Resolution

Gemeinsamer Bundesausschuss

of the Federal Joint Committee on an amendment to the Pharmaceuticals Directive Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V Sofosbuvir/Velpatasvir (New Therapeutic Indication: Chronic Hepatitis C, ≥ 6 and < 18 years of age)

From 1 April2021
At its session on 1 April 2021, the Federal Joint Committee (G-BA) resolved to amend the Directive on the Prescription of Medicinal Products in SHI-accredited Medical Care (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 on 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 **sofosbuvir/velpatasvir in accordance with the resolution of 5 January 2017:**

sofosbuvir/velpatasvir

Resolution from: 1 April 2021
Entry into force on: 1 April 2021
BAnz AT DD MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 28 August 2020:):

Epclusa is used to treat patients from 6 years of age and weighing at least 17 kg with chronic hepatitis C (HCV) (see Sections 4.2, 4.4 and 5.1).

Therapeutic indication of the resolution (resolution from 1 April 2021):

Epclusa is used to treat patients from 6 to 18 years of age and weighing at least 17 kg with chronic hepatitis C (HCV).

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

a) Patients between 6 and < 12 years of age with chronic hepatitis C (genotypes 1, 4, 5 or 6)

Appropriate comparator therapy for sofosbuvir/velpatasvir:

- Ledipasvir/sofosbuvir

Extent and probability of the additional benefit of sofosbuvir/velpatasvir compared to the appropriate comparator therapy:

An additional benefit is not proven.

b) Patients between 6 and < 12 years of age with chronic hepatitis C (genotypes 2 or 3)

Appropriate comparator therapy for sofosbuvir/velpatasvir:

- Sofosbuvir plus ribavirin

Extent and probability of the additional benefit of sofosbuvir/velpatasvir compared to the appropriate comparator therapy:

An additional benefit is not proven.

c) Patients between 12 and < 18 years of age with chronic hepatitis C (genotypes 1, 4, 5 or 6):

Appropriate comparator therapy for sofosbuvir/velpatasvir:

- Ledipasvir/sofosbuvir
  or

- Glecaprevir/pibrentasvir

Extent and probability of the additional benefit of sofosbuvir/velpatasvircompared tothe appropriate comparator therapy:

An additional benefit is not proven.

d) Patients between 12 and < 18 years of age with chronic hepatitis C (genotypes 2 or 3):

Appropriate comparator therapy for sofosbuvir/velpatasvir:

- Sofosbuvir plus ribavirin
  or
- Glecaprevir/pibrentasvir

Extent and probability of the additional benefit of sofosbuvir/velpatasvir compared to the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:[1]

1143 study (non-RCT, single-arm study with sofosbuvir/velpatasvir (SOF/VEL) without comparison with appropriate comparator therapy, patient population a) and b))

a) Patients between 6 and < 12 years of age with chronic hepatitis C (genotypes 1, 4, 5 or 6)

b) Patients between 6 and < 12 years of age with chronic hepatitis C (genotypes 2 or 3)

Summary of results for relevant clinical endpoints

a) Patients between 6 and < 12 years of age with chronic hepatitis C (genotypes 1, 4, 5 or 6)		
Endpoint category	**Direction of effect/ Risk of bias**	**Summary**
Mortality	n.a.	There are no comparative data
Morbidity	n.a.	no comparative data; results of SVR with the same size as respective appropriate comparator therapy
Health-related quality of life	n.a.	There are no comparative data
Side effects	n.a.	There are no comparative data
Explanations:		

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

↑: 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

b) Patients between 6 and < 12 years of age with chronic hepatitis C (genotypes 2 or 3)		
Endpoint category	**Direction of effect/ Risk of bias**	**Summary**
Mortality	n.a.	There are no comparative data
Morbidity	n.a.	no comparative data; results of SVR with the same size as respective appropriate comparator therapy
Health-related quality of life	n.a.	There are no comparative data
Side effects	n.a.	There are no comparative data

