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 Abrocitinib (atopic dermatitis)

of 7 July 2022

At its session on 7 July 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. Annex XII shall be amended in alphabetical order to include the active ingredient abrocitinib as follows:

Abrocitinib

Resolution of: 7 July 2022
Entry into force on: 7 July 2022
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 9 December 2021):

Cibinqo is indicated for the treatment of moderate-to-severe atopic dermatitis in adults who are candidates for systemic therapy.

Therapeutic indication of the resolution (resolution of 7 July 2022):

See therapeutic indication according to marketing authorisation.

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

Adults with moderate-to-severe atopic dermatitis who are candidates for a continuous systemic therapy

Appropriate comparator therapy:

Dupilumab (in combination with topical glucocorticoids and/or topical calcineurin inhibitors if required)

Extent and probability of the additional benefit of abrocitinib compared to dupilumab:

Hint for a considerable additional benefit.

Study results according to endpoints:[1]

Adults with moderate-to-severe atopic dermatitis who are candidates for a continuous systemic therapy

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	No relevant differences for the benefit assessment.
Morbidity	↑↑	Advantages in remission (EASI 100; SCORAD 100), SCORAD 90 and patient-reported symptomatology.
Health-related quality of life	↔	No relevant differences for the benefit assessment.
Side effects	↔	No relevant differences for the benefit assessment. Advantages and disadvantages in the specific AEs, in detail.
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		

JADE DARE study: RCT, direct comparison of abrocitinib 200 mg versus dupilumab in adults over 26 weeks

Mortality

Endpoint	Abrocitinib		Dupilumab		Abrocitinib vs Dupilumab
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value[a]
Overall mortality[b]	362	2 (0.6[c])	365	0 (0)	-

[1] Data from the dossier assessment of the IQWiG (A22-06) and from the addendum (A22-60), unless otherwise indicated.

Morbidity

Endpoint Characteristic Subgroup	Abrocitinib		Dupilumab		Abrocitinib vs Dupilumab
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value[a]
Symptomatology[d,e]					
Remission (EASI 100)	362	79 (21.8)	365	50 (13.7[c])	1.59 [1.15; 2.20]; 0.005
Remission (SCORAD 100)	362	37 (10.2)	365	22 (6.0)	1.70 [1.02; 2.82]; 0.041
Response (EASI 90)	362	190 (52.5)	365	172 (47.1)	1.11 [0.96; 1.29]; 0.147
Response (EASI 75)	362	254 (70.2)	365	261 (71.5)	0.98 [0.89; 1.08]; 0.698
Response (SCORAD 90)	362	80 (22.1)	365	52 (14.2)	1.55 [1.13; 2.13]; 0.007
Response (SCORAD 75)	362	152 (42.0)	365	133 (36.4)	1.15 [0.96; 1.38]; 0.128
Itching (Peak pruritus NRS 0-1)	362	139 (38.4[c])	365	114 (31.2[c])	1.23 [0.99; 1.52]; 0.058[f]
Itching (Peak pruritus NRS, improvement by ≥ 4 points[p])	357	241 (67.5)	364	229 (62.9)	1.07 [0.96; 1.19]; 0.198
Sleep disorders (MOS sleep scale) SPI I (improvement by ≥ 15 points[g])	362	131 (36.2)	363	117 (32.2)	1.12 [0.92; 1.37]; 0.264
Sleep disorders (MOS sleep scale) SPI II (improvement by ≥ 15 points[g])	362	139 (38.4)	364	140 (38.5)	1.00 [0.83; 1.20]; 0.972
Pain (skin pain NRS, improvement by ≥ 4 points[p])	316	205 (64.9)	325	202 (62.2)	1.04 [0.93; 1.17]; 0.475
Patient-reported symptomatology (POEM 0-2)	358	106 (29.6)	363	69 (19.0)	1.56 [1.19; 2.03]; 0.001
Patient-reported symptomatology (POEM 0)	359	49 (13.6)	365	26 (7.1)	1.92 [1.22; 3.01]; 0.005

