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 Apremilast (new therapeutic indication: moderate to severe plaque psoriasis; 6 to < 18 years)

of 15 May 2025

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 active ingredient apremilast (Otezla) was listed for the first time on 15 February 2015 in the “LAUER-TAXE®”, the extensive German registry of available drugs and their prices.

On 21 October 2024, apremilast received marketing authorisation for a new therapeutic indication to be classified as a major type 2 variation as defined according to Annex 2, number 2, letter a to Regulation (EC) No. 1234/2008 of the Commission of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334, 12.12.2008, sentence 7).

On 15 November 2024, the pharmaceutical company has submitted a dossier in accordance with Section 4, paragraph 3, number 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5, Section 8, paragraph 1, number 2 of the Rules of Procedure (VerfO) of the G-BA on the active ingredient apremilast with the new therapeutic indication "for the treatment of moderate to severe plaque psoriasis in children and adolescents from the age of 6 years and weighing at least 20 kg who are candidates for systemic therapy" in due time (i.e. at the latest within four weeks after informing the pharmaceutical company about the approval for a new therapeutic indication).

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 17 February 2025 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 apremilast 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 apremilast.

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 Apremilast (Otezla) in accordance with the product information

Otezla is indicated for the treatment of moderate to severe plaque psoriasis in children and adolescents from the age of 6 years and weighing at least 20 kg who are candidates for systemic therapy.

Therapeutic indication of the resolution (resolution of 15.05.2025):

Otezla is indicated for the treatment of moderate to severe plaque psoriasis in children and adolescents aged 6 to < 18 years and weighing at least 20 kg who are candidates for systemic therapy.

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Children and adolescents aged 6 to < 18 years and weighing at least 20 kg with moderate to severe plaque psoriasis who are candidates for systemic therapy

Appropriate comparator therapy for apremilast:

- Adalimumab or etanercept or secukinumab or ustekinumab

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

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

The appropriate comparator therapy must be an appropriate therapy in the therapeutic indication 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 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.

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

On 1. The following active ingredients are generally approved for children and adolescents in the present therapeutic indication:

- ciclosporin,
- methotrexate,

- the TNF-alpha inhibitors adalimumab and etanercept,
- the interleukin inhibitors ixekizumab, secukinumab and ustekinumab.

On 2. Non-medicinal measures as sole appropriate comparator therapy are not considered in the present therapeutic indication.

On 3. In the therapeutic indication under consideration here (plaque psoriasis in children and adolescents), the following resolutions of the G-BA are available:

- Resolution on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V for the active ingredient ixekizumab dated 21 January 2021.
- Resolution on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V for the active ingredient secukinumab dated 18 February 2021.

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 therapeutic indication according to Section 35a, paragraph 7 SGB V.

The TNF-alpha inhibitors adalimumab and etanercept (severe form of plaque psoriasis) and the interleukin inhibitors ixekizumab, secukinumab and ustekinumab (moderate to severe plaque psoriasis) are approved for the treatment of plaque psoriasis in children and adolescents aged 6 to < 18 years who are candidates for systemic therapy.

The interleukin inhibitors ixekizumab and secukinumab were assessed as part of the benefit assessment in accordance with Section 35a SGB V. A minor additional benefit of secukinumab over etanercept could be observed. Therefore, secukinumab is to be considered appropriate. In contrast, an additional benefit of ixekizumab compared to the active ingredients of the appropriate comparator therapy could not observed in the benefit assessment according to Section 35a SGB V, so that it is not considered to be an equally appropriate alternative treatment.

The marketing authorisation of the active ingredient ciclosporin (severe form of plaque psoriasis) does not recommend its use in children under 16 years of age. Ciclosporin is not included in the appropriate comparator therapy as it is not a therapy option for the majority of paediatric and adolescent patients and its recommendation is also only secondary to therapy with biologic agents.

In view of the recommendations of lower priority in the guidelines for this age group, the active ingredient methotrexate also does not represent an equally appropriate therapy option and is therefore not part of the appropriate comparator therapy.

As a result, the active ingredients adalimumab, etanercept, secukinumab and ustekinumab are considered equally appropriate therapy options for children and adolescents from the age of 6 years with plaque psoriasis who are candidates for systemic therapy.

The authorisation status and the product information of the respective medicinal products must be taken into account. Adalimumab and etanercept are only approved for the treatment of severe plaque psoriasis. Etanercept and ustekinumab are only indicated for patients who have responded inadequately to other systemic therapies or phototherapies, or have not tolerated them.

The appropriate comparator therapy determined here includes several therapy options. These therapeutic alternatives are equally appropriate for the comparator 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.

2.1.3 Extent and probability of the additional benefit

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

For children and adolescents aged 6 to < 18 years and weighing at least 20 kg with moderate to severe plaque psoriasis who are candidates for systemic therapy, the additional benefit compared with the appropriate comparator therapy is not proven.

