Gemeinsamer Bundesausschuss

Resolution

of the Federal Joint Committee 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

At its session on 16 December 2021, the Federal Joint Committee (G-BA) resolved to amend the Pharmaceuticals Directive (AM-RL) in the version dated 18 December 2008 / 22 January 2009 (Federal Gazette, BAnz. No. 49a of 31 March 2009), as last amended by the publication of the resolution of DD Month YYYY (Federal Gazette, BAnz AT DD.MM.YYYY BX), as follows:

I. In Annex XII, the following information shall be added after No. 4 to the information on the benefit assessment of Glecaprevir/ Pibrentasvir in accordance with the resolution of 17 October 2019:

Glecaprevir/ Pibrentasvir

Resolution of: 16 December 2021
Entry into force on: 16 December 2021
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 22 June 2021):

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.

1. Additional benefit of the medicinal product in relation to the appropriate comparator therapy

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

Appropriate comparator therapy:

Ledipasvir/sofosbuvir or sofosbuvir/velpatasvir[1]

Extent and probability of the additional benefit of Glecaprevir/ Pibrentasvir compared to the appropriate comparator therapy

An additional benefit is not proven.

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

Appropriate comparator therapy:

Sofosbuvir plus ribavirin or sofosbuvir/velpatasvir[1]

Extent and probability of the additional benefit of Glecaprevir/ Pibrentasvir compared to the appropriate comparator therapy

An additional benefit is not proven.

[1] approved above the age of 6

Study results according to endpoints:[2]

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

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.a.	There are no assessable data.
Morbidity	n.a.	There are no assessable data.
Health-related quality of life	n.a.	There are no assessable data.
Side effects	n.a.	There are no assessable data.
Explanations: ↑: statistically significant and relevant positive effect with low/unclear reliability of data ↓: statistically significant and relevant negative effect with low/unclear reliability of data ↑↑: statistically significant and relevant positive effect with high reliability of data ↓↓: statistically significant and relevant negative effect with high reliability of data ↔: no statistically significant or relevant difference ∅: There are no usable data for the benefit assessment. n.a.: not assessable		

No assessable data versus the appropriate comparator therapy were presented.

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

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.a.	There are no assessable data.
Morbidity	n.a.	There are no assessable data.
Health-related quality of life	n.a.	There are no assessable data.
Side effects	n.a.	There are no assessable data.
Explanations: ↑: statistically significant and relevant positive effect with low/unclear reliability of data ↓: statistically significant and relevant negative effect with low/unclear reliability of data ↑↑: statistically significant and relevant positive effect with high reliability of data ↓↓: statistically significant and relevant negative effect with high reliability of data ↔: no statistically significant or relevant difference ∅: There are no usable data for the benefit assessment. n.a.: not assessable		

No assessable data versus the appropriate comparator therapy were presented.

[2] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A21-88) unless otherwise indicated.

M16-123 (DORA) study (single-arm study with glecaprevir/ pibrentasvir without comparison to the appropriate comparator therapy, patient population a) and b))

Cohorts 2 to 4: Children with chronic hepatitis C aged 3 to < 12 years; treated for 8 to 16 weeks with glecaprevir/ pibrentasvir

Mortality

DORA study (cohorts 2 to 4) Endpoint category Endpoint	Glecaprevir/ Pibrentasvir			
	N	HCV-GT 1/4/5/6[1] Patients with event n (%)	N	HCV-GT 2/3 Patients with event n (%)
Mortality				
Overall mortality	60	0 (0)	20	0 (0)

Morbidity

DORA study (cohorts 2 to 4) Endpoint category Endpoint	Glecaprevir/ Pibrentasvir			
	N	HCV-GT 1/4/5/6[1] Patients with event n (%)	N	HCV-GT 2/3 Patients with event n (%)
Morbidity				
SVR12[2]	60	59 (98.3)	20	18 (90)

