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
Glecaprevir/ Pibrentasvir (new therapeutic indication: chronic hepatitis C, 3 to < 12 years of age)

of 16 December 2021

Contents

1. Legal basis 2

2. Key points of the resolution 2

2.1 Additional benefit of the medicinal product in relation to the appropriate comparator therapy 3

2.1.1 Approved therapeutic indication of Glecaprevir/ Pibrentasvir (Maviret) according to the product information 3

2.1.2 Appropriate comparator therapy 3

2.1.3 Extent and probability of the additional benefit 6

2.1.4 Summary of the assessment 8

2.2 Number of patients or demarcation of patient groups eligible for treatment 8

2.3 Requirements for a quality-assured application 8

2.4 Treatment costs 9

3. Bureaucratic costs calculation 15

4. Process sequence 15

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 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 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 forms part of the Pharmaceuticals Directive.

2. Key points of the resolution

The combination of active ingredients glecaprevir/ pibrentasvir (Maviret) was listed for the first time on 1 September 2017 in the "LAUER-TAXE®", the extensive German registry of available medicinal products and their prices.

On 22 June 2021, Maviret 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 European 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, p. 7).

On 25 June 2021, i.e. at the latest within four weeks after informing the pharmaceutical company about the approval for a new therapeutic indication, the pharmaceutical company has submitted a dossier in due time in accordance with Section 4, paragraph 3, number 2 of

the 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 combination of active ingredients glecaprevir/ pibrentasvir with the new therapeutic indication ("Maviret is indicated for the treatment of chronic hepatitis C virus (HCV) infection in adults and children aged 3 years and older").

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 1 October 2021, 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 glecaprevir/ pibrentasvir 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 glecaprevir/ pibrentasvir.

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 Glecaprevir/ Pibrentasvir (Maviret) according to the product information

Maviret is indicated for the treatment of chronic hepatitis C virus (HCV) infection in adults and children aged 3 years and older.

Therapeutic indication of the resolution (resolution of 16 December 2021):

Maviret is indicated for the treatment of chronic hepatitis C virus (HCV) infection children aged 3 to < 12 years.

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

a) Children with chronic hepatitis C aged 3 to < 12 years, genotype 1, 4, 5 or 6

Appropriate comparator therapy for glecaprevir/ pibrentasvir:

- Ledipasvir/sofosbuvir or sofosbuvir/velpatasvir[2]

[1] General Methods, version 6.0 from 05.11.2020. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.
[2] approved above the age of 6

b) Children with chronic hepatitis C aged 3 to < 12 years, genotype 2 or 3

Appropriate comparator therapy for glecaprevir/ pibrentasvir:

- Sofosbuvir plus ribavirin or sofosbuvir/velpatasvir[2]

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 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, in principle, 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 advantage 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:

a) Children with chronic hepatitis C aged 3 to < 12 years, genotype 1, 4, 5 or 6

b) Children with chronic hepatitis C aged 3 to < 12 years, genotype 2 or 3

on 1. In the therapeutic indication of chronic hepatitis C, the active ingredients ribavirin, interferon alfa-2b, peginterferon alfa-2a[3], peginterferon alfa-2b, sofosbuvir and the combination of active ingredients ledipasvir/sofosbuvir and sofosbuvir/velpatasvir are approved for children aged 3 to < 12 years. Peginterferon alfa-2b is not currently marketed in Germany.

on 2. Non-medicinal treatments are not considered for the therapeutic indication.

on 3. In the therapeutic indication "chronic hepatitis C" there are resolutions of the G-BA on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V active ingredients/combinations of active ingredients. The G-BA has made the following resolutions for patients between the ages of 3 and <12 years of age with chronic hepatitis C:

[3] approved above the age of 5

- Sofosbuvir (in combination with ribavirin) from 21 January 2021
- Ledipasvir/sofosbuvir from 21 January 2021
- Sofosbuvir/velpatasvir from 1 April 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".

It can be stated that the data basis for drug therapies and treatment cascades in the present therapeutic indication is limited overall. In the present age group, therapy with the approved options (peg)interferon plus ribavirin is no longer considered adequate in accordance with the current guideline recommendations and is only used in exceptional cases. For example, therapy with (peg)interferon and ribavirin may be indicated in children with severe symptoms. The guidelines recommend treating patients in this age group with DAA in accordance with the recommendations for adulthood.

