Directive.

2. Key points of the resolution

The active ingredient selumetinib (Koselugo) was listed for the first time on 15 August 2021 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

On 9 January 2026, selumetinib received marketing authorisation for a new therapeutic indication to be classified as a major type 2 variation as defined according to Annex 2, number 2, letter a to Regulation (EC) No. 1234/2008 of the Commission of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334 from 12.12.2008, sentence 7).

On 4 February 2026, i.e. at the latest within four weeks of informing the pharmaceutical company about the approval for a new therapeutic indication, the pharmaceutical company submitted a dossier in accordance with Section 4, paragraph 3, number 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with

Chapter 5, Section 8, paragraph 1, number 2 of the Rules of Procedure (VerfO) of the G-BA on the active ingredient selumetinib with the new therapeutic indication

"Koselugo as monotherapy is indicated for the treatment of symptomatic, inoperable plexiform neurofibromas (PN) in patients with neurofibromatosis type 1 (NF1) aged 1 year to less than 7 years and for older patients with swallowing difficulties."

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 15 May 2026 on the G-BA website (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA came to a resolution on whether an additional benefit of selumetinib compared with the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG, the statements submitted in the written statement and oral hearing procedure, and the addendum to the benefit assessment prepared by the IQWiG. In order to determine the extent of the additional benefit, the G-BA have evaluated the data justifying the finding of an additional benefit on the basis of their therapeutic relevance (qualitative), in accordance with the criteria laid down in Chapter 5, Section 5, paragraph 7 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods[1] was not used in the benefit assessment of selumetinib.

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 selumetinib (Koselugo) in accordance with the product information

Koselugo as monotherapy is indicated for the treatment of symptomatic, inoperable plexiform neurofibromas (PN) in patients with neurofibromatosis type 1 (NF1) aged 1 year to less than 7 years and for older patients with swallowing difficulties.

Therapeutic indication of the resolution (resolution of 06.08.2026):

Koselugo as monotherapy is indicated for the treatment of symptomatic, inoperable plexiform neurofibromas (PN) in patients with neurofibromatosis type 1 (NF1) aged 1 year to less than 3 years.

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Children aged 1 year to less than 3 years with symptomatic, inoperable plexiform neurofibromas (PN) associated with neurofibromatosis type 1 (NF1)

Appropriate comparator therapy for selumetinib as monotherapy:

Best supportive care

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

Criteria according to Chapter 5 Section 6 of the Rules of Procedure of the G-BA and Section 6 paragraph 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV):

The appropriate comparator therapy must be an appropriate therapy in the therapeutic indication according to the generally recognised state of medical knowledge (Section 12 SGB V), preferably a therapy for which endpoint studies are available and which has proven its worth in practical application unless contradicted by the guidelines under Section 92, paragraph 1 SGB V or the principle of economic efficiency.

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

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

According to Section 6, paragraph 2, sentence 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the determination of the appropriate comparator therapy must be based on the actual medical treatment situation as it would be without the medicinal product to be assessed. According to Section 6, paragraph 2, sentence 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the G-BA may exceptionally determine the off-label use of medicinal products as an appropriate comparator therapy or as part of the appropriate comparator therapy if they determine by resolution on the benefit assessment according to Section 7, paragraph 4 that, according to the generally recognised state of medical knowledge, this is considered a therapy standard in the therapeutic indication to be assessed or as part of the therapy standard in the medical treatment situation to be taken into account according to sentence 2, and

1. for the first time, a medicinal product approved in the therapeutic indication is available with the medicinal product to be assessed,
2. according to the generally recognised state of medical knowledge, the off-label use is generally preferable to the medicinal products previously approved for the therapeutic indication, or
3. according to the generally recognised state of medical knowledge, the off-label use for relevant patient groups or indication areas is generally preferable to the medicinal products previously approved for the therapeutic indication.

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

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

On 1. In addition to selumetinib, the active ingredient mirdametinib is approved in the present therapeutic indication.

On 2. Non-medicinal treatments as part of the appropriate comparator therapy are not considered in the present therapeutic indication.

