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
Cabotegravir (new therapeutic indication: HIV-1 infection, therapy-experienced adolescents, combination with rilpivirine)

of 7 August 2025

Contents

1. Legal basis

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

1. approved therapeutic indications,
2. medical benefit,
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.
7. Number of study participants who participated in the clinical studies at study sites within the scope of SGB V, and total number of study participants.

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 cabotegravir (Vocabria) was listed for the first time on 1 May 2021 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

On 13 January 2025, cabotegravir 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 7 February 2025, 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 cabotegravir with the new therapeutic indication "for the treatment of Human Immunodeficiency Virus type 1 (HIV-1) infection in adolescents (12 to 17 years of age and weighing at least 35 kg), who are virologically suppressed (HIV-1 RNA <50 copies/mL) on a stable antiretroviral regimen without present or past evidence of viral resistance to, and no prior virological failure with agents of the non-nucleoside reverse transcriptase inhibitor (NNRTI) and integrase inhibitor (INI) class" 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 15 May 2025 on the G-BA website (www.g-ba.de), thus initiating the written statement procedure.

The oral hearing has been dispensed with since all assessment experts who submitted a written statement waived their right to make an oral statement or did not register for the oral hearing.

As part of a therapy concept, cabotegravir is used in combination with rilpivirine for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adolescents according to the information in the therapeutic indication. The therapy concept includes an oral lead-in phase of at least 28 days, during which cabotegravir is to be taken orally (Vocabria) together with rilpivirine orally (Edurant) in order to assess the tolerability of cabotegravir and rilpivirine prior to the use of long-acting cabotegravir injection plus long-acting rilpivirine injection. This is followed by the maintenance phase with intramuscular cabotegravir injection (Vocabria) in combination with intramuscular rilpivirine injection (Rekambys). Oral therapy (cabotegravir oral + rilpivirine oral) is also used for adolescents who miss the scheduled dose of cabotegravir injection plus rilpivirine injection. The assessment of the additional benefit of cabotegravir in combination with rilpivirine relates to the entire therapy concept consisting of the oral lead-in phase, the intramuscular maintenance phase and the oral bridging therapy.

The G-BA came to a resolution on whether an additional benefit of cabotegravir 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 written statements. In order to determine the extent of the additional benefit, the G-BA have evaluated the data justifying the finding of an additional benefit on the basis of their therapeutic relevance (qualitative), in accordance with the criteria laid down in Chapter 5 Section 5, paragraph 7 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of cabotegravir.

In the light of the above, and taking into account the statements received, the G-BA has come to the following assessment:

[1] General Methods, version 7.0 from 19.09.2023. 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 Cabotegravir (Vocabria) in accordance with the product information

Vocabria injection is indicated, in combination with rilpivirine injection, for the treatment of Human Immunodeficiency Virus type 1 (HIV-1) infection in adults and adolescents (at least 12 years of age and weighing at least 35 kg), who are virologically suppressed (HIV-1 RNA <50 copies/mL) on a stable antiretroviral regimen without present or past evidence of viral resistance to, and no prior virological failure with agents of the non-nucleoside reverse transcriptase inhibitor (NNRTI) and integrase inhibitor (INI) class.

Vocabria tablets are indicated in combination with rilpivirine tablets for the short-term treatment of Human Immunodeficiency Virus type 1 (HIV-1) infection in adults and adolescents (at least 12 years of age and weighing at least 35 kg) who are virologically suppressed (HIV-1 RNA <50 copies/mL) on a stable antiretroviral regimen without present or past evidence of viral resistance to, and no prior virological failure with agents of the non-nucleoside reverse transcriptase inhibitor (NNRTI) and integrase inhibitor (INI) class for:

- Oral lead-in to assess tolerability of Vocabria and rilpivirine prior to administration of long acting cabotegravir injection plus long acting rilpivirine injection.
- Oral therapy for adults and adolescents who will miss planned dosing with cabotegravir injection plus rilpivirine injection.

Therapeutic indication of the resolution (resolution of 07.08.2025):

Vocabria injection is indicated, in combination with rilpivirine injection, for the treatment of Human Immunodeficiency Virus type 1 (HIV-1) infection in adolescents (12 to 17 years of age and weighing at least 35 kg), who are virologically suppressed (HIV-1 RNA <50 copies/mL) on a stable antiretroviral regimen without present or past evidence of viral resistance to, and no prior virological failure with agents of the non-nucleoside reverse transcriptase inhibitor (NNRTI) and integrase inhibitor (INI) class.

