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
Entrectinib (new therapeutic indication: solid tumours, neurotrophic tyrosine receptor kinase (NTRK) gene fusion, histology-independent, > 1 month to < 12 years)

of 6 February 2025

At its session on 6 February 2025, 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:

I. In Annex XII, the following information shall be added after No. 4 to the information on the benefit assessment of Entrectinib in accordance with the resolution of 18 February 2021:

Entrectinib

Resolution of: 6 February 2025
Entry into force on: 6 February 2025
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 27 June 2024):

Rozlytrek as monotherapy is indicated for the treatment of adult and paediatric patients older than 1 month with solid tumours expressing a NTRK gene fusion,

- who have a disease that is locally advanced, metastatic or where surgical resection is likely to result in severe morbidity, and
- who have not received a prior NTRK inhibitor
- who have no satisfactory treatment options.

Therapeutic indication of the resolution (resolution of 6 February 2025):

Rozlytrek as monotherapy is indicated for the treatment of paediatric patients older than 1 month up to 12 years of age with solid tumours expressing a NTRK gene fusion,

- who have a disease that is locally advanced, metastatic or where surgical resection is likely to result in severe morbidity, and
- who have not received a prior NTRK inhibitor
- who have no satisfactory treatment options.

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

Paediatric patients (older than one month up to 12 years of age) with solid tumours expressing a neurotrophic tyrosine receptor kinase (NTRK) gene fusion, who have a disease that is locally advanced, metastatic or where surgical resection is likely to result in severe morbidity, and who have not received a prior NTRK inhibitor and who have no satisfactory treatment options other than larotrectinib

Appropriate comparator therapy:

Individualised therapy with selection of

- larotrectinib
- best supportive care
- surgical resection which is likely to result in severe morbidity, but for which a patient-individual clinical benefit can nevertheless be expected in individual cases

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

An additional benefit is not proven.

Study results according to endpoints:[1]

Paediatric patients (older than one month up to 12 years of age) with solid tumours expressing a neurotrophic tyrosine receptor kinase (NTRK) gene fusion, who have a disease that is locally advanced, metastatic or where surgical resection is likely to result in severe morbidity, and who have not received a prior NTRK inhibitor and who have no satisfactory treatment options other than larotrectinib

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	n.a.	There are no assessable data.
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		

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

Paediatric patients (older than one month up to 12 years of age) with solid tumours expressing a neurotrophic tyrosine receptor kinase (NTRK) gene fusion, who have a disease that is locally advanced, metastatic or where surgical resection is likely to result in severe morbidity, and who have not received a prior NTRK inhibitor and who have no satisfactory treatment options other than larotrectinib

Approx. 3 patients

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A24-78) unless otherwise indicated.

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 Rozlytrek (active ingredient: entrectinib) at the following publicly accessible link (last access: 3 January 2025):

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

Treatment with entrectinib should only be initiated and monitored by specialists in paediatrics and adolescent medicine with a focus on paediatric haematology and oncology who are experienced in the treatment of paediatric patients with solid tumours.

Prior to initiation of treatment with entrectinib, the presence of an NTRK gene fusion in a tumour sample must be confirmed by a validated test.

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 will evaluate new information on this medicinal product at a minimum once per year and update the product information where necessary.

4. Treatment costs

Annual treatment costs[2]:

Paediatric patients (older than one month up to 12 years of age) with solid tumours expressing a neurotrophic tyrosine receptor kinase (NTRK) gene fusion, who have a disease that is locally advanced, metastatic or where surgical resection is likely to result in severe morbidity, and who have not received a prior NTRK inhibitor and who have no satisfactory treatment options other than larotrectinib

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Entrectinib	€ 11,201.00 – € 43,367.60
Appropriate comparator therapy:	
larotrectinib	€ 17,150.18 – € 66,639.09
Best supportive care[3]	Different from patient to patient
Surgical resection	Different from patient to patient

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 January 2025

[2] Only the costs for the first year of treatment are presented.

[3] When comparing entrectinib versus best supportive care, the costs of best supportive care must also be additionally considered for the medicinal product to be assessed.

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:

Paediatric patients (older than one month up to 12 years of age) with solid tumours expressing a neurotrophic tyrosine receptor kinase (NTRK) gene fusion, who have a disease that is locally advanced, metastatic or where surgical resection is likely to result in severe morbidity, and who have not received a prior NTRK inhibitor and who have no satisfactory treatment options other than larotrectinib

- No designation of medicinal products with new active ingredients that can be used in combination therapy pursuant to Section 35a, paragraph 3, sentence 4 SGB V, as the active ingredient to be assessed is an active ingredient authorised in monotherapy.

The designation of combinations exclusively serves the implementation of the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. The findings made neither restrict the scope of treatment required to fulfil the medical treatment mandate, nor do they make statements about expediency or economic feasibility.

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 6 February 2025.

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

Berlin, 6 February 2025

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

Prof. Hecken