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: Tofacitinib (new therapeutic indication: Polyarticular juvenile idiopathic arthritis, RF+ or RF- polyarthritis and extended oligoarthritis, and juvenile psoriatic arthritis, ≥ 2 years)

of 3 March 2022

At its session on 3 March 2022, 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 Tofacitinib in accordance with the resolution of 17 February 2022:

Tofacitinib

Resolution of: 3 March 2022
Entry into force on: 3 March 2022
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 18 August 2021):

Tofacitinib is indicated for the treatment of active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), and juvenile psoriatic arthritis (PsA) in patients 2 years of age and older, who have responded inadequately to previous therapy with DMARDs.
Tofacitinib can be given in combination with methotrexate (MTX) or as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate.

Therapeutic indication of the resolution (resolution of 3 March 2022):

See new therapeutic indication according to marketing authorisation

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

a1) Patients aged 2 years and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor-positive [RF+] or -negative [RF-] polyarthritis and extended oligoarthritis) who have responded inadequately to previous treatment with conventional DMARDs (including MTX); tofacitinib in monotherapy in the case of MTX intolerance or MTX unsuitability

Appropriate comparator therapy:

a bDMARD (adalimumab or etanercept or tocilizumab) as monotherapy

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

An additional benefit is not proven.

a2) Patients aged 2 years and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor-positive [RF+] or -negative [RF-] polyarthritis and extended oligoarthritis) who have responded inadequately to previous treatment with conventional DMARDs (including MTX); tofacitinib in combination with MTX

Appropriate comparator therapy:

a bDMARD (adalimumab or etanercept or golimumab or tocilizumab) in combination with MTX

Extent and probability of the additional benefit of Tofacitinib in combination with MTX compared to the appropriate comparator therapy:

An additional benefit is not proven.

b1) Patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), who have responded inadequately to previous therapy with one or more bDMARDs; tofacitinib as monotherapy in case of intolerance to MTX or MTX unsuitability

Appropriate comparator therapy:

a change in bDMARD therapy (adalimumab or etanercept or tocilizumab) as monotherapy, depending on previous therapy.

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

An additional benefit is not proven.

b2) Patients aged 2 years and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor-positive [RF+] or -negative [RF-] polyarthritis and extended oligoarthritis) who have responded inadequately to previous treatment with one or more bDMARDs; tofacitinib in combination with MTX

Appropriate comparator therapy:

a change in bDMARD therapy (abatacept or adalimumab or etanercept or golimumab or tocilizumab) in combination with MTX, depending on the previous therapy.

Extent and probability of the additional benefit of Tofacitinib in combination with MTX compared to the appropriate comparator therapy:

An additional benefit is not proven.

c) Patients 2 years of age and older with juvenile psoriatic arthritis who have responded inadequately to previous DMARD therapy

Appropriate comparator therapy:

Therapy according to doctor's instructions

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

An additional benefit is not proven.

Study results according to endpoints:[1]

a1) Patients aged 2 years and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor-positive [RF+] or -negative [RF-] polyarthritis and extended oligoarthritis) who have responded inadequately to previous treatment with conventional DMARDs (including MTX); tofacitinib in monotherapy in the case of MTX intolerance or MTX unsuitability

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	∅	No data submitted.
Morbidity	∅	No data submitted.
Health-related quality of life	∅	No data submitted.
Side effects	∅	No data submitted.
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		

No suitable data submitted.

a2) Patients aged 2 years and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor-positive [RF+] or -negative [RF-] polyarthritis and extended oligoarthritis) who have responded inadequately to previous treatment with conventional DMARDs (including MTX); tofacitinib in combination with MTX

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	∅	No data submitted.
Morbidity	∅	No data submitted.
Health-related quality of life	∅	No data submitted.
Side effects	∅	No data submitted.
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		

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A21-121) unless otherwise indicated.