On 3. Resolutions on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V:

- Mirdametinib: Resolution of 19 March 2026

On 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as systematic reviews of clinical studies in the present indication and is presented in the "Research and synopsis of the evidence to determine the appropriate comparator therapy according to Section 35a SGB V". The scientific-medical societies and the Drugs Commission of the German Medical Association (AkdÄ) were also involved in writing on questions relating to the comparator therapy in the present therapeutic indication according to Section 35a, paragraph 7 SGB V. In this regard, a joint written statement from the Society for Neuropaediatrics (GNP) and the German Society of Neurology (Deutsche Gesellschaft für Neurologie e.V. [DGN]) has been received.

The evidence in the present therapeutic indication is very limited. No methodologically sound reviews or guidelines could be identified during the systematic search. A total of four guidelines subject to methodological limitations were presented additionally. These also include the S2k guideline issued by the German Society for Neurosurgery (DGNC) on the diagnosis and treatment of peripheral nerve tumours.

Surgical intervention for plexiform neurofibromas is not an option as they are classified as inoperable according to the therapeutic indication.

According to the guidelines, a therapy trial with selumetinib may be carried out as a non-surgical therapeutic concept. As selumetinib is the medicinal product to be assessed, this therapy option is not considered as the appropriate comparator therapy.

With regard to the issue of comparator therapy, the scientific-medical societies explain in their written statement that the MEK inhibitor mirdametinib is available for children aged two years and older, whereas there is no medicinal therapy option for younger children.

By resolution of 19 March 2026, a hint of non-quantifiable additional benefit of mirdametinib was identified in the benefit assessment thereof, since the scientific data did not allow quantification. The assessment was based on a single-arm study. This revealed an improvement in therapeutic benefit due to a significant reduction in tumour volume compared with baseline. The active ingredient mirdametinib is a new treatment option for adults and children aged 2 years and older with symptomatic, inoperable plexiform neurofibromas associated with neurofibromatosis type 1. The active ingredient was only recently approved (marketing authorisation on 17 July 2025). According to the generally recognised state of medical knowledge, the significance of this treatment option in this patient population cannot yet be conclusively assessed; consequently, mirdametinib is not determined as the appropriate comparator therapy for the present resolution.

In the overall assessment, best supportive care (BSC) is determined as the appropriate comparator therapy for selumetinib in children aged 1 year to less than 3 years with symptomatic, inoperable plexiform neurofibromas associated with neurofibromatosis type 1. Best supportive care (BSC) is defined as the therapy that provides the best possible, patient-individually optimised, supportive treatment to alleviate symptoms and improve quality of life.

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

Any change to the appropriate comparator therapy requires a decision by the G-BA based on a prior review of the criteria set out in Chapter 5, Section 6, paragraph 3 VerfO.

2.1.3 Extent and probability of the additional benefit

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

Children aged 1 year to less than 3 years with symptomatic, inoperable plexiform neurofibromas (PN) associated with neurofibromatosis type 1 (NF1)

Hint of non-quantifiable additional benefit.

Justification:

Data basis

The pharmaceutical company presented the SPRINKLE, SPRINT and KOMET studies in the dossier for the benefit assessment of selumetinib in patients aged 1 year to less than 3 years with symptomatic, inoperable plexiform neurofibromas (PN) associated with neurofibromatosis type 1 (NF1).

SPRINKLE study

The SPRINKLE study is a single-arm, open-label phase I/II study investigating selumetinib in granule form in children aged 1 year to less than 7 years with PN associated with NF1. The 1st data cut-off from 8 April 2024 containing results for the endpoint categories of mortality and safety was presented in the dossier. Furthermore, the 2nd data cut-off from 16 December 2025 containing results for the endpoint categories of mortality, morbidity, health-related quality of life and safety was presented in the written statement procedure.

The SPRINT and KOMET studies

The SPRINT study is a single-arm, open-label phase I/II study investigating selumetinib in capsule form in children aged 3 years and older and adolescents with PN associated with NF1.

The KOMET study is a double-blind phase III randomised controlled trial comparing selumetinib capsules with placebo in adults with PN associated with NF1.

