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) Momelotinib (myelofibrosis)

of 15 August 2024

At its session on 15 August 2024, 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 Momelotinib as follows:

Momelotinib

Resolution of: 15 August 2024
Entry into force on: 15 August 2024
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 25 January 2024):

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

Therapeutic indication of the resolution (resolution of 15 August 2024):

See therapeutic indication according to marketing authorisation.

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

Momelotinib 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 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) Adults with moderate to severe anaemia who have primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis and who are Janus Kinase (JAK) inhibitor naïve; for the treatment of disease-related splenomegaly or symptoms

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

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

b) Adults with moderate to severe anaemia who have primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis and who have been treated with ruxolitinib; for the treatment of disease-related splenomegaly or symptoms

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

Hint for a minor additional benefit

Study results according to endpoints:[1]

a) Adults with moderate to severe anaemia who have primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis and who are Janus Kinase (JAK) inhibitor naïve; for the 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 relevant difference for the benefit assessment.
Morbidity	↔	No relevant differences for the benefit assessment.
Health-related quality of life	↔	No relevant differences for the benefit assessment.
Side effects	↓	Disadvantage in the endpoint of therapy discontinuation due to AE. In detail, advantage in a specific AE.
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		

SIMPLIFY-1 study

- Randomised, double-blind, active-controlled, multicentre phase-III study
- Relevant sub-population: Patients with a haemoglobin (Hb) value < 10 g/dl at baseline

[1] Data from the dossier assessment of the G-BA (published on 15. Mai 2024), and from the amendment to the dossier assessment from 27 June 2024, unless otherwise indicated.

Mortality

Endpoint	Momelotinib		Ruxolitinib		Momelotinib vs ruxolitinib
	N	Median survival time in months [95% CI] Patients with event n (%)[a]	N	Median survival time in months [95% CI] Patients with event n (%)	HR [95% CI] p value
Overall survival					
	86	n.r. [5.68; n.r.] 5 (5.8)	94	n.a. 1 (1.1)	6.04 [0.69; 53.18]; 0.08[b]

Morbidity

Endpoint	Momelotinib		Ruxolitinib		Momelotinib vs ruxolitinib
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value
Spleen response by MRI/CT (≥ 35% at week 24)					
	86	27 (31.4)	94	31 (33.0)	1.00 [0.65; 1.52]; 0.98[c]
Transfusion independence (no RBC transfusions during the 24-week treatment phase) (presented additionally)					
	86	33 (38.4)	94	19 (20.2)	0.47 [0.30; 0.75]; 0.001[c]
Endpoint	**Momelotinib**		**Ruxolitinib**		**Momelotinib vs ruxolitinib**
	N	Median survival time in months [95% CI] Patients with event n (%)	N	Median survival time in months [95% CI] Patients with event n (%)	HR [95% CI] p value
Leukaemic transformation					
	86	n.a. 1 (1.2)	94	n.a. 0	n.a.[b]
Endpoint	**Momelotinib**		**Ruxolitinib**		**Momelotinib vs ruxolitinib**
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value
MPN-SAF[d] - Improvement in symptomatology at week 24 by ≥ 15%					

