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 Pemigatinib (cholangiocarcinoma with FGFR2 fusion or FGFR2 rearrangement, after at least one prior therapy)

of 7 October 2021

At its session on 7 October 2021, 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 DD. 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 pemigatinib as follows:

Courtesy translation – only the German version is legally binding.

Pemigatinib

Resolution of: 7 October 2021
Entry into force on: 7 October 2021
BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 26 March 2021):

Pemazyre monotherapy is indicated for the treatment of adults with locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or rearrangement that have progressed after at least one prior line of systemic therapy.

Therapeutic indication of the resolution (resolution of 7 October 2021):

see therapeutic indication according to marketing authorisation

1. Extent of the additional benefit and significance of the evidence

Pemigatinib is approved as a medicinal product for the treatment of rare diseases in accordance with Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999 on orphan drugs. In accordance with section 35a, paragraph 1, sentence 11, 1st half of the sentence German Social Code, Book Five (SGB V), the additional medical benefit is considered to be proven through the grant of the marketing authorisation.

The Federal Joint Committee (G-BA) determines the extent of the additional benefit for the number of patients and patient groups for which there is a therapeutically significant additional benefit in accordance with Chapter 5, Section 12, paragraph 1, number 1, sentence 2 of its Rules of Procedure (VerfO) in conjunction with Section 5, paragraph 8 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), indicating the significance of the evidence. This quantification of the additional benefit is based on the criteria laid out in Chapter 5, Section 5, paragraph 7, numbers 1 to 4 of the Rules of Procedure (VerfO).

<u>Adults with locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or rearrangement that have progressed after at least one prior line of systemic therapy</u>

Extent of the additional benefit and significance of the evidence of pemigatinib:

In conclusion, there is a hint for a non-quantifiable additional benefit since the scientific data does not allow quantification.

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Study results according to endpoints:[1]

Adults with locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or rearrangement that have progressed after at least one prior line of systemic therapy

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.a.	not assessable
Morbidity	n.a.	not assessable
Health-related quality of life	n.a.	not assessable
Side effects	n.a.	not assessable
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		

FIGHT-202 study: open-label, uncontrolled, multicentre Phase 2 study

Data cut-off of 7 April 2020: Mortality and safety

Data cut-off of 22 March 2019: Endpoints of the PRO instruments used

Mortality

Endpoint	**Cohort A[a] of the FIGHT-202 study Data cut-off of 07April 2020 Efficacy Evaluable Population n = 108**
	Median time to event in months [95 %- CI] *Patients n (%)*
Overall survival	17.5 [14.4; 22.9] *63 (58.3)*

[1]Data from the dossier assessment of the G-BA (published on the 15 Juli 2021), unless otherwise indicated.

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Morbidity

Endpoint	Cohort A of the FIGHT-202 study Data cut-off of 07 April 2020 Efficacy Evaluable Population n = 108
	Median time to event in months [95 %- CI] *Patients n (%)*
Progression-free survival (PFS)[b]	7.03 [6.08; 10.48] *81 (75)*