Justification:

For the assessment of the additional benefit of apremilast, the pharmaceutical company did not identify any comparator studies versus the appropriate comparator therapy.

The pharmaceutical company presented the label-enabling SPROUT study, which compared apremilast with placebo in children and adolescents over a period of 16 weeks. Due to the lack of comparison with the appropriate comparator therapy, the study is not appropriate for the assessment of the additional benefit.

In the overall assessment, the G-BA therefore came to the conclusion that the additional benefit of apremilast compared with the appropriate comparator therapy is not proven for children and adolescents aged 6 to < 18 years and weighing at least 20 kg with moderate to severe plaque psoriasis who are candidates for systemic therapy.

2.1.4 Summary of the assessment

The present assessment is the benefit assessment of a new therapeutic indication for the active ingredient apremilast.

The therapeutic indication assessed here is as follows: Apremilast (Otezla) is indicated for the treatment of moderate to severe plaque psoriasis in children and adolescents aged 6 to < 18 years and weighing at least 20 kg who are candidates for systemic therapy.

The G-BA determined adalimumab or etanercept or secukinumab or ustekinumab as the appropriate comparator therapy.

For the benefit assessment of apremilast, no comparator studies versus the appropriate comparator therapy were presented in the present therapeutic indication.

Against this background, the additional benefit of apremilast compared with the appropriate comparator therapy is not proven for children and adolescents aged 6 to < 18 years and

weighing at least 20 kg with moderate to severe plaque psoriasis who are candidates for systemic therapy.

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 information is based on the data provided by the pharmaceutical company in the dossier.

The figures presented are based on prevalence and incidence data from routine data analyses of children and adolescents diagnosed with plaque psoriasis. The calculation of the lower limit appears plausible in principle. The calculation of the upper limit is however subject to uncertainties. These uncertainties result from the prevalence rate used, the sole determination of disease severity via the additional code L40.70! and the lack of limitation with regard to body weight. Overall, the upper limit for the number of patients is an underestimate.

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 Otezla (active ingredient: apremilast) at the following publicly accessible link (last access: 6 May 2025):

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

Treatment with apremilast should only be initiated and monitored by doctors experienced in treating patients with psoriasis.

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 April 2025).

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

In general, initial induction regimens are not taken into account for the cost representation, since the present indication is a chronic disease with a continuous need for therapy and, as a rule, no new titration or dose adjustment is required after initial titration.

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 etanercept for the treatment of plaque psoriasis is intended for 24 weeks according to the product information, but renewed treatment with etanercept may be indicated.

Children and adolescents aged 6 to < 18 years and weighing at least 20 kg with moderate to severe plaque psoriasis who are candidates for systemic therapy

Treatment period:

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Apremilast	Continuously, 2 x daily	365.0	1	365.0
Appropriate comparator therapy				
Adalimumab or etanercept or secukinumab or ustekinumab				
Adalimumab	Continuously, 1 x every 14 days	26.1	1	26.1
Etanercept	Continuously, 1 x in 7 days	24.0	24.0	24.0
Secukinumab	Continuously, 1 x monthly	12.0	1	12.0
Ustekinumab	Continuously, 1 x every 84 days	4.3	1	4.3

Consumption:

For calculating the dosages depending on body weight, the average body measurements from the official representative statistics "Microcensus 2017 – body measurements of the population" as well as "Microcensus 2021 – body measurements of the population" were applied (average body weight of 6 to < 7-year-olds: 23.6 kg[2] and of 17 to < 18-year-olds: 67.2 kg[3]).

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					

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

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

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Apremilast	20 – < 50 kg: 20 mg ≥ 50 kg: 30 mg	40 mg – 60 mg	2 x 20 mg – 2 x 30 mg	365.0	730 x 20 mg – 730 x 30 mg
Appropriate comparator therapy					
Adalimumab or etanercept or secukinumab or ustekinumab					
Adalimumab	15 - < 30 kg: 20 mg ≥ 30 kg: 40 mg	20 mg 40 mg	1 x 20 mg 1 x 40 mg	26.1 26.1	26.1 x 20 mg 26.1 x 40 mg
Etanercept	0.8 mg/kg BW – 50 mg	18.9 mg – 50 mg	2 x 10 mg – 1 x 50 mg	24.0	48 x 10 mg – 24 x 50 mg
Secukinumab	< 25 - < 50 kg 75 mg ≥ 50 mg 150 mg – 300 mg	75 mg 150 mg – 300 mg	1 x 75 mg 1 x 150 mg – 1 x 300 mg	12.0 12.0	12 x 75 mg 12 x 150 mg – 12 x 300 mg
Ustekinumab	0.75 mg/kg BW – 45 mg	17.7 – 45 mg	1 x 45 mg[4]	4.3	4.3 x 45 mg

Costs:

In order to improve comparability, the costs of the medicinal products were approximated both on the basis of the pharmacy sales price level and also deducting the statutory rebates in accordance with Sections 130 and 130 a 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:

[4] According to the PI, a 45 mg vial is available for children and adolescents who require less than the full 45 mg dose. The calculated dose is administered using a scaled 1 ml syringe. Discard the rest of the solution from the vial. A pre-filled pen can be used for children and adolescents who require a full 45 mg dose.