Health-related quality of life

DORA study (cohorts 2 to 4) Endpoint category Endpoint	Glecaprevir/ Pibrentasvir					
	HCV-GT 1/4/5/6[1]			HCV-GT 2/3		
	N[3]	Values at the start of study MV (SD)	Change to FU week 12c[4] MV (SD)	N[3]	Values at the start of study MV (SD)	Change to FU week 12[4] MV (SD)
Health-related quality of life						
PedsQL (total score, patient-reported)[5]	53	75.30 (n.d.)	-1.12 (23.25)	17	87.40 (n.d.)	-8.66 (22.66)

Side effects

DORA study (cohorts 2 to 4) Endpoint category Endpoint	Glecaprevir/ Pibrentasvir			
	N	HCV-GT 1/4/5/6[1] Patients with event n (%)	N	HCV-GT 2/3 Patients with event n (%)
Side effects				
AEs (presented additionally)	60	43 (71.1)	20	14 (70.0)
SAEs	60	0 (0)	20	0 (0)
Discontinuation due to AEs	60	1 (1.7)	20	0 (0)

1) Children with HCV-GT 1, 4, 5 or 6 were to be enrolled in the study. However, the enrolled population included only children with GT 1 or 4.
2) Sufficiently valid surrogate for the patient-relevant endpoint hepatocellular carcinoma
3) Number of patients who were taken into account in the evaluation; the values at the start of study (possibly at other times) can be based on other patient numbers.
4) Questionnaire was completed 12 weeks after treatment, which lasted 8, 12, or 16 weeks
5) Scale range 0-100. Higher (increasing) values mean better quality of life. According to information on the study, the questionnaire was completed by parents or legal guardians for children aged 5 years or younger or for children who had difficulty reading the questions.

FU: follow-up; GT: genotype; HCV: hepatitis C virus; n.d.: no data available: CI: confidence interval; MV: mean value; N: number of patients evaluated; n: number of patients with (at least 1) event; PedsQL: Paediatric Quality of Life Inventory; RCT: randomised controlled trial; SD: standard deviation; SAE: serious adverse event; SVR: sustained virologic response 12 weeks after end of therapy; AE: adverse event

2. Number of patients or demarcation of patient groups eligible for treatment

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

approx. 95 – 155 patients

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

approx. 51 – 83 patients

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: 1 December 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.

4. Treatment costs

Annual treatment costs:

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

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Glecaprevir / pibrentasvir 8 weeks	€ 17,983.44 - € 29,972.40
Glecaprevir / pibrentasvir 12 weeks	€ 26,975.16 - € 44,958.60
Glecaprevir / pibrentasvir 16 weeks	€ 35,966.88 - € 59,944.80
Appropriate comparator therapy:	
Ledipasvir / sofosbuvir 8 weeks	€ 29,986.58
Ledipasvir / sofosbuvir 12 weeks	€ 44,979.87
Ledipasvir / sofosbuvir 24 weeks	€ 89,959.74
Sofosbuvir / velpatasvir 12 weeks[3]	€ 29,984.82

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 1 December 2021)

Costs for additionally required SHI services: not applicable

[3] approved above the age of 6

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

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Glecaprevir / pibrentasvir 8 weeks	€ 17,983.44 - € 29,972.40
Glecaprevir / pibrentasvir 12 weeks	€ 26,975.16 - € 44,958.60
Glecaprevir / pibrentasvir 16 weeks	€ 35,966.88 - € 59,944.80
Appropriate comparator therapy:	
Sofosbuvir 12 weeks	€ 43,041.81
Sofosbuvir 24 weeks	€ 86,083.62
Ribavirin 12 weeks	€ 627.78 - € 1,674.09
Ribavirin 24 weeks	€ 1,255.56 - € 3,348.17
Total 12 weeks:	€ 43,669.59 - € 44,715.90
Total 24 weeks:	€ 87,339.18 - € 89,431.79
Sofosbuvir / velpatasvir 12 weeks[4]	€ 29,984.82

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 1 December 2021)

Costs for additionally required SHI services: not applicable

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 16 December 2021.

The justification to this resolution will be published on the website of the G-BA at www.g-ba.de.

Berlin, 16 December 2021

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

Prof. Hecken

[4] approved above the age of 6