Endpoint	Cohort A[a] of the FIGHT-202 study Data cut-off 22 March 2019 Efficacy Evaluable Population[c]				
EORTC-QLQ-C30 symptom scale/item					
	Baseline	Cycle 3 day 1		Cycle 6 day 1	
	Absolute score N (%) MV (SD) Median (min; max)	Absolute score N (%) MV (SD) Median (min; max)	Change from baseline N (%) MV (SD) Median (min; max)	Absolute score N (%) MV (SD) Median (min; max)	Change from baseline N (%) MV (SD) Median (min; max)
Fatigue	103 (96.3) 32.8 (24.5) 33.3 (0; 100)	92 (86.0) 34.3 (22.2) 33.3 (0; 100)	89 (83.2) 2.3 (22.4) 0 (-67; 67)	77 (72.0) 37.1 (25.9) 33.3 (0; 100)	75 (70.1) 6.7 (23.9) 11.1 (-78; 56)
Nausea and vomiting	102 (95.3) 9.8 (15.6) 0 (0; 67)	92 (86.0) 10.9 (19.5) 0 (0; 100)	88 (82.2) 2.1 (20.5) 0 (-33; 100)	77 (72.0) 10.4 (15.3) 0 (0; 67)	74 (69.2) 1.6 (16.4) 0 (-33; 50)
Pain	103 (96.3) 25.2 (24.0) 16.7 (0; 100)	90 (84.1) 23.5 (23.8) 16.7 (0; 100)	87 (81.3) -1.5 (25.1) 0 (-83; 67)	76 (71.0) 30.3 (30.3) 33.3 (0; 100)	74 (69.2) 8.6 (27.2) 0 (-67; 100)
Dyspnoea	103 (96.3) 21.4 (25.9) 0 (0; 100)	91 (85.0) 15.4 (24.0) 0 (0; 100)	88 (82.2) -5.7 (19.1) 0 (-67; 33)	77 (72.0) 17.3 (25.7) 0 (0; 100)	75 (70.1) -4.9 (21.7) 0 (-67; 33)
Loss of appetite	102 (95.3) 21.2 (26.9) 0 (0; 100)	92 (86.0) 24.6 (31.6) 0 (0; 100)	88 (82.2) 4.2 (37.1) 0 (-100; 100)	77 (72.0) 29.0 (28.8) 33.3 (0; 100)	74 (69.2) 9.0 (33.2) 0 (-100; 100)
Insomnia	102 (95.3) 24.2 (27.4) 33.3 (0; 100)	92 (86.0) 22.1 (25.8) 33.3 (0; 100)	88 (82.2) -1.1 (24.0) 0.0 (-67; 67)	77 (72.0) 26.8 (30.1) 33.3 (0; 100)	74 (69.2) 5.0 (31.1) 0.0 (-67; 100)

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Endpoint	Cohort A[a] of the FIGHT-202 study Data cut-off 22 March 2019 Efficacy Evaluable Population[c]				
Constipation	103 (96.3) 18.4 (27.9) 0 (0; 100)	92 (86.0) 22.5 (30.1) 0 (0; 100)	89 (83.2) 4.1 (33.6) 0 (-100; 100)	77 (72.0) 23.8 (25.9) 33.3 (0; 100)	75 (70.1) 7.6 (26.0) 0 (-67; 100)
Diarrhoea	103 (96.3) 12.0 (20.8) 0 (0; 100)	91 (85.0) 16.1 (25.5) 0 (0; 100)	88 (82.2) 3.0 (22.4) 0 (-33; 67)	77 (72.0) 15.2 (23.3) 0 (0; 100)	75 (70.1) 4.0 (27.4) 0 (-100; 100)

Health-related quality of life

	Cohort A[a] of the FIGHT-202 study Data cut-off 22March 2019 Efficacy Evaluable Population[c]				
Health-specific quality of life					
EORTC QLQ-C30 symptom scale/item					
	Baseline	Cycle 3 day 1		Cycle 6 day 1	
	Absolute score N (%) MV (SD) Median (min; max)	Absolute score N (%) MV (SD) Median (min; max)	Change from baseline N (%) MV (SD) Median (min; max)	Absolute score N (%) MV (SD) Median (min; max)	Change from baseline N (%) MV (SD) Median (min; max)
Physical functioning	103 (96.3) 80.0 (18.6) 86.7 (13; 100)	92 (86.0) 78.1 (19.1) 80 (20; 100)	89 (83.2) -2.7 (16.7) 0.0 (-53; 33)	77 (72.0) 76.6 (19.7) 80 (20; 100)	75 (70.1) -4.0 (16.1) 0.0 (-47; 33)
Role functioning	103 (96.3) 75.1 (25.8) 83.3 (0; 100)	92 (86.0) 77.5 (25.4) 83.3 (0; 100)	89 (83.2) 0.2 (26.9) 0.0 (-67; 67)	76 (71.0) 67.3 (26.9) 66.7 (0; 100)	74 (69.2) -9.0 (25.6) 0.0 (-100; 50)
Emotional functioning	103 (96.3) 78.1 (21.9) 83.3 (17; 100)	91 (85.0) 79.3 (22.2) 83.3 (0; 100)	88 (82.2) 1.8 (17.2) 0.0 (-33; 75)	77 (72.0) 79.8 (22.6) 83.3 (0; 100)	75 (70.1) -0.1 (16.6) 0.0 (-42; 42)
Cognitive functioning	102 (95.3) 86.9 (16.7) 83.3 (17; 100)	91 (85.0) 85.2 (18.8) 83.3 (0; 100)	87 (81.3) -1.9 (17.7) 0.0 (-67; 33)	76 (71.0) 81.4 (19.2) 83.3 (33; 100)	73 (68.2) -5.5 (19.1) 0.0 (-67; 50)
Social functioning	103 (96.3) 77.2 (26.3) 83.3 (0; 100)	90 (84.1) 76.3 (26.4) 83.3 (0; 100)	87 (81.3) -2.1 (25.0) 0.0 (-100; 50)	77 (72.0) 71.6 (28.1) 66.7 (0; 100)	75 (70.1) -8.4 (26.1) 0.0 (-100; 50)
Overall assessment	102 (95.3) 67.3 (19.2) 66.7 (25; 100)	91 (85.0) 65.7 (19.5) 66.7 (0; 100)	87 (81.3) -2.2 (19.9) 0.0 (-50; 50)	76 (71.0) 63.0 (20.2) 66.7 (0; 100)	73 (68.2) -6.4 (19.2) -8.3 (-50; 50)

