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)
Abaloparatide (osteoporosis, postmenopausal women)

of 2 October 2024

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 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 trials the pharmaceutical company has conducted or commissioned, at the latest at the time of the first placing on the market as well as the marketing authorisation of new therapeutic indications of the medicinal product, and which must contain the following information in particular:

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

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 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 start of the benefit assessment procedure was the first placing on the (German) market of the active ingredient abaloparatide on 15 April 2024 in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure (VerfO) of the G-BA. 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 11 April 2024.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 15 July 2024 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 abaloparatide compared with the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG, and the statements submitted in the written statement and oral hearing procedure. In order to determine the extent of the additional benefit, the G-BA has 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 abaloparatide.

In the light of the above, and taking into account the statements received and the oral hearing, the G-BA has come to 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 Abaloparatide (Eladynos) in accordance with the product information

Treatment of osteoporosis in postmenopausal women at increased risk of fracture.

Therapeutic indication of the resolution (resolution of 2 October 2024):

see the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

<u>Postmenopausal women with osteoporosis at increased risk of fracture</u>

Appropriate comparator therapy for abaloparatide:

Patient-individual therapy taking into account risk of fracture and previous therapy with selection of:

Alendronic acid, risedronic acid, zoledronic acid, denosumab, romosozumab (women at significantly increased risk of fracture) and teriparatide

<u>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):</u>

The appropriate comparator therapy must be an appropriate therapy in the therapeutic indication in accordance with the generally recognised state of medical knowledge (Section 12 SGB V), preferably a therapy for which endpoint studies are available and which has proven

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

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 it determines 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.

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

on 1. Medicinal products with the following active ingredients are approved for the present therapeutic indication:

- Bisphosphonates (in combination with colecalciferol, if necessary):
  Alendronic acid, ibandronic acid, risedronic acid and zoledronic acid

- Other active ingredients with an influence on bone structure and mineralisation: Denosumab, sodium fluoride and romosozumab
- Selective oestrogen receptor modulators: Raloxifene and bazedoxifene
- Parathyroid hormones and analogues, parathyroid antagonists: Calcitonin and teriparatide
- Vitamin D3 and analogues
- Calcium preparations and combinations

on 2. A non-medicinal treatment is unsuitable as a comparator therapy in this therapeutic indication.

on 3. In the present therapeutic indication, the following resolutions and guidelines of the G-BA are available:

- Annex I of the Pharmaceuticals Directive (AM-RL) regulates the prescribability of calcium compounds and vitamin D (monopreparations or in combination) (points 11 and 12).
- Resolution on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V for the active ingredient romosozumab dated 3 September 2020.

on 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as 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 indication according to Section 35a paragraph 7 SGB V (see “Information on Appropriate Comparator Therapy”).

The S3 guideline on the *prevention, diagnosis and therapy of osteoporosis*[2] is particularly relevant for the German healthcare context.

The present therapeutic indication concerns the treatment of osteoporosis in postmenopausal women at increased risk of fracture. According to the guideline, specific medicinal treatment of osteoporosis is recommended in this treatment setting. In principle, bisphosphonates, selective oestrogen receptor modulators (raloxifene and bazedoxifene) and the active ingredients denosumab, romosozumab and teriparatide are available for this purpose.

Based on the available evidence, only subordinate recommendations are available for the active ingredient ibandronate (bisphosphonate) and for the selective oestrogen receptor modulators raloxifene and bazedoxifene. These active ingredients are therefore not determined as appropriate comparator therapy.

2 S3 guideline on prevention, diagnosis and therapy of osteoporosis in postmenopausal women and men over the age of 50. Version 2.1, 2023. https://register.awmf.org/assets/guidelines/183-001l_S3_Prophylaxe-Diagnostik-Therapie-der-Osteoporose_2023-11.pdf

According to the S3 guideline, specific medicinal therapy should be initiated and the osteoanabolic active ingredients romosozumab and teriparatide should be used, depending on the extent of the absolute risk of fracture in postmenopausal women.

