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
Sofosbuvir/ Velpatasvir (new therapeutic indication: chronic hepatitis C, 3 to < 6 years)

of 4 August 2022

At its session on 4 August 2022, 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 D Month YYYY (Federal Gazette, BAnz AT DD.MM.YYYY BX), as follows:

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 1 April 2021 last modified on 7 December 2021:

Sofosbuvir/ Velpatasvir

Resolution of: 4 August 2022
Entry into force on: 4 August 2022
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 7 January 2022):

Epclusa is indicated for the treatment of chronic hepatitis C virus (HCV) infection in patients 3 years of age and older.

Therapeutic indication of the resolution (resolution of 4 August 2022):

Treatment of chronic hepatitis C virus infection in children aged 3 to < 6 years.

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

Children with chronic hepatitis C aged 3 to < 6 years

Appropriate comparator therapy:

Ledipasvir/ sofosbuvir (only for genotypes 1, 4, 5 and 6) 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]

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.a.	No comparator data available.
Morbidity	n.a.	No comparator data available.
Health-related quality of life	n.a.	No comparator data available.
Side effects	n.a.	No comparator data available.
Explanations: ↑: statistically significant and relevant positive effect with low/unclear reliability of data		

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A22-26) unless otherwise indicated.

↓: 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 suitable data versus the appropriate comparator therapy were presented.

GS-US-342-1143 study – non-randomised, open-label, single-arm study with sofosbuvir/ velpatasvir without comparison to the appropriate comparator therapy. (Cohort 3: non-pretreated children aged 3 to < 6 years)

Mortality

Endpoint	**Sofosbuvir/ velpatasvir**	
	HCV-GT 1/4/5/6[a] **(Patient group a)**	HCV-GT 2/3[a] **(Patient group b)**
	Patients with event n (%)	Patients with event n (%)
Overall mortality[b]	0 (0)	0 (0)

Morbidity

Endpoint	**Sofosbuvir/ velpatasvir**			
	HCV-GT 1/4/5/6[a] **(Patient group a)**		HCV-GT 2/3[a] **(Patient group b)**	
	N	Patients with event n (%)	N	Patients with event n (%)
SVR_{12}[c,d]	33	29 (87.9)	8	5 (62.5)
SVR_{24}[c,e]	33	29 (87.9)	8	5 (62.5)

Health-related quality of life

Endpoint	**Sofosbuvir/ velpatasvir**		
	N[e]	Values at the start of the study MV (SD)	Change to FU week 24[f] MV (SD)
PedsQL total score)[g,h]	35	86.5 (12.43)	1.9 (14.26)

Side effects

Endpoint	**Sofosbuvir/ velpatasvir**			
	HCV-GT 1/4/5/6[a] **(Patient group a)**		HCV-GT 2/3[a] **(Patient group b)**	
	N	Patients with event n (%)	N	Patients with event n (%)

AEs (presented additionally)[i]	41	32 (78.0)
SAEs[i]	41	0 (0)
Severe AEs[i,j]	41	0 (0)
Discontinuation due to AEs[i]	41	1 (2.4)

a. For cohort 3, the inclusion of children with chronic HCV infection of all 6 genotypes was planned. Ultimately, however, only children with HCV genotypes 1 to 4 were included in this cohort.
b. Was assessed using AEs
c. Sufficiently valid surrogate for the patient-relevant endpoint of hepatocellular carcinoma
d. In the case of missing values at FU week 12, the missing value was imputed. According to the pharmaceutical company, this was the case for 7 children in cohort 3. A missing value at FU week 12 was imputed as a responder if the measurement before and after it was considered a response. Otherwise, a missing value was imputed as a non-responder. At least 6 of the 7 children who discontinued therapy prematurely and did not participate in follow-up examinations were imputed as non-responders.
e. 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.
f. The questionnaire was completed 24 weeks after treatment, which lasted 12 weeks.
g. Results for all children in cohort 3; no data available that is broken down by question.
h. Higher (increasing) values mean better quality of life. According to information provided by the pharmaceutical company in module 4 A of the dossier, these values are based on the questionnaire for parents.
i. Results for all children in cohort 3; no data available that is broken down by question.
j. Operationalised as CTCAE grade ≥ 3

Abbreviations used: CTCAE: Common Terminology Criteria for Adverse Events; FU: follow-up; GT: genotype; HCV: hepatitis C virus; MV: mean value; n: number of patients with (at least 1) event; N: Number of patients evaluated; PedsQL: Paediatric Quality of Life Inventory; RCT: randomised controlled trial; SD: standard deviation SAE: serious adverse event; SVR12: sustained virological response 12 weeks after end of therapy; SVR24: sustained virological response 24 weeks after end of therapy; AE: adverse event

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

Children with chronic hepatitis C aged 3 to < 6 years

approx. 1 – 12 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 (active ingredient: sofosbuvir/ velpatasvir) at the following publicly accessible link (last access: 28 June 2022):
https://www.ema.europa.eu/en/documents/product-information/epclusa-epar-product-information_en.pdf

Treatment with sofosbuvir/ velpatasvir should only be initiated and monitored by doctors experienced in treating hepatitis C.

4. Treatment costs

Annual treatment costs:

Children with chronic hepatitis C aged 3 to < 6 years

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Sofosbuvir/ velpatasvir 12 weeks	€ 29,985.54
Appropriate comparator therapy:	
Ledipasvir/ sofosbuvir 8 weeks	€ 29,987.06
Ledipasvir/ sofosbuvir 12 weeks	€ 44,980.59
Ledipasvir/ sofosbuvir 24 weeks	€ 89,961.18
Glecaprevir/ pibrentasvir 8 weeks	€ 17,984.88 - € 23,979.84
Glecaprevir/ pibrentasvir 12 weeks	€ 26,977.32 - € 35,969.76
Glecaprevir/ pibrentasvir 16 weeks	€ 35,969.76 - € 47,959.68

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 July 2022)

Costs for additionally required SHI services: not applicable

I. The resolution will enter into force on the day of its publication on the website of the G-BA on 4 August 2022.

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

Berlin, 4 August 2022

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

Prof. Hecken