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	Cohort A[a] of the FIGHT-202 study Data cut-off 22March 2019 Efficacy Evaluable Population[c]		
Disease-specific quality of life			
EORTC QLQ-BIL21 symptom scale/item			
	Baseline	Cycle 3 day 1	
	Absolute score N (%) MV (SD) Median (min; max)	Absolute score N (%) MV (SD) Median (min; max)	Change to Baseline N (%) MV (SD) Median (min; max)
Anxiety	82 (93.2) 42.4 (24.7) 41.7 (0; 100)	70 (79.5) 38.9 (26.1) 33.3 (0; 100)	67 (76.1) -4.3 (16.9) 0.0 (-50; 42)
Drainage	80 (90.9) 3.3 (11.2) 0.0 (0; 67)	63 (71.6) 1.6 (9.3) 0.0 (0; 67)	62 (70.5) -1.6 (11.2) 0.0 (-67; 33)
Food intake	83 (94.3) 17.7 (17.3) 16.7 (0; 67)	70 (79.5) 28.5 (22.9) 25.0 (0; 100)	68 (77.3) 13.4 (26.4) 8.3 (-42; 83)
Icterus	83 (94.3) 6.4 (12.2) 0.0 (0; 67)	70 (79.5) 7.1 (10.2) 0.0 (0; 33)	68 (77.3) 2.5 (10.5) 0.0 (-33; 33)
Pain	83 (94.3) 24.9 (19.5) 25.0 (0; 83)	70 (79.5) 20.2 (18.4) 16.7 (0; 100)	68 (77.3) -4.0 (17.5) 0.0 (-75; 42)
Side-effects	80 (90.9) 28.3 (31.4) 33.3 (0; 100)	69 (78.4) 29.5 (22.5) 33.3 (0; 100)	64 (72.7) 4.7 (33.5) 0.0 (-100; 67)
Fatigue	83 (94.3) 43.0 (30.5) 33.3 (0; 100)	70 (79.5) 38.9 (27.3) 33.3 (0; 100)	68 (77.3) -2.5 (30.3) 0.0 (-78; 78)
Weight loss	82 (93.2) 19.1 (30.1) 0.0 (0; 100)	70 (79.5) 14.3 (26.4) 0.0 (0; 100)	67 (76.1) -4.0 (25.6) 0.0 (-100; 67)

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Side effects

Endpoint	**Cohort A[a] of the FIGHT-202 study, data cut-off 07 April 2020; safety population N=108**
	Patients with event n (%)
Adverse events in total	*108 (100.0)*
Serious adverse events (SAE)	*46 (42.6)*
Severe adverse events (NCI-CTCAE grades 3 and 4)	*72 (66.7)*
AE, which led to the discontinuation of the study medication	*7 (6.5)*
AE with NCI-CTCAE severity grade 3 and 4 with incidence ≥ 5 % **SOC** PT	
Gastrointestinal disorders	*25 (23.1)*
Abdominal pain	*6 (5.6)*
Stomatitis	*9 (8.3)*
General disorders and administration site conditions	*9 (8.3)*
Fatigue	*5 (4.6)*
Diseases of the liver and gall bladder	*11 (10.2)*
Infections and infestations	*15 (13.9)*
Investigations	*14 (13.0)*
Metabolism and nutrition disorders	*22 (20.4)*
Hypophosphatemia	*16 (14.8)*
Musculoskeletal and connective tissue disorders	*10 (9.3)*
Arthralgia	*7 (6.5)*
Respiratory, thoracic and mediastinal disorders	*6 (5.6)*
Skin and subcutaneous tissue disorders	*8 (7.4)*
Hand-foot syndrome	*7 (6.5)*
Vascular disorders	*7 (6.5)*

