

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 (reassessment of an orphan drug after exceeding
the EUR 30 million limit: neurofibromatosis type 1 (≥ 3 to < 18
years))

dated 7 May 2026

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1. Legal basis

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

1. approved therapeutic indications,
2. medical benefit,
3. additional medical benefit in relation to the appropriate comparator therapy,
4. number of patients and patient groups for whom there is a therapeutically significant additional benefit,
5. treatment costs for the statutory health insurance funds,
6. requirement 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.

Koselugo for the treatment of symptomatic, inoperable plexiform neurofibromas (PN) in neurofibromatosis type 1 (NF1) is approved 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.

At their session on 21 December 2023, the G-BA decided on the benefit assessment of selumetinib in the therapeutic indication

"Koselugo as monotherapy is indicated for the treatment of symptomatic, inoperable plexiform neurofibromas (PN) in paediatric patients with neurofibromatosis type 1 (NF1) aged 3 years and older."

in accordance with Section 35a SGB V.

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

By letter dated 14 October 2025, the pharmaceutical company was requested to submit a dossier for the benefit assessment according to Section 35a SGB V by 15 January 2026, due to exceeding the EUR 30 million turnover limit. Pursuant to Section 4, paragraph 3, number 4 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 8, paragraph 1, number 6 Rules of Procedure (VerfO), the pharmaceutical company submitted the final dossier to the G-BA on 14 November 2025.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 16 February 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 to the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG and the statements submitted in the written statement and oral hearing procedure.

In order to determine the extent of the additional benefit, the G-BA have assessed the studies relevant to the marketing authorisation on the basis of their therapeutic relevance (qualitative), in accordance with the criteria laid down in Chapter 5 Section 5, paragraph 7, sentence 1, numbers 1 to 4 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods¹ 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:

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

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 adult and paediatric patients with neurofibromatosis type 1 (NF1) aged 3 years and older.

Therapeutic indication of the resolution (resolution of 7 May 2026):

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

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Paediatric patients aged 3 years and older with symptomatic, inoperable plexiform neurofibromas (PN) in neurofibromatosis type 1 (NF1)

Appropriate comparator therapy for selumetinib as monotherapy:

- Best supportive care

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

The appropriate comparator therapy must be an appropriate therapy in the therapeutic indication 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 in the therapeutic indication, or
3. according to the generally recognised state of medical knowledge, the off-label use for relevant patient groups or indication areas is generally preferable to the medicinal products previously approved in the therapeutic indication.

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

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

- On 1. 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
 - Selumetinib: resolution of 21 December 2023
- 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. There are no written statements.

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. This should be carried out in consultation with a paediatric oncology centre and under close supervision, with regular neurological and functional assessments, preferably at an NF centre or a centre for rare diseases.

The two MEK inhibitors, selumetinib and mirdametininib, are approved for the therapeutic indication. As selumetinib is the medicinal product to be assessed, this therapy option is not considered as the appropriate comparator therapy.

By resolution of 19 March 2026, a hint for a non-quantifiable additional benefit of mirdametininib was identified in the benefit assessment thereof, since the scientific data did not allow quantification. The assessment was based on a single-arm study. The active ingredient mirdametininib is a new treatment option for adults and children aged 2 years and older with symptomatic, inoperable PN in NF1. 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 the present treatment setting cannot yet be conclusively assessed; consequently, mirdametininib 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 paediatric patients aged 3 years and older with symptomatic, inoperable plexiform neurofibromas in neurofibromatosis type 1 (NF1). 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:

Paediatric patients aged 3 years and older with symptomatic, inoperable plexiform neurofibromas (PN) in neurofibromatosis type 1 (NF1)

Hint for a non-quantifiable additional benefit.