Vocabria tablets are indicated in combination with rilpivirine tablets for the short-term treatment to assess tolerability of Vocabria and rilpivirine prior to administration of long acting cabotegravir injection plus long acting rilpivirine injection. Oral therapy is indicated for adolescents who will miss planned dosing with cabotegravir injection plus rilpivirine injection. The present assessment refers to the entire therapy concept consisting of the oral lead-in phase, the intramuscular maintenance phase and the oral bridging therapy.

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adolescents 12 to 17 years of age and weighing at least 35 kg with HIV-1 infection, who are virologically suppressed (HIV-1 RNA <50 copies/mL) on a stable antiretroviral regimen without present or past evidence of viral resistance to, and no prior virological failure with agents of the non-nucleoside reverse transcriptase inhibitor (NNRTI) and integrase inhibitor (INI) class.

Appropriate comparator therapy for cabotegravir in combination with rilpivirine:

- An individualised therapy with selection of approved antiretroviral agents

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. In addition to cabotegravir, the following active ingredients are generally approved for the treatment of HIV-1 infection in adolescents 12 to 17 years of age in the present therapeutic indication:

- Protease inhibitors (PI): Atazanavir, darunavir, fosamprenavir lopinavir, ritonavir, tipranavir
- Nucleoside and nucleotide reverse transcriptase inhibitors (NRTI): Abacavir, didanosine, emtricitabine, lamivudine, tenofovir alafenamide, tenofovir disoproxil, zidovudine
- Non-nucleoside reverse transcriptase inhibitors (NNRTI): Doravirine, efavirenz, etravirine, nevirapine, rilpivirine
- Integrase inhibitors (INI): Dolutegravir, elvitegravir, raltegravir
- Other antivirals: Enfuvirtide (entry inhibitor), maraviroc (entry inhibitor)
- Other therapeutic agents: Cobicistat (pharmacokinetic enhancer)

On 2. A non-medicinal treatment cannot be considered in the present therapeutic indication.

On 3. The following resolutions in accordance with Section 35a SGB V are available in the therapeutic indication to be considered here:

- Bictegravir/ emtricitabine/ tenofovir alafenamide (resolution of 15.06.2023)
- Doravirine (nAWG) *(resolution of 20 October 2022)*
- Doravirine/ lamivudine/ tenofovir disoproxil (nAWG) (resolution of 20 October 2022)
- Cobicistat (resolution of 1 October 2020)
- Dolutegravir/ lamivudine (resolution of 6 February 2020)
- Elvitegravir/ cobicistat/ emtricitabine/ tenofovir alafenamide (nAWG) (resolution of 5 July 2018)
- Elvitegravir/ cobicistat/ emtricitabine/ tenofovir disoproxil (nAWG) (resolution of 3 May 2018)
- Darunavir/ cobicistat/ emtricitabine/ tenofovir alafenamide (resolution of 16 March 2018)
- Rilpivirine/ emtricitabine/ tenofovir alafenamide (resolution of 5 January 2017)
- Emtricitabine/ tenofovir alafenamide (resolution of 3 November 2016)
- Rilpivirine (nAWG) (resolution of 16 June 2016)
- Elvitegravir/ cobicistat/ emtricitabine/ tenofovir alafenamide (resolution of 16 June 2016)
- Dolutegravir/ abacavir/ lamivudine (resolution of 19 March 2015)
- Dolutegravir (resolution of 7 August 2014)

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.

Based on the available evidence and the written statement of the German AIDS Society, which makes statements on the German healthcare context, in particular on the resistance situation, an individualised pharmacotherapy coordinated with the patient is recommended for therapy-experienced adolescents with HIV-1 in the present therapeutic indication after one or more previous treatment(s), depending on the active ingredients/ product classes used and the reason for the change of therapy (e.g. side effects). The naming of a defined combination of active ingredients in the sense of a therapy standard cannot be deduced based on the evidence available and because of the patient-individual selection of the therapy regimen depending on the previous therapy. In principle, all possible combinations of active ingredients can therefore be regarded as appropriate.

In the overall assessment, an individualised therapy with selection of approved antiretroviral agents is therefore determined for cabotegravir in combination with rilpivirine for the treatment of Human Immunodeficiency Virus type 1 (HIV-1) infection in adolescents (12 to 17 years of age and weighing at least 35 kg), who are virologically suppressed (HIV-1 RNA <50 copies/mL) on a stable antiretroviral regimen without present or past evidence of viral resistance to, and no prior virological failure with agents of the non-nucleoside reverse transcriptase inhibitor (NNRTI) and integrase inhibitor (INI) class. The treatment decision should be made in particular taking into account the previous treatment(s) and any side effects that may occur.