The SPRINT (phase II, stratum 1, data cut-off from 31 March 2021) and KOMET (data cut-offs from 5 August 2024 and 17 March 2025) studies were presented by the pharmaceutical company as supporting evidence. In this context, the pharmaceutical company refers to the patient populations comprising children aged 3 years and older, adolescents and adults within the same therapeutic indication. These populations were assessed in the benefit assessment procedures for selumetinib in the resolutions of 7 May 2026.[2,3]

The benefit assessment procedure for children aged 3 years and older and adolescents with symptomatic, inoperable PN associated with NF1[2] was based on the single-arm SPRINT study, which investigated the efficacy and safety of selumetinib. As part of the benefit assessment procedure, a non-quantifiable additional benefit of selumetinib in this therapeutic indication was identified for children aged 3 years and older and adolescents, based on "change in tumour volume" data.

[2]Selumetinib for the treatment of symptomatic, inoperable plexiform neurofibromas (PN) associated with neurofibromatosis type 1 (NF1) in children aged 3 years and older and adolescents – resolution of 7 May 2026

[3]Selumetinib for the treatment of symptomatic, inoperable plexiform neurofibromas (PN) associated with neurofibromatosis type 1 (NF1) in adults – resolution of 7 May 2026

The benefit assessment procedure for adults with symptomatic, inoperable PN associated with NF1[3] was based on the randomised controlled trial KOMET, which investigated the efficacy and safety of selumetinib compared with placebo. As part of the benefit assessment procedure, a minor additional benefit of selumetinib in this therapeutic indication was identified for adults, based on data relating to change in tumour volume, chronic pain, pain spikes and side effects.

The pharmaceutical company considered this data to be transferable to the analysed patient population of children aged 1 year to less than 3 years.

Assessment

A cross-endpoint analysis of the results of the SPRINKLE study

With the 2nd data cut-off submitted subsequently during the written statement procedure, the pharmaceutical company presented data on the endpoint categories of mortality, morbidity, health-related quality of life and side effects. The single-arm design of the SPRINKLE study precludes a comparative assessment of the data presented. The data are therefore generally unsuitable for the benefit assessment.

One exception to this is the morbidity endpoint of change in volume of the target lesion. The target lesion was defined as the most clinically relevant, inoperable PN that could be visualised using volumetric 3D MRI measurements. This endpoint was assessed as a secondary endpoint in the SPRINKLE study and operationalised as the change in volume of the target lesion from baseline, as measured by volumetric 3D MRI.

Based on the statements made by the clinical experts at the oral hearing, it can be assumed that no spontaneous remissions occur in the natural history of the disease in the present clinical picture and stage. The present indication represents a special case due to the partial external visibility of the tumours, which in some cases manifest themselves in clearly visible deformations, but can also be characterised by functional impairments independent of the visibility of the tumours. Consequently, the endpoint of change in volume of the target lesion is considered a patient-relevant endpoint in this indication, provided that significant reduction in the tumour size is shown by appropriate operationalisation. In this assessment, the endpoint of change in volume of the target lesion therefore constitutes an exception and is used here to derive the additional benefit.

The SPRINKLE study demonstrated a reduction in the target lesion (best percentage change in volume achieved) by –10%.

Due to the lack of a control group, the first fundamental question is to what extent this is an effect of the treatment. Furthermore, the results are subject to further uncertainty due to the major patient-individual fluctuations and the small number of study participants. Moreover, the effect of treatment with selumetinib on other existing plexiform neurofibromas that were not classified as target lesions was not assessed due to the operationalisation of the endpoint. Furthermore, due to the lack of a control group, it is not possible to distinguish naturally occurring fluctuations (e.g. due to the fluid content in the tumour caused by external factors) from changes observed since the enrolment in the study. However, a reduction in tumour volume in this therapeutic indication should generally be regarded as a therapeutic goal. The volume of PN represents the relevant manifestation of the disease and is the cause of any existing symptomatology with functional impairments and may also be accompanied by deformation.

Against this background, despite remaining uncertainties, an improvement in the therapeutic benefit of treatment with selumetinib in terms of a relevant reduction in tumour volume from

baseline can be identified, thereby demonstrating an advantage of selumetinib in the endpoint of change in tumour volume.

No suitable data are available on other patient-relevant endpoints. The results on other endpoints of the SPRINKLE study are presented additionally.