Endpoint Characteristic Subgroup	Abrocitinib		Dupilumab		Abrocitinib vs Dupilumab
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value[a]
Patient-reported symptomatology (POEM 0[e]) Age					
< 40 years	227	22 (9.7)	247	19 (7.7)	1.26 [0.70; 2.27]; 0.514[v]
≥ 40 years	132	27 (20.5)	118	7 (5.9)	3.45 [1.56; 7.62]; < 0.001[v]
Total				Interaction:	0.009[w]

Endpoint	Abrocitinib			Dupilumab			Abrocitinib vs dupilumab
	N[l]	Values at the start of the study MV (SD)	Change at week 26 MV[m] (SE)	N[l]	Values at the start of the study MV (SD)	Change at week 26 MV[m] (SE)	MD [95% CI]; p value[m]
Symptomatology							
Health status (EQ-5D VAS[o])	362	68.4 (19.5)	13.48 (0.76)	364	67.7 (18.3)	14.30 (0.75)	-0.82 [-2.91; 1.28]; 0.445

Health-related quality of life

Endpoint	Abrocitinib		Dupilumab		Abrocitinib vs Dupilumab
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value[a]
DLQI 0-1[d,e]	358	137 (38.3)	361	114 (31.6)	1.21 [0.99; 1.48]; 0.060

Side effects

Endpoint[d]	Abrocitinib		Dupilumab		Abrocitinib vs Dupilumab
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value[a]
AEs[h] (presented additionally)	362	268 (74.0)	365	239 (65.5)	-
SAEs[h]	362	6 (1.7)	365	6 (1.6)	1.01 [0.33; 3.10]; 0.989
Discontinuation due to AEs[h,i]	362	9 (2.5)	365	9 (2.5)	1.01 [0.40; 2.51]; 0.986
Infections (SOC, AEs)[j]	362	110 (30.4)	365	109 (29.9)	1.02 [0.82; 1.27]; 0.916[k]
Serious infections (SOC, SAEs)[j]	362	3 (0.8)	365	0 (0)	-
Conjunctivitis (PT, AEs)	362	8 (2.2)	365	35 (9.6)	0.23 [0.11; 0.49]; < 0.001
Eye disorders (SOC, AEs)	362	17 (4.7)	365	28 (7.7)	0.61 [0.34; 1.10]; 0.103[k]
Nervous system disorders (SOC, AEs)	362	70 (19.3)	365	33 (9.0)	2.14 [1.45; 3.15] < 0.001[k]
Nausea (PT, AEs)	362	70 (19.3)	365	8 (2.2)	8.82 [4.31; 18.07]; < 0.001
Acne (PT, AEs)	362	46 (12.7)	365	10 (2.7)	4.64 [2.38; 9.05]; < 0.001

a. Unless otherwise stated, endpoints of the morbidity and health-related quality of life categories: Cochran-Mantel-Haenszel method, stratified by disease severity at the start of the study (IGA = 3 vs IGA = 4); endpoints of the side effects category: asymptotic, unstratified
b. Fatalities were recorded as part of AEs.
c. IQWiG calculation
d. Morbidity and health-related quality of life: Evaluation at week 26; side effects: Evaluation up to week 26 and plus 28 days if follow-up phase has been completed
e. Values after therapy discontinuation or after rescue therapy as well as missing values were replaced by means of non-response imputation.
f. IQWiG calculation of RR, 95% CI and p value; asymptotic, with variance correction according to the data-set resizing approach