Change of the appropriate comparator therapy

To date, ledipasvir/sofosbuvir for children with chronic hepatitis C aged 3 to < 12 years, genotype 1, 4, 5 or 6 and sofosbuvir in combination with ribavirin for children with chronic hepatitis C aged 3 to < 12 years, genotype 2 or 3 have been considered as the sole appropriate comparator therapies.

However, in the course of the written statement procedure on the present benefit assessment of glecaprevir/ pibrentasvir, it became clear that the clinical significance of sofosbuvir/velpatasvir in the treatment of chronic hepatitis C in children with HCV infection of any genotype is comparable with the specific appropriate comparator therapies ledipasvir/sofosbuvir or sofosbuvir in combination with ribavirin.

In addition, the observed virologic response rates of sofosbuvir/velpatasvir (see resolution of 1 April 2021) are of the same order of magnitude as those of the specific appropriate comparator therapies ledipasvir/sofosbuvir or sofosbuvir in combination with ribavirin.

In light of the aforementioned guideline recommendations to treat children with DAA, as well as the findings from the benefit assessment procedures conducted, the approved options ledipasvir/sofosbuvir or sofosbuvir/velpatasvir or sofosbuvir plus ribavirin or sofosbuvir/velpatasvir are considered equally appropriate treatment options in the present age group and are therefore determined as appropriate comparator therapies.

The distribution of the patient groups follows the treatment recommendations and the additional benefit of ledipasvir/sofosbuvir and sofosbuvir, respectively, identified for the infection with the respective HCV genotypes.

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

Overall, taking into account the clinical treatment situation and the findings from the written statement procedure, the G-BA therefore considers it appropriate to expand the specific appropriate comparator therapies for the above-mentioned patient

populations to include sofosbuvir/velpatasvir and thus, to adapt them to the current state of medical knowledge.

2.1.3 Extent and probability of the additional benefit

In summary, the additional benefit of glecaprevir/ pibrentasvir is assessed as follows:

a) Children with chronic hepatitis C aged 3 to < 12 years, genotype 1, 4, 5 or 6

Additional benefit not proven

b) Children with chronic hepatitis C aged 3 to < 12 years, genotype 2 or 3

Additional benefit not proven

Justification:

The pharmaceutical company presents the ongoing single-arm M16-123 (DORA) study for children with chronic hepatitis C aged 3 to < 12 years. This is an open-label, multicentre, single-arm study investigating glecaprevir/ pibrentasvir in children and adolescents aged 3 to < 18 years with chronic hepatitis C infections. In cohorts 2 to 4 of the study, children aged 3 to <12 years were treated with glecaprevir/ pibrentasvir for 8 to 16 weeks. The pharmaceutical company does not present data on the appropriate comparator therapy. It does not compare individual arms of different studies.

The study examined mortality, sustained virologic response (SVR) as the endpoints of morbidity, as well as health-related quality of life and side effects. These endpoints are fundamentally patient-relevant.

Due to the lack of a comparison, the single-arm study is not suitable for assessing an additional benefit; this would only be possible with very large effects compared to the appropriate comparator therapy. The results of the M16-123 (DORA) study on the endpoint categories of mortality, morbidity, health-related quality of life and side effects are therefore only presented additionally in the resolution.

Mortality

There were no deaths

Morbidity

Sustained virologic response 12 (SVR12) weeks after the end of treatment was achieved in 59 (98.3%) of children with chronic hepatitis C aged 3 to < 12 years (hepatitis C virus (HCV) genotype 1 or 4) and in 18 (90%) of children with chronic hepatitis C aged 3 to < 12 years (HCV genotype 2 or 3). The results of cohorts 2 to 4 of the M16-123 (DORA) study are in the same

order of magnitude as those of the appropriate comparator therapy ledipasvir/sofosbuvir or sofosbuvir/velpatasvir or sofosbuvir plus ribavirin or sofosbuvir/velpatasvir. For ledipasvir/sofosbuvir, SVR12 and SVR 24 of 95-100% were observed (see G-BA resolution of 21 January 2021) . For sofosbuvir/velpatasvir, SVR12 and SVR 24 of 93.2% were observed (see G-BA resolution of 1 April 2021). For sofosbuvir plus ribavirin, SVR12 and SVR 24 of 94.4-100% were observed (see G-BA resolution of 21 January 2021). Great effects compared to the newly determined appropriate comparator therapy can therefore not be assumed.

