Bimekizumab (new therapeutic indication: psoriatic arthritis, monotherapy or in combination with methotrexate)

Resolution of: 21 December 2023
Entry into force on: 21 December 2023
Federal Gazette, BAnz AT 21 02 2024 B2

Valid until: unlimited

New therapeutic indication (according to the marketing authorisation of 5 June 2023):

Bimzelx, alone or in combination with methotrexate, is indicated for the treatment of active psoriatic arthritis in adults who have had an inadequate response or who have been intolerant to one or more disease-modifying antirheumatic drugs (DMARDs).

Therapeutic indication of the resolution (resolution of 21 December 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 active psoriatic arthritis who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug (DMARD) therapy

Appropriate comparator therapy:

– a TNF-alpha antagonist (adalimumab or certolizumab pegol or etanercept or golimumab or infliximab) or an interleukin inhibitor (ixekizumab or secukinumab or ustekinumab), if necessary in combination with methotrexate

Extent and probability of the additional benefit of bimekizumab compared to adalimumab:

An additional benefit is not proven.

b) Adults with active psoriatic arthritis who have had an inadequate response or have been intolerant to a prior biological disease-modifying antirheumatic drug (bDMARD) therapy

Appropriate comparator therapy:

– switching to another biological disease-modifying antirheumatic drug (adalimumab or certolizumab pegol or etanercept or golimumab or infliximab or ixekizumab or secukinumab or ustekinumab), if necessary in combination with methotrexate

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

An additional benefit is not proven.

Study results according to endpoints:1

a) Adults with active psoriatic arthritis who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug (DMARD) therapy

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	No statistically significant difference
Morbidity	↔	No statistically significant difference
Health-related quality of life	↔	No statistically significant difference
Side effects	↔	No relevant differences for the benefit assessment, in detail disadvantage in the endpoint of fungal infections
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		

RCT BE OPTIMAL: Bimekizumab vs adalimamab (each as monotherapy or with csDMARD concomitant therapy); treatment duration of 52 weeks.

Mortality

Endpoint	Bimekizumab		Adalimumab		Bimekizumab vs adalimumab
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	RR [95 % CI]; p-value[a]
Overall mortality[b]	339	0 (0)	108	0 (0)	-

1 Data from the dossier assessment of the IQWiG (A23-60) and from the addendum (A23-105), unless otherwise indicated.

Morbidity

Endpoint	Bimekizumab		Adalimumab		Bimekizumab vs adalimumab
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	RR [95 % CI]; p-value[a]
Minimal disease activity (MDA)[d]	339	181 (53.4)	108	59 (54.6)	1.00 [0.82; 1.22]; 0.975
Remission (DAPSA ≤ 4)[e]	339	78 (23.0)	108	32 (29.6)	0.79 [0.56; 1.12]; 0.189
Joints sensitive to pressure pain (TJC68 ≤ 1)	339	157 (46.3)	108	52 (48.1)	0.97 [0.78; 1.22]; 0.825
Swollen joints (SJC66 ≤ 1)	339	241 (71.1)	108	72 (66.7)	1.09 [0.95; 1.26]; 0.227
Enthesitis (SPARCC Enthesitis Index = 0)	No suitable data				
Dactylitis (LDI = 0)	No suitable data				
Axial involvement (BASDAI; improvement by ≥ 1.5 points)[f]	243	175 (72.0)	83	60 (72.3)	1.00 [0.86; 1.17]; 0.984
Skin symptomatology (PASI)	No suitable data				
Involvement of the fingernails (mNAPSI)	No suitable data				

Endpoint	Bimekizumab		Adalimumab		Bimekizumab vs adalimumab
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	RR [95 % CI]; p-value[a]
Arthritic pain (PtAAP VAS, improvement by ≥ 15 points)[g]	339	215 (63.4)	108	69 (63.9)	1.00 [0.85; 1.18]; 0.992
Disease activity (PGA-PsA VAS, improvement by ≥ 15 points)[g]	339	228 (67.3)	108	72 (66.7)	1.02 [0.88; 1.19]; 0.811
Impairment due to the disease (PsAID-12, improvement by ≥ 3 points)[h]	230	113 (49.1)	86	42 (48.8)	1.02 [0.79; 1.32]; 0.864
Health status (EQ-5D VAS, improvement by ≥ 15 points)[i]	339	158 (46.6)	108	54 (50.0)	0.95 [0.76; 1.18]; 0.642
Fatigue (FACIT fatigue, improvement by ≥ 7.8 points)[j]	246	110 (44.7)	91	35 (38.5)	1.17 [0.87; 1.57]; 0.302

