Gemeinsamer Bundesausschuss

Resolution

of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive (AM-RL)

Annex XII - Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V:

Fedratinib (myelofibrosis)

of 2 September 2021

At its session on 2 September 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 on 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 fedratinib as follows:

Fedratinib

Resolution of: 18.08.2021
Entry into force on: 18.08.2021
BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 8 February 2021):

Inrebic is indicated for the treatment of disease-related splenomegaly or symptoms in adult patients with primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis who are Janus Associated Kinase (JAK) inhibitor naïve or have been treated with ruxolitinib.

Therapeutic indication of the resolution (resolution of 2 September 2021):

see therapeutic indication according to marketing authorisation.

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

Fedratinib 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 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).

(a) <u>adult patients with primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis who are Janus Associated Kinase (JAK) inhibitor naïve, treatment of disease-related splenomegaly or symptoms</u>

Extend of the additional benefit and significance of the evidence of fedratinib:

Hint for a non-quantifiable additional benefit since the scientific data does not allow quantification.

(b) <u>adult patients with primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis who have been treated with Ruxolitinib, treatment of disease-related splenomegaly or symptoms</u>

Extend of the additional benefit and significance of the evidence of fedratinib:

Hint for a non-quantifiable additional benefit since the scientific data does not allow quantification.

Study results according to endpoints:[1]

(a) adult patients with primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis who are Janus Associated Kinase (JAK) inhibitor naïve, treatment of disease-related splenomegaly or symptoms

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	no statistically significant or relevant difference
Morbidity	↑	Advantage in spleen response and symptom response
Health-related quality of life	∅	There are no usable data for the benefit assessment.
Side effects	↓ ↓	Disadvantage in severe AE CTCAE grade ≥ 3, advantage and disadvantage in AE of special interest
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		

[1] Data from the dossier assessment of the G-BA (published on 15. Juni 2021), and from the amendment to the dossier assessment from 13 August 2021 unless otherwise indicated.

JAKARTA study: RCT; fedratinib vs placebo, patients not pre-treated with JAK inhibitor

Mortality

Endpoint	**Fedratinib 400 mg**		**placebo**		Fedratinib vs placebo
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	RR [95 % CI] p-value
Overall survival					
Safety population - additional analyses[a] (at the end of treatment cycle 6)	96	*7 (7.3 %)*	95	*12 (12.6 %)*	0.58 [0.24; 1.40] 0.2188

Morbidity

	N	*Patients with event n (%) without event n (%) with imputed values (non responder) n (%)*	N	*Patients with event n (%) without event n (%) with imputed values (non responder) n (%)*	RR [95 % CI] p-value
Spleen response by MRI / CT (≥ 35%) at the end of treatment cycle 6					
with reconfirmation of a spleen response rate ≥ 35% 4 weeks later					
	96	*35 (36.5)* *40 (41.7)* *21 (21.9)*	96	*1 (1.0)* *57 (59.4)* *38 (39.6)*	35.00 [4.89; 250.36] < 0.0001
without reconfirmation of a spleen response rate ≥ 35% 4 weeks later					
	96	*45 (46.9)* *30 (31.3)* *21 (21.9)*	96	*1 (1.0)* *57 (59.4)* *38 (39.6)*	45.00 [6.33; 319.89] < 0.0001
	~~N~~	*Patients with event n (%)* [95 % CI]	N	*Patients with event n (%)* [95 % CI]	RR [95 % CI] p-value
Symptom response using modified MFSAF					
Symptom response rate (≥ 50% reduction in TSS) at the end of cycle 6[b]					
	89	36 (40.4) [30.2; 51.4]	81	7 (8.6) [30.2; 51.4]	4.68 [2.21; 9.92] < 0.0001
	N	Median time to event in weeks	N	Median time to event in weeks	HR [95 % CI] p-value