Early satiety	86	17 (19.8)	94	30 (31.9)	1.67 [1.00; 2.78][c]; 0.05
Abdominal pain	86	16 (18.6)	94	22 (23.4)	1.26 (0.71; 2.23)[e]; 0.43[f]
Abdominal discomfort	86	21 (24.4)	94	23 (24.5)	1.00 (0.60; 1.68)[e]; 0.99[f]
Inactivity	86	13 (15.1)	94	23 (24.5)	1.59 [0.86; 2.92][c]; 0.14
Problems with headaches	86	14 (16.3)	94	13 (13.8)	0.85 [0.42; 1.70][e]; 0.65[f]
Concentration problems	86	14 (16.3)	94	22 (23.4)	1.44 (0.79; 2.63)[e]; 0.24[f]
Dizziness	86	19 (22.1)	94	16 (17.0)	0.82 [0.45; 1.47][c]; 0.50
Numbness in the hands and feet	86	17 (19.8)	94	16 (17.0)	0.86 (0.46; 1.60)[e]; 0.63[f]
Difficulty sleeping	86	24 (27.9)	94	29 (30.9)	1.14 [0.73; 1.79][c]; 0.57
Depression or sad mood	86	13 (15.1)	94	18 (19.1)	1.27 (0.66; 2.43)[e]; 0.48[f]
Problems with sexual desire or function	86	12 (14.0)	94	11 (11.7)	0.84 [0.39; 1.83][c]; 0.67
Cough	86	10 (11.6)	94	19 (20.2)	1.68 [0.85; 3.33][c]; 0.14
Night sweats	86	27 (31.4)	94	33 (35.1)	1.09 [0.72; 1.64][c]; 0.68
Itching	86	15 (17.4)	94	17 (18.1)	1.04 (0.55; 1.95)[e]; 0.91[f]
Bone pain (not joint pain or arthritis)	86	21 (24.4)	94	18 (19.1)	0.85 [0.49; 1.46][c]; 0.56
Fever (> 37.8 degrees Celsius)	86	4 (4.7)	94	6 (6.4)	1.37 [0.40; 4.70][c]; 0.61[e]
Unintentional weight loss last 6 months	86	28 (32.6)	94	28 (29.8)	0.91 [0.59; 1.41][c]; 0.69
Overall quality of life	86	15 (17.4)	94	24 (25.5)	1.49 [0.84; 2.62][c]; 0.17

BFI - Improvement in symptomatology by ≥ 15% at week 24					
BFI total score[g]	86	21 (24.4)	94	26 (27.7)	1.13 [0.69; 1.86][e]; 0.62[f]
BFI fatigue score[h]	86	23 (26.7)	94	23 (24.5)	0.98 [0.60; 1.58][c]; 0.92
BFI interference score[i]	86	20 (23.3)	94	27 (28.7)	1.24 [0.75; 2.03][e]; 0.41[f]
PGIC[j] - Improvement in symptomatology by ≥ 15% at week 24					
	86	55 (64.0)	94	70 (74.5)	1.19 [0.97; 1.44][c]; 0.09
EQ-5D-VAS[k] - Improvement by ≥ 15 points at week 24					
	86	20 (23.3)	94	21 (22.3)	0.96 [0.56; 1.65][e]; 0.88[f]

Health-related quality of life

Endpoint	**Momelotinib**		**Ruxolitinib**		**Momelotinib vs ruxolitinib**
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value
SF-36					
SF-36 – Physical Component Summary (PCS) score[l]	86	13 (15.1)	94	9 (9.6)	0.67 [0.30; 1.48][c]; 0.32
SF-36 – Mental Component Summary (MCS) score[l]	86	6 (7.0)	94	10 (10.6)	1.52 [0.58; 4.02][e]; 0.39[f]

Side effects

Endpoint **MedDRA system organ classes[m]/ preferred terms/ AEs of special interest**	**Momelotinib**		**Ruxolitinib**		Momelotinib vs ruxolitinib
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI][e] p value[f]
Total adverse events (presented additionally)	86	81 (94.2)	94	91 (96.8)	-
Serious adverse events (SAE)	86	26 (30.2)	94	23 (24.5)	1.24 [0.77; 1.99]; 0.39
Severe adverse events (CTCAE grade ≥ 3)	86	42 (48.8)	94	52 (55.3)	0.88 [0.67; 1.17]; 0.39
Therapy discontinuation due to adverse events	86	17 (19.8)	94	5 (5.3)	3.72 [1.43; 9.64]; 0.01
Severe adverse events according to MedDRA (with an incidence ≥ 5% in one study arm and statistically significant difference between the treatment arms; SOC and PT)					
Anaemia, PT	86	10 (11.6)	94	26 (27.7)	0.42 [0.22; 0.82]; 0.01
SAEs according to MedDRA (with an incidence ≥ 5% in one study arm and statistically significant difference between the treatment arms; SOC and PT)					
No significant differences					
Adverse events of special interest (with statistically significant difference between the treatment arms)					
No significant differences					