Justification:

The pharmaceutical company presented the results of the single-arm, open-label SPRINT, D1346C00013, D1346C00011, D1346C00015, SPRINKLE and ESR-17-12847 studies for the benefit assessment of selumetinib. The SPRINT study is used for the present benefit assessment. The D1346C00013, D1346C00011, D1346C00015, SPRINKLE and ESR-17-12847 studies are not used for the present benefit assessment for the following reasons:

With regard to the D1346C00015, ESR-17-12847 and SPRINKLE studies, it is unclear whether, and if so to what percentage patients, who were not covered by the approved therapeutic indication for selumetinib, were enrolled. Furthermore, the D1346C00015 study has a very brief duration of observation. Moreover, due to the age restrictions in the inclusion criteria, the D1346C00015, ESR-17-12847 and SPRINKLE studies represent only a sub-population of the therapeutic indication for selumetinib. In addition, with regard to the D1346C00013, D1346C00011 and ESR-17-12847 studies, there is uncertainty regarding the transferability of the study results to the German healthcare context, as these studies were conducted exclusively in Asia. Furthermore, the D1346C00013, D1346C00011, D1346C00015, SPRINKLE and ESR-17-12847 studies are characterised by a relatively small number of study participants. Overall, the D1346C00013, D1346C00011, D1346C00015, SPRINKLE and ESR-17-12847 studies are therefore unsuitable for the benefit assessment.

SPRINT study

The SPRINT study is an ongoing, multicentre, open-label, single-arm phase I/II study. The study has been conducted in 4 study sites in the USA since August 2011.

For the phase II, study participants with type 1 neurofibromatosis with at least one inoperable PN were enrolled in one of two strata based on whether PN-related morbidity was already present at the time of enrolment (stratum 1) or whether there was no significant clinical morbidity but the potential for such morbidity (stratum 2). PN-related morbidity included PN-induced pain, deformation or functional impairment such as vision loss, facial motor impairment, hearing loss, swallowing problems, speech impairment, airway obstruction, respiratory impairment, bladder dysfunction, bowel dysfunction, muscle weakness, restricted range of motion or sensory impairment.

Stratum 1 of phase II is used for the present benefit assessment. Recruitment of patients for phase II began in August 2015. Stratum 2 of phase II comprises asymptomatic subjects who are not included in the therapeutic indication of selumetinib. A total of 50 children 3 years and older and adolescents were enrolled in stratum 1 of phase II.

In the SPRINT study, the most clinically relevant, inoperable PN that could be detected using volumetric 3D MRI measurement was defined as the target PN. The primary study endpoint of phase II was the objective response rate (ORR). In addition, data on mortality, morbidity, quality of life and side effects were collected.

In the dossier, the pharmaceutical company presented the results of the data cut-off from 31 March 2021, which was required by the European Medicines Agency (EMA) in connection with the conditional marketing authorisation of selumetinib. Further data cut-offs were carried out on 29 June 2018 (primary interim analysis) and 29 March 2019.

Studies on the appropriate comparator therapy

The pharmaceutical company did not provide any comparative analyses between selumetinib and the appropriate comparator therapy for the benefit assessment. Instead, data on annualized growth rates of the PN from the studies by Fisher 2008², Kotch 2023³, Nguyen 2012⁴, Nguyen 2013⁵ and Well 2021⁶ on the natural history of the disease are presented.

The studies are subject to uncertainty: With regard to the studies, the pharmaceutical company merely presented the relevant publications, but did not provide the corresponding study protocols or study reports. There is therefore a lack of relevant information regarding the conduct of the studies and the baseline characteristics of the study populations. This information is required for assessing the relevance of the study. It is therefore not possible to adequately assess the comparability with the SPRINT study. For example, it is not possible to derive the percentage of patients who had symptomatic and inoperable PN at baseline according to the present therapeutic indication. It is therefore not possible to assess whether these patients are sufficiently similar to the populations in the studies on selumetinib. Overall, there is insufficient comparability with the studies on selumetinib, or it cannot be adequately assessed due to a lack of information. The publications provided do not offer sufficient information on the use of best supportive care either. In the overall assessment, the data are unsuitable for the benefit assessment.