Explanations:
↑: statistically significant and relevant positive effect with low/unclear reliability of data
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↑↑: statistically significant and relevant positive effect with high reliability of data
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n.a.: not assessable

Mortality

1143 study Endpoint category Endpoint	**SOF/VEL**			
	Cohort 2 (6 to <12 years of age)		**Presented additionally: Cohort 2 (6 to <12 years of age; ≥ 17 to < 30 kg body weight)**	
	N	**Patients with event n (%)**	**N**	**Patients with event n (%)**
Mortality				
Overall mortality[1)]	73	0 (0)	45	0 (0)

Morbidity

1143 study Endpoint category	**SOF/VEL**	
	Cohort 2	**Presented additionally:**

Endpoint	(6 to <12 years of age)		Cohort 2 (6 to <12 years of age; ≥ 17 to < 30 kg body weight)	
	N	Patients with event n (%)	N	Patients with event n (%)
Morbidity				
SVR12[2)]	73	68 (93.2)	45	42 (93.3)
SVR24[2)]	73	68 (93.2)	45	42 (93.3)

Health-related quality of life

1143 study Endpoint category Endpoint	SOF/VEL					
	Cohort 2 (6 to <12 years of age)			Presented additionally: Cohort 2 (6 to <12 years of age; ≥ 17 to < 30 kg body weight)		
	N[3)]	Values at the start of the study MV (SD)	Change to FU week 24 MVb (SD)[4)]	N[3)]	Values Start of the study MV (SD)	Change to FU week 24 MVb (SD)[4)]
Health-related quality of life						
PedsQL (total score, patient-reported)[5)]	69	77.9 (13.3)	4.2 (13.7)	45	78.9 (12.0)	0.9 (12.8)

Side effects

1143 study Endpoint category Endpoint	SOF/VEL			
	Cohort 2 (6 to <12 years of age)		Presented additionally: Cohort 2 (6 to <12 years of age; ≥ 17 to < 30 kg body weight)	
	N	Patients with event n (%)	N	Patients with event n (%)
Side effects				
AEs (presented additionally	73	59 (80.8)	45	37 (82.2)
SAEs[6)]	73	2 (2.7)	45	2 (4.4)
Discontinuation because of AEs	73	2 (2.7)	45	2 (4.4)

1) was collected via SUE
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 the study (possibly at other times) can be based on other patient numbers.

4) If the values for the FU week 24 were missing, the last available value was imputed after the end of treatment.
5) Higher (increasing) values mean better quality of life.
6) The two events are the PTs constipation and acoustic hallucination, the latter leading to therapy discontinuation. It is not clear from the study documents whether this information is based on a follow-up period of 30 days or 24 weeks.

FU: Follow-up; MV: mean value; N: number of patients evaluated; n: number of patients with (at least one) event; PedsQL 4.0 SF15: Pediatric Quality of Life Inventory Version 4.0 Short Form 15; PT: preferred term; RCT: randomised controlled trial; RR: relative risk; SD: Standard deviation; SOF: sofosbuvir; SAE: serious adverse event; SVR12 and SVR24: sustained virological response 12 and 24 weeks after the end of therapy; UE: adverse event; VEL: velpatasvir

c) Patients between 12 and < 18 years of age with chronic hepatitis C (genotypes 1, 4, 5 or 6):

No data submitted.

Endpoint category	Direction of effect/ Risk of bias	Summary
Mortality	∅	No data available
Morbidity	∅	No data available
Health-related quality of life	∅	No data available
Side effects	∅	No data available

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

d) Patients between 12 and < 18 years of age with chronic hepatitis C (genotypes 2 or 3):

No data submitted.