a. Death during the 24-week treatment phase is defined as death at or after the first dose of study medication until the last dose + 30 days or the first dose of study medication of the open-label treatment phase - 1 day.
b. Cox proportional hazards model with the covariates treatment, transfusion dependence at baseline (yes/ no) and baseline platelet count (< 100 x 10^9/l / ≥ 100 x 10^9/l and ≤ 200 x 10^9/l / > 200 x 10^9/l). p value based on two-tailed stratified log-rank test with the strata variables transfusion dependence (yes/ no) and platelet count (< 100 x 10^9/l / ≥ 100 x 10^9/l and ≤ 200 x 10^9/l / > 200 x 10^9/l).
c. Adjusted inverse relative risk including 95% CI and associated p value; calculated using a modified Poisson regression model with robust sandwich matrix estimators with the covariates treatment, transfusion dependence at baseline (yes/ no) and baseline platelet count (< 100 x 10^9/l / ≥ 100 x 10^9/l and ≤ 200 x 10^9/l / > 200 x 10^9/l).
d. The MPN-SAF is rated on an 11-point scale (0-10) for each item. Higher values in the respective items indicate greater symptom severity.
e. Unadjusted relative risk
f. Calculated with the Z-test.
g. The BFI comprises 9 items, which are answered on a scale from 0 ("no fatigue" or "no limitations") to 10 ("worst perceivable fatigue" or "complete limitation"). If more than 4 items were answered, a total value is calculated from the 9 items.
h. The BFI fatigue score comprises the mean value of 3 items. It is not clear from the documents how many items had to be present for a score to be calculated.
i. The BFI interference score comprises the mean value of 6 items. It is not clear from the documents how many items had to be present for a score to be calculated.

j. The subjects rate the change in their MF symptoms since the start of treatment with the study medication over time using a 7-point scale.
k. Scale from 0 to 100; higher values correspond to better health status.
l. The calculation was based on T-scores of the SF-36. A higher T-score represents a higher quality of life.
m. MedDRA version 22.0, CTCAE version 4.03.

Abbreviations used:
BFI = Brief Fatigue Inventory; CT = computed tomography; CTCAE = Common Terminology Criteria for Adverse Events; EQ-5D-VAS = Visual Analogue Scale of the EuroQoL 5-Dimensions; HR = hazard ratio; CI = confidence interval; MedDRA = Medical Dictionary for Regulatory Activities; MFSAF = Myelofibrosis Symptom Assessment Form; (m) MPN-SAF = (modified) Myeloproliferative Neoplasm Symptom Assessment Form; MRI = magnetic resonance imaging; N = number of patients evaluated; n = number of patients with (at least one) event; n.a. = not applicable; n.c. = not calculable; n.r. = not reached; PGIC = Patient Global Impression of Change; RBC = red blood cell count; RR = relative risk; SF-36 = 36-Item Short-Form Health Survey; SAE = serious adverse event; TD = transfusion dependence; TSS = total symptom score; AE = adverse event

b) Adults with moderate to severe anaemia who have primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis and who have been treated with ruxolitinib; for the 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 relevant difference for the benefit assessment.
Morbidity	↑	Advantage in the endpoint of spleen response in conjunction with an improvement in symptomatology (symptom response (MFSAF), advantage in the endpoint of severity of symptoms (PGIC).
Health-related quality of life	↔	No relevant differences for the benefit assessment.
Side effects	↓	Disadvantage in the endpoint of therapy discontinuation due to AE. In detail, advantages in some specific AEs.