² Fisher MJ, Basu S, Dombi E et al. The role of [18F]-fluorodeoxyglucose positron emission tomography in predicting plexiform neurofibroma progression. *J Neurooncol* 2008; 87(2): 165-171. <https://doi.org/10.1007/s11060-007-9501-5>.

³ Kotch C, Dombi E, Shah AC et al. Retrospective Cohort Analysis of the Impact of Puberty on Plexiform Neurofibroma Growth in Patients with Neurofibromatosis Type 1. *J Pediatr* 2023; 260: 113513. <https://doi.org/10.1016/j.jpeds.2023.113513>.

⁴ Nguyen R, Dombi E, Widemann BC et al. Growth dynamics of plexiform neurofibromas: a retrospective cohort study of 201 patients with neurofibromatosis 1. *Orphanet J Rare Dis* 2012; 7: 75. <https://doi.org/10.1186/1750-1172-7-75>.

⁵ 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>.

⁶ Well L, Dobel K, Kluwe L et al. Genotype-phenotype correlation in neurofibromatosis type-1: NF1 whole gene deletions lead to high tumour-burden and increased tumour-growth. *PLoS Genet* 2021; 17(5): e1009517. <https://doi.org/10.1371/journal.pgen.1009517>.

Extent and probability of the additional benefit

Analysis across endpoints

The pharmaceutical company presented data on the endpoint categories of mortality, morbidity, quality of life and side effects. The single-arm design of the SPRINT 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. This endpoint was assessed as a secondary endpoint in the SPRINT study and operationalised as the change in volume of the PN - defined as the target lesion - from baseline, measured by 3D volumetric 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.

In the SPRINT study, a -27% reduction in the target lesion (best percentage volume reduction achieved) could be demonstrated. A volume reduction was observed in 96% of patients.

Due to the lack of a control group, the first fundamental question is to what extent this is an effect of the treatment. The results are also subject to a number of other uncertainties: On the one hand, due to the operationalisation of the endpoint, the effect of treatment with selumetinib on other existing plexiform neurofibromas that were not classified as target lesions was not assessed in the majority of study participants. 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 always 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 SPRINT study are presented additionally.

Conclusion:

Given the present data constellation, it is possible, despite the single-arm study design, to derive an additional benefit of selumetinib for the treatment of symptomatic, inoperable plexiform neurofibromas (PN) in paediatric patients with neurofibromatosis type 1 (NF1) aged 3 years and older.

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. 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.

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 in paediatric patients with NF1 aged 3 years and older.

Reliability of data (probability of additional benefit)

Being a single-arm study, the SPRINT 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 a new benefit assessment of the medicinal product Koselugo with the active ingredient selumetinib due to exceeding the EUR 30 million turnover limit. Koselugo was approved as an orphan drug. The therapeutic indication assessed here is as follows:

Treatment of symptomatic, inoperable plexiform neurofibromas (PN) in paediatric patients with neurofibromatosis type 1 (NF1) aged 3 years and older.

Best supportive care was determined as the appropriate comparator therapy.

The SPRINT study is used for the present benefit assessment. This is an ongoing, open-label, single-arm phase I/II study. 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. 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. In the SPRINT study, a -27% reduction in the target lesion (best percentage volume reduction achieved) was demonstrated.

Despite remaining uncertainties, an improvement in the therapeutic benefit of treatment with selumetinib can be identified 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).

In order to ensure consistent determination of patient numbers in the present therapeutic indication, this resolution is based on the information from the resolution on the benefit assessment of mirdametininib (resolution of 19 March 2026).

The patient numbers presented by the pharmaceutical company in the present benefit assessment procedure are subject to uncertainty. On the one hand, the limited transferability of percentages of patients with NF1, as well as patients with NF1 and at least one PN is a key factor for this. On the other, the uncertainties involved in the determination of the percentage of patients with symptomatic and inoperable PN are significant.