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					
Apremilast 20 mg	56 FCT	€ 630.99	€ 1.77	€ 34.31	€ 594.91
Apremilast 30 mg	168 FCT	€ 2,760.99	€ 1.77	€ 154.39	€ 2,604.83
Appropriate comparator therapy					
Adalimumab 20 mg	2 SFI	€ 499.99	€ 1.77	€ 27.06	€ 471.16
Adalimumab 40 mg[Fehler! Textmarke nicht definiert.]	6 SFI	€ 2,804.97	€ 1.77	€ 0.00	€ 2,803.20
Etanercept 10 mg	4 DSS	€ 194.34	€ 1.77	€ 10.13	€ 182.44
Etanercept 50 mg[Fehler! Textmarke nicht definiert.]	12 SFI	€ 2,548.84	€ 1.77	€ 0.00	€ 2,547.07
Secukinumab 75 mg	1 SFI	€ 352.09	€ 1.77	€ 0.00	€ 350.32
Secukinumab 150 mg	6 PEN	€ 4,022.03	€ 1.77	€ 0.00	€ 4,020.26
Secukinumab 300 mg	3 SFI	€ 4,022.03	€ 1.77	€ 0.00	€ 4,020.26
Ustekinumab 45 mg	1 SFI	€ 2,938.11	€ 1.77	€ 164.50	€ 2,771.84
Ustekinumab 45 mg	1 SFI	€ 2,934.37	€ 1.77	€ 164.29	€ 2,768.31
Abbreviations: FCT = film-coated tablets; SFIPFS = solution for injection in a pre-filled syringe; SFI = solution for injection; PEN = solution for injection in a pre-filled pen; DSS = dry substance with solvent					

LAUER-TAXE® last revised: 15 April 2025

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.

Prior to administration of the active ingredients of the appropriate comparator therapy adalimumab, etanercept and ustekinumab, patients must be examined for active and inactive ("latent") tuberculosis infections. In addition, patients must be tested for the presence of a hepatitis B infection prior to initiation of treatment with adalimumab. Diagnostics to rule out chronic hepatitis B requires sensibly coordinated steps. A step-by-step serological diagnosis initially consists of the examination of HBs antigen and anti-HBc antibodies. If both are negative, a past HBV infection can be excluded. In certain case constellations, further steps may be necessary in accordance with current guideline recommendations[5].

[5] S3 guideline on prevention, diagnosis and therapy of hepatitis B virus infection AWMF registry no.: 021/011 https://register.awmf.org/assets/guidelines/021-011l_S3_Prophylaxe-Diagnostik-Therapie-der-Hepatitis-B-Virusinfektion_2021-07.pdf

Designation of the therapy	Designation of the service	Number	Unit cost	Costs per patient per year
Adalimumab Etanercept Ustekinumab	Quantitative determination of an in vitro interferon-gamma release after ex vivo stimulation with antigens (at least ESAT-6 and CFP-10) specific for Mycobacterium tuberculosis-complex (except BCG) (GOP 32670)	1	€ 53.36	€ 53.36
	Chest radiograph (GOP 34241)	1	€ 18.09	€ 18.09
Adalimumab	HBs antigen (GOP 32781)	1	€ 5.06	€ 5.06
Adalimumab	Anti-HBc antibody (GOP 32614)	1	€ 5.43	€ 5.43

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.

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:

Children and adolescents aged 6 to < 18 years and weighing at least 20 kg with moderate to severe plaque psoriasis who are candidates for systemic therapy

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

References:
Product information for apremilast (Otezla); Otezla film-coated tablets; last revised: October 2024

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 26 March 2024, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

A review of the appropriate comparator therapy took place. The Subcommittee on Medicinal Products determined the appropriate comparator therapy at their session on 6 November 2024.

On 15 November 2024, the pharmaceutical company submitted a dossier for the benefit assessment of apremilast to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 2, sentence 2 VerfO.

By letter dated 18 November 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 apremilast.

The dossier assessment by the IQWiG was submitted to the G-BA on 13 February 2025, and the written statement procedure was initiated with publication on the G-BA website on 17 February 2025. The deadline for submitting statements was 10 March 2025.

The oral hearing was held on 24 March 2025.

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 6 May 2025, and the proposed draft resolution was approved.

At their session on 15 May 2025, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	26 March 2024	Determination of the appropriate comparator therapy
Subcommittee on Medicinal Products	6 November 2024	Examination of the appropriate comparator therapy
Working group Section 35a	19 March 2025	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	24 March 2025	Conduct of the oral hearing,
Working group Section 35a	2 April 2025 30 April 2025	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	6 May 2025	Concluding discussion of the draft resolution
Plenum	15 May 2025	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 15 May 2025

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

Prof. Hecken