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

SIMPLIFY-2 study

– Randomised, open-label, multicentre phase III study on the efficacy of momelotinib vs BAT (best available therapy)

– Relevant sub-population: Patients with an Hb value < 10 g/dl at baseline

MOMENTUM study

– Randomised, double-blind, phase III study with subsequent open-label phase
– Momelotinib vs danazol

Mortality

Endpoint	**Momelotinib**		**Control**		**Momelotinib vs control**
	N	Median survival time in months [95% CI] Patients with event n (%)	N	Median survival time in months [95% CI] Patients with event n (%)	HR [95% CI] p value
Overall survival					
SIMPLIFY-2	66	n.a. 4 (6.1)[a]	39	n.a. 5 (12.8)	0.46 [0.12; 1.74]; 0.29[b]
MOMENTUM	130	n.a. 15 (11.5)[c]	65	n.a. 13 (20.0)	0.51 [0.24; 1.08]; 0.07[d]

Morbidity

Endpoint	**Momelotinib**		**Control**		**Momelotinib vs control**
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value
Spleen response by MRI/CT (≥ 35% at week 24)					
SIMPLIFY-2	66	6 (9.1)	39	2 (5.1)	0.60 [0.12; 2.93]; 0.53[e]
MOMENTUM	130	29 (22.3)	65	2 (3.1)	0.15 [0.04; 0.58]; 0.01[f]
Transfusion independence (no RBC transfusions during the 24-week treatment phase) (presented additionally)					
SIMPLIFY-2	66	12 (18.2)	39	4 (10.3)	0.47 [0.19; 1.21]; 0.12[e]
MOMENTUM	130	46 (35.4)	65	11 (16.9)	0.48 [0.27; 0.860][g]; 0.02[h]
Endpoint	**Momelotinib**		**Control**		**Momelotinib vs control**

	N	Median survival time in months [95% CI] Patients with event n (%)	N	Median survival time in months [95% CI] Patients with event n (%)	HR [95% CI] p value
Leukaemic transformation					
SIMPLIFY-2	66	2 (2.3)	39	1 (2.6)	1.51 [0.13; 17.97]; 0.67[b]
Endpoint	**Momelotinib**		**Control**		**Momelotinib vs control**
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value Absolute difference (AD)
MPN-SAF2 - Improvement in symptomatology by ≥ 15% at week 24					
SIMPLIFY-2	No usable data available				
MFSAF v4.0[i] - Improvement in symptomatology by ≥ 15% at week 24					
MOMENTUM	130	39 (30.0)	65	9 (13.8)	0.46 [0.24; 0.89][g]; 0.02[h]
BFI - Improvement in symptomatology by ≥ 15% at week 24					
BFI total score SIMPLIFY-2	No usable results				
BFI fatigue score SIMPLIFY-2	No usable results				
BFI interference score SIMPLIFY-2	No usable results				
PGIC[j] - Improvement in symptomatology by ≥ 15% at week 24					
SIMPLIFY-2	66	35 (53.0)	39	10 (25.6)	0.48 [0.27; 0.85][e]; 0.01
EQ-5D-VAS - Improvement by ≥ 15 points					
SIMPLIFY-2	No usable data available				
Endpoint	**Momelotinib**		**Control**		**Momelotinib vs control**
	BL MV (SD)	*Change Week 24 LS MV (SE)[k]*	BL MV (SD)	*Change Week 24 LS MV (SE)[k]*	LS mean difference [95% CI][k]; p value[m]

