GBA
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
Tovorafenib (malignant low-grade glioma (LGG) harbouring a BRAF fusion or rearrangement or a BRAF V600 mutation, after at least 1 prior therapy, ≥ 6 months)

of 5 November 2026

At their session on 5 November 2026, the Federal Joint Committee (GBA) 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:

I. In Annex XII, information on the active ingredient tovorafenib shall be added in alphabetical order as follows:

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Tovorafenib

Resolution of: 5 November 2026
Entry into force on: 5 November 2026
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 20 April 2026):

Ojemda is indicated as monotherapy for the treatment of patients 6 months of age and older with paediatric low-grade glioma (LGG) harbouring a BRAF fusion or rearrangement, or BRAF V600 mutation, who have progressed after one or more prior systemic therapies (for biomarkers-based patient selection, see section 4.2).

Therapeutic indication of the resolution (resolution of 5 November 2026):

See therapeutic indication according to marketing authorisation.

1. Extent of the additional benefit and significance of the evidence

Tovorafenib is approved as a medicinal product for the treatment of rare diseases under Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999 on orphan drugs. In accordance with Section 35a, paragraph 1, sentence 11, 1st half of the sentence German Social Code, Book Five (SGB V), the additional medical benefit is considered to be proven through the grant of the marketing authorisation.

The GBA determines the extent of the additional benefit for the number of patients and patient groups for which there is a therapeutically significant additional benefit in accordance with Chapter 5, Section 12, paragraph 1, number 1, sentence 2 of their Rules of Procedure (VerfO) in conjunction with Section 5, paragraph 8 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), indicating the significance of the evidence. This quantification of the additional benefit is based on the criteria laid out in Chapter 5, Section 5, paragraph 7, numbers 1 to 4 of the Rules of Procedure (VerfO).

<u>Patients 6 months of age and older with paediatric low-grade glioma (LGG) harbouring a BRAF fusion or rearrangement, or BRAF V600 mutation, who have progressed after one or more prior systemic therapies</u>

Extent of the additional benefit and significance of the evidence of tovorafenib:

Hint of a non-quantifiable additional benefit since the scientific data does not allow quantification.

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Study results according to endpoints:[1]

Patients 6 months of age and older with paediatric low-grade glioma (LGG) harbouring a BRAF fusion or rearrangement, or BRAF V600 mutation, who have progressed after one or more prior systemic therapies

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.a.	The data are not assessable.
Morbidity	n.a.	The data are not assessable.
Health-related quality of life	n.a.	The data are not assessable.
Side effects	n.a.	The data are not assessable.
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		

FIREFLY-1 study

- Uncontrolled, multicentre phase II study with 3 study arms
- Results for the third data cut-off from 6 June 2025
- Relevant study arms:
    - Arm 1 - Patients with paediatric low-grade glioma (pLGG) and an activating BRAF alteration (including BRAF V600 mutations or KIAA1549:BRAF fusions)
    - Arm 2 - Patients with pLGG and an activating or putatively activating RAF alteration (e.g. BRAF or CRAF/RAF1 fusions)

[1] Data from the GBA's benefit assessment (published on 17 August 2026), unless otherwise indicated.

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Mortality

Endpoint	**Tovorafenib** *Patients with event n (%)*		
	Arm 1 N = 77	Arm 2 N = 60	Arm 1+2 N = 137
Overall survival/ mortality			
	4 (5.19)	5 (8.33)	9 (6.57)

Morbidity

Endpoint	**Tovorafenib** *Median time to event in months [95% CI]* *Patients with event n (%)*		
	Arm 1 N = 77	Arm 2 N = 60	Arm 1+2 N = 137
Progression-free survival[b]			
RANO-LGG analysis population time to event Subjects with event	76 (n.d.) 14.0 [11.1; 19.1] 65 (85.5)	n.d.	n.d.
RAPNO-LGG analysis population time to event Subjects with event	76 (n.d.) 16.6 [8.3; 19.1] 59 (77.6)	n.d.	n.d.

Endpoint	**Tovorafenib** *Patients with event n (%)*		
	Arm 1 N = 77	Arm 2 N = 60	Arm 1+2 N = 137
Overall response rate (presented additionally)			
RANO-HGG analysis population[a] Subjects with event	69 (89.6) 49 (71.0)	n.d.	n.d.
RANO-LGG analysis population Subjects with event	76 (98.7) 41 (54.0)	n.d.	n.d.
RAPNO-LGG analysis population Subjects with event	76 (98.7) 40 (52.6)	n.d.	n.d.
Visual acuity	There are no assessable data.		
Cognitive functioning using PROMIS CSF7a	There are no assessable data.		
Fatigue using	There are no assessable data.		