		[95 % CI] *Patients with event n (%)*		[95 % CI] *Patients with event n (%)*	
Symptom response using modified MFSAF[c]					
Time to improvement of ≥ 50 % compared to baseline					
Total symptom score (TSS)[d]	91	11.9 [8.0; 20.0] *56 (61.5)*	85	n.c. *22 (25.9)*	2.760 [1.678; 4.538] 0.0001
Night sweats	91	4.1 [4.0; 7.6] *60 (65.9)*	85	12.6 [8.0; n.c.] *30 (35.3)*	2.225 [1.428; 3.468] 0.0004
Itching	91	8.0 [7.9; 20.0] *44 (48.4)*	85	n.c. [12.0; n.c.] *20 (23.5)*	1.797 [1.058; 3.052] 0.0301
Abdominal disorders	91	8.1 [8.0; 16.1] *52 (57.1)*	85	n.c. [18.0; n.c.] *25 (29.4)*	1.980 [1.227; 3.195] 0.0051
Fullness	91	11.9 [8.0; 12.3] *53 (58.2)*	85	n.c. [12.0; n.c.] *24 (28.2)*	2.240 [1.377; 3.645] 0.0012
Pain under the ribs on the left side	91	8.0 [4.3; 12.0] *50 (54.9)*	85	24.0 [8.0; n.c.] *24 (28.2)*	1.854 [1.137; 3.023] 0.0133
Muscle / bone pain	91	24.0 [8.1; n.c.] *37 (40.7)*	85	n.c. *21 (24.7)*	1.682 [0.978; 2.893] 0.0602
Health status - EQ 5D-VAS[e]					
Time to improvement by ≥ 15 %[f]					
	91	26.4 [25.0; 26.4] *17 (18.7)*	88	24.9 [24.3; n.c.] *12 (13.6)*	0.866 [0.401; 1.870] 0.7148

Health-related quality of life

No data collected.

Side effects

Endpoint	Fedratinib (400 mg)		placebo		Fedratinib vs placebo
	N	Median in days [95 % CI] *Patients with event n (%)*	N	Median in days [95 % CI] *Patients with event n (%)*	HR [95 % CI] p-value
Adverse events in total					
	96	- *95 (99.0)*	95	- *89 (93.7)*	-
Serious adverse events (SAE)					
	96	n.c. *20 (20.8)*		n.c. *22 (23.2)*	0.84 [0.46; 1.54]; 0.5698
Severe adverse events (CTCAE grade ≥ 3)					
	96	115.0 [60.00; n.c.] *52 (54.2)*	95	n.c. [168.00; n.c.] *35 (36.8)*	1.67 [1.09; 2.57] 0.0178
Therapy discontinuation due to adverse events					
	96	n.c. *13 (13.5)*	95	n.c. *8 (8.4)*	1.41 [0.58; 3.42] 0.4511
Serious AEs with incidence ≥ 5% by system organ class and preferred term in either treatment group up to cycle 6 in the JAKARTA study; safety population **SOC** PT					
General disorders and administration site conditions	96	n.c. 5 (5.2)	95	n.c. 4 (4.2)	1.17 [0.31; 4.35] 0.8166
Blood and lymphatic system disorders	96	n.c. 33 (34.4)	95	n.c. 14 (14.7)	2.45 [1.31; 4.58] 0.0037
Anaemia	96	n.c. 29 (30.2)	95	n.c. 7 (7.4)	4.30 [1.88; 9.82] 0.0002
Thrombocytopenia	96	n.c. 5 (5.2)	95	n.c. 6 (6.3)	0.68 [0.20; 2.27] 0.5272
Gastrointestinal disorders	96	n.c. 8 (8.3)	95	n.c. 5 (5.3)	1.51 [0.49; 4.61] 0.4699
Diarrhoea	96	n.c. 5 (5.2)	95	n.c. 0 (0.0)	2,69E7 [0.00; n. c.] 0.0338
Heart diseases	96	n.c. 9 (9.4)	95	n.c. 6 (6.3)	1.40 [0.50; 3.92] 0.5256

