The day you choose JAKAVI® (ruxolitinib)

is the day you could begin to change their life[1–7]

Polycythaemia vera

For your patients with polycythaemia vera (PV) who are resistant to or intolerant of hydroxyurea.[1,2,7]

NOVARTIS

JAKAVI® ruxolitinib

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Prescribing information can be found on the back cover of this leave piece.
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References: 1. Novartis Pharmaceuticals NI Ltd. JAKAVI® summary of product characteristics. Last accessed May 2024. **2.** Scottish Medicines Consortium. Ruxolitinib (Jakavi). Available at: https://www.scottishmedicines.org.uk/medicines-advice/ruxolitinib-jakavi-full-smc2213/. Last accessed May 2024. **3.** Vannucchi AM, et al. N Engl J Med. 2015;372:426–435. **4.** Verstovsek S, et al. Haematologica. 2016;101:821–829. **5.** Griesshammer M, et al. Ann Hematol. 2018;97:1591–1600. **6.** Griesshammer M, et al. Ann Hematol. 2018;97:1591–1600. Supplementary appendix. **7.** NICE. Ruxolitinib for treating polycythaemia vera. Available at: https://www.nice.org.uk/guidance/ta921/chapter/1-Recommendations/. Last accessed May 2024.

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JAKAVI® is indicated for the treatment of disease-related splenomegaly or symptoms in adult patients with primary myelofibrosis (also known as chronic idiopathic myelofibrosis), post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis. JAKAVI® is also indicated for adult patients with polycythaemia vera who are resistant to or intolerant of hydroxyurea.[1]

How do PV symptoms impair patients' QoL?

Symptom reduction was reported as the primary goal of treatment by 61% of patients with PV in the MPN Landmark Survey‡[3]

* Data from patients with an MPN (N=286) surveyed in the UK MPN Landmark Survey.[1] † Data from patients with PV (n=78) surveyed in the UK MPN Landmark Survey (N=286).[1]
‡ Data from patients with MPNs (ET, n=302; MF, n=174; PV, n=223) surveyed in the International MPN Landmark Survey (N=699).[3]

References: 1. Harrison CN, et al. BSH 2017. 27–29 March, Brighton, UK. **2.** Data on file. Novartis. Patient Quotes in PV from Advisory Board [MPN_PV_2020_001]. November 2020. **3.** Harrison CN, et al. Ann Hematol. 2017;96:1653–1665.

Study design: RESPONSE Phase 3, randomised, open-label, multicentre study[1]

(N=222)

Eligibility criteria:

- Age ≥18
- PV with intolerance or resistance to HU
- Venesection requirement for HCT control
- Splenomegaly (MRI volume ≥450 cm^2)
- Platelets >100x10^9 cells/L
- HCT 40–45%
- No prior JAK inhibitor treatment

1:1 randomisation

JAKAVI® (n=110)
PV patients: 10 mg BID

BAT‡ (n=112)
(n=96 crossed over to JAKAVI® at 32 weeks/ disease progression)

Primary outcomes:

- Composite of HCT control in absence of venesection (defined as HCT of >45% and ≥3% above baseline or HCT >48%) and ≥35% reduction in spleen volume at Week 32

Key secondary outcomes:

- Complete haematological remission at Week 32
- % patients maintaining primary response at 48 weeks
- Duration of spleen volume reduction
- Symptom reduction†
- Safety profile

Week 32 (primary endpoint) — **Week 48** (primary data cut-off) — **Week 80** (planned analysis) — **Week 256** (final planned analysis)

Crossover of BAT to JAKAVI®

JAKAVI® extended treatment phase

Study design: RESPONSE-2 Phase 3b, randomised, open-label, multicentre study[2]

(N=149)

Eligibility criteria:

- Age ≥18
- Patients with intolerance or resistance to HU
- Venesection requirement for HCT control
- No requirement for splenomegaly
- No prior JAK inhibitor treatment

1:1 randomisation

JAKAVI® (n=74)
10 mg BID

BAT‡ (n=75)
(n=58 crossed over to JAKAVI® after 28 weeks)

Primary outcomes:

- HCT control (Week 16 and maintained) defined as no venesection eligibility (defined as HCT of >45% and ≥3% above baseline or HCT >48% (Week 8–28) at Week 28

Key secondary outcomes:

- % patients achieving complete haematological remission at Week 28

Other secondary outcomes:

- Durability of HCT control and complete haematological remission at Weeks 52 and 80
- Change in venesection eligibility over time
- Change in HCT level over time
- Change in spleen length
- Change in ECOG status
- Transformation-free survival
- OS
- Safety profile
- Changes in PROs†

Crossover of BAT to JAKAVI® — BAT end of treatment follow-up — JAKAVI® end of treatment follow-up

Week 28 (primary endpoint) — **Week 80** — **Week 260**

JAKAVI® extended treatment phase

BAT, best available therapy; BID, twice daily; CHR, complete haematologic response; HCT, haematocrit test; HU, hydroxyurea; JAK, janus kinase; MPN-SAF TSS, Myeloproliferative Neoplasm-Symptom Assessment Form Total Symptom Score; MRI, magnetic resonance imaging; OS, overall survival; PRO, patient reported outcome; PV, polycythaemia vera; RCT, randomised controlled clinical trial.