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Endpoint	Cohort A[a] of the FIGHT-202 study, data cut-off 07 April 2020; safety population N=108	
	Patients with event n (%)	
SAE with an incidence ≥ 5% **SOC** PT		
Gastrointestinal disorders	*12 (11.1)*	
General disorders and administration site conditions	*6 (5.6)*	
Pyrexia	*5 (4.6)*	
Diseases of the liver and gall bladder	*9 (8.3)*	
Cholangitis	*5 (4.6)*	
Infections and infestations	*15 (13.9)*	
Metabolism and nutrition disorders	*8 (7.4)*	
Respiratory, thoracic and mediastinal disorders	*5 (4.6)*	
AE of special clinical interest PT		
	Total *n (%)*	**NCI-CTCAE grades 3 and 4** *n (%)*
AE of special clinical interest	*91 (84.3)*	*20 (18.5)*
Nail toxicity[d]	*60 (55.6)*	*3 (2.8)*
Severe retinal detachments[d]	*5 (4.6)*	*1 (0.9)*
Hyperphosphatemia	*63 (58.3)*	-
Hypophosphatemia	*29 (26.9)*	*16 (14.8)*

[a] Patients with FGFR2 fusion or FGFR2 rearrangement according to central laboratory report
[b] Data from the dossier of the pharmaceutical company Module 4 A, last revised 30 March 2021
[c] Efficacy evaluable population of cohort A includes 107 subjects as of the data cut-off of 22 March 2019
[d] There are discrepancies between the PT set forth in SAP Amendment 1 dated 15 April 2019, and the PT presented in Addendum 2 of the study report. It is unclear which PTs make up the groups of AEs of special interest.

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Endpoint	Cohort A[a] of the FIGHT-202 study, data cut-off 07 April 2020; safety population N=108
	Patients with event *n (%)*
Abbreviations used: EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer, Quality of Life Questionnaire – Core Module; EORTC QLQ-BIL21= European Organisation for Research and Treatment of Cancer, Quality of Life Questionnaire - Cholangiocarcinoma and Gallbladder Cancer Module; FGFR2 = fibroblast growth factor receptor-2; n. d.= no data; CI = confidence interval; MV= mean value; N = number of patients evaluated; n = number of patients with (at least one) event; NCI-CTCAE = National Cancer Institute - Common Terminology Criteria for Adverse Events; PT = preferred term; SAP = statistical analysis plan; SD = standard deviation; SOC = system organ class; SAE = serious adverse event; AE = adverse event	

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

Adults with locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or rearrangement that have progressed after at least one prior line of systemic

35 – 300 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 Pemazyre (active ingredient: pemigatinib) at the following publicly accessible link (last access: 15 September 2021):
https://www.ema.europa.eu/en/documents/product-information/pemazyre-epar-product-information_de.pdf

Treatment with pemigatinib should only be initiated and monitored by specialists in internal medicine, haematology, and oncology, internal medicine and gastroenterology, and specialists participating in the Oncology Agreement experienced in the treatment of adults with cholangiocarcinoma.

This medicinal product was approved under "special conditions". This means that further evidence of the benefit of the medicinal product is anticipated. The European Medicines Agency will evaluate new information on this medicinal product at a minimum once per year and update the product information where necessary.

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4. Treatment costs

Annual treatment costs:

Adults with locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or rearrangement that have progressed after at least one prior line of systemic

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Pemigatinib	€ 156,451.75
additionally required SHI services	patient-individual
Total:	patient-individual

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 September 2021)

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 7 October 2021.

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

Berlin, 7 October 2021

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

Prof. Hecken

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