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: Rilpivirine (HIV-1 infection, combination with cabotegravir)

of 21 October 2021

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 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 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 benefits,
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. Costs of therapy for the statutory health insurance,
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 forms part of the Pharmaceuticals Directive.

2. Key points of the resolution

The relevant date for the first placing on the (German) market of the active ingredient rilpivirine in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure of the G-BA (VerfO) is 1st May 2021. 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 14 April 2021.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on the website of the G-BA (www.g-ba.de), on 2 August 2021, thus initiating the written statement procedure. In addition, an oral hearing was held.

As part of a therapy concept, rilpivirine is used in combination with cabotegravir for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults according to the information in the therapeutic indication. The therapy concept includes an oral lead-in phase of at least 28 days, during which rilpivirine is to be taken orally (Edurant) together with

cabotegravir orally (Vocabria) in order to assess the tolerability of rilpivirine and cabotegravir prior to the use of long-acting rilpivirine injection plus long-acting cabotegravir injection. This is followed by the maintenance phase with intramuscular rilpivirine injection (Rekambys) in combination with intramuscular cabotegravir injection (Vocabria). Oral therapy (cabotegravir oral + rilpivirine oral) is also used for adults to replace up to 2 consecutive monthly injection dates or one of the every 2-month injection dates. The assessment of the additional benefit of rilpivirine + cabotegravir 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 rilpivirine 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, the statements submitted in the written statement and oral hearing procedure, and the addenda to the benefit assessment prepared by the IQWiG. 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 rilpivirine.

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 rilpivirine (Rekambys) in accordance with the product information

Rekambys is indicated, in combination with cabotegravir injection, for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults 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 NNRTI and INI class.

Therapeutic indication of the resolution (resolution from 21.10.2021):

Rekambys is indicated, in combination with cabotegravir injection, for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults 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 NNRTI and INI class.

[1] General Methods, version 6.0 from 05.11.2020. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

Prior to the initiation of Rekambys, rilpivirine oral tablets, together with cabotegravir oral tablets, should be taken for approximately 1 month (at least 28 days) to assess tolerability to rilpivirine and cabotegravir.

If a patient plans to miss a scheduled injection by more than 7 days, daily oral therapy (one rilpivirine tablet [25 mg] and one cabotegravir tablet [30 mg]) may be used to replace up to 2 consecutive monthly injection visits.

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:

Adults 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 NNRTI and INI class.

an patient-individual antiretroviral therapy using a selection of approved active ingredients; taking into account the previous therapy(ies) and, if applicable, side effects

Criteria according to Chapter 5, Section 6 of the Rules of Procedure of the G-BA:

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

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

1. To be considered as a comparator therapy, the medicinal product must, principally, have a marketing authorisation for the therapeutic indication
2. If a non-medicinal treatment is considered as a comparator therapy, this must be available within the framework of the SHI system.
3. As comparator therapy, medicinal products or non-medicinal treatments for which the Federal Joint Committee has already determined the patient-relevant benefit 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.

Justification based on the criteria set out in Chapter 5, Section 6, paragraph 3 VerfO:

on 1. Besides rilpivirine, the following active ingredients are approved in principle for the treatment of adults infected with human immunodeficiency virus 1 (HIV-1):

Protease inhibitors (PI): Atazanavir, darunavir, fosamprenavir, indinavir[2], ritonavir, saquinavir, tipranavir, lopinavir

Nucleoside and nucleotide reverse transcriptase inhibitors (NRTI): Abacavir, didanosine[2], emtricitabine, lamivudine, stavudine[2], tenofovir alafenamide, tenofovir disoproxil, zidovudine

Non-nucleoside reverse transcriptase inhibitors (NNRTI): Efavirenz, etravirine, nevirapine, doravirine

Integrase inhibitors (INI): Dolutegravir, elvitegravir, raltegravir, bictegravir, cabotegravir

Other anti-virals: Enfuvirtide (fusion inhibitor), maraviroc (fusion inhibitor), ibalizumab and fostemsavir (post-attachment inhibitors)