* HU, interferon, pipobroman (not licensed for PV in the UK), anagrelide (not licensed for PV in the UK),[3] immunomodulators or observation only. † Measured using MPN-SAF TSS.[1,2]
‡ HU, interferon, immunomodulators and others.

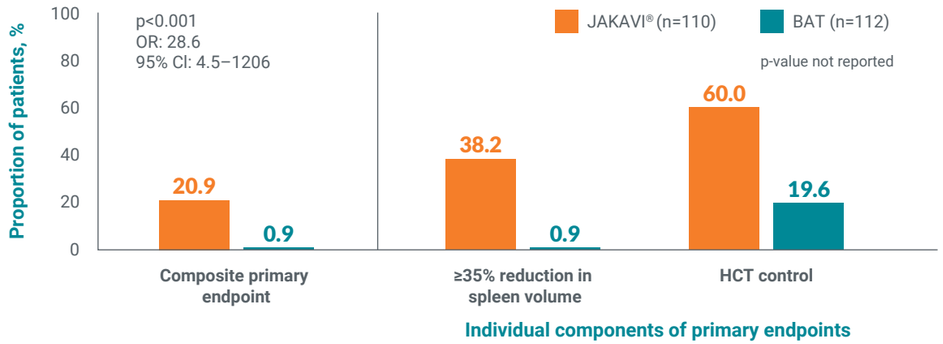
References: 1. Vannucchi A, et al. N Engl J Med. 2015;375:426–435. **2.** Griesshammer M, et al. Ann Hematol. 2018;97:1591–1600. **3.** Mylan. Anagrelide summary of product characteristics. Available at: https://www.medicines.org.uk/emc/product/9255/smpc/print. Last accessed May 2024.

JAKAVI® demonstrated superior HCT control* and spleen size reduction (composite primary endpoint) vs BAT[1,2]

RESPONSE (patients with splenomegaly)

More patients achieved HCT control* and ≥35% reduction in spleen size at Week 32 with JAKAVI® vs BAT[2]

Composite primary endpoint (Week 32)



Adapted from Vannucchi AM, et al. N Engl J Med. 2015.

No statistical testing was conducted

74% of patients with PV maintained primary response from Week 32 to 5 years (n=25)†[3]

Other endpoint (Week 256)

73% of patients with PV **maintained HCT control** from Week 32 to **5 years** (n=48/66)*[3]

72% of patients with PV had a probability of **maintaining ≥35% reduction in spleen volume** from Week 32 to **5 years** (n=31/44)[3,4]

Patients receiving BAT could cross over to JAKAVI® after Week 32. It was therefore impossible to compare results at 5 years to BAT due to crossover.[3]

RESPONSE is a Phase 3, randomised, open-label, multicentre study evaluating the efficacy and safety of JAKAVI® (n=110) vs BAT (n=112) in venesection-dependent patients with splenomegaly, who have HU-resistant or intolerant PV.[2]

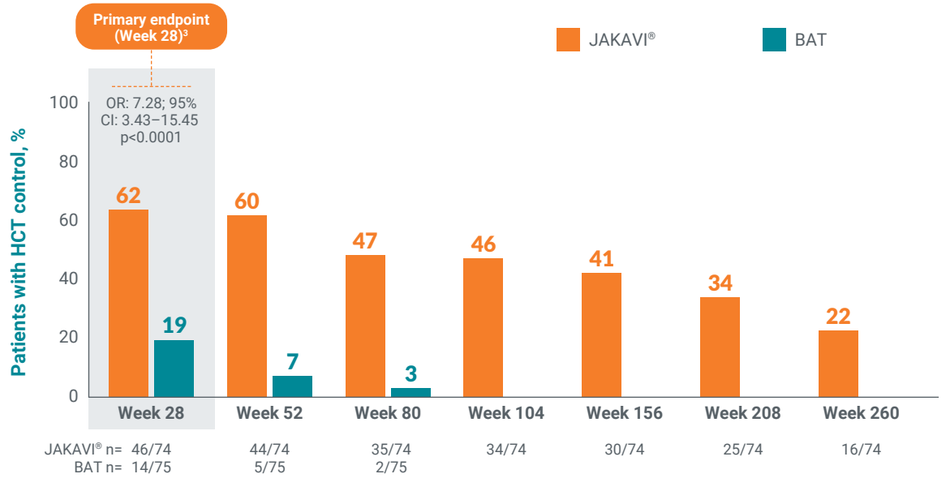
* HCT control defined as no venesection eligibility between Weeks 8 and 32, with venesection eligibility occurring only once after randomisation and before Week 8. Venesection eligibility was defined as HCT >45% and at least 3 percentage points higher than baseline or HCT >48%.[3] † There were 25 responders, six events and 19 censored.[3]

References: 1. Novartis Pharmaceuticals NI Ltd. JAKAVI® summary of product characteristics. Last accessed May 2024. **2.** Vannucchi AM, et al. N Engl J Med. 2015;372:426–435. **3.** Kiladjian JJ, et al. Lancet Haematol. 2020;7:e226–e237. **4.** Kiladjian JJ, et al. Lancet Haematol. 2020;7:e226–e237. Supplementary appendix.