Treatment with selumetinib should be continued for as long as clinical benefit is observed, or until progression of plexiform neurofibromas or occurrence of unacceptable toxicity.

On the transferability of the results of the SPRINT and KOMET studies

This benefit assessment is based on the results of the 2nd data cut-off for the SPRINKLE study. By contrast, the marketing authorisation of selumetinib for this therapeutic indication was based on the results of the 1st data cut-off from the SPRINKLE study in the endpoint categories of mortality and safety, as well as pharmacokinetics. At that time, results on efficacy in children aged 1 year to less than 3 years were not yet available. The European Medicines Agency (EMA) assessment report on selumetinib[4] also states that the uncontrolled SPRINT study was used as the basis for extrapolating efficacy data from already approved older patient populations to children aged 1 year to less than 3 years. In this context, the EMA carried out population pharmacokinetic (Pop-PK) modelling using data from children aged 3 years and older and adolescents (the SPRINT study; reference population), as well as from children aged 1 year to less than 7 years (the SPRINKLE study; target population). The extrapolation of efficacy data carried out by the EMA is therefore primarily based on exposure modelling and not on clinical data in the present therapeutic indication.

NF1 is a clinically heterogeneous genetic disorder characterised by progressive cutaneous, neurological, skeletal and neoplastic symptoms, and is caused by mutations in the NF1 tumour suppressor gene (17q11.2). The underlying pathophysiological mechanisms of the patient population relevant here – children aged 1 year to less than 3 years – are identical to those of older patients.

According to the statements made by clinical experts, the early juvenile tumour growth rate is, in turn, significantly higher than that in older patients. Furthermore, the clinical experts explained that pain occurs significantly less frequently in the patient population relevant here – children aged 1 year to less than 3 years – than in older patients.

Overall, the transferability of the results of the SPRINT and KOMET studies to the results of the 2nd data cut-off for the SPRINKLE study is therefore limited.

Nevertheless, the consistent findings in the next patient population – children aged 3 years and older and adolescents – from the SPRINT study support the findings of the SPRINKLE study regarding the endpoint of change in tumour volume in children aged 1 year to less than 3 years.

<u>Overall assessment</u>

Given the present data constellation, it is possible, despite the single-arm study design, to derive an additional benefit of selumetinib for the treatment ofsymptomatic, inoperable plexiform neurofibromas (PN) associated with neurofibromatosis type 1 (NF1) in children aged 1 year to less than 3 years.

[4] European Medicines Agency. Koselugo; assessment report [online]. 2025 [accessed: 21.07.2026]. URL: https://www.ema.europa.eu/en/documents/variation-report/koselugo-h-c-005244-x-0018-g-epar-assessment-report-variation_en.pdf.

Based on the statements made by the clinical experts, it can be assumed that no spontaneous remissions occur in the natural history of the disease in the present clinical picture and stage. Furthermore, the tumour growth rate is significantly higher, particularly in the early juvenile period, than in older patients. At the endpoint level, despite remaining uncertainties, an improvement in the therapeutic benefit of treatment with selumetinib in terms of a relevant reduction in tumour volume from baseline can be identified, thereby demonstrating an advantage of selumetinib in the endpoint of change in tumour volume.

Due to the single-arm study design, no suitable data are available on other patient-relevant endpoints in the categories of mortality, morbidity, quality of life and side effects. Consequently, it is also not possible to weigh against potential disadvantages in the overall assessment.

Quantification of the additional benefit is made more difficult by the wide patient-individual fluctuations, the small number of study participants and the comparison with baseline. By contrast, the findings of the SPRINKLE study regarding reduction in tumour volume are supported by the consistent findings of the SPRINT study in the next patient population of children aged 3 years and older and adolescents.

Given the relevant limitations in the data basis, it is therefore not possible to quantify the extent of the additional benefit. Consequently, a non-quantifiable additional benefit of selumetinib has been identified in the present assessment for the treatment of symptomatic, inoperable PN associated with NF1 in children aged 1 year to less than 3 years.

Reliability of data (probability of additional benefit)

Being a single-arm study, the SPRINKLE study does not allow a comparative assessment.

The advantage of selumetinib in terms of a relevant reduction in tumour volume from baseline is identified. Against this background, the reliability of data is classified under the "hint" category.