The patient numbers in the mirdametininib procedure was deemed to have been overestimated for the (broader) therapeutic indication to be assessed. For the target population to be assessed in the current procedure, the pharmaceutical company stated the patient numbers of a similar magnitude. Due to the absence of more suitable data, the information from the mirdametininib procedure – taking into account the uncertainties addressed in the assessment – should also be used for the present (narrower) therapeutic indication.

The resolution is therefore based on the information from the resolution on the benefit assessment of mirdametininib (resolution of 19 March 2026), which can be used despite the continuing uncertainties.

Additional uncertainties remain, as the number of patients in this therapeutic indication (NF1-PN; ≥ 3 to < 18 years) is expected to be lower than in the mirdametininib procedure (NF1-PN; ≥ 2 years).

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 Koselugo (active ingredient: selumetinib) at the following publicly accessible link (last access: 23 March 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 received a conditional marketing authorisation. This means that further evidence of the benefit of the medicinal product is anticipated. The European Medicines Agency (EMA) will assess new information on this medicinal product at least annually and update the product information where 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 March 2026). The calculation of treatment costs is generally based on the last revised LAUER-TAXE® version following the publication of the benefit assessment.

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.

In this particular patient population, it is up to the physician to decide the most appropriate dosage form for the respective child < 6 years of age, depending on body weight and dose. For this reason, where available, the dosages of both solid (tablet or hard capsule) and additional child-friendly dosage forms are shown for each active ingredient, if no limitations are described 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.

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.

Paediatric patients aged 3 years and older with symptomatic, inoperable plexiform neurofibromas (PN) in neurofibromatosis type 1 (NF1)

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 surface area, the average body measurements from the official representative statistics "Microcensus 2017 – body measurements of the population" and "Microcensus 2021 – body measurements of the population" were applied⁷. Average body height and weight for children aged 3 years are 1.01 m and 16.2 kg respectively⁸. 17-year-olds are on average 1.74 metres tall and weigh 67.2 kg⁸. This results in body surface areas (BSA) of 0.67 m² for 3-year-olds and 1.81 m² for 17-year-olds (calculation according to Du Bois 1916).

The doses per m² body surface area recommended in the product information were used as the calculation basis.

⁷ Federal Health Reporting. Average body measurements of the population (2021, both sexes, 15 years and older), www.gbe-bund.de

⁸ Federal Health Reporting. Average body measurements of the population (2017, both sexes, 1 year and older), www.gbe-bund.de

Paediatric patients aged 3 years and older with symptomatic, inoperable plexiform neurofibromas (PN) in neurofibromatosis type 1 (NF1)

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					
3 years HC	25 mg/m ² BSA = 20 mg + 10 mg ⁹	30 mg	3 x 10 mg	365.0	1,095 x 10 mg
3 years GRC	25 mg/m ² BSA = 15 mg + 15 mg ⁹	30 mg	4 x 7.5 mg	365.0	1,460 x 7.5 mg
17 years HC	25 mg/m ² BSA = 45 mg + 45 mg ⁹	90 mg	2 x 25 mg + 4 x 10 mg	365.0	730 x 25 mg + 1,460 x 10 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.

⁹ Dosage according to the regimen in the product information for selumetinib

Paediatric patients aged 3 years and older with symptomatic, inoperable plexiform neurofibromas (PN) in neurofibromatosis type 1 (NF1)

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 7.5 mg	60 GRC	€ 4,006.28	€ 1.77	€ 0.00	€ 4,004.51
Selumetinib 10 mg	60 HC	€ 5,338.22	€ 1.77	€ 0.00	€ 5,336.45
Selumetinib 25 mg	60 HC	€ 13,329.94	€ 1.77	€ 0.00	€ 13,328.17
Best supportive care	Different from patient to patient				
Appropriate comparator therapy					
Best supportive care	Different from patient to patient				
Abbreviations: GRC = granules for release from capsules; HC = hard capsules					

LAUER-TAXE® last revised: 1 March 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.