Individualised therapy is based on the assumption that several treatment options, which allow an individualised medical treatment decision, are available.

In therapy-experienced adolescents with HIV-1 infection, the on-label use of the medicinal products, in particular the age-appropriate use, must be observed.

The term "individualised therapy" is used instead of previously used terms such as "patient-individual therapy" or "therapy according to doctor's instructions". This harmonises the terms used in the European assessment procedures (EU-HTA).

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 cabotegravir in combination with rilpivirine is assessed as follows:

An additional benefit is not proven.

Justification:

In the therapy concept of combination therapy with cabotegravir and rilpivirine, the active ingredients cabotegravir and rilpivirine are initially administered orally for 4 weeks in the lead-in phase. Thereafter, in the maintenance phase, the switch to the intramuscular form of administration of both active ingredients is made according to one of 2 approved treatment regimens either every 2 months (Q2M) or 1 time per month (Q1M). Oral therapy (cabotegravir oral + rilpivirine oral) is also used for adolescents who miss the scheduled dose of cabotegravir injection plus rilpivirine injection. The assessment of the additional benefit of cabotegravir + rilpivirine relates to the entire therapy concept consisting of the oral lead-in phase, the intramuscular application and the oral bridging therapy.

The pharmaceutical company did not present any data for the benefit assessment of cabotegravir in combination with rilpivirine compared to the appropriate comparator therapy for the treatment of Human Immunodeficiency Virus type 1 (HIV-1) infection in adolescents (12 to 17 years of age and weighing at least 35 kg), who are virologically suppressed (HIV-1 RNA <50 copies/mL) on a stable antiretroviral regimen without present or past evidence of viral resistance to, and no prior virological failure with agents of the non-nucleoside reverse transcriptase inhibitor (NNRTI) and integrase inhibitor (INI) class.

The pharmaceutical company did not use the single-arm, label-enabling IMPAACT 2017 study for the assessment of the additional benefit due to the lack of comparison with the appropriate comparator therapy.

For the present therapeutic indication, the pharmaceutical company did not present any data overall for the assessment of the additional benefit of cabotegravir in combination with rilpivirine compared to the appropriate comparator therapy. An additional benefit of cabotegravir in combination with rilpivirine versus the appropriate comparator therapy is therefore not proven.

2.1.4 Summary of the assessment

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

Cabotegravir is indicated for the treatment of Human Immunodeficiency Virus type 1 (HIV-1) infection in adolescents (12 to 17 years of age and weighing at least 35 kg), who are virologically suppressed (HIV-1 RNA <50 copies/mL) on a stable antiretroviral regimen without present or past evidence of viral resistance to, and no prior virological failure with agents of the non-nucleoside reverse transcriptase inhibitor (NNRTI) and integrase inhibitor (INI) class.

The G-BA determined the appropriate comparator therapy to be an individualised therapy with selection of approved antiretroviral agents.

For the present therapeutic indication, the pharmaceutical company did not present any data overall for the assessment of the additional benefit of cabotegravir in combination with rilpivirine compared to the appropriate comparator therapy. An additional benefit of cabotegravir in combination with rilpivirine versus the appropriate comparator therapy is therefore not proven.

2.2 Number of patients or demarcation of patient groups eligible for treatment

The number of patients is the target population in statutory health insurance (SHI).

The information is based on patient numbers based on the information provided by the pharmaceutical company in the dossier. The number of patients based on the pharmaceutical company's query of the reported cases from the SurvStat@RKI2.0[2] database submitted to the Robert Koch Institute (RKI) in accordance with the Infection Protection Act is 147 adolescents 12 to 17 years of age who were infected with HIV in 2025.

In addition, the pharmaceutical company makes assumptions about the pretreated adolescents as well as the existing resistance situation. Assuming that approx. 87.7% of the German resident population has statutory health insurance, approx. 65 adolescents are eligible for the administration of cabotegravir in combination with rilpivirine according to the pharmaceutical company.

The number of patients in the SHI target population stated by the pharmaceutical company is underestimated overall due to the possible higher number of HIV-infected adolescents (e.g. due to the lack of consideration of refugees, non-consideration of reported cases from 2024, unclear transfer of the percentage of successfully treated patients in Germany to the present target population, uncertainty in the transfer of resistance data from adults to adolescents) in the therapeutic indication.