Quality of life

Health-related quality of life was assessed in the M16-123 (DORA) study using the Paediatric Quality of Life Inventory (PedsQL) at the start of study and 12 weeks after the end of treatment. Over the course of the study, there is a change of -1.12 points in the total score for children with HCV genotype 1 or 4 and -8.66 points for children with HCV genotype 2 or 3.

However, the results cannot be sufficiently interpreted due to the non-comparative data.

Side effects

In cohorts 2 to 4 of the M16-123 (DORA) study, discontinuation due to AEs (1.7%) but no serious adverse events (SAEs) occurred in children with HCV genotype 1 or 4. No SAEs or discontinuations due to AEs occurred in children with HCV genotype 2 or 3.

Overall assessment / conclusion

The presented single-arm M16-123 (DORA) study is not suitable for the assessment of an additional benefit due to the lack of a comparison with the respective appropriate comparator therapy; this would only be possible with very large effects compared to the appropriate comparator therapy. Sustained virologic response 12 (SVR12) weeks after the end of treatment was achieved with glecaprivir/ pibrentasvir in 98.3% of children with chronic hepatitis C aged 3 to < 12 years (hepatitis C virus (HCV) genotype 1 or 4) and in 90% of children with chronic hepatitis C aged 3 to < 12 years (HCV genotype 2 or 3). The results of cohorts 2 to 4 of the M16-123 (DORA) study are in the same order of magnitude as those of the appropriate comparator therapies ledipasvir/sofosbuvir or sofosbuvir/velpatasvir or sofosbuvir plus ribavirin or sofosbuvir/velpatasvir.

There were no deaths, no serious adverse events, and only one adverse event that led to therapy discontinuation.

The available data on health-related quality of life cannot be adequately interpreted.

Overall, no additional benefit can be derived on the basis of the data presented.

2.1.4 Summary of the assessment

The present benefit assessment concerns the benefit assessment of the medicinal product Maviret with the combination of active ingredients glecaprevir / pibrentasvir. Glecaprivir/ pibrentasvir is approved for the treatment of chronic hepatitis C virus (HCV) infection in adults and in children aged 3 years and older.

In the therapeutic indication to be considered, two patient groups were distinguished:

a) Children with chronic hepatitis C aged 3 to < 12 years, genotype 1, 4, 5 or 6

b) Children with chronic hepatitis C aged 3 to < 12 years, genotype 2 or 3

The G-BA determined ledipasvir/sofosbuvir or sofosbuvir/velpatasvir as the appropriate comparator therapy for patient population a) and sofosbuvir in combination with ribavirin or sofosbuvir/velpatasvir for patient population b). For the benefit assessment of glecaprivir/ pibrentasvir for the treatment of children aged 3 to <12 years with chronic hepatitis C, only data from the single-arm, non-comparative M16-123 (DORA) study were presented. Due to the lack of comparison, the data are not suitable for the derivation of an additional benefit compared to the appropriate comparator therapies.

In addition, the observed virologic response rates are in the same order of magnitude as for the respective appropriate comparator therapies.

An additional benefit of glecaprivir/ pibrentasvir versus the appropriate comparator therapies is therefore not proven.

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. The G-BA bases its resolution on the patient numbers from the dossier submitted by the pharmaceutical company. Overall, it can be assumed that the number of patients in the SHI target population (total across all genotypes) is closer to the lower limit specified by the pharmaceutical company. Each of the numbers given by the pharmaceutical company for the genotypes is subject to uncertainty due to the transfer of percentage values for adults to the age group relevant here.

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 Maviret (active ingredient: glecaprevir/ pibrentasvir) at the following publicly accessible link (last access: 5 November 2021):

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

Treatment with glecaprevir/ pibrentasvir should only be initiated and monitored by specialists who are experienced in the treatment of children with chronic hepatitis C.

2.4 Treatment costs

The treatment costs are based on the specifications of the product information as well as the information in the LAUER-TAXE® (last revised: 1 December 2021).