RESPONSE-2 (patients without splenomegaly)

Durability of HCT control* with JAKAVI® up to 5 years[3]

Primary endpoint (Week 28)



Adapted from Passamonti F, et al. Lancet Haematol. 2022.

Patients receiving BAT could cross over to JAKAVI® after Week 28. It was therefore impossible to compare results at 5 years to BAT due to crossover.[3]

22% of patients receiving JAKAVI® achieved and sustained HCT control* through **5 years** (n=16/74)[3]

RESPONSE-2 is a Phase 3b, prospective, randomised, open-label, multicentre study assessing the efficacy and safety of JAKAVI® (n=74) vs BAT (n=75) in venesection-dependent patients with PV without splenomegaly who are resistant to or intolerant of HU.[4]

* HCT control defined as no venesection eligibility between Weeks 8 and 28, with venesection eligibility occurring only once after randomisation and before Week 8. Venesection eligibility was defined as HCT >45% and at least 3 percentage points higher than baseline or HCT >48%.[5]

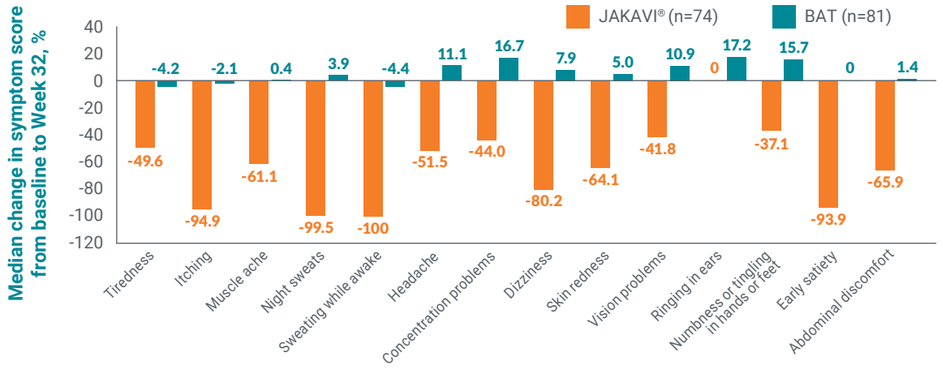
References: 1. Novartis Pharmaceuticals NI Ltd. JAKAVI® summary of product characteristics. Last accessed May 2024. **2.** Vannucchi AM, et al. N Engl J Med. 2015;372:426–435. **3.** Passamonti F, et al. Lancet Haematol. 2022;9:e480–e492. **4.** Griesshammer M, et al. Ann Hematol.2018;97:1591–1665. **5.** Passamonti F, et al. Lancet Oncol. 2017;18:88–99.

JAKAVI® is associated with a reduced symptom burden and improved QoL*[1,2]

RESPONSE (patients with splenomegaly)

Median change in PV symptom score at Week 32 with JAKAVI® vs BAT†[3]

Other endpoint (Week 32)



Adapted from Vannucchi AM, et al. N Engl J Med. 2015.

p-value not reported

Mean change in global health status–QoL scale in patients originally randomised to JAKAVI® (Week 32 and 256) and BAT (Week 32)[1,3,4]

Other endpoint (Week 256)

Adapted from Kiladjian JJ, et al. Lancet Haematol. 2020. Supplementary appendix.

p-value not reported

In RESPONSE, patients receiving BAT could cross over to JAKAVI® after Week 32. It was therefore impossible to compare results at 5 years to BAT due to crossover.[1]

RESPONSE is a Phase 3, randomised, open-label, multicentre study evaluating the efficacy and safety of JAKAVI® (n=110) vs BAT (n=112) in venesection-dependent patients with splenomegaly, who have HU-resistant or intolerant PV.[3]

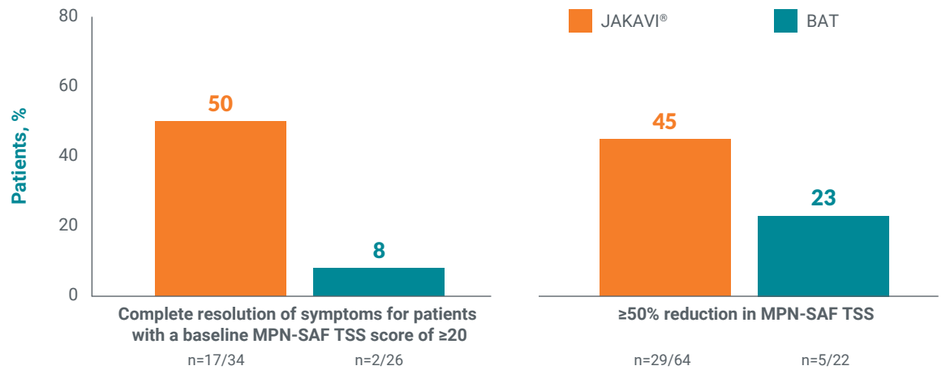
* Symptom score was assessed using MPN-SAF and MPN-SAF TSS questionnaire.[2,3] QoL was assessed using the EORTC QLQ-C30 questionnaire.[1,3] † Patients with data at both baseline (value >0) and Week 32 were included in the analysis.[3]

References: 1. Kiladjian JJ, et al. Lancet Haematol. 2020;7:e226–e237. **2.** Passamonti F, et al. Lancet Haematol. 2022;9:e480–e492. **3.** Vannucchi AM, et al. N Engl J Med. 2015;372:426–435. **4.** Kiladjian JJ, et al. Lancet Haematol. 2020;7:e226–e237. Supplementary appendix.