Other therapeutic agents: Cobicistat (pharmacokinetic amplifier)

on 2. A non-medicinal treatment cannot be considered as an appropriate comparator therapy in this therapeutic indication.

on 3. Resolutions on procedures according to Section 35a SGB V:

Fostemsavir of 16 September 2021

Dolutegravir (new therapeutic indication) of 15 July 2021

Ibalizumab of 18 February 2021

Cobicistat of 1st October 2020

Dolutegravir/lamivudine of 6 February 2020

Doravirin/lamivudine/tenofovir disoproxil of 4 July 2019

Doravirin of 4 July 2019

Bictegravir/emtricitabine/tenofovir alafenamide of 20 December 2018

Dolutegravir/rilpivirine of 6 December 2018

Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (new therapeutic indication) of 5 July 2018

Elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil (new therapeutic indication) of 3 May 2018

Darunavir/cobicistat/emtricitabine/tenofovir alafenamide of 16 March 2018

Dolutegravir (new therapeutic indication) of 21 September 2017

[2] Currently not placed on the German market

Emtricitabine/rilpivirine/tenofovir alafenamide of 5 January 2017

Emtricitabine/tenofovir alafenamide of 3 November 2016

Rilpivirine (nAWG) of 16 June 2016

Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide of 16 June 2016

Dolutegravir/abacavir/lamivudine of 19 March 2015

Cobicistat of 18 September 2014

Dolutegravir of 7 August 2014

Emtricitabine/rilpivirine/tenofovir disoproxil (new therapeutic indication) of 19 June 2014

Elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil of 5 December 2013

Emtricitabine/rilpivirine/tenofovir disoproxil of 5 July 2012

Rilpivirine of 5 July 2012

on 4. The general state of medical knowledge, on which the finding of the G-BA is based, was illustrated by systematic research for guidelines as well as reviews of clinical studies in the present therapeutic indication. For the treatment of adults infected with human immunodeficiency virus type 1 (HIV-1), the active ingredients listed under 1 are available according to the respective approved therapeutic indication. When determining the appropriate comparator therapy for therapy experienced adults with HIV-1, the evidence search showed that after one or more previous therapies, depending on the active ingredients/medicinal product classes used and the reason for the change of therapy (e.g. side effects), patient-individual pharmacotherapy coordinated with the patient is recommended. 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 scheme depending on the previous therapy. In principle, all possible combinations of active ingredients can therefore be regarded as appropriate.

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

2.1.3 Extent and probability of the additional benefit

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

Adults 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 NNRTI and INI class.

An additional benefit is not proven.

Justification:

In the therapy concept of combination therapy with rilpivirine and cabotegravir, the active ingredients rilpivirine and cabotegravir 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 (rilpivirine oral + cabotegravir oral) is also used for adults to replace up to 2 consecutive monthly injection dates or one of the every 2-month injection dates. The assessment of the additional benefit of rilpivirine + cabotegravir relates to the entire therapy concept consisting of oral lead-in phase, intramuscular application and oral bridging therapy.

For the assessment of the additional benefit of rilpivirine in combination with cabotegravir for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults 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 NNRTI and INI class, an adjusted indirect comparison for the Q2M treatment regimen versus individual ART via the bridge comparator rilpivirine + cabotegravir Q1M was submitted by the pharmaceutical company. The pharmaceutical company uses the two studies ATLAS-2M and FLAIR with data cut-off at week 96 for their indirect comparison.

The ATLAS-2M study is an open-label, randomised, parallel-group study evaluating the therapy concept of rilpivirine and cabotegravir Q2M versus Q1M. The study included treatment-experienced adult patients with HIV-1 infection who had been receiving therapy for at least 6 months without interruption consisting of 2 nucleoside reverse transcriptase inhibitors (NRTIs) in combination with a 3rd active ingredient from the NNRTI, protease inhibitor (PI) or INI product classes and were stable virologically suppressed (HIV-1 RNA < 50 copies/ml). Furthermore, patients from the ATLAS study were able to transfer to the ATLAS-2M study.