↔: no statistically significant or relevant difference ∅: There are no usable data for the benefit assessment. n.a.: not assessable

No suitable data submitted.

b1) Patients 2 years of age and older with active pJIA - polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), who have responded inadequately to previous therapy with one or more bDMARDs; tofacitinib as monotherapy in case of intolerance to MTX or MTX unsuitability

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	∅	No data submitted.
Morbidity	∅	No data submitted.
Health-related quality of life	∅	No data submitted.
Side effects	∅	No data submitted.
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		

No suitable data submitted.

b2) Patients 2 years of age and older with active pJIA - polyarticular juvenile idiopathic arthritis(rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), who have responded inadequately to previous therapy with one or more bDMARDs; tofacitinib in combination with MTX

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	∅	No data submitted.
Morbidity	∅	No data submitted.
Health-related quality of life	∅	No data submitted.
Side effects	∅	No data submitted.

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

No suitable data submitted.

c) Patients 2 years of age and older with juvenile psoriatic arthritis who have responded inadequately to previous DMARD therapy

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	∅	No data submitted.
Morbidity	∅	No data submitted.
Health-related quality of life	∅	No data submitted.
Side effects	∅	No data submitted.

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

No data submitted.

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

a) Patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), who have responded inadequately to previous therapy with conventional DMARDs (including MTX) (a1 + a2)

approx. 990 patients

b) Patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), who have responded inadequately to previous therapy with one or more bDMARDs (b1 + b2)

approx. 380 patients

c) Patients 2 years of age and older with juvenile psoriatic arthritis who have responded inadequately to previous DMARD therapy

approx. 180 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 Xeljanz (active ingredient: tofacitinib) at the following publicly accessible link (last access: 1 February 2022):
https://www.ema.europa.eu/en/documents/product-information/xeljanz-epar-product-information_en.pdf

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. The training material includes instructions on how to manage the potential side effects associated with tofacitinib, particularly severe and opportunistic infections including tuberculosis and herpes zoster. It also points out the need for an effective contraceptive method.

Treatment with tofacitinib should only be initiated and monitored by doctors experienced in treating patients with JIA (juvenile idiopathic arthritis) and jPsA (juvenile psoriatic arthritis).

4. Treatment costs

Annual treatment costs:

a1) Patients aged 2 years and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor-positive [RF+] or -negative [RF-] polyarthritis and extended oligoarthritis) who have responded inadequately to previous treatment with conventional DMARDs (including MTX); tofacitinib in monotherapy in the case of MTX intolerance or MTX unsuitability

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Tofacitinib Additionally required SHI services Total	€ 8,240.82 - € 12,876.29 € 106.40 € 8,347.22 - € 12,982.69
Appropriate comparator therapy:	
Adalimumab Additionally required SHI services	€ 6,286.19 - € 11,435.41 € 106.40

Designation of the therapy	Annual treatment costs/ patient
Total	€ 6,392.59 - € 11,541.81
Etanercept Additionally required SHI services Total	€ 5,064.90 - € 11,413.50 € 106.40 € 5,171.30 - € 11,519.90
Tocilizumab	€ 7,529.60 - € 22,545.54

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 March 2022)

a2) Patients aged 2 years and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor-positive [RF+] or -negative [RF-] polyarthritis and extended oligoarthritis) who have responded inadequately to previous treatment with conventional DMARDs (including MTX); tofacitinib in combination with MTX

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Tofacitinib Methotrexate Additionally required SHI services Total	€ 8,240.82 - € 12,876.29 € 52.40 - € 1,079.47[2] € 106.40 € 8,958.96 €[3] - € 14,062.16
Appropriate comparator therapy:	
Adalimumab Methotrexate Additionally required SHI services Total	€ 6,286.19 - € 11,435.41 € 52.40 - € 1,079.47[2] € 106.40 € 7,004.33[Fehler! Textmarke nicht definiert.] - € 11,671.78[4]
Etanercept Methotrexate Additionally required SHI services Total	€ 5,064.90 - € 11,413.50 € 52.40 - € 1,079.47[2] € 106.40 € 5,783.04[3] - € 11,649.87[4]
Golimumab Methotrexate Additionally required SHI services Total	€ 10,416.60 - 20,903.76[5] € 52.40 - € 1,079.47[2] € 106.40 € 10,575.40 - € 22,089.63
Tocilizumab Methotrexate Total	€ 7,529.60 - € 22,545.54 € 52.40 - € 1,079.47[2] € 8,141.34[3] - € 22,675.51[4]