2.1.4 Summary of the assessment

The present assessment is the benefit assessment of a new therapeutic indication for the medicinal product Koselugo with the active ingredient selumetinib. Koselugo was approved as an orphan drug. Since the EUR 30 million turnover limit has been exceeded, a standard assessment of the new therapeutic indication outlined below is carried out:

Koselugo as monotherapy is indicated for the treatment of symptomatic, inoperable plexiform neurofibromas (PN) in patients with neurofibromatosis type 1 (NF1) aged 1 year to less than 7 years and for older patients with swallowing difficulties.

This benefit assessment only covers children aged 1 year to less than 3 years and not the entire therapeutic indication as set out in the marketing authorisation, since assessments are already available for children aged 3 years and older, adolescents and adults (resolutions of 7 May 2026).

Best supportive care was determined as the appropriate comparator therapy.

The single-arm study design precludes a comparative assessment. However, there is a special case regarding the endpoint "change in volume of the target lesion". In the present therapeutic indication, this endpoint should generally be regarded as a therapeutic goal. Based on the statements made by the clinical experts, it can be assumed that no spontaneous remissions occur in the natural history of the disease in the present clinical picture/ stage. Furthermore, the tumour growth rate is significantly higher, particularly in the early juvenile period, than in older patients. The volume of plexiform neurofibromas (PN) represents the

relevant manifestation of the disease and is the cause of any existing symptomatology with functional impairments and may also be accompanied by deformation. The SPRINKLE study demonstrated a reduction in the target lesion (best percentage volume reduction achieved) by –10%. The findings of the SPRINKLE study are supported by the consistent findings of the SPRINT study in the directly adjacent patient population of children aged 3 years and older and adolescents.

Despite remaining uncertainties, an improvement in the therapeutic benefit of treatment with selumetinib can be identified overall due to a relevant reduction in tumour volume from baseline.

Due to the single-arm study design, no suitable data are available on other patient-relevant endpoints.

In the overall assessment, a non-quantifiable additional benefit of selumetinib was identified.

Due to the limitations mentioned, the reliability of data is classified in the "hint" category.

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 written statement procedure. Uncertainties exist in particular for the following reasons:

The used prevalence rates for NF1 are based on a study of 6-year-olds. Transferring this to 1- to 2-year-olds leads to an overestimation, as a significant percentage do not yet meet all the diagnostic criteria.

The study[5] used to calculate the percentage of paediatric patients with at least one PN out of the total number of paediatric patients with NF1 may lead to an overestimation, as the study includes only a small percentage of paediatric patients with NF1 and it is unclear whether this constitutes a selected patient group. A nationwide Danish cohort study[6] reports significantly lower percentage values.

Furthermore, the studies[5][7] used to calculate the percentages of patients with at least one PN, symptomatic PNs as well as symptomatic, inoperable PNs included older children and adolescents who are not part of the age group under assessment. Transferring this to 1- to 2-year-olds may lead to an overestimation.

Overall, an 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

[5] Nguyen R, Kluwe L, Fuensterer C et al. Plexiform neurofibromas in children with neurofibromatosis type 1: frequency and associated clinical deficits. J Pediatr 2011; 159(4): 652-5.e2. https://doi.org/10.1016/j.jpeds.2011.04.008.

[6] Ejerskov C, Farholt S, Nielsen FSK et al. Clinical Characteristics and Management of Children and Adults with Neurofibromatosis Type 1 and Plexiform Neurofibromas in Denmark: A Nationwide Study. Oncol Ther 2023; 11(1): 97-110. https://doi.org/10.1007/s40487-022-00213-4.

[7] Nguyen R, Ibrahim C, Friedrich RE et al. Growth behaviour of plexiform neurofibromas after surgery. Genet Med 2013; 15(9): 691-697. https://doi.org/10.1038/gim.2013.30.

product characteristics, SmPC) for Koselugo (active ingredient: selumetinib) at the following publicly accessible link (last access: 24 June 2026):

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

Treatment with selumetinib should only be initiated and monitored by specialists in internal medicine, haematology and oncology or specialists in paediatrics and adolescent medicine specialising in neuropaediatrics, paediatric haematology and oncology, all of whom are experienced in the treatment of patients with NF1-related tumours.