RESPONSE-2 (patients without splenomegaly)

More patients with PV reported complete resolution of symptoms with JAKAVI® vs BAT†[3]

Secondary endpoint (Week 28)



Adapted from Passamonti F, et al. Lancet Oncol.2017.

p-value not reported

More patients on JAKAVI® reported ≥50% reduction from baseline in MPN-SAF TSS vs BAT at the end-of-treatment visit‡[2]

Secondary endpoint (5-year follow-up)

JAKAVI® (n=28/62)

BAT (n=10/63)

(OR: 4.36; 95% CI: 1.88–10.12)[2]

p-value not reported

Patients receiving JAKAVI® at Week 80, including patients who had crossed over, could enter an extended treatment period up to Week 260. At Week 80, patients receiving BAT who did not cross over to JAKAVI® were not eligible for the extended treatment period but had an end-of-treatment visit at Week 80, or at the time of discontinuation.[2]

RESPONSE-2 is a Phase 3b, prospective, randomised, open-label, multicentre study assessing the efficacy and safety of JAKAVI® (n=74) vs BAT (n=75) in venesection-dependent patients with PV without splenomegaly who are resistant to or intolerant of HU.[4]

* Symptom score was assessed using MPN-SAF and MPN-SAF TSS questionnaire.[2,5] QoL was assessed using the EORTC QLQ-C30 questionnaire.[1,5] † Complete resolution of symptoms is defined as MPN-SAF TSS reduction of ≥10 points from baseline at Week 16 and maintained until Week 28 (for patients with a baseline score of ≥20).[5] ‡ Median follow-up was 67 months.[2]

References: 1. Kiladjian JJ, et al. Lancet Haematol. 2020;7:e226–e237. **2.** Passamonti F, et al. Lancet Haematol. 2022;9:e480–92. **3.** Passamonti F, et al. Lancet Oncol. 2017;18:88–99. **4.** Griesshammer M, et al. Ann Hematol.2018;97:1591–1665. **5.** Vannucchi AM, et al. N Engl J Med. 2015;372:426–435.

JAKAVI® has a well-characterised safety profile[1]

Haematological AEs

Anaemia

Thrombocytopenia

Neutropenia

Non-haematological AEs

Weight gain

Dizziness

Headache

45.3% increased alanine aminotransferase
42.6% increased aspartate aminotransferase
34.7% Hypercholesterolaemia

Discontinuation due to adverse events, regardless of causality, was observed in **19.4%** of patients.[1]
Please refer to the SmPC for full safety profile.

Reference: 1. Novartis Pharmaceuticals NI Ltd. JAKAVI® summary of product characteristics. Last accessed May 2024.

Frequency category of ADRs reported with JAKAVI® in Phase 3 studies in PV[1]

	Very common (≥1/10)	Common (≥1/100 to <1/10)	Uncommon (≥1/1000 to <1/100)	Not known
Infections and infestations	• Urinary tract infections • Herpes zoster	• Pneumonia	• Sepsis • HBV reactivation	• Tuberculosis*
Blood and lymphatic system disorders†	• Anaemia† of any CTCAE‡ Grade • Thrombocytopenia† of any CTCAE‡ Grade • Bleeding (any bleeding including intracranial, gastrointestinal, bruising and other bleeding) • Bruising • Other bleeding (including epistaxis, post-procedural haemorrhage and haematuria)	• Anaemia† CTCAE‡ Grade 3 (<8.0–6.5 g/dL) • Thrombocytopenia† CTCAE‡ Grade 3 (50,000–25,000/mm^3) • Neutropenia† of any CTCAE‡ Grade • Pancytopenia†§ • Gastrointestinal bleeding	• Anaemia† CTCAE‡ Grade 4 (<6.5 g/dL) • Thrombocytopenia† CTCAE‡ Grade 4 (<25,000/mm^3) • Neutropenia† – CTCAE‡ Grade 4 (<500/mm^3) – CTCAE‡ Grade 3 (<1000–500/mm^3) • Intracranial bleeding	
Metabolism and nutrition disorders	• Weight gain • Hypercholesterolaemia† of any CTCAE‡ Grade • Hypertriglyceridaemia† of any CTCAE‡ Grade			
Nervous system disorders	• Dizziness • Headache			
Gastrointestinal disorders	• Elevated lipase of any CTCAE‡ Grade • Constipation	• Flatulence		
Hepatobiliary disorders	• Raised alanine aminotransferase† of any CTCAE‡ Grade • Raised aspartate aminotransferase† of any CTCAE‡ Grade	• Raised alanine aminotransferase† CTCAE‡ Grade 3 (>5x–20x ULN)		
Vascular disorders	• Hypertension			

Selected special warnings and precautions for JAKAVI® include myelosuppression, infections, progressive multifocal leukoencephalopathy, lipid abnormalities/elevations, herpes zoster, MACE, thrombosis, second primary malignancies such as lymphoma and non-melanoma skin cancers.[1] Please refer to the SmPC for full information.

