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 and Annex XIIa – Combinations with New Active Ingredients according to Section 35a SGB V
Dolutegravir/ abacavir/ lamivudine (new therapeutic indication: HIV infection, ≥ 14 kg to < 12 years)

of 17 August 2023

At its session on 17 August 2023, 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 Dolutegravir/ abacavir/ lamivudine in accordance with the resolution of 19 March 2015:

Dolutegravir/ abacavir/ lamivudine

Resolution of: 17 August 2023
Entry into force on: 17 August 2023
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 20 February 2023):

Triumeq is indicated for the treatment of Human Immunodeficiency Virus (HIV) infected children weighing at least 14 kg to less than 25 kg.

Triumeq is indicated for the treatment of Human Immunodeficiency Virus (HIV) infected adults, adolescents and children weighing at least 25 kg.

Before initiating treatment with abacavir-containing products, screening for carriage of the HLAB*5701 allele should be performed in any HIV-infected patient, irrespective of racial origin. Abacavir should not be used in patients known to carry the HLA-B*5701 allele.

Therapeutic indication of the resolution (resolution of 17 August 2023):

Triumeq is indicated for the treatment of Human Immunodeficiency Virus (HIV) infected children weighing at least 14 kg to < 12 years.

Before initiating treatment with abacavir-containing products, screening for carriage of the HLAB*5701 allele should be performed in any HIV-infected patient, irrespective of racial origin. Abacavir should not be used in patients known to carry the HLA-B*5701 allele.

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

   a) <u>Therapy naive children with HIV-1 infection ≥ 14 kg to < 6 years</u>

   Appropriate comparator therapy:

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

   - lopinavir/ ritonavir or
   - raltegravir or
   - nevirapine or
   - atazanavir + ritonavir or
   - darunavir + ritonavir

   or dolutegravir + abacavir + emtricitabine

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

   An additional benefit is not proven.

b) Therapy naive children with HIV-1 infection ≥ 14 kg from 6 to < 12 years

Appropriate comparator therapy:

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

- atazanavir + ritonavir or
- darunavir + ritonavir

or dolutegravir + abacavir + emtricitabine

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

An additional benefit is not proven.

c) Therapy experienced children with HIV-1 infection ≥ 14 kg to < 12 years

Appropriate comparator therapy:

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

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

An additional benefit is not proven.

Study results according to endpoints:

a) Therapy naive children with HIV-1 infection ≥ 14 kg to < 6 years

No suitable data versus the appropriate comparator therapy were presented.

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	∅	No data available.
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 ∅: No data available. n.a.: not assessable		

b) Therapy naive children with HIV-1 infection ≥ 14 kg from 6 to < 12 years

No suitable data versus the appropriate comparator therapy were presented.

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	∅	No data available.
Side effects	n.a.	There are no assessable data.
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c) Therapy experienced children with HIV-1 infection ≥ 14 kg to < 12 years

No suitable data versus the appropriate comparator therapy were presented.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.a.	There are no assessable data.
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Health-related quality of life	∅	No data available.
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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 ∅: No data available. n.a.: not assessable		

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

a) Therapy naive children with HIV-1 infection ≥ 14 kg to < 6 years

approx. 4 patients

b) Therapy naive children with HIV-1 infection ≥ 14 kg from 6 to < 12 years

approx. 15 patients

c) Therapy experienced children with HIV-1 infection ≥ 14 kg to < 12 years

approx. 67 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 Triumeq (combination of active ingredients: dolutegravir/ abacavir/ lamivudine) at the following publicly accessible link (last access: 16 May 2023):

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

Treatment with dolutegravir/ abacavir/ lamivudine should only be initiated and monitored by doctors experienced in treating patients with HIV-1.