According to the product information, the following therapy options are available:

Designation of the therapy	**Duration of the treatment cycle**	**Use according to product information:**
Medicinal product to be assessed:		
Children aged 3 to < 12 years and with a body weight between 12 and < 45 kg		
Glecaprevir/ Pibrentasvir	8 weeks	Therapy naive patients with genotype 1, 2, 3, 4, 5 or 6 with or without cirrhosis
Glecaprevir/ Pibrentasvir	8 weeks	Pretreated patients with genotype 1, 2, 4 – 6 without cirrhosis
Glecaprevir/ Pibrentasvir	12 weeks	Pretreated patients with genotype 1, 2, 4 – 6 with cirrhosis
Glecaprevir/ Pibrentasvir	16 weeks	Pretreated patients with genotype 3 with or without cirrhosis
Appropriate comparator therapy		
Patients aged 3 to < 12 years with chronic hepatitis C (genotypes 1, 4, 5 or 6)		
Ledipasvir/Sofosbuvir	8 weeks	Can be considered in genotype 1 patients without cirrhosis.
Ledipasvir/Sofosbuvir	12 weeks	Patients with genotype 1, 4, 5, or 6 without cirrhosis or with compensated cirrhosis, a low risk of progression and retreatment option.
Ledipasvir/Sofosbuvir	24 weeks	Patients with genotype 1, 4, 5 or 6 and compensated cirrhosis.
Sofosbuvir/Velpatasvir	12 weeks	Patients aged 6 to <18 years and weighing at least 17 kg regardless of the HCV genotype
Patients aged 3 to < 12 years with chronic hepatitis C (genotype 2 or 3)		
Sofosbuvir + Ribavirin	12 weeks	Patients with genotype 2
Sofosbuvir + Ribavirin	24 weeks	Patients with genotype 3
Sofosbuvir/Velpatasvir	12 weeks	Patients aged 6 to <18 years and weighing at least 17 kg regardless of the HCV genotype

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:				
Glecaprevir / Pibrentasvir	1 x daily for 8 weeks	56	1	56
Glecaprevir / Pibrentasvir	1 x daily for 12 weeks	84	1	84
Glecaprevir / Pibrentasvir	1 x daily for 16 weeks	112	1	112
Appropriate comparator therapy				
a) Children with chronic hepatitis C aged 3 to < 12 years, genotype 1, 4, 5 or 6				
Ledipasvir / Sofosbuvir	1 x daily for 8 weeks	56	1	56
Ledipasvir / Sofosbuvir	1 x daily for 12 weeks	84	1	84
Ledipasvir / Sofosbuvir	1 x daily for 24 weeks	168	1	168
Sofosbuvir/Velpatasvir	1 x daily for 12 weeks	84	1	84
b) Children with chronic hepatitis C aged 3 to < 12 years, genotype 2 or 3				
Sofosbuvir + Ribavirin	1 x daily for 12 weeks 2 x daily for 12 weeks	84 84	1 1	84 84
Sofosbuvir + Ribavirin	1 x daily for 24 weeks 2 x daily for 24 weeks	168 168	1 1	168 168
Sofosbuvir/Velpatasvir	1 x daily for 12 weeks	84	1	84

Consumption:

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.

The cost calculation was based on standard patients with an average body weight of 16.2 kg for patients aged 3 years, 23.6 kg for patients aged 6 years and 42.1 kg for patients aged 11 years.[4]

Ledipasvir / sofosbuvir and sofosbuvir are available in both liquid and solid dosage forms. However, the potencies ledipasvir 90 mg / sofosbuvir 400 mg and sofosbuvir 400 mg, which correspond to the dosage for patients weighing 35 kg or more, are only available as a solid dosage form (film-coated tablets). For the cost representation, it is assumed that patients with a body weight of 35 kg or more (corresponding to an age of approx. 9 to 10 years) can usually take the more economical option of the solid dosage form in the appropriate potency. The dosage of the liquid formulation of these active ingredients is therefore only presented for patients weighing 16.2 kg or more and less than 35 kg. Ledipasvir / sofosbuvir film-coated tablets and sofosbuvir are only approved for patients weighing 17 kg or more.