EQ-5D-VAS[l] at week 12					
MOMENTUM	49.63 (19.96)	*7.07 (2.04)*	53.77 (19.83)	*3.55 (3.10)*	3.53 [-3.58; 10.63]; 0.33
PGIS[n] (severity of symptoms)					
MOMENTUM	3.07 (0.72)	*-0.47 (0.09)*	2.97 (0.68)	*-0.15 (0.12)*	-0.32 [-0.61; -0.03]; 0.03
PGIS[n] (severity of fatigue)					
MOMENTUM	3.27 (0.71)	*-0.48 (0.08)*	3.05 (0.72)	*-0.21 (0.11)*	-0.27 [-0.54; 0.00]; 0.048
EORTC QLQ-C30[o] - Change at week 12					
MOMENTUM					
Appetite loss	42.38 (31.94)	*-15.18 (3.35)*	37.44 (32.01)	*-11.63 (5.02)*	-3.54 [-15.10; 8.01]; 0.55
Constipation	16.41 (23.66)	*-2.23 (2.89)*	13.54 (24.28)	*3.03 (4.36)*	-5.26 [-15.29; 4.77]; 0.30
Diarrhoea	17.31 (26.39)	*-1.45 (2.77)*	21.54 (25.30)	*-9.65 (4.13)*	8.21 [-1.32; 17.74]; 0.09
Dyspnoea	40.57 (31.99)	*-11.56 (2.96)*	42.05 (32.95)	*-5.45 (4.43)*	-6.11 [-16.30; 4.07]; 0.24
Fatigue	63.82 (24.07)	*-12.55 (2.22)*	55.38 (24.81)	*-2.39 (3.32)*	10.17 [-17.83; - 2.50]; 0.01
Insomnia	44.19 (34.15)	*11.29 (3.43)*	37.44 (30.91)	*-4.00 (5.15)*	7.29 [-19.12; 4.54]; 0.23
Nausea and vomiting	11.63 (15.95)	*1.09 (1.67)*	9.23 (16.15)	*-4.42 (2.50)*	-3.33 [-2.43; 9.09]; 0.26
Pain	40.83 (29.83)	*-8.91 (2.70)*	32.56 (25.59)	*1.69 (4.05)*	-10.59 [-19.91; -1.28]; 0.026

Health-related quality of life

Endpoint	**Momelotinib**		**Control**		**Momelotinib vs control**
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value
SF-36					
SF-36 – PCS SIMPLIFY-2	No usable results				

SF-36 – MCS SIMPLIFY-2	No usable results				
Endpoint	**Momelotinib**		**Control**		**Momelotinib vs control**
	BL MV (SD)	*Change Week 24 LS MV (SE)*[k]	BL MV (SD)	*Change Week 24 LS MV (SE)*[k]	LS mean difference [95% CI][k]; p value[m]
EORTC QLQ-C30[p] **- Change at week 12**					
MOMENTUM					
Cognitive functioning	76.61 (22.78)	*4.99 (2.25)*	77.95 (21.47)	*3.88 (3.38)*	1.11 [-6.67; 8.89]; 0.78
Emotional functioning	66.49 (24.22)	*8.14 (2.18)*	70.90 (19.88)	*2.93 (3.27)*	5.21 [-2.32; 12.73]; 0.17
Physical functioning	52.89 (20.38)	*6.53 (1.88)*	56.13 (22.72)	*6.78 (2.82)*	-0.25 [-6.77; 6.27]; 0.94
Role functioning	55.56 (29.85)	*5.06 (2.94)*	59.23 (28.11)	*4.10 (4.41)*	0.95 [-9.20; 11.11]; 0.85
Social functioning	67.31 (29.05)	*8.64 (2.99)*	72.56 (27.86)	*1.65 (4.48)*	6.99 [-3.36; 17.33]; 0.18
Global health status/ quality of life	45.99 (22.37)	*3.06 (2.75)*	48.08 (18.56)	*0.21 (4.13)*	2.85 [-6.65; 12.36]; 0.55

Side effects

Endpoint MedDRA system organ classes/ preferred terms/ AEs of special interest	**Momelotinib**		**Control**		**Momelotinib vs control**
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value
Total adverse events (presented additionally)					
SIMPLIFY-2	66	66 (100)	39	35 (89.7)	-
MOMENTUM	130	122 (93.8)	65	62 (95.4)	-
Serious adverse events (SAE)					
SIMPLIFY-2	66	23 (34.8)	39	9 (23.1)	1.44 [0.74; 2.80][e]; 0.28[e]
MOMENTUM	130	45 (34.6)	65	26 (40.0)	0.87 [0.59; 1.27][g];

