Gemeinsamer Bundesausschuss

Resolution

of the Resolution of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive (AM-L):

Annex XII - Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V: Dolutegravir (New Therapeutic Indication: HIV infection, children ≥ 4 weeks to < 6 years)

of 15 July 2021

At its session on 15 July 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 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 dolutegravir in accordance with the resolution of 21 September 2017:

Dolutegravir

Resolution of: 15 July 2021
Entry into force on: 15 July 2021
BAnz AT TT. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 11 January 2021):

Tivicay is indicated in combination with other anti-retroviral medicinal products for the treatment of Human Immunodeficiency Virus (HIV) infected adults, adolescents and children of at least 4 weeks of age or older and weighing at least 3 kg.

Therapeutic indication of the resolution (resolution of 15 July 2021):

Tivicay is indicated in combination with other anti-retroviral medicinal products for the treatment of Human Immunodeficiency Virus (HIV) paediatric patients aged 4 weeks to below 6 years and weighing at least 3 kg.

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

a) <u>Therapy naïve children with HIV-1 infection aged ≥ 4 weeks to < 6 years</u>

Appropriate comparator therapy for dolutegravir in combination with other anti-retroviral drugs:

Abacavir with lamivudine or abacavir with emtricitabine, in each case in combination with

- Lopinavir/ritonavir or
- Raltegravir or
- Nevirapine

Extent and probability of the additional benefit of dolutegravir compared to the appropriate comparator therapy:

An additional benefit is not proven.

b) <u>Therapy-experienced children with HIV-1 infection aged ≥ 4 weeks to < 6 years</u>

Appropriate comparator therapy for dolutegravir in combination with other anti-retroviral drugs:

- A patient-individual anti-retroviral therapy using a selection of approved active ingredients; taking into account the previous therapy(ies) and the reason for the change of therapy, in particular therapy failure because of virological failure and possible associated development of resistance or because of side effects.

Extent and probability of the additional benefit of dolutegravir compared to the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:

a) Therapy naïve children with HIV-1 infection aged ≥ 4 weeks to < 6 years

No adequate data are available to allow an assessment of the additional benefit.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.c.	There are no assessable data.
Morbidity	n.c.	There are no assessable data.
Health-related quality of life	n.c.	There are no assessable data.
Side effects	n.c.	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		

b) Therapy-experienced children with HIV-1 infection aged ≥ 4 weeks to < 6 years

No adequate data are available to allow an assessment of the additional benefit.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.c.	There are no assessable data.
Morbidity	n.c.	There are no assessable data.
Health-related quality of life	n.c.	There are no assessable data.
Side effects	n.c.	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	

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

Children with HIV-1 infection aged ≥ 4 weeks to < 6 years

approx. 29 patient

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 Tivicay (active ingredient: dolutegravir) at the following publicly accessible link (last access: 5 March 2021):

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

Treatment with dolutegravir should only be initiated and monitored by doctors experienced in treating patients with HIV infection.

4. Treatment costs

Annual treatment costs:

a) Therapy naïve children with HIV-1 infection aged ≥ 4 weeks to < 6 years

Designation of the therapy	Annual treatment costs/person
Medicinal product to be assessed:	
Dolutegravir	€ 872.11 - € 5,232.64
Appropriate comparator therapy:	
Lopinavir/ritonavir	€ 1,515.44 - € 4,377.93
Raltegravir, granules (up to 20 kg bw)	€ 2,623.74
Raltegravir, chewable tablets (from 11 kg BW)	€ 2,221.76 - € 3,935.61
Nevirapine	€ 823.99 - € 4,943.93

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

Costs for additionally required SHI services: not applicable

b) Therapy-experienced children with HIV-1 infection aged ≥ 4 weeks to < 6 years

Designation of the therapy	Annual treatment costs/person
Medicinal product to be assessed:	
Dolutegravir	€ 872.11 - € 5,232.64
Appropriate comparator therapy:	
Lopinavir/ritonavir	€ 1,515.44 - € 4,377.93
Raltegravir, GSE (up to 20 kg bw)	€ 2,623.74
Raltegravir, CT (from 11 kg BW)	€ 2,221.76 - € 3,935.61
Nevirapine	€ 823.99 - € 4,943.93
Atazanavir + ritonavir	
Atazanavir, POS	€ 7,223.11 - € 90,28.88
Ritonavir, POS	€ 655.78
Total:	*€ 7,878.89 - € 9,684.67*
Atazanavir + ritonavir (from 15 kg bw)	
Atazanavir, HC	€ 2,923.41
Ritonavir, FCT	€ 487.07
Total:	*€ 3,410.48*
Darunavir + ritonavir (3 years and older)	
Darunavir OSUS	€ 7,721.50
Ritonavir POS	€ 655.78
Total:	*€ 8,377.28*
Darunavir + ritonavir (3 years and older)	
Darunavir FCT	€ 2,977.63
Ritonavir FCT	€ 487.07
Total:	*€ 3,464.70*
Etravirenz (3 months and older)	€ 1,444.91 - € 2,756.85
Etravirine (2 years and older)	
Etravirine	€ 3,808.47 - € 4,843.00
+ boosted PI	€ 3,536.02 - € 4,377.93
Total:	*€ 7,344.49 - € 9,220.93*
Maraviroc (2 years and older)	€ 3,281.51 - € 6,563.02

Designation of the therapy	Annual treatment costs/person
Abbreviations: FCT = film-coated tablets, GSE = granules for oral suspension; HC = hard capsules; CT = chewable tablets; TOS/POS= tablet/powder for oral suspension; OSUS = oral suspension; SUS = suspension; TAB= tablets	

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

Costs for additionally required SHI services: not applicable

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 15 July 2021.**
2. **The period of validity of the resolution is limited to 1 April 2022.**

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

Berlin, 15 July 2021

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

Prof. Hecken