2.5 Designation of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V that can be used in a combination therapy with the assessed medicinal product

According to Section 35a, paragraph 3, sentence 4, the G-BA designate all medicinal products with new active ingredients that can be used in a combination therapy with the assessed medicinal product for the therapeutic indication to be assessed on the basis of the marketing authorisation under Medicinal Products Act.

Basic principles of the assessed medicinal product

A designation in accordance with Section 35a, paragraph 3, sentence 4 SGB V requires that it is examined based on the product information for the assessed medicinal product whether it can be used in a combination therapy with other medicinal products in the assessed therapeutic indication. In the first step, the examination is carried out on the basis of all sections of the currently valid product information for the assessed medicinal product.

If the assessed medicinal product contains an active ingredient or a fixed combination of active ingredients in the therapeutic indication of the resolution (assessed therapeutic indication) and is approved exclusively for use in monotherapy, a combination therapy is not considered due to the marketing authorisation under Medicinal Products Act, which is why no designation is made.

A designation is also not considered if the G-BA have decided on an exemption as a reserve antibiotic for the assessed medicinal product in accordance with Section 35a, paragraph 1c, sentence 1 SGB V. The additional benefit is deemed to be proven if the G-BA have decided on an exemption for a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V; the extent of the additional benefit and its therapeutic significance are not to be assessed by the G-BA. Due to the lack of an assessment mandate by the G-BA following the resolution on an exemption according to Section 35a, paragraph 1c, sentence 1 SGB V with regard to the extent of the additional benefit and the therapeutic significance of the reserve antibiotic to be assessed, there is a limitation due to the procedural privileging of the pharmaceutical companies to the effect that neither the proof of an existing nor an expected at least considerable additional benefit is possible for exempted reserve antibiotics in the procedures according to Section 35a paragraph 1 or 6 SGB V and Section 35a paragraph 1d SGB V. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V must therefore also be taken into account at the level of designation according to Section 35a, paragraph 3, sentence 4 SGB V in order to avoid valuation contradictions.

With regard to the further examination steps, a differentiation is made between a "determined" or "undetermined" combination, which may also be the basis for a designation.

A "determined combination" exists if one or more individual active ingredients which can be used in combination with the assessed medicinal product in the assessed therapeutic indication are specifically named.

An "undetermined combination" exists if there is information on a combination therapy, but no specific active ingredients are named. An undetermined combination may be present if the

information on a combination therapy:

- names a product class or group from which some active ingredients not specified in detail can be used in combination therapy with the assessed medicinal product, or
- does not name any active ingredients, product classes or groups, but the assessed medicinal product is used in addition to a therapeutic indication described in more detail in the relevant product information, which, however, does not include data from the product information on active ingredients within the scope of this therapeutic indication.

Concomitant active ingredient

The concomitant active ingredient is a medicinal product with new active ingredients that can be used in combination therapy with the assessed medicinal product for the therapeutic indication to be assessed.

For a medicinal product to be considered as a concomitant active ingredient, it must be classified as a medicinal product with new active ingredients according to Section 2 paragraph 1 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with the corresponding regulations in Chapter 5 of the Rules of Procedure of the G-BA as of the date of the present resolution. In addition, the medicinal product must be approved in the assessed therapeutic indication, whereby a marketing authorisation is sufficient only for a sub-area of the assessed therapeutic indication.

Based on an "undetermined combination", the concomitant active ingredient must be attributable to the information on the product class or group or the therapeutic indication according to the product information of the assessed medicinal product in the assessed therapeutic indication, whereby the definition of a product class or group is based on the corresponding requirements in the product information of the assessed medicinal product.

In addition, there must be no reasons for exclusion of the concomitant active ingredient from a combination therapy with the assessed medicinal product, in particular no exclusive marketing authorisation as monotherapy.

In addition, all sections of the currently valid product information of the eligible concomitant active ingredient are checked to see whether there is any information that excludes its use in combination therapy with the assessed medicinal product in the assessed therapeutic indication under marketing authorisation regulations. Corresponding information can be, for example, dosage information or warnings. In the event that the medicinal product is used as part of a determined or undetermined combination which does not include the assessed medicinal product, a combination with the assessed medicinal product shall be excluded.