Cardiac insufficiency	96	n.c. 6 (6.3)	95	n.c. 2 (2.1)	2.76 [0.56; 13.71] 0.1945
Infections and infestations	96	n.c. 1 (1.0)	95	n.c. 6 (6.3)	0.14 [0.02; 1.20] 0.0369
Metabolic and nutritional disorders	96	n.c. 4 (4.2)	95	n.c. 5 (5.3)	0.75 [0.20; 2.81] 0.6722
Investigations	96	n.c. 7 (7.3)	95	n.c. 1 (1.1)	6.76 [0.83; 54.98] 0.0384
SAE with incidence ≥ 5% by system organ class and preferred term in either treatment group through cycle 6 in the JAKARTA study ; safety population					
Gastrointestinal disorders	96	n.c. 3 (3.1)	95	n.c. 5 (5.3)	0.52 [0.12; 2.17] 0.3586
Heart diseases	96	n.c. 9 (9.4)	95	n.c. 5 (5.3)	1.62 [0.54; 4.84] 0.3828
Cardiac insufficiency	96	n.c. 5 (5.2)	95	n.c. 3 (3.2)	1.54 [0.37; 6.45] 0.5521
Infections and infestations	96	n.c. 3 (3.1)	95	n.c. 5 (5.3)	0.54 [0.13; 2.25] 0.3876
AE of special interest up to cycle 6 in the JAKARTA study; safety population					
	N	Median in days / subjects with event	N	Median in days / subjects with event	HR [95 % CI] p-value
Time to onset of first potential Wernicke's encephalopathy					
Total Serious Severe (CTCAE grade ≥ 3)	96	n.c./10 (10.4) n.c./0 (0.0) n.c./1 (1.0)	95	4 (4.2) 0 (0.0) 0 (0.0)	2.39 [0.75; 7.63] 0.1288 n.c. 2,93E7 [0,00; n. c.] 0.3198
Time to first bleeding (SMQ bleeding, narrow definition)					
Total	96	n.c./0	95	n.c./0	n.c.
Time to first bleeding (SMQ bleeding, broad definition)					
Total Serious Severe (CTCAE grade ≥ 3)	96	n.c./1 (1.0) n.c./0 (0.0) n.c./1 (1.0)	95	n.c./0 (0) n.c./0 (0) n.c./0 (0)	2,9E7 [0,00; n. c.] 0.3224 n.c. 2,9E7 [0,00; n. c.] 0.3224
Time to onset of first cardiac insufficiency/cardiomyopathy					
Total Serious	96	n.c./21 (21.9) n.c./9 (9.4) n.c./8 (8.3)	95	n.c./18 (18.9) n.c./8 (8.4) n.c./8 (8.4)	1.11 [0.59; 2.08] 0.7519 1.00 [0.38; 2.59] 0.9948

Severe (CTCAE grade ≥ 3)					0.90 [0.34; 2.39] 0.8290
Time until the appearance of the first anaemia					
Total (CTCAE grade 3 or 4) Serious	96	n.c./30 (31.2) n.c./2 (2.1)	95	n.c./7 (7.4) n.c./1 (1.1)	4.48 [1.97; 10.21] < 0.0001 1.97 [0.18; 21.74] 0.5720
Time to first thrombocytopenia, CTCAE grade 3 or 4					
Total (CTCAE grade 3 or 4) Serious	96	n.c./1 (1.0) n.c./0 (0.0)	95	n.c./3 (3.2) n.c./3 (3.2)	0.31 [0.03; 2.98] 0.2831 0.00 [0.00; n. a.] 0.0679
Time to first elevation of ALT, AST or bilirubin in the blood					
Total (CTCAE grade 3 or 4) Serious	96	n.c./1 (1.0) n.c./0 (0.0)	95	n.c./3 (3.2) n.c./3 (3.2)	0.31 [0.03; 2.98] 0.2831 0.00 [0.00; n. a.] 0.0679
Time to first hyperamylasaemia or hyperlipasemia, CTCAE grade 3 or 4					
Total (grade 3 or 4) Serious	96	n.c./3 (3.1) n.c./1 (1.0)	95	n.c./1 (1.1) n.c./0 (0.0)	2.96 [0.31; 28.44] 0.3243 2,93E7 [0,00; n. c.] 0.3198
Time to first appearance of secondary malignancy					
Total Serious Severe (CTCAE grade ≥ 3)	96	n.c. / 0 (0) n.c. / 0 (0) n.c. / 0 (0)	95	n.c./ 5 (5.3) n.c./ 3 (3.2) n.c./ 3 (3.2)	0.00 [0.00; n. a.] 0.0154 0.00 [0.00; n. a.] 0.0611 0.00 [0.00; n. a.] 0.0514