This medicinal product was approved under "exceptional circumstances". This means that further evidence of the benefit of the medicinal product is anticipated. The EMA will assess new information on this medicinal product at least annually and update the product information as necessary.

2.4 Treatment costs

The treatment costs are based on the contents of the product information and the information listed in the LAUER-TAXE® (last revised: 1 June 2026).The calculation of treatment costs is generally based on the last revised LAUER-TAXE® version following the publication of the benefit assessment.

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.

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.

The treatment costs for best supportive care are different for each individual 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:

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Selumetinib	Continuously, 2 x daily	365.0	1	365.0
Best supportive care	Different from patient to patient			
Appropriate comparator therapy				
Best supportive care	Different from patient to patient			

Consumption:

For the calculation of the dosages depending on body weight (BW) or body surface area (BSA), the average body measurements from the official representative statistics "2025 Microcensus – body measurements of the population" were applied. The average body weight of children aged 1 year to less than 2 years is 12.7 kg, with a body height of 0.84 m. This results in a body surface area of 0.53 m² (calculated according to Du Bois 1916)[8]. The average body weight of children aged 2 years to less than 3 years is 14.8 kg, with a body height of 0.93 m. This results in a body surface area of 0.60 m² (calculated according to Du Bois 1916)[8].

The calculation was based on the dosage regimen recommended in the product information for selumetinib and determined by body surface area.

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					
Selumetinib					
Child BSA of 0.53 m²	12.5 mg 2 x daily	25 mg	2 x 7.5 mg + 2 x 5 mg	365.0	730 x 7.5 mg + 730 x 5 mg
Child BSA of 0.60 m²	15 mg 2 x daily	30 mg	4 x 7.5 mg	365.0	1,460 x 7.5 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.

[8] Federal Health Reporting. Average body measurements of the population (2025, both sexes), 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					
Selumetinib 5 mg granules in capsule for opening	60 GRC	€ 2,674.32	€ 1.77	€ 0.00	€ 2,672.55
Selumetinib 7.5 mg granules in capsule for opening	60 GRC	€ 4,006.28	€ 1.77	€ 0.00	€ 4,004.51
Best supportive care	Different from patient to patient				
Appropriate comparator therapy					
Best supportive care	Different from patient to patient				
Abbreviations: GRC = granules in capsules for opening					

LAUER-TAXE® last revised: 1 June 2026

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

At their session on 7 April 2021, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

A review of the appropriate comparator therapy took place once the positive opinion was granted. At their session on 27 January 2026, the Subcommittee on Medicinal Products newly determined the appropriate comparator therapy.

On 4 February 2026, the pharmaceutical company submitted a dossier for the benefit assessment of selumetinib to the G-BA in due time in accordance with Chapter 5 Section 8,

paragraph 1, No. 2 VerfO.

By letter dated 5 February 2026 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefit of medicinal products with new active ingredients in accordance with Section 35a SGB V, the G-BA commissioned the IQWiG to assess the dossier concerning the active ingredient selumetinib.

The dossier assessment by the IQWiG was submitted to the G-BA on 13 May 2026, and the written statement procedure was initiated with publication on the G-BA website on 15 May 2026. The deadline for submitting written statements was 5 June 2026.

The oral hearing was held on 22 June 2026.

By letter dated 23 June 2026, the IQWiG was commissioned with a supplementary assessment of data submitted in the written statement procedure. The addendum prepared by the IQWiG was submitted to the G-BA on 10 July 2026.

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

The evaluation of the written statements received and the oral hearing were discussed at the Subcommittee's session on 28 July 2026, and the draft resolution was conclusively discussed.

At their session on 6 August 2026, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	7 April 2021	Determination of the appropriate comparator therapy
Subcommittee on Medicinal Products	27 January 2026	New determination of the appropriate comparator therapy
Working group Section 35a	17 June 2026	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	22 June 2026 23 June 2026	Conduct of the oral hearing, commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	30 June 2026 14 July 2026	Consultation on the dossier assessment by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	28 July 2026	Concluding discussion of the draft resolution
Plenum	6 August 2026	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 6 August 2026

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

Dr Optendrenk