As part of the update of the S3 guideline in 2023, a new method for determining the patient-individual 3-year risk of fracture using the DVO risk calculator was presented, which is explicitly referred to in the therapy recommendations.

A specific medicinal therapy should be recommended above a 5% 3-year risk of fracture. In the presence of severe or irreversible risk factors or a very high risk of imminent fractures, medicinal therapy should be considered even if the 3-year risk of fracture is between 3% and 5%.

If the absolute risk of fracture is above the osteoanabolic threshold (above 10%/ 3years), an osteoanabolic substance should be recommended. If the absolute risk of fracture is above the therapy threshold and below the osteoanabolic threshold (between 5 and 10%/ 3 years), the use of an osteoanabolic substance can be considered, taking into account the authorisation status and contraindications.

Treatment with the osteoanabolic active ingredients romosozumab and teriparatide is limited to one and two years respectively, according to the product information. According to the S3 guideline, antiresorptive follow-up therapy should be given at the end of romosozumab and teriparatide therapy.

In the overall assessment, it is therefore considered appropriate to determine a patient-individual therapy in the present indication, taking into account the risk of fracture and previous therapy by selecting alendronic acid, risedronic acid, zoledronic acid, denosumab as well as romosozumab and teriparatide.

With regard to the use of the active ingredient romosozumab, it should be noted that it is only approved for postmenopausal women at significantly increased risk of fracture.

It is pointed out that all patients with osteoporosis should receive sufficient calcium and vitamin D supplements as part of a basic therapy.

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

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

Change of the appropriate comparator therapy

The adjustment of the appropriate comparator therapy particularly takes account of the update of the S3-guideline (November 2023). To date, therapy with one of the following active ingredients has been considered appropriate for the treatment of all postmenopausal women with osteoporosis at increased risk of fracture: Alendronic acid, risedronic acid, zoledronic acid, denosumab, romosozumab (women at significantly increased risk of fracture) or teriparatide.

With the introduction of the DVO risk calculator, reference values for fracture risk were added to the current therapy recommendations.

According to the current S3 guideline, the initiation of specific medicinal therapy and the use of the osteoanabolic active ingredients romosozumab or teriparatide are recommended, depending on the absolute risk of fracture in postmenopausal women. A specific medicinal therapy should be recommended above a 5% 3-year risk of fracture. In the presence of severe or irreversible risk factors or a very high risk of imminent fractures, medicinal therapy should be considered even if the 3-year risk of fracture is between 3% and 5%. Treatment with the osteoanabolic substances teriparatide or romosozumab should be recommended to women at a risk of fracture ≥ 10%/ 3 years. If the risk is between 5% and 10%/ 3 years, the use of an osteoanabolic substance can also be considered, taking into account the authorisation status and contraindications.

Based on these recommendations, it appears necessary to change the appropriate comparator therapy to a patient-individual therapy, taking into account the risk of fracture and previous therapy by selecting alendronic acid, risedronic acid, zoledronic acid, denosumab as well as romosozumab and teriparatide.

The G-BA therefore considers it appropriate to change the appropriate comparator therapy at this point in time and to adapt it to the current state of medical knowledge.

2.1.3 Extent and probability of the additional benefit

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

For postmenopausal women with osteoporosis at increased risk of fracture, the additional benefit of abaloparatide compared with the appropriate comparator therapy is not proven.

Justification:

To demonstrate the additional benefit of abaloparatide in the treatment of postmenopausal osteoporosis, the pharmaceutical company presented the results of the multicentre, randomised, phase III ACTIVE study. The study compared the efficacy and safety of abaloparatide versus teriparatide and placebo over a period of 18 months. While the abaloparatide and placebo arms were blinded, teriparatide was administered to the study participants without blinding. In the subsequent ACTIVExtend study, only patients in the abaloparatide and placebo groups were given the option of receiving follow-up treatment

with alendronic acid for 24 months. This option was not available for participants in the teriparatide group.

2,463 osteoporosis patients aged between 50 and 85 years with amenorrhoea that had been present for at least 5 years and an FSH serum value of ≥ 30 IU/l were enrolled in the ACTIVE study. Bone mineral density and fracture history were used to assess the severity of the disease. The participants were allocated to one of the three treatment groups in a 1:1:1 ratio. Stratifications, e.g. with regard to possible risk factors, did not take place during randomisation.