Furthermore, the product information of the assessed medicinal product must not contain any specific information that excludes its use in combination therapy with the eligible concomitant active ingredient in the assessed therapeutic indication under marketing authorisation regulations.

Medicinal products with new active ingredients for which the G-BA have decided on an exemption as a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V are ineligible as concomitant active ingredients. The procedural privileging of the

reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V also applies accordingly to the medicinal product eligible as a concomitant active ingredient.

Designation

The medicinal products which have been determined as concomitant active ingredients in accordance with the above points of examination are named by indicating the relevant active ingredient and the invented name. The designation may include several active ingredients, provided that several medicinal products with new active ingredients may be used in the same combination therapy with the assessed medicinal product or different combinations with different medicinal products with new active ingredients form the basis of the designation.

If the present resolution on the assessed medicinal product in the assessed therapeutic indication contains several patient groups, the designation of concomitant active ingredients shall be made separately for each of the patient groups.

Exception to the designation

The designation excludes combination therapies for which - patient group-related - a considerable or major additional benefit has been determined by resolution according to Section 35a, paragraph 3, sentence 1 SGB V or it has been determined according to Section 35a, paragraph 1d, sentence 1 SGB V that at least considerable additional benefit of the combination can be expected. In this context, the combination therapy that is excluded from the designation must, as a rule, be identical to the combination therapy on which the preceding findings were based.

In the case of designations based on undetermined combinations, only those concomitant active ingredients - based on a resolution according to Section 35a, paragraph 3, sentence 1 SGB V on the assessed medicinal product in which a considerable or major additional benefit had been determined - which were approved at the time of this resolution are excluded from the designation.

Legal effects of the designation

The designation of combinations is carried out in accordance with the legal requirements according to Section 35a, paragraph 3, sentence 4 and is used exclusively to implement the combination discount according to Section 130e SGB V between statutory health insurance funds and pharmaceutical companies. The designation is not associated with a statement as to the extent to which a therapy with the assessed medicinal products in combination with the designated medicinal products corresponds to the generally recognised state of medical knowledge. The examination was carried out exclusively on the basis of the possibility under Medicinal Products Act to use the medicinal products in combination therapy in the assessed therapeutic indication based on the product information; the generally recognised state of medical knowledge or the use of the medicinal products in the reality of care were not the subject of the examination due to the lack of an assessment mandate of the G-BA within the framework of Section 35a, paragraph 3, sentence 4 SGB V.

The findings made neither restrict the scope of treatment required to fulfil the medical treatment mandate, nor do they make statements about expediency or economic feasibility.

Justification for the findings on designation in the present resolution:

Paediatric patients aged 3 years and older with symptomatic, inoperable plexiform neurofibromas (PN) in neurofibromatosis type 1 (NF1)

- No designation of medicinal products with new active ingredients that can be used in combination therapy pursuant to Section 35a, paragraph 3, sentence 4 SGB V, as the active ingredient to be assessed is an active ingredient approved in monotherapy.

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. The Subcommittee on Medicinal Products newly determined the appropriate comparator therapy at their session on 9 December 2025.

On 14 November 2025, 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 5, paragraphs 1 - 6 VerfO.

By letter dated 17 November 2025 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 11 February 2026, and the written statement procedure was initiated with publication on the G-BA website on 16 February 2026. The deadline for submitting statements was 9 March 2026.

The oral hearing was held on 23 March 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 session of the Subcommittee on 28 April 2026, and the draft resolution was approved.

At their session on 7 May 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	9 December 2025	New determination of the appropriate comparator therapy
Working group Section 35a	18 March 2026	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	23 March 2026	Conduct of the oral hearing
Working group Section 35a	01.04.2026; 15.04.2026	Consultation on the dossier assessment by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	28 April 2026	Concluding discussion of the draft resolution
Plenum	7 May 2026	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 7 May 2026

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

Prof. Hecken