* ADR derived from post-marketing experience.[1] † Frequency is based on new or worsened laboratory abnormalities compared to baseline.[1] ‡ Common Terminology Criteria for Adverse Events (CTCAE) version 3.0; Grade 1 = mild, Grade 2 = moderate, Grade 3 = severe, Grade 4 = life-threatening.[1] § Pancytopenia is defined as haemoglobin level <100 g/L, platelet count <100x10^9/L, and neutrophil count <1.5x10^9/L (or low white blood cell count of Grade 2 if neutrophil count is missing), simultaneously in the same lab assessment.[1]

Reference: 1. Novartis Pharmaceuticals NI Ltd. JAKAVI® summary of product characteristics. Last accessed May 2024.

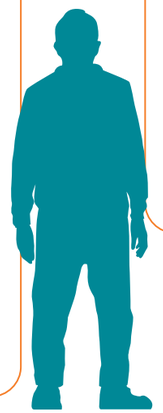
Don’t leave HU-resistant or HU-intolerant patients behind[1–5]

1 in 5 patients with PV may become resistant to or intolerant of HU treatment*[1,6,7]

ELN recommends switching patients to an alternative cytoreductive therapy if any one of the criteria are met[5]

HU resistance†[5]

- Persistent disease-related symptoms: TSS of at least 20 or an itching score of at least 10 for at least 6 months
- Persistent thrombocytosis: a platelet count >1000×10^9 cells/L, microvascular symptoms, or both, persisting for more than 3 months
- Symptomatic or progressive splenomegaly: increase in spleen size by more than 5 cm from the left costal margin in 1 year
- Progressive and persistent leukocytosis: (at least 100% increase if BL count is <10×10^9 cells/L or at least 50% increase if BL count is >10×10^9 cells/L) (leukocyte count >15×10^9 cells/L confirmed at 3 months)
- Insufficient HCT control: need for six or more venesections per year to keep HCT <45%



HU intolerance[5]

- Grade 3–4 or prolonged Grade 2 non-haematological toxicity (e.g., mucocutaneous manifestations, gastrointestinal symptoms, fever or pneumonitis) at any dose
- Haematological toxicity (Hb <100 g/L, platelet count <100×10^9 cells/L, or neutrophil count <1×10^9 cells/L) at the lowest dose of HU to achieve a response
- Development of non-melanoma skin cancers
- Development of vascular events: either clinically relevant bleeding, venous thrombosis or arterial thrombosis

ELN recommends switching patients with HU resistance or intolerance to JAKAVI® or IFN-α based on individual clinical features‡[5]

* HU resistance or intolerance was defined using the 2010 ELN criteria.[2,7] In a retrospective analysis of 106 patients with PV in Belgium, when using the original and modified ELN criteria, 20.7% and 39.6% of patients were resistant to or intolerant of HU, respectively.[2,4,7] † HU dosed at ≥1.5 g per day for at least 4 months and without reporting intolerance.[5] ‡ In particular, age, spleen size, symptoms, history of skin cancers and patient preferences.[5] Not all IFN-α therapies are approved for use in PV.[5]

References: 1. Alvarez-Larrán A, et al. Blood. 2012;119:1363–1369. **2.** Barosi G, et al. Br J Haematol. 2010;148:961–963. **3.** McMullin MF, et al. Br J Haematol. 2019;184:176–191. **4.** McMullin MF, et al. Br J Haematol. 2016;172:337–349. **5.** Marchetti M, et al. Lancet Haematol. 2022;9:e301–e311. **6.** Geyer H, et al. J Clin Oncol. 2016;34:151–159. **7.** Demuynck T, et al. Ann Hematol. 2019;98:1421–1426.

The day you choose JAKAVI® (ruxolitinib) is the day you could begin to change their life[1–7]

Durable HCT control* and **reduction in spleen size** vs baseline†[1,3,8]

Marked reductions in **PV-related symptoms** vs BAT (no p-value reported)‡[3,9]

Generally **well-characterised** safety profile with over **5 years** of safety data[1,8,10]

JAKAVI® (ruxolitinib) is recommended by NICE for treating polycythaemia vera in eligible adult patients who are resistant to or intolerant of hydroxyurea (please refer to the guidance for the full criteria)[7]