The pharmaceutical company presents the results of a sub-population of those patients who have previously been treated with ART consisting of 2 NRTIs in combination with a 3rd active ingredient from the NNRTI, PI or INI product classes. The sub-population of the ATLAS-2M study includes 327 patients in the intervention arm and 327 in the comparator arm.

The FLAIR study is an open-label, randomised, parallel-group study evaluating rilpivirine + cabotegravir Q1M versus abacavir/dolutegravir/lamivudine (ABC/DTG/3TC). The study included therapy naïve patients with HIV-1 infection (HIV-1 RNA ≥ 1000 copies/ml) who received therapy with ABC/DTG/3TC for 20 weeks prior to randomisation. After 16 weeks of treatment with ABC/DTG/3TC, patients had to be virologically suppressed (HIV-1 RNA < 50 copies/mL) to be randomised to one of the two treatment arms (rilpivirine + cabotegravir Q1M or ABC/DTG/3TC) after an additional 4 weeks. A total of 566 patients were randomised to the intervention arm (N = 283) or the comparator arm (N = 283).

Treatment with rilpivirine + cabotegravir in the ATLAS-2M and Flair studies was done according to the requirements in the product information.

The primary endpoint of the ATLAS-2M and FLAIR studies is virologic non-response (HIV RNA ≥ 50 copies/ml) at week 48. Other patient-relevant endpoints include mortality, morbidity, health-related quality of life, and adverse events (AEs).

It is assumed that the ATLAS-2M and FLAIR studies included only patients for whom there was no medically necessary changeover indication of the existing previous therapy.

No data are available for adult patients with a medically necessary indication for conversion (e.g. due to side effects).

The indirect comparison presented for the Q2M treatment regimen in the dossier cannot be considered for the present benefit assessment due to methodological deficiencies (e.g. lack of similarity test, lack of information on disease-specific patient characteristics of the ATLAS-2M study). The conduct of a similarity test is a fundamental prerequisite for the recognition of an indirect comparison, so that it should have been submitted with the dossier.

For the Q1M treatment regimen, the pharmaceutical company does not use the results of the two RCTs FLAIR and ATLAS (rilpivirine + cabotegravir Q1M vs individual ART, 48 weeks), which are potentially suitable for the benefit assessment, to derive the additional benefit, although these were available for the Q1M treatment regimen.

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

2.1.4 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product Rekambys with the active ingredient rilpivirine.

Rilpivirine in combination with cabotegravir is approved for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable antiretroviral regimen. Patients must have no current or previous evidence of viral resistance to non-nucleoside reverse transcriptase inhibitors (NNRTIs) or integrase inhibitors (INIs) and must not have experienced virological failure with these inhibitors.

The appropriate comparator therapy was determined to be a patient-individual antiretroviral therapy, selecting the approved active ingredients, taking into account the previous therapy(ies) and, if applicable, side effects.

For the assessment of the additional benefit of rilpivirine in combination with cabotegravir, an adjusted indirect comparison of the ATLAS-2M and FLAIR studies for the Q2M treatment regimen versus individual ART via the bridge comparator rilpivirine + cabotegravir Q1M was submitted by the pharmaceutical company for patients without a medically necessary changeover indication.

The indirect comparison presented for the Q2M treatment regimen in the dossier cannot be considered for the present benefit assessment due to methodological deficiencies (e.g. lack of similarity test, lack of information on disease-specific patient characteristics of the ATLAS-2M study). The conduct of a similarity test is a fundamental prerequisite for the recognition of an indirect comparison so that it should have been submitted with the dossier.

No data are available for adult patients with a medically necessary indication for conversion (e.g. due to side effects).