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 01 March 2022)

[2] The parenteral dosage form is used for the calculation of the annual treatment costs for the lower range of children ≥ 2 years.
[3] Arithmetically, the lower limit of the total range is € 611.74, taking into account the lower limit of methotrexate (parenteral) for children.
[4] Arithmetically, the upper limit of the total range is € 129.97, taking into account the upper limit of methotrexate (oral) for adults.
[5] Golimumab for children < 40 kg BW is administered by means of an injector according to the product information, which is not the most economical form of administration available.

b1) Patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), who have responded inadequately to previous therapy with one or more bDMARDs; tofacitinib as monotherapy in case of intolerance to MTX or MTX unsuitability

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Tofacitinib Additionally required SHI services Total	€ 8,240.82 - € 12,876.29 € 106.40 € 8,347.22 - € 12,982.69
Appropriate comparator therapy:	
Adalimumab Additionally required SHI services Total	€ 6,286.19 - € 11,435.41 € 106.40 € 6,392.59 - € 11,541.81
Etanercept Additionally required SHI services Total	€ 5,064.90 - € 11,413.50 € 106.40 € 5,171.30 - € 11,519.90
Tocilizumab	€ 7,529.60 - € 22,545.54

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 01 March 2022)

b2) Patients aged 2 years and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor-positive [RF+] or -negative [RF-] polyarthritis and extended oligoarthritis) who have responded inadequately to previous treatment with one or more bDMARDs; tofacitinib in combination with MTX

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Tofacitinib Methotrexate Additionally required SHI services Total	€ 8,240.82 - € 12,876.29 € 52.40 - € 1,079.47[2] € 106.40 € 8,958.96[3] - € 14,062.16
Appropriate comparator therapy:	
Abatacept Methotrexate Additionally required SHI services Total	€ 7,887.68 - € 19,024.53[6] € 52.40 - € 1,079.47[2] € 106.40 € 8,605.82[3] - € 19,260.90[4]
Adalimumab Methotrexate Additionally required SHI services Total	€ 6,286.19 - € 11,435.41 € 52.40 - € 1079.47[2] € 106.40 € 7,004.33[3] - € 11,671.78[4]
Etanercept	€ 5,064.90 - € 11,413.50

[6] According to the product information, the use of abatacept is only approved with the dosage form of the injection solution for children 2 years and older.

Designation of the therapy	Annual treatment costs/ patient
Methotrexate Additionally required SHI services Total	€ 52.40 - € 1,079.47[2] € 106.40 € 5,783.04[3] - € 11,649.87[4]
Golimumab Methotrexate Additionally required SHI services Total	€ 10,416.60 - € 20,903.76[5] € 52.40 - € 1,079.47[2] € 106.40 € 10,575.40 - € 22,089.63
Tocilizumab Methotrexate Total	€ 7,529.60 - € 22,545.54 € 52.40 - € 1,079.47[2] € 8,141.34[3] - € 22,675.51[4]

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 01 March 2022)

c) Patients 2 years of age and older with juvenile psoriatic arthritis who have responded inadequately to previous DMARD therapy

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Tofacitinib monotherapy	
Tofacitinib Additionally required SHI services Total	€ 8,240.82 - € 12,876.29 € 106.40 € 8,347.22 - € 12,982.69
Tofacitinib in combination with MTX	
Tofacitinib Methotrexate Additionally required SHI services Total	€ 7,911.19 - € 12,566.75 € 52.40 - € 1,079.47[2] € 106.40 € 8,958.96[3] - € 14,062.16
Appropriate comparator therapy:	
Therapy according to doctor's instructions	Different from patient to patient

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 01 March 2022)

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 3 March 2022.

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

Berlin, 3 March 2022

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

Prof. Hecken