* HCT control was defined as no venesection eligibility (venesection eligibility defined as HCT of >45% and ≥3% above baseline or HCT >48%).[3,8] † In RESPONSE at Week 32, JAKAVI® (n=110) demonstrated significantly higher rates of HCT control* and ≥35% reductions in spleen volume vs BAT (n=112; p<0.001),[1,3] which was maintained by 74% of patients on JAKAVI® (n=25) at Week 256.[10] In RESPONSE-2 at Week 28, JAKAVI® (n=74) demonstrated higher rates of HCT control* vs BAT (n=75; p<0.0001).[9] At Week 260, 22% of patients on JAKAVI® had maintained or achieved HCT control (n=74).[8] RESPONSE-2 was conducted in patients without splenomegaly.[8,9] In RESPONSE and RESPONSE-2, patients receiving BAT could cross over to JAKAVI® after Week 32 and 28, respectively. It was therefore impossible to compare results at 5 years to BAT due to crossover.[8,10] ‡ In RESPONSE at Week 32, 49% vs 5% of patients achieved ≥50% reduction in MPN-SAF TSS for JAKAVI® (n=74) vs BAT (n=81).[3] In RESPONSE-2 at Week 28, 45% vs 23% of patients achieved ≥50% reduction in MPN-SAF TSS for JAKAVI® (n=64) vs BAT (n=22).[9]

References: 1. Novartis Pharmaceuticals NI Ltd. JAKAVI® summary of product characteristics. Last accessed May 2024. **2.** Scottish Medicines Consortium. Ruxolitinib (Jakavi). Available at: https://www.scottishmedicines.org.uk/medicines-advice/ruxolitinib-jakavi-full-smc2213/. Last accessed May 2024. **3.** Vannucchi AM, et al. N Engl J Med. 2015;372:426–435. **4.** Verstovsek S, et al. Haematologica. 2016;101:821–829. **5.** Griesshammer M, et al. Ann Hematol. 2018;97:1591–1600. **6.** Griesshammer M, et al. Ann Hematol. 2018;97:1591–1600. Supplementary appendix. **7.** NICE. Ruxolitinib for treating polycythaemia vera. TA921, 2023. Available at: https://www.nice.org.uk/guidance/ta921. Last accessed May 2024. **8.** Passamonti F, et al. Lancet Haematol. 2022;9:e480–e492. **9.** Passamonti F, et al. Lancet Oncol. 2017;18:88–99. **10.** Kiladjian JJ, et al. Lancet Haematol. 2020;7:e226–e237.

Abbreviations: ADR, adverse drug reaction; AE, adverse event; BAT, best available therapy; BID, twice daily; BL, baseline; CBC, complete blood count; CI, confidence interval; CTCAE, common terminology criteria for adverse events; ELN, European LeukemiaNet; EORTC QLQ-C30, European Organization for the Research and Treatment of Cancer core quality of life questionnaire; ET, essential thrombocythaemia; Hb, haemoglobin; HBV, hepatitis B virus; HCT, haematocrit; HU, hydroxyurea; IFN, interferon; MACE, major adverse cardiac event; MF, myelofibrosis; MPN-SAF TSS, Myeloproliferative Neoplasms Symptom Assessment Form Total Symptom Score; NICE, National Institute for Health and Care Excellence; OR, odds ratio; OS, overall survival; PV, polycythaemia vera; QoL, quality of life; SmPC, summary of product characteristics; TSS, total symptom score; ULN, upper limit of normal; WBC, white blood cell.