Patient-relevant endpoints were collected in the categories of morbidity (e.g. occurrence of new vertebral fractures) and side effects.

The ACTIVE study cannot be used to derive the additional benefit of abaloparatide, as the sole comparison between abaloparatide and teriparatide does not correspond to the currently determined appropriate comparator therapy.

For the implementation of patient-individual therapy in a direct comparator study, it is expected that the investigators will have a choice of several active ingredients named in the appropriate comparator therapy (multi-comparator study). This should enable a patient-individual treatment decision to be made, taking into account the risk of fracture and previous therapy.

In addition, there is also insufficient information as to whether teriparatide therapy is the most suitable patient-individual therapy for the patients in the ACTIVE study, taking into account the risk of fracture and previous therapy. It therefore remains unclear whether the treatment with teriparatide in a single comparator study corresponds to an adequate implementation of the appropriate comparator therapy for all patients in the ACTIVE study.

2.1.4 Limitation of the period of validity of the resolution

The limitation of the period of validity of the resolution on the present benefit assessment of abaloparatide finds its legal basis in Section 35a, paragraph 3, sentence 5 SGB V. Thereafter, the G-BA may limit the validity of the resolution on the benefit assessment of a medicinal product. In the present case, the limitation is justified by objective reasons consistent with the purpose of the benefit assessment according to Section 35a paragraph 1 SGB V.

For postmenopausal women with osteoporosis at increased risk of fracture, the pharmaceutical company presented direct comparator data of abaloparatide versus teriparatide therapy. As part of the written statement procedure, it became clear that the recommendations of the S3 guideline *Prevention, diagnosis and therapy of osteoporosis*, which were updated in November 2023, make an adjustment of the appropriate comparator therapy necessary. According to this S3 guideline, the initiation of specific medicinal therapy and the use of the osteoanabolic active ingredients romosozumab or teriparatide are recommended, depending on the absolute risk of fracture in postmenopausal women.

Since the appropriate comparator therapy was adapted during the ongoing process, the pharmaceutical company is given the opportunity to submit a new benefit assessment dossier to the G-BA, taking into account the current appropriate comparator therapy.

The aim of this assessment is to be able to make statements about the additional benefit of abaloparatide compared to a patient-individual therapy, taking into account the risk of fracture and previous therapy by selecting alendronic acid, risedronic acid, zoledronic acid, denosumab as well as romosozumab and teriparatide.

The selection and, if necessary, limitation of treatment options must be justified. If only a single comparator study is presented, the extent to which conclusions can be drawn about a sub-population will be examined as part of the new benefit assessment. For this purpose, specific information on the risk of fracture and previous therapy of the enrolled patients should be submitted with the dossier.

For the new benefit assessment after the expiry of the deadline, the results of a comparison of abaloparatide with the appropriate comparator therapy must be presented in the dossier. For this purpose, the G-BA considers a limitation for the resolution until 1 April 2025 to be appropriate.

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

A new assessment according to Section 3, paragraph 1, No. 5 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 1, paragraph 2, No. 7 Rules of the Procedure (VerfO) will not take place if the pharmaceutical company does not wish to make use of the option to submit suitable evaluations corresponding to the appropriate comparator therapy specified in this resolution and irrevocably applies in writing to the G-BA for the resolution to be cancelled within 3 months of this resolution coming into force. In the event of a timely application for cancellation of the time limit, the G-BA shall cancel the limitation on the validity of this resolution with the consequence that the findings of this resolution shall then continue to apply beyond the end of the time limit.

2.1.5 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product Eladynos with the active ingredient abaloparatide. Abaloparatide is approved for the treatment of osteoporosis in postmenopausal women at increased risk of fracture.

The G-BA determined the appropriate comparator therapy to be a patient-individual therapy, taking into account the risk of fracture and previous therapy by selecting alendronic acid, risedronic acid, zoledronic acid, denosumab, romosozumab (women at significantly increased risk of fracture) and teriparatide.