Endpoint category	Direction of effect/ Risk of bias	Summary
Mortality	∅	No data available
Morbidity	∅	No data available
Health-related quality of life	∅	No data available
Side effects	∅	No data available

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
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∅: There are no usable data for the benefit assessment.
n.a.: not assessable

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

A) Patients between 6 and < 12 years of age with chronic hepatitis C (genotypes 1, 4, 5 or 6)

b) Patients between 6 and < 12 years of age with chronic hepatitis C (genotypes 2 or 3)

approx. 40 patients

c) Patients between 12 and < 18 years of age with chronic hepatitis C (genotypes 1, 4, 5 or 6):

d)) Patients between 12 and < 18 years of age with chronic hepatitis C (genotypes 2 or 3):

approx. 80 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 Epclusa (sofosbuvir/velpatasvir) at the following publicly accessible link (last access: 29 March 2021):

https://www.ema.europa.eu/en/documents/product-information/epclusa-epar-product-information_de.pdf.

Treatment with sofosbuvir/velpatasvir should only be initiated and monitored by specialists experienced in the treatment of patients with chronic hepatitis C.

4. Treatment costs

Annual treatment costs:

a) Patient populations

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Sofosbuvir/velpatasvir	€ 29,984.82
Appropriate comparator therapy:	
Ledipasvir/sofosbuvir	€ 29,986.58 – € 89,959.74

Costs after deduction of statutory rebates (LAUER-TAXE®, as last revised: 15 March 2021)

Costs for additionally required SHI services: not applicable

b) Patient populations

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Sofosbuvir/velpatasvir	€ 29,984.82
Appropriate comparator therapy:	
Sofosbuvir 12 weeks	€ 43,041.81
Ribavirin 12 weeks	€ 941.67 – € 1,674.09
Total:	€ 43,983.48 – € 44,715.90
Sofosbuvir 24 weeks	€ 86,083.62
Ribavirin 24 weeks	€ 1,883.35 – € 3,348.17
Total:	€ 87,966.97 – € 89,431.79

Costs after deduction of statutory rebates (LAUER-TAXE®, as last revised: 15 March 2021)

Costs for additionally required SHI services: not applicable

c) Patient population

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Sofosbuvir/velpatasvir	€ 29,984.82
Appropriate comparator therapy:	
Ledipasvir / sofosbuvir 8 weeks	€ 29,986.58
Ledipasvir / sofosbuvir 12 weeks	€ 44,979.87
Ledipasvir / sofosbuvir 24 weeks	€ 89,959.74
Glecaprevir / pibrentasvir 8 weeks	€ 29,986.58
Glecaprevir / pibrentasvir 12 weeks	€ 44,979.87

Costs after deduction of statutory rebates (LAUER-TAXE®, as last revised: 15 March 2021)

Costs for additionally required SHI services: not applicable

d) Patient population

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Sofosbuvir/velpatasvir	€ 29,984.82

Designation of the therapy	Annual treatment costs/patient
Appropriate comparator therapy:	
Sofosbuvir 12 weeks	€ 43,041.81
Ribavirin 12 weeks	€ 1,096.65 – € 1,827.75
Total:	€ 44,138.46 – € 44,869.56
Sofosbuvir 24 weeks	€ 86,083.62
Ribavirin 24 weeks	€ 2,193.30 – € 3,655.50
Total:	€ 88,276.92 – € 89,739.12
Glecaprevir / pibrentasvir 8 weeks	€ 29,986.58
Glecaprevir / pibrentasvir 12 weeks	€ 44,979.87
Glecaprevir / pibrentasvir 24 weeks	€ 59,973.16

Costs after deduction of statutory rebates (LAUER-TAXE®, as last revised: 15 March 2021).

II. Entry into force

1. **The resolution will enter into force on the day of its publication on the internet on the website of the G-BA on 1 April 2021.**
2. **The validity of the resolution for patient populations a) and b) is limited to 1 October 2021.**

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

Berlin, 1 April 2021

Federal Joint Committee in accordance with Section 91 SGB V The chair

Prof. Hecken