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:					
Glecaprevir / Pibrentasvir 8 weeks Granules	150 mg/60 mg - 250 mg/100 mg	150mg/60 mg - 250 mg/100 mg	3 x 50 mg/20 mg - 5 x 50 mg/20 mg	56 56	168 x 50 mg/20 mg - 280 x 50 mg/20 mg
Glecaprevir / Pibrentasvir 12 weeks granules	150 mg/60 mg - 250 mg/100 mg	150mg/60 mg - 250 mg/100 mg	3 x 50 mg/20 mg - 5 x 50 mg/20 mg	84 84	252 x 50 mg/20 mg - 420 x 50 mg/20 mg
Glecaprevir / Pibrentasvir 16 weeks granules	150 mg/60 mg - 250 mg/100 mg	150mg/60 mg - 250 mg/100 mg	3 x 50 mg/20 mg - 5 x 50 mg/20 mg	112 112	336 x 50 mg/20 mg - 560 x 50 mg/20 mg

[4] Federal Statistical Office, Wiesbaden 2018: http://www.gbe-bund.de/

Appropriate comparator therapy					
a) Children with chronic hepatitis C aged 3 to < 12 years, genotype 1, 4, 5 or 6					
Ledipasvir / Sofosbuvir 8 weeks Granules	33.75 mg/150 mg - 45 mg/200 mg	45mg/200 mg - 45 mg/200 mg	1 x 33.75 mg/150 mg - 1 x 45 mg/200 mg	56	56 x 33.75 mg/150 mg - 56 x 45 mg/200 mg
Ledipasvir / Sofosbuvir 12 weeks granules	33.75 mg/150 mg - 45 mg/200 mg	45mg/200 mg - 45 mg/200 mg	1 x 33.75 mg/150 mg - 1 x 45 mg/200 mg	84	84 x 33.75 mg/150 mg - 84 x 45 mg/200 mg
Ledipasvir / Sofosbuvir 24 weeks granules	33.75 mg/150 mg - 45 mg/200 mg	45mg/200 mg - 45 mg/200 mg	1 x 33.75 mg/150 mg - 1 x 45 mg/200 mg	168	168 x 33.75 mg/150 mg - 168 x 45 mg/200 mg
Ledipasvir / Sofosbuvir 8 weeks FCT[5]	45 mg/200 mg - 90 mg/400 mg	45mg/200 mg - 90 mg/400 mg	1 x 45 mg/200 mg - 1 x 90 mg/400 mg	56	56 x 45 mg/200 mg - 56 x 90 mg/400 mg
Ledipasvir / sofosbuvir 12 weeks FCT[5]	45 mg/200 mg - 90 mg/400 mg	45mg/200 mg - 90 mg/400 mg	1 x 45 mg/200 mg - 1 x 90 mg/400 mg	84	84 x 45 mg/200 mg - 84 x 90 mg/400 mg
Ledipasvir / Sofosbuvir 24 weeks FCT[5]	45 mg/200 mg - 90 mg/400 mg	45mg/200 mg - 90 mg/400 mg	1 x 45 mg/200 mg - 1 x 90 mg/400 mg	168	168 x 45 mg/200 mg - 168 x 90 mg/400 mg
Sofosbuvir/Velpatasvir 12 weeks FCT[5]	200 mg/50 mg - 400 mg/100 mg	200 mg/50 mg - 400 mg/100 mg	1 x 200 mg/50 mg - 1 x 400 mg/100 mg	84	84 x 200 mg/50 mg - 84 x 400 mg/100 mg

[5]For body weight above 17 kg.