Endpoint MedDRA system organ classes/ preferred terms/ AEs of special interest	Momelotinib		Control		Momelotinib vs control
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value
					0.46[h]
Severe adverse events (CTCAE grade ≥ 3)					
SIMPLIFY-2	66	40 (60.6)	39	18 (46.2)	1.35 [0.91; 1.98][e]; 0.13[e]
MOMENTUM	130	70 (53.8)	65	42 (64.6)	0.83 [0.66; 1.06][g]; 0.14[h]
Therapy discontinuation due to adverse events					
SIMPLIFY-2	66	14 (21.2)	39	1 (2.6)	8.66 [1.16; 64.73][e]; 0.04[e]
MOMENTUM	130	23 (17.7)	65	15 (23.1)	0.77 [0.43; 1.37][g]; 0.37[g]
Severe adverse events according to MedDRA (with an incidence ≥ 5% in one study arm and statistically significant difference between the treatment arms; SOC and PT)					
SIMPLIFY-2	No significant differences				
MOMENTUM					
Pneumonia, PT	130	3 (2.3)	65	6 (9.2)	0.25 [0.06; 0.97][g]; 0.045[h]
Renal and urinary disorders, SOC	130	6 (4.6)	65	9 (13.8)	0.33 [0.12; 0.90][g]; 0.03[h]
SAEs according to MedDRA (with an incidence ≥ 5% in one study arm and statistically significant difference between the treatment arms; SOC and PT)					
SIMPLIFY-2	No significant differences				
MOMENTUM					
Pneumonia, PT	130	3 (2.3)	65	6 (9.2)	0.25 [0.06; 0.97][g]; 0.045[h]
Adverse events of special interest (with statistically significant difference between the treatment arms)					
SIMPLIFY-2	No significant differences				

a. Death during the 24-week treatment phase is defined as death at or after the first dose of study medication until the last dose + 30 days or the first dose of study medication of the open-label treatment phase - 1 day.
b. Calculated with the Cox proportional hazards model with the covariates treatment, transfusion dependence at baseline (yes/ no) and TSS at baseline (< 18/ ≥ 18). p value based on two-tailed stratified log-rank test with the strata variables transfusion dependence (yes/ no) and TSS baseline value (< 18/ ≥ 18).
c. Deaths were collected up to week 24 and every 3 months thereafter.

Endpoint MedDRA system organ classes/ preferred terms/ AEs of special interest	Momelotinib		Control		Momelotinib vs control
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value

d. According to the Cox proportional hazards model with the covariates treatment, MFSAF-TSS baseline value (≥ 22/ < 22), palpable spleen length below the left costal arch (≥ 12 cm/ < 12 cm) and the number of transfused erythrocyte units in the 8 weeks prior to randomisation (0/ 1 to 4/ 5+). The p value is based on a two-tailed stratified log-rank test with the strata variables MFSAF-TSS baseline value (≥ 22/ < 22), palpable spleen length below the left costal arch (≥ 12 cm/ < 12 cm) and transfused erythrocyte or whole blood units in the 8 weeks prior to randomisation (0/ 1 to 4/ 5+) at baseline.
e. Adjusted inverse relative risk including 95% CI and associated p value; calculated with a modified Poisson regression model with robust sandwich matrix estimators with the covariates treatment, TD at baseline (yes/ no), TSS at baseline (< 18/ ≥ 18).
f. Adjusted inverse relative risk including 95% CI and associated p value; calculated with a modified Poisson regression model with robust sandwich matrix estimators with the covariates treatment, baseline MFSAF-TSS (< 22/ ≥ 22), palpable spleen length below the left costal arch at baseline (< 12 cm/ ≥ 12 cm) and erythrocyte units at baseline transfused in the 8 weeks prior to randomisation (0/ 1 to 4/ 5+).
g. Unadjusted relative risk
h. Calculated with the Z-test.
i. The MFSAF v4.0 consists of 7 items, which are rated on an 11-point numerical scale from 0 (not present) to 10 (worst perceivable). The MFSAF-TSS is then calculated as the sum of the individual scores of the 7 items and can assume a range of values between 0 and 70, with a higher MFSAF-TSS value indicating more severe symptomatology.
j. In the PGIC, patients rate the change in their myelofibrosis symptoms since the start of treatment with the study medication over time using a 7-point scale.
k. MMRM with the covariates treatment, time point (week), interaction for treatment x time point, baseline MFSAF TSS (< 22/ ≥ 22), palpable spleen length below the left costal arch at baseline (< 12 cm/ ≥ 12 cm) and erythrocyte units at baseline that were transfused in the 8 weeks prior to randomisation (0/ 1 to 4/ 5+).
l. Scale from 0 to 100, higher values there correspond to better health status.
m. p value from the MMRM.
n. The PGIS is assessed using a 4-point scale (1 = "no symptoms"; 2 = "mild symptoms"; 3 = "moderate symptoms"; 4 = "severe symptoms").
o. Scale from 0 to 100; higher values correspond to more severe disease symptomatology.
p. Values from 0 to 100; higher values correspond to better functioning or health or quality of life.