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

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

Based on the data on patient numbers from the Robert Koch Institute, the pharmaceutical company assumes 74,100 (95% CI: 70,600 to 77,500)[3] patients on stable antiretroviral therapy (ART). The pharmaceutical company delimits those patients who show resistance to INI (0.2%) or NNRTI (7.8%). In this context, the pharmaceutical company shall only take into account transferred resistances. Assuming that approx. 87.81% of the German resident population has statutory health insurance, approx. 59,900 patients are eligible for the administration of rilpivirine in combination with cabotegravir, according to the pharmaceutical company.

The number of patients in the SHI target population reported by the pharmaceutical company is overestimated overall due to an underestimation of the percentage of patients with resistance.

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

[3] Robert Koch Institute. Estimate of the number of new HIV infections and the total number of people living with HIV in Germany, last revised end of 2019. Epidemiological Bulletin 2020; 48

(summary of product characteristics, SmPC) for Rekambys (active ingredient: rilpivirine) at the following publicly accessible link (last access: 12 July 2021):

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

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

Prior to initiating treatment with Rekambys, healthcare professionals should carefully select 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 associated with missed doses.

Following discontinuation of Rekambys in combination with cabotegravir injection, it is essential to adopt an alternative, fully suppressive antiretroviral regimen no later than one month after the last every 1-month injection of Rekambys and two months after the last every 2-months injection of Rekambys.

2.4 Treatment costs

The treatment costs are based on the contents of the product information and the information listed in the LAUER-TAXE® (last revised: 1 October 2021).

If no maximum treatment duration is specified in the product information, the treatment duration is assumed to be one year (365 days), even if the actual treatment duration is patient-individual 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. If the treatment duration is not limited, initial induction schemes are not considered for the cost representation. 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 induction is required after the initial induction. For this reason, the first year of treatment with induction therapy is not presented below but rather the maintenance treatment of a subsequent year of treatment.

Rilpivirine injection in combination with cabotegravir injection 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 2 months (Q2M).

Cabotegravir injection 400 mg and rilpivirine injection 600 mg for the Q1M treatment regimen are currently 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 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 + lamivudine/tenofovir disoproxil) and a cost-intensive therapy (maraviroc + abacavir + emtricitabine) as examples.

According to the current German-Austrian guidelines[4], different alternatives ("backbone" with combination partners) are recommended that were considered for the cost representation.

Treatment period:

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Days of treatment/ patient/ year
Medicinal product to be assessed				
Rilpivirine + cabotegravir				
Rilpivirine	1 x every 2 months	6	1	6
Cabotegravir	1 x every 2 months	6	1	6
or				
Rilpivirine	1 x month	12	1	12
Cabotegravir	1 x month	12	1	12
Appropriate comparator therapy				
Nevirapine + lamivudine / tenofovir disoproxil				
Nevirapine	continuously, 2 x daily	365	1	365

German-Austrian guidelines on antiretroviral therapy for HIV-1 infection, AWMF 055-001, version 8 of 10.04.2019 and version 9 of 01.09.2020.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Days of treatment/ patient/ year
Lamivudine / tenofovir disoproxil	continuously, 1 x daily	365	1	365
Maraviroc + abacavir + emtricitabine				
Maraviroc	continuously, 2 x daily	365	1	365
Abacavir	continuously, 2 x daily	365	1	365
Emtricitabine	continuously, 1 x daily	365	1	365

Consumption:

Designation of the therapy	Dosage/ application	Dosage/ patient/ treatment days	Usage by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Rilpivirine + cabotegravir					
Rilpivirine	900 mg	900 mg	1 x 900 mg	6	6 x 900 mg
Cabotegravir	600 mg	600 mg	1 x 600 mg	6	6 x 600 mg
or					
Rilpivirine	600 mg[5]	600 mg	1 x 600 mg	12	12 x 600 mg
Cabotegravir	400 mg[5]	400 mg	1 x 400 mg	12	12 x 400 mg
Appropriate comparator therapy					