g. An improvement is defined as a decrease of ≥ 15 points compared to the start of the study with a scale range of 0 to 100. Lower (decreasing) values mean an improvement of symptomatology.
h. Includes events of the underlying disease (PT atopic dermatitis); in Annex 4-G of the pharmaceutical company's dossier, the results on AEs and SAEs are presented without disease progression events in each case. However, no data was available on the events that were not taken into account.
i. In module 5 of the pharmaceutical company's dossier, in addition to the information on discontinuation due to AEs, there is also information on study discontinuation due to AEs presumably including death (12 [3.3%] vs 9 [2.5%] patients) as well as on therapy discontinuation due to AEs with simultaneous study continuation (0 [0%] vs 1 [0.3%] patients). Thus, 12 [3.3%] vs 10 [2.7%] therapy discontinuations due to AEs would be expected.
j. All AEs of the MedDRA SOC Infections and infestations are used for the assessment of infections, all SAEs are used for the assessment of serious infections
k. IQWiG calculation of RR, 95% CI (asymptotic) and p value (unconditional exact test, CSZ method)).
l. Number of patients who were taken into account in the evaluation for calculating the effect estimate; the values at start of study can be based on other patient numbers.
m. MV and SE (per treatment group at week 26) as well as MD, 95% CI and p value (group comparison): MMRM with the factors treatment and visit, the interaction term visit x treatment as well as the respective value at the start of the study and disease severity at the start of the study as covariates; effect represents the difference between the treatment groups of the changes since the start of the study at week 26; values after therapy discontinuation and after rescue therapy were considered missing values
n. Lower (decreasing) values mean better symptomatology; negative effects (intervention minus control) mean an advantage for the intervention (scale range 0 to 10).
o. Higher (increasing) values mean better symptomatology; positive effects (intervention minus control) mean an advantage for the intervention (scale range 0 to 100).
p. An improvement is defined as a decrease of ≥ 4 points compared to the start of the study with a scale range of 0 to 10. Lower (decreasing) values mean an improvement of symptomatology. Patients with a baseline ≥ 4 points were included in the evaluation.
q. Patients with a baseline ≥ 1 point were included in the evaluation
v. Unstratified
w. Logistic regression model with corresponding interaction term; unstratified

DLQI: Dermatology Life Quality Index; EASI: Eczema Area and Severity Index; IGA: Investigator Global Assessment; CI: Confidence interval; MD: Mean difference; MedDRA: Medical Dictionary for Regulatory Activities; MMRM: Mixed model for repeated measures; MOS: Medical Outcome Study; MV: mean Value; n: number of patients with (at least 1) event; N: number of patients evaluated; NRS: Numerical Rating Scale; POEM: Patient-Oriented Eczema Measure;; PT: preferred term; RCT: randomised controlled study; RR: relative risk; SD: standard deviation; SE: standard error; SOC: system organ class; SPI: sleep problem index; SAE: serious adverse event; AE: adverse event; VAS: visual analogue scale

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

Adults with moderate-to-severe atopic dermatitis who are candidates for a continuous systemic therapy

approx. 52,000 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 Cibinqo (active ingredient: abrocitinib) at the following publicly accessible link (last access: 24 June 2022):

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

Treatment with abrocitinib should only be initiated and monitored by specialists experienced in treating atopic dermatitis.

In patients in whom no therapeutic benefit can be demonstrated after 24 weeks of treatment, discontinuation of treatment should be considered.

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 abrocitinib, particularly severe and opportunistic infections including tuberculosis and herpes zoster. It also points out the need for an effective contraceptive method.

Furthermore, against the background of the ongoing EMA PRAC procedure, the safety profile of the JAK inhibitors such as abrocitinib cannot be conclusively assessed at present.

4. Treatment costs

Annual treatment costs:

Adults with moderate-to-severe atopic dermatitis who are candidates for a continuous systemic therapy

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Abrocitinib Additionally required SHI services Total:	€ 16,266.85 - € 20,277.60 € 180.85 € 16,447.70 - € 20,458.45
Appropriate comparator therapy:	
Dupilumab	€ 17,796.15

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 15 June 2022)

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 7 July 2022.

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

Berlin, 7 July 2022

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

Prof. Hecken