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 Vocabria (active ingredient: cabotegravir) at the following publicly accessible link (last access: 3 June 2025):

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

Treatment with cabotegravir should only be initiated and monitored by specialists who are experienced in the treatment of patients with HIV-1.

Prior to starting Vocabria injection, healthcare professionals should have carefully selected patients who agree to the required injection schedule and counsel patients about the importance of adherence to scheduled dosing visits to help maintain viral suppression and reduce the risk of viral rebound and potential development of resistance with missed doses**.** Following discontinuation of Vocabria and rilpivirine injection, it is essential to adopt an alternative, fully suppressive antiretroviral regimen no later than one month after the final injection of Vocabria when dosed monthly and no later than two months after the final injection of Vocabria when dosed every 2 months.

[2] Robert Koch Institute. Query parameter SurvStat@RKI 2.0, query date 08.01.2025 [online]. URL: https://survstat.rki.de/

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: 15 July 2025).

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.

For the cost representation, only the dosages of the general case are considered. Patient-individual dose adjustments (e.g. because of side effects or comorbidities) are not taken into account when calculating the annual treatment costs. In general, initial induction regimens are not taken into account for the cost representation, since the present indication is a chronic disease with a continuous need for therapy and, as a rule, no new titration or dose adjustment is required after initial titration.

The injection of cabotegravir in combination with rilpivirine is approved for two different treatment regimens: 400 mg cabotegravir/ 600mg rilpivirine prolonged-release suspension for injection for administration once monthly (Q1M) and 600 mg cabotegravir/ 900 mg rilpivirine prolonged-release suspension for injection for administration every two months (Q2M). Cabotegravir injection 400 mg and rilpivirine injection 600 mg for the Q1M treatment regimen are not available on the German market.

It is assumed that in clinical practice, for economic reasons, the dosage for Q1M application is not taken from the 600 mg cabotegravir/ 900 mg rilpivirine prolonged-release suspension for injection. Therefore, no costs are shown for the Q1M treatment regimens.

For dosages depending on body weight (BW), the average body measurements from the official representative statistics "Microcensus 2017 – body measurements of the population"[3] (average body weight of children aged 12 years and over 47.1 kg) and "Microcensus 2021 – body measurements of the population"[4] (average body weight of adolescents aged up to 17 years 67.2 kg) were used as the basis.

For the appropriate comparator therapy, the range of treatment costs incurred depending on the individual choice of therapy is shown. Because of the different combination possibilities in individual therapy, not all possible combination therapies are presented but a cost-effective (nevirapine + emtricitabine/ tenofovir disoproxil) and a cost-intensive therapy (lopinavir/ ritonavir + abacavir + emtricitabine) as examples.

Based on the marketing authorisations and the evidence in the present therapeutic indication, including the recommendations of the German AIDS Society, which reflect the German healthcare context, various alternatives ("backbone" with concomitant active ingredient) are recommended, which were taken into account for the cost representation.

Adolescents 12 to 17 years of age and weighing at least 35 kg with HIV-1 infection, who are virologically suppressed (HIV-1 RNA <50 copies/mL) on a stable antiretroviral regimen without

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

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

present or past evidence of viral resistance to, and no prior virological failure with agents of the non-nucleoside reverse transcriptase inhibitor (NNRTI) and integrase inhibitor (INI) class.