4. Treatment costs

Annual treatment costs:

a) Therapy naive children with HIV-1 infection ≥ 14 kg to < 6 years

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Dolutegravir/ abacavir/ lamivudine	€ 9,791.53 - € 11,749.84
Appropriate comparator therapy:	
Base therapy	
Abacavir	€ 1,999.47 - € 2,832.58
Emtricitabine	€ 1,603.08 - € 2,315.56
Lamivudine	€ 1,337.45 - € 2,006.18
Abacavir + emtricitabine	€ 3,602.55 - € 5,148.14
Abacavir + lamivudine	€ 3,336.92 - € 4,838.76
Concomitant active ingredient:	
Atazanavir	€ 7,638.23 - € 9,547.79[1]
Ritonavir	€ 413.50 - € 722.70
Darunavir	€ 2,977.63[1]
Lopinavir/ ritonavir	€ 2,629.37 - € 4,319.68
Nevirapine	€ 3,170.03 - € 4,755.04
Raltegravir	€ 2,518.62 - € 3,777.93
Dolutegravir	€ 4,199.63 - € 5,039.56
Total	
Abacavir + emtricitabine + atazanavir + ritonavir	€ 11,963.48 - € 15,418.63
Abacavir + emtricitabine + darunavir + ritonavir	€ 8,539.28
Abacavir + emtricitabine + lopinavir/ ritonavir	€ 6,231.92 - € 9,467.82
Abacavir + emtricitabine + nevirapine	€ 6,772.58 - € 9,903.18
Abacavir + emtricitabine + raltegravir	€ 6,121.17 - € 8,926.08

[1] According to the product information, darunavir is approved for children weighing 15 kg or more. The indicated annual treatment costs for the combinations with darunavir represent the dosage for children weighing more than 15 kg.

Designation of the therapy	Annual treatment costs/ patient
Abacavir + emtricitabine + dolutegravir	€ 7,802.18 - € 10,187.70
Abacavir + lamivudine + atazanavir + ritonavir	€ 11,697.85 - € 15,109.25
Abacavir + lamivudine + darunavir + ritonavir	€ 8,229.89
Abacavir + lamivudine + lopinavir/ ritonavir	€ 5,966.29 - € 9,158.43
Abacavir + lamivudine + nevirapine	€ 6,506.95 - € 9,593.80
Abacavir + lamivudine + raltegravir	€ 5,855.54 - € 8,616.69

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 August 2023)

Costs for additionally required SHI services: not applicable

b) Therapy naive children with HIV-1 infection ≥ 14 kg from 6 to < 12 years

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Dolutegravir/ abacavir/ lamivudine	€ 11,382.97 - € -11,749.84
Appropriate comparator therapy:	
Base therapy	
Abacavir	€ 3,866.99 - € 5,155.99
Emtricitabine	€ 2,671.80 - € 3,322.11
Lamivudine	€ 2,006.18 - € 2,465.12
Abacavir/ lamivudine	€ 743.18[2]
Abacavir + emtricitabine	€ 6,538.79 - € 8,478.10
Abacavir + lamivudine	€ 743.18 [2] - € 5,873.17
Concomitant active ingredient:	
Atazanavir	€ 2,923.29 - € 4,337.78
Ritonavir	€ 413.50
Darunavir	€ 2,977.63 - € 3,805.04
Dolutegravir	€ 8,307.52
Total:	
Abacavir + emtricitabine + atazanavir + ritonavir	€ 9,875.58 - € 13,229.93
Abacavir + emtricitabine + darunavir + ritonavir	€ 9,929.93 - € 12,696.65
Abacavir + emtricitabine + dolutegravir	€ 14,846.31 - € 16,785.62
Abacavir + lamivudine + atazanavir + ritonavir	€ 5,494.47 - € 9,209.96

[2] Fixed combination of abacavir/ lamivudine not approved for children <25 kg

Designation of the therapy	Annual treatment costs/ patient
Abacavir + lamivudine + darunavir + ritonavir	€ 4,961.73 - € 9,264.30

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 August 2023)