Northern Ireland Prescribing Information: JAKAVI® (ruxolitinib) 5mg, 10mg, 15mg and 20mg tablets. **Important note: Before prescribing, consult Summary of Product Characteristics (SmPC). Presentation**: Tablet (containing lactose). White to almost white tablets with imprints (NVR on one face and L5, L10, L15 or L20 debossed on the other side). **Indications:** Myelofibrosis (MF): Jakavi is indicated for the treatment of disease related splenomegaly or symptoms in adult patients with primary myelofibrosis (also known as chronic idiopathic myelofibrosis), post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis. Polycythaemia vera (PV): Jakavi is indicated for the treatment of adult patients with polycythaemia vera who are resistant to or intolerant of hydroxyurea. **Dosage:** *Starting dose*: The recommended starting dose of Jakavi in myelofibrosis is 5 mg twice daily for patients with a platelet count between 50,000/mm^3 and < 75,000/mm^3, 10 mg twice daily for patients with a platelet count between 75,000/mm^3 and < 100,000/mm^3, 15 mg twice daily for patients with a platelet count between 100,000/mm^3 and 200,000/mm^3 and 20 mg twice daily for patients with a platelet count of >200,000/mm^3. The recommended starting dose of Jakavi in polycythaemia vera is 10 mg given orally twice daily. *Dose modifications*: Doses may be titrated based on efficacy and safety. If efficacy is considered insufficient and blood counts are adequate, doses may be increased by a maximum of 5 mg twice daily, up to the maximum dose of 25 mg twice daily. The starting dose should not be increased within the first four weeks of treatment and thereafter no more frequently than at 2-week intervals. Treatment should be discontinued for platelet counts less than 50,000/mm^3 or absolute neutrophil counts less than 500/mm^3. In PV, treatment should also be interrupted when haemoglobin is below 8 g/dl. After recovery of blood counts above these levels, dosing may be re-started at 5 mg twice daily and gradually increased based on careful monitoring of complete blood cell count, including a white blood cell count differential. Dose reductions should be considered if the platelet count decreases below 100,000/mm^3, with the goal of avoiding dose interruptions for thrombocytopenia. Refer to the full SmPC for details. In PV, dose reductions should also be considered if haemoglobin decreases below 12 g/dl and is recommended if it decreases below 10 g/dl. **Contraindications:** Jakavi contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product. Hypersensitivity to the active substance or to any of the excipients listed: cellulose, microcrystalline, magnesium stearate, silica, colloidal anhydrous, sodium starch glycolate (Type A), povidone hydroxypropylcellulose, lactose monohydrate. Pregnancy and lactation. **Warnings and Precautions:** ***Myelosuppression***: Treatment with Jakavi can cause haematological adverse drug reactions, including thrombocytopenia, anaemia and neutropenia. A complete blood count, including a white blood cell count differential, must be performed before initiating therapy with Jakavi. Treatment should be discontinued in patients with platelet count less than 50,000/mm^3 or absolute neutrophil count less than 500/mm^3. It has been observed that patients with low platelet counts (<200,000/mm^3) at the start of therapy are more likely to develop thrombocytopenia during treatment. Thrombocytopenia is generally reversible and is usually managed by reducing the dose or temporarily withholding Jakavi. However, platelet transfusions may be required as clinically indicated. Patients with a haemoglobin level below 10.0 g/dl at the beginning of the treatment have a higher risk of developing a haemoglobin level below 8.0 g/dl during treatment compared to patients with a higher baseline haemoglobin level (79.3% versus 30.1%). More frequent monitoring of haematology parameters and of clinical signs and symptoms of Jakavi-related adverse drug reactions is recommended for patients with baseline haemoglobin below 10 g/dl. Patients developing anaemia may require blood transfusions. Dose modifications or interruption for patients developing anaemia may also be considered. ***Infections***: Serious bacterial, mycobacterial, fungal, viral and other opportunistic infections have occurred in patients treated with Jakavi. Patients should be assessed for the risk of developing serious infections. Physicians should carefully observe patients receiving Jakavi for signs and symptoms of infections and initiate appropriate treatment promptly. Treatment with Jakavi should not be started until active serious infections have resolved. Tuberculosis has been reported in patients receiving Jakavi. Before starting treatment, patients should be evaluated for active and inactive ("latent") tuberculosis has per local recommendations. Hepatitis B viral load (HBV-DNA titre) increases, with and without associated elevations in alanine aminotransferase and aspartate aminotransferase, have been reported in patients with chronic HBV infections taking Jakavi. It is recommended to screen for HBV prior to commencing treatment. Patients with chronic HBV infection should be treated and monitored according to clinical guidelines. *Herpes zoster*: Physicians should educate patients about early signs and symptoms of herpes zoster, advising that treatment should be sought as early as possible. *Progressive multifocal leukoencephalopathy*: Progressive multifocal leukoencephalopathy (PML) has been reported with Jakavi treatment. Physicians should be particularly alert to symptoms suggestive of PML that patients may not notice (e.g., cognitive, neurological or psychiatric symptoms or signs). Patients should be monitored for any of these new or worsening symptoms or signs, and if such symptoms/signs occur, referral to a neurologist and appropriate diagnostic measures for PML should be considered. If PML is suspected, further dosing must be suspended until PML has been excluded. *Second primary malignancies*: Lymphoma and other malignancies have been reported in patients receiving JAK inhibitors, including Jakavi. Non-melanoma skin cancers (NMSCs) have been reported in patients treated with ruxolitinib. Most of these patients had histories of extended treatment with hydroxyurea and prior NMSC or pre-malignant skin lesions. Periodic skin examination is recommended for patients who are at increased risk for skin cancer. *Lipid abnormalities/elevations*: Treatment with Jakavi has been associated with increases in lipid parameters. Lipid monitoring and treatment of dyslipidaemia according to clinical guidelines is recommended. *Major Adverse Cardiac Events*: Major adverse cardiac events have been