Abbreviations used:

BAT = Best Available Therapy; BFI = Brief Fatigue Inventory; BL = baseline; CT = computed tomography; CTCAE = Common Terminology Criteria for Adverse Events; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer, Quality of Life Questionnaire - Cancer 30EQ-5D-VAS = Visual Analogue Scale of the EuroQoL 5-Dimensions; Hb = haemoglobin; HR = hazard ratio; CI = confidence interval; LS = least squares; MedDRA = Medical Dictionary for Regulatory Activities; MFSAF = Myelofibrosis Symptom Assessment Form; (m) MPN-SAF = (modified) Myeloproliferative Neoplasm Symptom Assessment Form; MMRM = Mixed Model for Repeated Measurement; MRI = magnetic resonance imaging; MV = mean value; N = number of patients evaluated; n = number of patients with (at least one) event; n.a. = not applicable; n.c. = not calculable; n.r. = not reached; PGIC = Patient Global Impression of Change; PGIS = Patient Global Impression of Severity; RBC = red blood cell count; RR = relative risk; SD = standard deviation; SE = standard error; SF-36 = 36-Item Short-Form Health Survey; SAE = serious adverse event; TD = transfusion dependence; TSS = total symptom score; AE = adverse event

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

a) Adults with moderate to severe anaemia who have primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis and who are Janus Kinase (JAK) inhibitor naïve; for the treatment of disease-related splenomegaly or symptoms

Approx. 460 to 1,470 patients

b) Adults with moderate to severe anaemia who have primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis and who have been treated with ruxolitinib; for the treatment of disease-related splenomegaly or symptoms

Approx. 210 to 1,160 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 Omjjara (active ingredient: momelotinib) agreed upon in the context of the marketing authorisation at the following publicly accessible link (last access: 23 July 2024):

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

Treatment with momelotinib should only be initiated and monitored by specialists in internal medicine, haematology and oncology experienced in the treatment of patients with myelofibrosis.

4. Treatment costs

Annual treatment costs:

a) Adults with moderate to severe anaemia who have primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis and who are Janus Kinase (JAK) inhibitor naïve; for the treatment of disease-related splenomegaly or symptoms

and

b) Adults with moderate to severe anaemia who have primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis and who have been treated with ruxolitinib; for the treatment of disease-related splenomegaly or symptoms

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Momelotinib	€ 68,117.15

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 July 2024)

Costs for additionally required SHI services: not applicable

5. Designation of 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 the assessed medicinal product

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 moderate to severe anaemia who have primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis and who are Janus Kinase (JAK) inhibitor naïve; for the treatment of disease-related splenomegaly or symptoms

- No medicinal product with new active ingredients that can be used in a combination therapy and fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

b) Adults with moderate to severe anaemia who have primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis and who have been treated with ruxolitinib; for the treatment of disease-related splenomegaly or symptoms

- No medicinal product with new active ingredients 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.

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 15 August 2024.

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

Berlin, 15 August 2024

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

Prof. Hecken