[a] Due to the early study discontinuation and the associated short follow-up, no a priori defined analyses were performed according to the information provided by the pharmaceutical company.
[b] Symptom analysis population
[c] The evaluation was based on the ITT population using the Modified MFSAF HRQoL-evaluable population, defined as all patients in the ITT population for whom a baseline value was available (at least 5 of the 7 daily values in a week).
[d] The TSS is defined as the average of the daily total score of the six items of the MFSAF when at least 5 of the 7 daily scores were available in a week: Night sweats, itching, abdominal discomfort, early satiety, pain under the ribs on the left side, and bone or muscle pain.
[e] Evaluation was based on the ITT population using the EQ-5D-VAS HRQoL-evaluable population, defined as all subjects in the ITT population for whom a baseline value was available.
[f] Values between 0 (worst possible health status) and 100 (best possible health status).

Abbreviations used: CTCAE = Common Terminology Criteria for Adverse Events; HR = hazard ratio; CI = confidence interval; MFSAF = Myelofibrosis Symptom Assessment Form; N = number of patients evaluated; n = number of patients with (at least one) event; n. c. = not calculable; n. a. = not achieved; PT = preferred term; RR = relative risk; SOC = system organ class; TSS = total symptom score vs = versus

(b) adult patients with primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis who have been treated with Ruxolitinib, treatment of disease-related splenomegaly or symptoms

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		

JAKARTA2: single-arm phase II study, patients after treatment with ruxolitinib

Mortality

Endpoint	Fedratinib	
	N	*Patients with event n (%)* [95% CI]
Overall survival		
Safety population	97	4 (4.1 %) [1.12; 10.2]

Morbidity

	N	Fedratinib
Spleen response by MRI / CT (≥ 35%) at the end of treatment cycle 6		
Spleen response (≥ 35%) according to MRI/CT at the end of treatment cycle 6 (incl. subjects with dose increase non-compliant with marketing authorisation)		
Patients with event n (%) [95 % CI]	97	*30 (30.9)* [21.9, 41.1]
Spleen response (≥ 35%) according to MRI/CT at the end of treatment cycle 6		

(Imputation: NRI of subjects with dose increase non-compliant with marketing authorisation)		
Patients with event n (%) [95 % CI] *without event n (%)* *with imputed values (non responder) n (%)*	97	*20 (20.6)* [13.1; 30.0] *10 (10.3)* *67 (69.1)*
	N	*Patients with event n (%)* [95% CI]
Symptom response using modified MFSAF[a]		
Symptom response (≥ 50% reduction in TSS)) using modified MFSAF at the end of treatment cycle 6		
MFSAF analysis population	89	24 (26.7) [17.9; 37]
	N	Median time to event in weeks [95 % CI] *Patients with event n (%)*
Symptom response using modified MFSAF[a]		
Time to improvement of ≥ 50 % compared to baseline		
Total symptom score (TSS)[b]	89	23.7 [8.4; n.c.] *40 (44.4)*
Night sweats	89	4.3 [4.0; 8.0] *55 (61.1)*
Itching	89	8.0 [7.7; n.c.] *33 (36.7)*
Abdominal disorders	89	15.9 [8.1; 23.9] *45 (50.0)*
Fullness	89	9.6 [8.0; 16.0] *49 (54.4)*
Pain under the ribs on the left side	89	7.7 [4.1; 8.0] *54 (60.0)*
Muscle / bone pain	89	16.0 [8.1; n.c.] *39 (43.3)*
EORTC QLQ-C30 symptom scales		
Time to improvement in health status by ≥ 10 points		