reported in patients receiving Jakavi. Prior to initiating or continuing therapy with Jakavi, the benefits and risks for the individual patient should be considered particularly in patients 65 years of age and older, patients who are current or past longtime smokers, and patients with a history of atherosclerotic cardiovascular disease or other cardiovascular risk factors. *Thrombosis*: Events of deep venous thrombosis (DVT) and pulmonary embolism (PE) have been reported in patients receiving Jakavi. Prior to initiating or continuing therapy with Jakavi, the benefits and risks for the individual patient should be considered, particularly in patients with cardiovascular risk factors. Patients with symptoms of thrombosis should be promptly evaluated and treated appropriately. **Special populations**: *Renal impairment*: No specific dose adjustment is needed in patients with mild or moderate renal impairment. In patients with severe renal impairment (creatinine clearance less than 30 ml/min) the recommended starting dose based on platelet count for MF patients should be reduced by approximately 50% to be administered twice daily. The recommended starting dose for PV patients with severe renal impairment is 5 mg twice daily. Patients should be carefully monitored with regard to safety and efficacy during Jakavi treatment. For patients with end stage renal disease on haemodialysis the starting dose for MF patients should be based on platelet counts. Subsequent doses (single dose of 20 mg or two doses of 10 mg given 12 hours apart in MF patients; single dose of 10 mg or two doses of 5 mg given 12 hours apart in PV patients) should be administered only on haemodialysis days following each dialysis session. Additional dose modifications should be made with careful monitoring of safety and efficacy. The recommended starting dose for PV patients with ESRD on haemodialysis is a single dose of 10 mg or two doses of 5 mg given 12 hours apart, to be administered post-dialysis and only on the day of haemodialysis. These dose recommendations are based on simulations and any dose modification in ESRD should be followed by careful monitoring of safety and efficacy in individual patients. Please refer to Summary of Product Characteristics for detailed information. *Hepatic impairment*: The starting dose of Jakavi should be reduced by approximately 50% in patients with hepatic impairment. Further dose modifications should be based on the safety and efficacy of the medicinal product. *Older people (>65 years)*: No additional dose adjustments are recommended for older people. *Paediatric population*: The safety and efficacy of Jakavi in children aged up to 18 years have not been established. *Withdrawal effects*: Following interruption or discontinuation of Jakavi, symptoms of myelofibrosis may return over a period of approximately one week. There have been cases of patients discontinuing Jakavi who sustained more severe events, particularly in the presence of acute intercurrent illness. It has not been established whether abrupt discontinuation of Jakavi contributed to these events. Unless abrupt discontinuation is required, gradual tapering of the dose of Jakavi may be considered, although the utility of the tapering is unproven. **Interaction with other medicinal product** *Strong CYP3A4 inhibitors*: When administering Jakavi with strong CYP3A4 inhibitors the unit dose of Jakavi should be reduced by approximately 50%, to be administered twice daily. Patients should be closely monitored (e.g. twice weekly) for cytopenias and dose titrated based on safety and efficacy (see section 4.2). *Dual CYP2C9 and CYP3A4 inhibitors*: the dose of ruxolitinib should be reduced by 50%. Avoid the concomitant use of Jakavi with fluconazole doses greater than 200 mg daily. *Mild or moderate CYP3A4 inhibitors*: No dose adjustment is recommended when Jakavi is co-administered with mild or moderate CYP3A4 inhibitors (e.g. erythromycin). However, patients should be closely monitored for cytopenias when initiating therapy with a mild/moderate CYP3A4 inhibitor. CYP3A4 inducers: Patients should be closely monitored and the dose titrated based on safety and efficacy. It is possible that in an individual patient, an increase of Jakavi dose is needed when initiating therapy with a strong enzyme inducer. *Cytoreductive therapies*: The concomitant use of cytoreductive therapies with Jakavi was associated with manageable cytopenias. *Oral contraceptives and substances metabolized by CYP3A4*: A study in healthy subjects indicated that ruxolitinib did not inhibit the metabolism of the oral CYP3A4 substrate midazolam. Therefore, no increase in exposure of CYP3A4 substrates is anticipated when combining them with Jakavi. Another study in healthy subjects indicated that Jakavi does not affect the pharmacokinetics of an oral contraceptive containing ethinylestradiol and levonorgestrel. Therefore, it is not anticipated that the contraceptive efficacy of this combination will be compromised by co-administration of ruxolitinib. **Side-effects:** The most frequently reported adverse drug reactions were thrombocytopenia and anaemia. *Very common*: anaemia, thrombocytopenia, neutropenia, bruising, dizziness, headache, raised alanine aminotransferase, raised aspartate aminotransferase, hypercholesterolaemia, hypertriglyceridaemia, elevated lipase, hypertension, urinary tract infections, pneumonia, herpes zoster, gastrointestinal bleeding, weight gain, constipation and bleeding. *Common*: sepsis, pancytopenia, intracranial bleeding and flatulence. *Uncommon*: Tuberculosis, HBV reactivation. Refer to the SmPC for a full list of all side effects. **Legal Category:** POM. PVC/PCTFE/Aluminium blister packs containing Jakavi 5mg x 56 tablets – MA Number: EU/1/12/773/004-006. Basic NHS price: £1,428; Jakavi 10mg x 56 tablets – MA Number EU/1/12/773/014-016. Basic NHS price: £2,856; Jakavi 15mg x 56 tablets – MA Number: EU/1/12/773/007-009. Basic NHS price: £2,856; Jakavi 20mg x 56 tablets – MA Number: EU/1/12/773/010-012. Basic NHS price: £2,856. Full prescribing information is available on request from Novartis Pharmaceuticals UK Ltd, 2nd Floor, The WestWorks Building, White City Place, 195 Wood Lane, London, W12 7FQ. Telephone (01276) 698370. **Date of revision:** April 2024 UK | 435755-1| May 2024

Adverse events should be reported.
Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Novartis via uk.patientsafety@novartis.com or online through the pharmacovigilance intake (PVI) tool at www.novartis.com/report. If you have any questions about the product, please contact Medical Information on 01276 698370 or by email at medinfo.uk@novartis.com

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