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 Upadacitinib (new therapeutic indication: ulcerative colitis, pretreated)

of 16 February 2023

At its session on 16 February 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:

I. In Annex XII, the following information shall be added after No. 4 to the information on the benefit assessment of Upadacitinib in accordance with the resolution of 17 February 2022:

Upadacitinib

Resolution of: 16 February 2023
Entry into force on: 16 February 2023
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 22 July 2022):

Rinvoq is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response, lost response or were intolerant to either conventional therapy or a biologic agent.

Therapeutic indication of the resolution (resolution of 16 February 2023):

See new therapeutic indication according to marketing authorisation.

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

a) Adults with moderately to severely active ulcerative colitis who have had an inadequate response, lost response or were intolerant to conventional therapy.

Appropriate comparator therapy:

- A TNF-α antagonist (adalimumab or infliximab or golimumab) or vedolizumab or ustekinumab

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

An additional benefit is not proven.

b) Adults with moderately to severely active ulcerative colitis who have had an inadequate response, lost response or were intolerant to a biologic agent (TNF-α antagonist or integrin inhibitor or interleukin inhibitor).

Appropriate comparator therapy:

- A change of therapy to vedolizumab or tofacitinib or ustekinumab or a TNF-α antagonist (adalimumab or infliximab or golimumab), in each case taking into account the marketing authorisation and the previous therapy/ therapies

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

An additional benefit is not proven.

Study results according to endpoints:[1]

a) Adults with moderately to severely active ulcerative colitis who have had an inadequate response, lost response or were intolerant to conventional therapy.

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	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 ∅: There are no usable data for the benefit assessment. n.a.: not assessable		

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A22-91) unless otherwise indicated.

b) Adults with moderately to severely active ulcerative colitis who have had an inadequate response, lost response or were intolerant to a biologic agent (TNF-α antagonist or integrin inhibitor or interleukin inhibitor).

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	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
∅: 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

a) Adults with moderately to severely active ulcerative colitis who have had an inadequate response, lost response or were intolerant to conventional therapy.

approx. 3,500 - 16,500 patients

b) Adults with moderately to severely active ulcerative colitis who have had an inadequate response, lost response or were intolerant to a biologic agent (TNF-α antagonist or integrin inhibitor or interleukin inhibitor).

approx. 1,800 – 8,500 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 Rinvoq (active ingredient: upadacitinib) at the following publicly accessible link (last access: 16 November 2022):

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

Treatment with upadacitinib should only be initiated and monitored by doctors experienced in treating ulcerative colitis.

In accordance with the European Medicines Agency (EMA) requirements regarding additional risk minimisation measures, the pharmaceutical company must provide training material that contains information for medical professionals and patients. In particular, the training and information material contains instructions on how to deal with any side effects caused by upadacitinib, especially in serious and opportunistic infections, including TB and herpes zoster, as well as birth defects (pregnancy risk), MACE and VTE.

Upadacitinib should be discontinued for patients who do not show any sign of therapeutic benefit by week 16.

The product class of Janus kinase inhibitors (JAK) is currently undergoing a risk assessment procedure by the Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (EMA)[2], which has not yet been concluded by a decision of the European Commission. The inclusion of new warnings and precautions in the product information is expected. These must then be observed accordingly.

[2] https://www.ema.europa.eu/en/documents/referral/rinvoq-epar-product-information-approved-chmp-23-january-2023-pending-endorsement-european_en.pdf

4. Treatment costs

Annual treatment costs:

a) Adults with moderately to severely active ulcerative colitis who have had an inadequate response, lost response or were intolerant to conventional therapy.

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Upadacitinib Additionally required SHI services:	€ 14,451.20 - € 18,444.99 € 106.40
Appropriate comparator therapy:	
Adalimumab Additionally required SHI services:	€ 11,434.41 € 106.40
Golimumab Additionally required SHI services:	€ 11,283.65 € 106.40
Infliximab Additionally required SHI services:	€ 16,683.94 € 106.40
Ustekinumab	€ 21,143.53
Vedolizumab	€ 14,808.40

b) Adults with moderately to severely active ulcerative colitis who have had an inadequate response, lost response or were intolerant to a biologic agent (TNF-α antagonist or integrin inhibitor or interleukin inhibitor).

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Upadacitinib Additionally required SHI services:	€ 14,451.20 - € 18,444.99 € 106.40
Appropriate comparator therapy:	
Adalimumab Additionally required SHI services:	€ 11,434.41 € 106.40
Golimumab Additionally required SHI services:	€ 11,283.65 € 106.40
Infliximab	€ 16,683.94

Designation of the therapy	Annual treatment costs/ patient
Additionally required SHI services:	€ 106.40
Tofacitinib Additionally required SHI services:	€ 11,474.52 € 106.40
Ustekinumab	€ 21,143.53
Vedolizumab	€ 14,808.40

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

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Appropriate comparator therapy for patient populations a) and b)					
Infliximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	6.5	€ 650

5. 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 Upadacitinib

Medicinal products with new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V are medicinal products with the following new active ingredients that can be used in a combination therapy with upadacitinib for the treatment of ulcerative colitis on the basis of the marketing authorisation granted under Medicinal Products Act:

a) Adults with moderately to severely active ulcerative colitis who have had an inadequate response, lost response or were intolerant to conventional therapy.

No active ingredient that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

b) Adults with moderately to severely active ulcerative colitis who have had an inadequate response, lost response or were intolerant to a biologic agent (TNF-α antagonist or integrin inhibitor or interleukin inhibitor).

No active ingredient that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 16 February 2023.

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

Berlin, 16 February 2023

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

Prof. Hecken