For the benefit assessment of abaloparatide, the pharmaceutical company presented the results of the phase III ACTIVE study. The study compared the safety and efficacy of abaloparatide versus teriparatide and placebo. While the abaloparatide and placebo arms were blinded, teriparatide was administered to the study participants without blinding.

The ACTIVE study cannot be used to derive the additional benefit of abaloparatide, as the sole comparison between abaloparatide and teriparatide does not correspond to the currently determined appropriate comparator therapy. For the implementation of patient-individual therapy in a direct comparator study, it is expected that the investigators will have a choice of several active ingredients named in the appropriate comparator therapy to enable a patient-

individual treatment decision to be made, taking into account the risk of fracture and previous therapy. There is insufficient information as to whether teriparatide therapy is the most suitable patient-individual therapy for all patients in the ACTIVE study, taking into account the risk of fracture and previous therapy.

For postmenopausal women with osteoporosis at increased risk of fracture, there are therefore no suitable data available to assess the additional benefit of abaloparatide compared with the appropriate comparator therapy. An additional benefit is therefore not proven.

The validity of the resolution is limited to 1 April 2025.

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 patient numbers stated in the pharmaceutical company's dossier.

The patient number estimated by the pharmaceutical company is subject to uncertainty overall and tends to be underestimated. The data record on which the estimate is based is from 2016. Despite the assumption of a currently higher prevalence, no extrapolation to the year under assessment 2024 was made. In addition, the lack of consideration of other risk factors for osteoporosis-related fractures could contribute to an underestimation of patient numbers. Due to an age restriction of the subjects assessed, postmenopausal women below 55 years of age, for example, are not taken into account.

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 Eladynos (active ingredient: abaloparatide) agreed upon in the context of the marketing authorisation at the following publicly accessible link (last access: 9 August 2024):

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

2.4 Treatment costs

The treatment costs are based on the requirements in the product information and the information listed in the LAUER-TAXE (last revised: 15 September 2024).

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 varies from patient to patient and/or is shorter on average. The time unit "days" is used to calculate the "number of treatments/ patient/ year", time intervals between individual treatments and for the maximum treatment duration, if specified in the product information.

The use of abaloparatide (Eladynos) is limited to 18 months. After completing therapy with abaloparatide, patients may resort to other osteoporosis treatments such as bisphosphonates.

The use of romosozumab (Evenity) is limited to 12 months. Therapy with romosozumab should preferably be followed by an anti-resorptive therapy in order to maintain the benefit achieved with romosozumab beyond 12 months.

The use of teriparatide (Movymia) is limited to 24 months.

Postmenopausal women with osteoporosis at increased risk of fracture

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				
Abaloparatide	Continuously, 1 x daily for 18 months	365.0	1	365.0
Appropriate comparator therapy				
Patient-individual therapy taking into account risk of fracture and previous therapy with selection of: Alendronic acid, risedronic acid, zoledronic acid, denosumab, romosozumab (women at significantly increased risk of fracture) and teriparatide				
Alendronic acid	Continuously, 1 x every 7 days	52.1	1	52.1
Risedronic acid	Continuously, 2 x monthly	12.0	2	24.0
Zoledronic acid	1 x every 12 months	1.0	1	1.0
Denosumab	1 x every 6 months	2.0	1	2.0
Romosozumab	1 x monthly for 12 months	12.0	1	12.0
Teriparatide	Continuously, 1 x daily for 24 months	365.0	1	365.0

Consumption:

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Abaloparatide	80 µg	80 µg	0.04 x 3,000 µg	365.0	14.6 x 3,000 µg
Appropriate comparator therapy					
Patient-individual therapy taking into account risk of fracture and previous therapy with selection of: Alendronic acid, risedronic acid, zoledronic acid, denosumab, romosozumab (women at significantly increased risk of fracture) and teriparatide					
Alendronic acid	70 mg	70 mg	1 x 70 mg	52.1	52.1 x 70 mg
Risedronic acid	75 mg	75 mg	1 x 75 mg	24.0	24 x 75 mg
Zoledronic acid	5 mg	5 mg	1 x 5 mg	1.0	1 x 5 mg
Denosumab	60 mg	60 mg	1 x 60 mg	2.0	2 x 60 mg
Romosozumab	210 mg	210 mg	2 x 105 mg	12.0	24 x 105 mg
Teriparatide	20 µg	20 µg	1 x 20 µg	365	365 x 20 µg