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- **PROMIS Paediatric Profile-49** - **PROMIS Parent-Proxy-49**	
Disease symptomatology using PedsQL Cancer	There are no assessable data.

Health-related quality of life

Endpoint	**Tovorafenib** *Patients with event n (%)*		
	Arm 1 N = 77	Arm 2 N = 60	Arm 1+2 N = 137
PedsQL Core	There are no assessable data.		

Side effects

Endpoint **MedDRA system organ classes/ Preferred terms/ AEs of special interest**	**Tovorafenib** *Patients with event n (%)*		
	Arm 1 N = 77	Arm 2 N = 60	Arm 1+2 N = 137
Total adverse events (presented additionally)	77 (100)	60 (100)	137 (100)
Serious adverse events (SAEs)	42 (54.5)	35 (58.3)	77 (56.2)
Severe adverse events (CTCAE grade 3 or 4)	64 (83.1)	49 (81.7)	113 (82.5)
Therapy discontinuation due to adverse events	8 (10.4)	11 (18.3)	19 (13.9)
Severe adverse events according to MedDRA system organ class (with an incidence ≥ 10%)			
Infections and infestations	21 (27.3)	27 (45.0)	48 (35.0)
Musculoskeletal and connective tissue disorders	24 (31.2)	24 (40.0)	48 (35.0)
Investigations	17 (22.1)	18 (30.0)	35 (25.5)
Nervous system disorders	13 (16.9)	13 (21.7)	26 (19.0)
Blood and lymphatic system disorders	11 (14.3)	13 (21.7)	24 (17.5)
Metabolism and nutrition disorders	13 (16.9)	9 (15.0)	22 (16.1)
Skin and subcutaneous tissue disorders	13 (16.9)	8 (13.3)	21 (15.3)
Gastrointestinal disorders	11 (14.3)	8 (13.3)	19 (13.9)
General disorders and administration site conditions	12 (15.6)	7 (11.7)	19 (13.9)

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SAEs according to MedDRA system organ class (with an incidence ≥ 10%)			
Infections and infestations	23 (29.9)	23 (38.3)	46 (33.6)
Nervous system disorders	13 (16.9)	13 (21.7)	26 (19.0)
General disorders and administration site conditions	11 (14.3)	11 (18.3)	22 (16.1)
Gastrointestinal disorders	8 (10.4)	8 (13.3)	16 (11.7)
Metabolism and nutrition disorders	6 (7.80)	8 (13.3)	14 (10.2)
Musculoskeletal and connective tissue disorders	8 (10.4)	2 (3.33)	10 (7.30)

a. Primary endpoint of the FIREFLY-1 study
b. Data from the pharmaceutical company's dossier on tovorafenib dated 13.05.2026

Abbreviations used:

CTCAE = Common Terminology Criteria for Adverse Events; HR = hazard ratio; n.d.= no data available; CI = confidence interval; N = number of patients evaluated; n = number of patients with (at least one) event; n.c. = not calculable; n.r. = not reached; vs = versus

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

Patients 6 months of age and older with paediatric low-grade glioma (LGG) harbouring a BRAF fusion or rearrangement, or BRAF V600 mutation, who have progressed after one or more prior systemic therapies

Approximately 5 to 160 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 Ojemda (active ingredient: tovorafenib) at the following publicly accessible link (last access: 21 October 2026):

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

Treatment with tovorafenib must only be initiated and monitored by specialists in internal medicine, haematology, and oncology experienced in the treatment of patients with gliomas, specialists in neurology, as well as specialists in neurosurgery or specialists in paediatrics and adolescent medicine with a specialisation in neuropaediatrics or paediatric haematology and oncology, and other specialists from other specialist groups participating in the Oncology Agreement.

Before taking tovorafenib, the presence of the BRAF fusion or rearrangement, or BRAF V600 mutation, must have been detected in patients by a validated test.

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This medicinal product received a conditional marketing authorisation. This means that further evidence of the benefit of the medicinal product is anticipated. The European Medicines Agency (EMA) will assess new information on this medicinal product at least annually and update the product information where necessary.

4. Treatment costs

Annual treatment costs

Patients 6 months of age and older with paediatric low-grade glioma (LGG) harbouring a BRAF fusion or rearrangement, or BRAF V600 mutation, who have progressed after one or more prior systemic therapies

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Tovorafenib	€ 239,405.23 - € 477,950.42

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 1 September 2026)

Costs for additionally required SHI services: not applicable

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II. The resolution will enter into force on the day of its publication on the GBA website on 5 November 2026.

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

Berlin, 5 November 2026

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

Dr Optendrenk

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