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: Crohn's disease, pretreated)

of 19 October 2023

At its session on 19 October 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. 5 to the information on the benefit assessment of Upadacitinib in accordance with the resolution of 16 February 2023:

Upadacitinib

Resolution of: 19 October 2023
Entry into force on: 19 October 2023
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 12 April 2023):

Crohn's disease

RINVOQ is indicated for the treatment of adult patients with moderately to severely active Crohn's disease 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 19 October 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 Crohn's disease who have had an inadequate response to, lost response to, or were intolerant to conventional therapy

Appropriate comparator therapy:

A TNF-α antagonist[1] (adalimumab or infliximab) or integrin inhibitor (vedolizumab) or interleukin inhibitor (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 Crohn's disease who have had an inadequate response to, lost response to, or were intolerant to a biologic agent (TNF-α antagonist or integrin inhibitor or interleukin inhibitor)

Appropriate comparator therapy:

A change of therapy to a TNF-α antagonist[1] (adalimumab or infliximab) or integrin inhibitors (vedolizumab) or interleukin inhibitors (ustekinumab)

1 The therapeutic indications for TNF-α inhibitors presuppose that patients have had an inadequate response to a complete and adequate therapy with a corticosteroid and/or an immunosuppressant (conventional therapy) or have an intolerance or a contraindication to such therapies (product information of Humira® as of January 2017).

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:[2]

a) Adults with moderately to severely active Crohn's disease who have had an inadequate response to, lost response to, 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 ∅: No data available. n.a.: not assessable		

2 Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A23-38) unless otherwise indicated.

b) Adults with moderately to severely active Crohn's disease who have had an inadequate response to, lost response to, 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

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Explanations:
↑: statistically significant and relevant positive effect with low/unclear reliability of data
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↓↓: 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) Adults with moderately to severely active Crohn's disease who have had an inadequate response to, lost response to, or were intolerant to conventional therapy

approx. 11,400 – 21,350 patients

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

approx. 7,500 – 14,000 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: 21 June 2023):

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 Crohn's disease.

The product class of Janus kinase (JAK) inhibitors underwent a risk assessment procedure by the Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (EMA), which has been concluded on 10 March 2023 by the European Commission's[3] legally binding decision in all EU Member States. The new warnings and precautions for use included in the product information must be followed.

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 (incl. patient card). 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, VTE and malignancies.

Prior to initiation of therapy with upadacitinib, it is recommended checking the vaccination status of the patients.

The recommended starting dose of upadacitinib is 45 mg once daily for 12 weeks. Prolonged induction for a further 12 weeks at a dose of 30 mg once daily may be considered for patients who have not achieved sufficient therapeutic benefit after the initial 12-week induction. Upadacitinib should be discontinued for these patients if there is no evidence of therapeutic benefit after 24 weeks of treatment.

4. Treatment costs

Annual treatment costs:

a) Adults with moderately to severely active Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to a conventional therapy or corresponding treatment

b) Adults with moderately to severely active Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to either a biologic agent (TNF-α antagonist or integrin inhibitor or interleukin inhibitor) or a corresponding treatment

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Upadacitinib	€ 13,882.33 - € 17,716.33

3 https://www.ema.europa.eu/en/documents/referral/janus-kinase-inhibitors-jaki-article-20-procedure-ema-confirms-measures-minimise-risk-serious-side_en.pdf

Designation of the therapy	Annual treatment costs/ patient
Appropriate comparator therapy:	
Adalimumab Additionally required SHI services: Total:	€ 11,434.54 € 106.40 € 11,540.94
Infliximab Additionally required SHI services: Total:	€ 16,684.15 € 106.40 € 16,790.55
Ustekinumab	€ 22,586.09
Vedolizumab	€ 14,364.35

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

a) Adults with moderately to severely active Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to a conventional therapy or corresponding treatment

No medicinal product with new active ingredients that can be used in a combination therapy and fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

b) Adults with moderately to severely active Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to either a biologic agent (TNF-α antagonist or integrin inhibitor or interleukin inhibitor) or a corresponding treatment

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

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 19 October 2023.

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

Berlin, 19 October 2023

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

Prof. Hecken