Fatigue	93	4.4 [4.1; 7.6] *70 (75.3)*
Nausea and vomiting	93	48.1 [48.1; n. a.] *27 (29.0)*
Pain	93	8.1 [4.4; 11.7] *54 (58.1)*
Dyspnoea	93	12.0 [5.4; 24.1] *48 (51.6)*
Insomnia	93	8.1 [4.7; 18.3] *49 (52.7)*
Appetite loss	93	5.4 [4.3; 12.1] *53 (57.0)*
Constipation	93	n. a. [27.1; n. a.] *25 (26.9)*
Diarrhoea	93	n.c. *24 (25.8)*

Health-related quality of life

EORTC QLQ-C30 – functional scales		
Time to improvement in health status by ≥ 10 points		
Global health status	93	8.1 [4.4; 48.1] *48 (51.6)*
Physical functioning	93	12.0 [5.4; 23.9] *48 (51.6)*
Role functioning	93	8.1 [4.3; 12.0] *55 (59.1)*
Emotional functioning	93	12.6 [8.0; n. a.] *44 (47.3)*
Cognitive functioning	93	16.0 [8.1; n. a.] *42 (45.2)*
Social functioning	93	16.1 [8.1; 36.1] *45 (48.4)*

Side effects

Endpoint	Fedratinib	
	N	Patients with event n (%) [95% CI]
Adverse events in total		
	97	95 (97.9) [92.7; 99.7]
Serious adverse events (SAE)		
	97	26 (26.8) [18.3; 36.8]
Severe adverse events (CTCAE grade ≥ 3)		
	97	59 (60.8) [50.4; 70.6]
Therapy discontinuation due to adverse events		
	97	13 (13.4) [7.3; 21.8]
SAE with incidence ≥ 5% by system organ class and preferred term; safety population **SOC** PT		
Respiratory, thoracic and mediastinal disorders	97	5 (5.2) [1.7; 11.6]
Cardiac disorders	97	5 (5.2) [1.7; 11.6]
Infections and infestations	97	6 (6.2) [2.3; 13.0]
Severe AEs with incidence ≥ 5% by system organ class and preferred term in either treatment group, safety population **SOC** PT		
Respiratory, thoracic and mediastinal disorders	97	5 (5.2) [1.7; 11.6]
Blood and lymphatic system disorders	97	40 (41.2) [31.3; 51.7]
Anaemia	97	31 (32.0) [22.9; 42.2]
Thrombocytopenia	97	19 (19.6) [12.2; 28.9]
Gastrointestinal disorders	97	10 (10.3) [5.1; 18.1]
Cardiac disorders	97	6 (6.2) [2.3; 13.0]
Infections and infestations	97	8 (8.2) [3.6; 15.6]