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				
Cabotegravir + rilpivirine				
Cabotegravir	1 x every 60.8 days	6.0	1	6.0
Rilpivirine	1 x every 60.8 days	6.0	1	6.0
or				
Cabotegravir	1 x every 30.4 days	12.0	1	12.0
Rilpivirine	1 x every 30.4 days	12.0	1	12.0
Appropriate comparator therapy				
An individualised antiretroviral therapy with selection of approved active ingredients				
Nevirapine + emtricitabine/ tenofovir disoproxil				
Nevirapine	Continuously, 1 x daily	365.0	1	365.0
Emtricitabine/ tenofovir disoproxil	Continuously, 1 x daily	365.0	1	365.0
Lopinavir/ ritonavir + abacavir + emtricitabine				
Lopinavir/ ritonavir	Continuously, 2 x daily	365.0	1	365.0
Abacavir	Continuously, 2 x daily	365.0	1	365.0
Emtricitabine	Continuously, 1 x daily	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					
Cabotegravir + rilpivirine					
Cabotegravir	600 mg	600 mg	1 x 600 mg	6	6 x 600 mg
Rilpivirine	900 mg	900 mg	1 x 900 mg	6	6 x 900 mg
or					
Cabotegravir	400 mg	400 mg	1 x 400 mg	12	12 x 400 mg
Rilpivirine	600 mg	600 mg	1 x 600 mg	12	12 x 600 mg
Appropriate comparator therapy					
Nevirapine + emtricitabine/ tenofovir disoproxil					
Nevirapine	400 mg	400 mg	1 x 400 mg	365.0	365 x 400 mg
Emtricitabine/ tenofovir disoproxil	200 mg/ 245 mg	200 mg/ 245 mg	1 x 200 mg/ 245 mg	365.0	365 x 200 mg/ 245 mg
Lopinavir/ ritonavir + abacavir + emtricitabine					
Lopinavir/ ritonavir	400 mg/ 100 mg	800 mg/ 200 mg	4 x 200 mg/ 50 mg	365.0	1460 x 200 mg/ 50 mg
Abacavir	300 mg	600 mg	2 x 300 mg	365.0	730 x 300 mg
Emtricitabine	200 mg	200 mg	1 x 200 mg	365.0	365 x 200 mg

Costs:

In order to improve comparability, the costs of the medicinal products were approximated both on the basis of the pharmacy sales price level and also deducting the statutory rebates in accordance with Section 130 and Section 130a SGB V. To calculate the annual treatment costs, the required number of packs of a particular potency was first determined on the basis of consumption. Having determined the number of packs of a particular potency, the costs of 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					
Cabotegravir 600 mg	1 PRJ	€ 1,272.93	€ 1.77	€ 69.85	€ 1,201.31
Rilpivirine 900 mg	1 PRJ	€ 552.02	€ 1.77	€ 29.94	€ 520.31
Cabotegravir 400 mg[5]	–	–	–	–	–
Rilpivirine 600 mg[5]	–	–	–	–	–
Appropriate comparator therapy					
Abacavir 300 mg	60 FCT	€ 485.88	€ 1.77	€ 26.27	€ 457.84
Emtricitabine 200 mg	30 HC	€ 302.76	€ 1.77	€ 16.14	€ 284.85
Emtricitabine/ tenofovir disoproxil 200 mg/ 245 mg[6]	90 FCT	€ 200.24	€ 1.77	€ 14.94	€ 183.53
Lopinavir/ ritonavir 200 mg/ 50 mg	360 FCT	€ 2,820.22	€ 1.77	€ 360.62	€ 2,457.83
Nevirapine 400 mg	30 SRT	€ 192.52	€ 1.77	€ 8.60	€ 182.15
Abbreviations: PRJ = prolonged-release suspension for injection; FCT = film-coated tablets; HC = hard capsules; SRT = sustained release tablet					

LAUER-TAXE® last revised: 15 July 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.

[5] currently not available on the German market
[6] Fixed reimbursement rate

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 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 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:

Adolescents 12 to 17 years of age and weighing at least 35 kg with HIV-1 infection, who are virologically suppressed (HIV-1 RNA <50 copies/mL) on a stable antiretroviral regimen without present or past evidence of viral resistance to, and no prior virological failure with agents of the non-nucleoside reverse transcriptase inhibitor (NNRTI) and integrase inhibitor (INI) class.

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 cabotegravir (Vocabria); Vocabria 400 mg/ 600mg prolonged-release suspension for injection, Vocabria 30 mg film-coated tablets; last revised: January 2025

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 9 July 2024, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 7 February 2025, the pharmaceutical company submitted a dossier for the benefit assessment of cabotegravir to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 2 VerfO.

By letter dated 12 February 2025 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefits 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 cabotegravir.

The dossier assessment by the IQWiG was submitted to the G-BA on 13 May 2025, and the written statement procedure was initiated with publication on the G-BA website on 15 May 2025. The deadline for submitting statements was 5 June 2025.

The oral hearing has been dispensed with since all assessment experts who submitted a written statement waived their right to make an oral statement or did not register for the oral hearing.

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 was discussed at the session of the subcommittee on 29 July 2025, and the draft resolution was approved.

At their session on 7 August 2025, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	9 July 2024	Determination of the appropriate comparator therapy
Working group Section 35a	18 June 2025	Information on statements received
Working group Section 35a	1 July 2025 15 July 2025	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	29 July 2025	Concluding discussion of the draft resolution
Plenum	7 August 2025	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 7 August 2025

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

Prof. Hecken