Health-related quality of life

Endpoint	Bimekizumab		Adalimumab		Bimekizumab vs adalimumab
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	RR [95 % CI]; p-value[a]
SF-36					
Mental component score (MCS, improvement by ≥ 9.6 points [15 %])[k]	339	29 (8.6)	108	11 (10.2)	0.84 [0.43; 1.62]; 0.604
Physical component score (PCS, improvement by ≥ 9.4 points [15 %])[l]	339	105 (31.0)	108	42 (38.9)	0.82 [0.62; 1.08]; 0.152
PsAQoL (improvement by ≥ 3 points)[m]	339	128 (37.8)	108	46 (42.6)	0.89 [0.69; 1.15]; 0.384

Side effects

Endpoint	Bimekizumab		Adalimumab		Bimekizumab vs adalimumab
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	RR [95 % CI]; p-value[a]
AEs[n]	339	284 (83.8)	108	83 (76.9)	
SAEs[n]	339	22 (6.5)	108	8 (7.4)	0.87 [0.40; 1.89]; 0.721
Discontinuation due to AEs[o]	339	12 (3.5)	108	6 (5.6)	0.61 [0.24; 1.59]; 0.311
Infections and infestations (SOC, AEs)	339	184 (54.3)	108	43 (39.8)	1.36 [1.06; 1.75]; 0.017
Fungal infections (HLGT, AEs)	339	44 (13.0)	108	2 (1.9)	7.01 [1.73; 28.43]; 0.006

a. Effect estimate and p value from a logistic regression, stratified by region; for morbidity endpoints and health-related quality of life endpoints, additionally adjusted for the value at start of study
b. operationalised as AEs that led to death
c. Missing values were replaced using non-responder imputation.
d. To be classified as an MDA responder, 5 of the following 7 criteria must be met: TJC68 ≤ 1; SJC66 ≤ 1; PASI ≤ 1 (for patients with BSA ≥ 3 at baseline) or BSA ≤ 3, PtAAP VAS ≤ 15; PGA-PsA VAS ≤ 20, HAQ-DI ≤ 0.5 and LEI ≤ 1
e. The DAPSA scale starts at 0 without an upper limit. A higher value reflects a higher disease activity. Remission is achieved when the patient reaches a DAPSA ≤ 4.
f. Percentage of patients with a decrease in the score by ≥ 1.5 points at week 52 compared to start of study, with a scale range of 0 to 10. Lower (decreasing) values mean an improvement of symptomatology. Evaluation refers to patients with a BASDAI ≥ 4 at the start of study.
g. Percentage of patients with a decrease in the score by ≥ 15 points at week 52 compared to start of study, with a scale range of 0 to 100. Lower (decreasing) values mean an improvement of symptomatology.
h. Percentage of patients with a decrease in the score by ≥ 3 points at week 52 compared to start of study, with a scale range of 0 to 10. Lower (decreasing) values mean an improvement of symptomatology. Evaluation refers to patients with a PsAID-12 ≥ 3 at the start of study.
i. Percentage of patients with an increase in the score by ≥ 15 points at week 52 compared to start of study, with a scale range of 0 to 100. Higher (increasing) values mean an improvement of symptomatology.
j. Percentage of patients with an increase in the score by ≥ 7.8 points at week 52 compared to start of study, with a scale range of 0 to 52. Higher (increasing) values mean an improvement of symptomatology. Evaluation refers to patients with a FACIT-F ≤ 44.2 at the start of study.
k. Percentage of patients with improvement: Increase in MCS score by ≥ 9.6 points at week 52 compared to start of study (corresponds to 15% of the scale range; normalised scale with a minimum of approximately 6 and a maximum of approximately 70)
l. Percentage of patients with improvement: Increase in PCS score by ≥ 9.4 points at week 52 compared to start of study (corresponds to 15% of the scale range; normalised scale with a minimum of approximately 7 and a maximum of approximately 70)
m. Percentage of patients with a decrease in the score by ≥ 3 points at week 52 compared to start of study, with a scale range of 0 to 20. Lower (decreasing) values mean an improvement of symptomatology.
n. Without taking into account the following PTs, which were defined as disease-related events by the pharmaceutical company in Module 4 C: Guttate psoriasis, psoriasis of the nails, psoriasis, pustular psoriasis, arthralgia, musculoskeletal stiffness, athropathic psoriasis and musculoskeletal pain
o. Operationalised as AEs that led to therapy discontinuation