Metabolism and nutrition disorders	97	8	(8.2) [3.6; 15.6]
Investigations	97	16	(16.5) [9.7; 25.4]
AE of special interest **SOC**			
Potential Wernicke's encephalopathy			
Total Serious Severe (CTCAE grade ≥ 3)	97	13 0 1	13.4 [7.3; 21.8] 0.0 [0.0; 3.7] 1.0 [0.0; 5.6]
SMQ "Bleeding" (narrow definition)			
Total Serious Severe (CTCAE grade ≥ 3)	97	22 4 5	22.7 [14.8; 32.3] 4.1 [1.1; 10.2] 5.2 [1.7; 11.6]
SMQ "Bleeding" (broad definition)			
Total Serious Severe (CTCAE grade ≥ 3)	97	22 4 5	22.7 [14.8; 32.3] 4.1 [1.1; 10.2] 5.2 [1.7; 11.6]
Cardiac insufficiency/cardiomyopathy			
Total Serious Severe (CTCAE grade ≥ 3)	97	11 2 3	11.3 [5.8; 19.4] 2.1 [0.3; 7.3] 3.1 [0.6; 8.8]
Anaemia, CTCAE grade 3 or 4			
Total Serious	97	31 1	32.0 [22.9; 42.2] 1.0 [0.0; 5.6]
Thrombocytopenia, CTCAE grade 3 or 4			
Total Serious	97	21 2	21.6 [13.9; 31.2] 2.1 [0.3; 7.3]
ALT, AST or bilirubin elevated in the blood, CTCAE grade 3 or 4			
Total Serious	97	5 0	5.2 [1.7; 11.6] 0.0 [0.0; 3.7]
Hyperamylasaemia or hyperlipasemia, CTCAE grade 3 or 4			
Total Serious	97	7 0	7.2 [3.0; 14.3] 0.0 [0.0; 3.7]
Secondary malignancies			
Total Serious Severe (CTCAE grade ≥ 3)	97	3 2 3	3.1 [0.6; 8.8] 2.1 [0.3; 7.3] 3.1 [0.6; 8.8]
Overdose with the test medication			
Total Serious Severe (CTCAE grade ≥ 3)	97	1 0 0	1.0 [0.0; 5.6] 0.0 [0.0; 3.7] 0.0 [0.0; 3.7]

[a] The evaluation was based on the ITT population using the modified MFSAF HRQoL-evaluable population, defined as all patients in the ITT population for whom a baseline value was available (at least 5 of the 7 daily values in a week).
[b] The TSS is defined as the average of the daily total score of the six items of the MFSAF when at least 5 of the 7 daily scores were available in a week: Night sweats, itching, abdominal discomfort, early satiety, pain under the ribs on the left side, and bone or muscle pain.

Abbreviations used:

CTCAE = Common Terminology Criteria for Adverse Events; CI = Confidence Interval; MFSAF = Myelofibrosis Symptom Assessment Form; N = Number of patients evaluated; n = Number of patients with (at least one) event; n. c. = not calculable; n. a. = not achieved; PT = Preferred Term; SOC = System Organ Class; TSS = total symptom score; vs = versus

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

(a) adult patients with primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis who are Janus Associated Kinase (JAK) inhibitor naïve, treatment of disease-related splenomegaly or symptoms

approx. 740 to 3,590 patients

(b) adult patients with primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis who have been treated with Ruxolitinib, treatment of disease-related splenomegaly or symptoms

approx. 630 to 1690 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 Inrebic (active ingredient: fedratinib) at the following publicly accessible link (last access: 29 July 2021):
https://www.ema.europa.eu/documents/product-information/inrebic-epar-product-information_de.pdf

Initiation and monitoring of treatment with fedratinib should be performed only by specialists in internal medicine and haematology and oncology experienced in the therapy of patients with myelofibrosis.

In view of the risk of occurrence of (Wernicke's) encephalopathies, patients' thiamine levels should be assessed prior to initiation and at regular intervals during treatment (e.g., monthly for the first 3 months and every 3 months thereafter) and as clinically indicated.

4. Treatment costs

Annual treatment costs:

(a) adult patients with primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis who are Janus Associated Kinase (JAK) inhibitor naïve, treatment of disease-related splenomegaly or symptoms

and

(b) adult patients with primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis who have been treated with Ruxolitinib, treatment of disease-related splenomegaly or symptoms

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Fedratinib	€ 65,005.77
Additionally required SHI services	€ 156.10

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

II. Entry into force

1. **The resolution will enter into force on the day of its publication on the internet on the website of the G-BA on 2 September 2021.**

2. **The period of validity of the resolution is limited in accordance with the following regulation:**

   The respective findings in points 1, 2, 3 and 4 regarding patient group b) "adult patients with primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis who have been treated with ruxolitinib" are limited until 1 March 2025.

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

Berlin, 2 September 2021

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

Prof. Hecken