Costs for additionally required SHI services: not applicable

c) Therapy experienced children with HIV-1 infection ≥ 14 kg to < 12 years

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Dolutegravir/ abacavir/ lamivudine	€ 9,791.53 - € 11,749.84
Appropriate comparator therapy:	
Individual antiretroviral therapy[3]	€ 2,126.10 - € 20,285.85
Lower range	
Abacavir/ lamivudine	€ 743.18
Nevirapine	€ 1,382.92
Abacavir/ lamivudine + nevirapine	€ 2,126.10
Upper range	
Abacavir	€ 5,155.99
Emtricitabine	€ 3,322.11
Maraviroc	€ 11,807.75
Abacavir + emtricitabine + maraviroc	€ 20,285.85

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 August 2023)

Costs for additionally required SHI services: not applicable

5. Designation of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V that can be used in a combination therapy with the assessed medicinal product

In the context of the designation of medicinal products with new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V, the following findings are made:

[3] Because of the different combination options in individual therapy, not all possible variants of combination therapies are presented and considered but the cost range from a cost-effective (abacavir/ lamivudine + nevirapine) to a cost-intensive therapy (abacavir + emtricitabine + maraviroc) is specified as an example.

a) Therapy naive children with HIV-1 infection ≥ 14 kg to < 6 years

The following medicinal products with new active ingredients that can be used in a combination therapy with dolutegravir/ abacavir/ lamivudine in the therapeutic indication of the resolution on the basis of the marketing authorisation under Medicinal Products Act are named (active ingredients and invented names) in accordance with Section 35a, paragraph 3, sentence 4 SGB V:

Dolutegravir (Tivicay)

b) Therapy naive children with HIV-1 infection ≥ 14 kg from 6 to < 12 years

The following medicinal products with new active ingredients that can be used in a combination therapy with dolutegravir/ abacavir/ lamivudine in the therapeutic indication of the resolution on the basis of the marketing authorisation under Medicinal Products Act are named (active ingredients and invented names) in accordance with Section 35a, paragraph 3, sentence 4 SGB V:

Dolutegravir (Tivicay)

c) Therapy experienced children with HIV-1 infection ≥ 14 kg to < 12 years

The following medicinal products with new active ingredients that can be used in a combination therapy with dolutegravir/ abacavir/ lamivudine in the therapeutic indication of the resolution on the basis of the marketing authorisation under Medicinal Products Act are named (active ingredients and invented names) in accordance with Section 35a, paragraph 3, sentence 4 SGB V:

Dolutegravir (Tivicay)

II. In Annex XIIa of the Pharmaceuticals Directive, the following information shall be added in alphabetical order:

"Active ingredient of the assessed medicinal product

Dolutegravir/ abacavir/ lamivudine

Resolution according to Section 35a paragraph 3 SGB V from

17 August 2023

Therapeutic indication of the resolution

Triumeq is indicated for the treatment of Human Immunodeficiency Virus (HIV) infected children weighing at least 14 kg to < 12 years.

Before initiating treatment with abacavir-containing products, screening for carriage of the HLAB*5701 allele should be performed in any HIV-infected patient, irrespective of racial origin. Abacavir should not be used in patients known to carry the HLA-B*5701 allele.

a) Therapy naive children with HIV-1 infection ≥ 14 kg to < 6 years

Naming of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V (active ingredients and invented names)

Dolutegravir (Tivicay)

b) Therapy naive children with HIV-1 infection ≥ 14 kg from 6 to < 12 years

Naming of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V (active ingredients and invented names)

Dolutegravir (Tivicay)

c) Therapy experienced children with HIV-1 infection ≥ 14 kg to < 12 years

Naming of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V (active ingredients and invented names)

Dolutegravir (Tivicay)

Period of validity of the designation (since... or from... to)

Since 17 August 2023"

III. The resolution will enter into force on the day of its publication on the website of the G-BA on 17 August 2023.

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

Berlin, 17 August 2023

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

Prof. Hecken