b) Children with chronic hepatitis C aged 3 to < 12 years, genotype 2 or 3					
Sofosbuvir 12 weeks granules	150 mg - 200 mg	150 mg - 200 mg	1 x 150 mg - 1 x 200 mg	84	84 x 150 mg - 84 x 200 mg
Sofosbuvir 24 weeks granules	150 mg - 200 mg	150 mg - 200 mg	1 x 150 mg - 1 x 200 mg	168	168 x 150 mg - 168 x 200 mg
Sofosbuvir 12 weeks FCT[5]	200 mg- 400 mg	200 mg- 400 mg	1 x 200 mg- 1 x 400 mg	84	84 x 200 mg- 84 x 400 mg
Sofosbuvir 24 weeks FCT[5]	200 mg- 400 mg	200 mg- 400 mg	1 x 200 mg- 1 x 400 mg	168	168 x 200 mg- 168 x 400 mg
Plus					
Ribavirin 12 weeks Solution	7.5 mg/kg = 120 mg 7.5 mg/kg = 320 mg	15 mg/ kg = 240 mg - 15 mg/kg = 640 mg	2 x 120 mg 2 x 320 mg	84 84	84 x 240 mg 84 x 640 mg
Ribavirin 24 weeks Solution	7.5 mg/kg = 120 mg 7.5 mg/kg = 320 mg	15 mg/ kg = 240 mg - 15 mg/kg = 640 mg	2 x 120 mg 2 x 320 mg	168 168	168 x 240 mg 168 x 640 mg
Sofosbuvir/Velpatasvir 12 weeks FCT[5]	200 mg/50 mg - 400 mg/100 mg	200 mg/50 mg - 400 mg/100 mg	1 x 200 mg/50 mg - 1 x 400 mg/100 mg	84	84 x 200 mg/50 mg - 84 x 400 mg/100 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 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.

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:					
Glecaprevir / Pibrentasvir 50 mg/20 mg	28 sachet GRA	€ 2,999.01	€ 1.77	€ 0.00	€ 2,997.24
Appropriate comparator therapy					
Ledipasvir 33.75 mg / Sofosbuvir 150 mg	28 sachet GRA	€ 14,995.06	€ 1.77	€ 0.00	€ 14,993.29
Ledipasvir 45 mg / Sofosbuvir 200 mg	28 sachet GRA	€ 14,995.06	€ 1.77	€ 0.00	€ 14,993.29
Ledipasvir 45 mg / Sofosbuvir 200 mg	28 FCT	€ 14,995.06	€ 1.77	€ 0.00	€ 14,993.29
Ledipasvir 90 mg / Sofosbuvir 400 mg	28 FCT	€ 14,995.06	€ 1.77	€ 0.00	€ 14,993.29
Sofosbuvir 150 mg	28 sachet GRA	€ 14,349.04	€ 1.77	€ 0.00	€ 14,347.27
Sofosbuvir 200 mg	28 sachet GRA	€ 14,349.04	€ 1.77	€ 0.00	€ 14,347.27
Sofosbuvir 200 mg	28 FCT	€ 14,349.04	€ 1.77	€ 0.00	€ 14,347.27
Sofosbuvir 400 mg	28 FCT	€ 14,349.04	€ 1.77	€ 0.00	€ 14,347.27
Ribavirin 40 mg/ml	100 ml OS	€ 133.09	€ 1.77	€ 6.76	€ 124.56
Sofosbuvir 200 mg/ Velpatasvir 50 mg	28 FCT	€ 9,996.71	€ 1.77	€ 0.00	€ 9,994.94
Sofosbuvir 400 mg/ Velpatasvir 100 mg	28 FCT	€ 9,996.71	€ 1.77	€ 0.00	€ 9,994.94
Abbreviations: FCT = film-coated tablets; GRA = granules; OS = oral solution					

LAUER-TAXE® last revised: 1 December 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 the standard expenditure in the course of the treatment are not shown.

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

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 23 March 2021, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 25 June 2021, the pharmaceutical company submitted a dossier for the benefit assessment of glecaprevir/ pibrentasvir to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 2, sentence 2 VerfO.

By letter dated 25 June 2021 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 glecaprevir/ pibrentasvir.

The dossier assessment by the IQWiG was submitted to the G-BA on 29 September 2021, and the written statement procedure was initiated with publication on the website of the G-BA on 01 October 2021. The deadline for submitting written statements was 22 October 2021.

The oral hearing was held on 8 November 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 7 December 2021, and the proposed resolution was approved.

At its session on 16 December 2021, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal product	23 March 2021	Determination of the appropriate comparator therapy
Working group Section 35a	2 November 2021	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal product	8 November 2021	Conduct of the oral hearing
Working group Section 35a	16 November 2021 30 November 2021	Consultation on the dossier assessment by the IQWiG, assessment of the written statement procedure
Subcommittee Medicinal product	7 December 2021	Concluding discussion of the draft resolution
Plenum	16 December 2021	Adoption of the resolution on the amendment of Annex XII AM-RL

Berlin, 16 December 2021

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

Prof. Hecken