Costs:

In order to improve comparability, the costs of the medicinal products were approximated both on the basis of the pharmacy sales price level and also deducting the statutory rebates in accordance with Section 130 and Section 130a SGB V. To calculate the annual treatment costs, the required number of packs of a particular potency was first determined on the basis of consumption. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated on the basis of the costs per pack after deduction of the statutory rebates. Any reference prices shown in the cost representation may not represent the cheapest available alternative.

Costs of the medicinal products:

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Medicinal product to be assessed					
Abaloparatide 3 mg PEN	3 SFI	€ 1,439.58	€ 2.00	€ 79.08	€ 1,358.50
Abaloparatide 3 mg PEN	1 SFI	€ 487.40	€ 2.00	€ 26.36	€ 459.04
Appropriate comparator therapy					
Patient-individual therapy taking into account risk of fracture and previous therapy with selection of: Alendronic acid, risedronic acid, zoledronic acid, denosumab, romosozumab (women at significantly increased risk of fracture) and teriparatide					
Alendronic acid 70 mg[3]	12 TAB	€ 50.92	€ 2.00	€ 3.13	€ 45.79
Risedronic acid 75 mg[3]	6 FCT	€ 59.94	€ 2.00	€ 3.85	€ 54.09
Zoledronic acid 5 mg[3]	1 INF	€ 268.79	€ 2.00	€ 20.36	€ 246.43
Denosumab 60 mg	1 PS	€ 381.07	€ 2.00	€ 20.47	€ 358.60
Romosozumab 105 mg	6 SFI	€ 1,783.20	€ 2.00	€ 98.55	€ 1,682.65
Teriparatide 0.6 mg[3] PEN	3 SFI	€ 1,264.18	€ 2.00	€ 99.09	€ 1,163.09
Abbreviations: PS = prefilled syringes; FCT = film-coated tablets; INF = infusion solution; SFI = solution for injection; TAB = tablets;					

LAUER-TAXE® last revised: 15 September 2024

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.

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 designates 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.

[3] Fixed reimbursement rate

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

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

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

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

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

Concomitant active ingredient

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

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

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

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

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

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

Medicinal products with new active ingredients for which the G-BA has decided on an exemption as a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V are ineligible as concomitant active ingredients. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V also applies accordingly to the medicinal product eligible as a concomitant active ingredient.

Designation

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

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

Exception to the designation

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

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

Legal effects of the designation

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

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

Justification for the findings on designation in the present resolution:

Postmenopausal women with osteoporosis at increased risk of fracture

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

References:
Product information for abaloparatide (Eladynos); Eladynos 80 micrograms/dose solution for injection in a pre-filled pen; last revised: December 2023

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 its session on 27 June 2023, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 11 April 2024, the pharmaceutical company submitted a dossier for the benefit assessment of abaloparatide to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 VerfO.

By letter dated 15 April 2024 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 abaloparatide.

The dossier assessment by the IQWiG was submitted to the G-BA on 2 July 2024, and the written statement procedure was initiated with publication on the G-BA website on 15 July 2024. The deadline for submitting written statements was 5 August 2024.

The oral hearing was held on 26 August 2024.

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

The evaluation of the written statements received and the oral hearing was discussed at the session of the subcommittee on 24 September 2024, and the proposed draft resolution was approved.

At its session on 2 October 2024, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	27 June 2023	Determination of the appropriate comparator therapy
Working group Section 35a	14 August 2024	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal products	26 August 2024	Conduct of the oral hearing
Working group Section 35a	4 September 2024 18 September 2024	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee Medicinal products	24 September 2024	Concluding discussion of the draft resolution
Plenum	2 October 2024	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 2 October 2024

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

Prof. Hecken