Abbreviations: BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BSA: BSA: Body Surface Area; DAPSA: Disease Activity in Psoriatic Arthritis; FACIT: Functional Assessment of Chronic Illness Therapy; HLGT: High Level Group Term; CI: confidence interval; LDI: Leeds Daktylitis Index; MCS: Mental Component Score; MDA: minimal disease activity; mNAPSI: modified nail psoriasis severity index; n: number of patients with (at least 1) event; N: number of patients evaluated; NRI: Non-Responder Imputation; PASI: Psoriasis Area and Severity Index; PCS: Physical Component Score; PGA-PsA: Patient's Global Assessment of Arthritis; PsAID-12: Psoriatic Arthritis Impact of Disease-12; PsAQoL: Psoriatic Arthritis Quality of Life; PtAAP: Patient's Assessment of Arthritis Pain; RCT: randomised controlled trial; RR: relative risk; SF-36: Short Form 36-Item Health Survey; SJC66: Swollen Joint Counts; SOC: system organ class; SPARCC: Spondyloarthritis Research Consortium of Canada; SAE: serious adverse event; TJC68: Tender Joint Counts; AE: adverse event; VAS: visual analogue scale

b) with active psoriatic arthritis who have had an inadequate response or have been intolerant to a prior biological disease-modifying antirheumatic drug (bDMARD) therapy

There are no assessable data.

Summary of results for relevant clinical endpoints

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

a) Adults with active psoriatic arthritis who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug (DMARD) therapy

approx. 20,900 patients

b) Adults with active psoriatic arthritis who have had an inadequate response or have been intolerant to a prior biological disease-modifying antirheumatic drug (bDMARD) therapy

approx. 9,400 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 Bimzelx (active ingredient: bimekizumab) at the following publicly accessible link (last access: 28 September 2023):

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

Treatment with bimekizumab should only be initiated and monitored by doctors experienced in treating psoriatic arthritis.

4. Treatment costs

Annual treatment costs:

a) Adults with active psoriatic arthritis who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug (DMARD) therapy

and

b) Adults with active psoriatic arthritis who have had an inadequate response or have been intolerant to a prior biological disease-modifying antirheumatic drug (bDMARD) therapy

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Bimekizumab Additionally required SHI services: Total:	€ 18,700.37 € 74.78 € 18,775.15
Appropriate comparator therapy:	
Adalimumab Additionally required SHI services: Total:	€ 11,434.54 € 181.18 € 11,615.72
Certolizumab pegol Additionally required SHI services: Total:	€ 12,381.20 - € 12,428.82 € 181.18 € 12,562.38 - € 12,610.00
Etanercept Additionally required SHI services: Total:	€ 11,412.64 € 181.18 € 11,593.82
Golimumab Additionally required SHI services: Total:	€ 10,415.84 € 181.18 € 10,597.02
Infliximab Additionally required SHI services: Total:	€ 16,177.17 € 181.18 € 16,358.35
Ixekizumab	€ 16,583.41
Secukinumab	€ 8,929.06 - € 17,858.12
Ustekinumab Additionally required SHI services: Total:	€ 22,586.09 € 74.78 € 22,660.87

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

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 Bimekizumab

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 active psoriatic arthritis who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug (DMARD) 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 active psoriatic arthritis who have had an inadequate response or have been intolerant to a prior biological disease-modifying antirheumatic drug (bDMARD) 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.

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.