[5] currently not available on the German market

Designation of the therapy	Dosage/ application	Dosage/ patient/ treatment days	Usage by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Nevirapine + lamivudine / tenofovir disoproxil					
Nevirapine	200 mg	400 mg	2 x 200 mg	365	730 x 200 mg
Lamivudine/ tenofovir disoproxil	245 mg / 300 mg	245 mg / 300 mg	1 x 245 mg / 300 mg	365	365 x 245 mg / 300 mg
Maraviroc + abacavir + emtricitabine					
Maraviroc	300 mg	600 mg	2 x 300 mg	365	730 x 300 mg
Abacavir	300 mg	600 mg	2 x 300 mg	365	730 x 300 mg
Emtricitabine	200 mg	200 mg	1 x 200 mg	365	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. The required number of packs of a particular potency was first determined based on consumption to calculate the annual treatment costs. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated based on the costs per pack after deduction of the statutory rebates.

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					
Rilpivirine + cabotegravir					
Rilpivirine 900 mg	1 PRJ	€ 782.91	€ 1.77	€ 42.74	€ 738.40
Cabotegravir 600 mg	1 PRJ	€ 1,408.12	€ 1.77	€ 77.35	€ 1,329.00
Rilpivirine 600 mg[5]	-	-	-	-	-
Cabotegravir 400 mg[5]	-	-	-	-	-
Appropriate comparator therapy					
Nevirapine + lamivudine / tenofovir disoproxil					
Nevirapine 200 mg	120 TAB	€ 266.98	€ 1.77	€ 12.73	€ 252.48
Lamivudine / tenofovir disoproxil 245 mg / 300 mg	30 FCT	€ 47.05	€ 1.77	€ 1.71	€ 43.57
Maraviroc + abacavir + emtricitabine					
Maraviroc 300 mg	60 FCT	€ 1,073.06	€ 1.77	€ 58.80	€ 1,012.49
Abacavir 300 mg	180 FCT	€ 1,107.09	€ 1.77	€ 52.01	€ 1,053.31
Emtricitabine 200 mg	30 HC	€ 302.47	€ 1.77	€ 16.14	€ 284.56
Abbreviations: PRJ = prolonged-release suspension for injection; HC = hard capsules, FCT = film-coated tablets, TAB = tablets					

LAUER-TAXE® last revised: 1st October 2021

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 standard expenditure in the course of the treatment are not shown.

Because there are no regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, no costs for additionally required SHI services had to be taken into account.

3. Bureaucratic costs calculation

The proposed resolution does not create any new or amended information obligations for care providers within the meaning of Annex II to Chapter 1 VerfO and, accordingly, no bureaucratic costs.

4. Process sequence

At its session on 8 October 2019, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

The appropriate comparator therapy determined by the G-BA was reviewed. The Subcommittee on Medicinal Products determined the appropriate comparator therapy at its session on 22 June 2021.

On 14 April 2021, the pharmaceutical company submitted a dossier for the benefit assessment of rilpivirine to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 VerfO.

By letter dated 03 May 2021, in conjunction with the resolution of the G-BA of 1st 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 rilpivirine.

The dossier assessment by the IQWiG was submitted to the G-BA on 29 July 2021, and the written statement procedure was initiated with publication on the website of the G-BA on 2 August 2021. The deadline for submitting written statements was 23 August 2021.

The oral hearing was held on 6 September 2021.

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 12 October 2021, and the proposed resolution was approved.

At its session on 21 October 2021, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal product	8 October 2019	Determination of the appropriate comparator therapy
Subcommittee Medicinal product	22 June 2021	New determination of the appropriate comparator therapy
Working group Section 35a	31 August 2021	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal product	6 September 2021	Conduct of the oral hearing
Working group Section 35a	14.09.2021; 05.10.2021	Consultation on the dossier assessment by the IQWiG, assessment of the written statement procedure
Subcommittee Medicinal product	12 October 2021	Concluding discussion of the draft resolution
Plenum	21 October 2021	Adoption of the resolution on the amendment of Annex XII AM-RL

Berlin, 21 October 2021

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

Prof. Hecken