

Monitor patients to find their optimal JAKAVI® (ruxolitinib) dose¹

Pre-initiation/ Initiation

Pre-initiation¹

A complete blood cell count, including a white blood cell count differential, must be performed before initiating therapy with JAKAVI®.

Starting dose^{1,2}

Based on platelet count:

- >200,000/mm³
– 20 mg twice daily.
- 100,000–200,000/mm³
– 15 mg twice daily.
- 75,000–<100,000/mm³
– 10 mg twice daily.
- 50,000–<75,000/mm³
– 5 mg twice daily.

Special populations such as those with severe renal impairment, end stage renal disease and hepatic impairment require adjusted starting and maintenance doses. Please refer to section 4.2 of the SmPC for full information.

Monitoring¹

Complete blood count, including a white blood cell count differential, should be monitored **every 2 to 4 weeks** until dose is stabilised, then as clinically indicated.

Approximately 4 weeks

Improvement in spleen size^{1,2}

Reduction in palpable spleen length may be **observed by Week 4**.
Reduction in spleen size may be observed later than Week 4 throughout the course of treatment.

Dose titration¹

The starting dose should not be increased during the **first 4 weeks** of therapy.
Doses should not be increased more frequently than at **2-week intervals**.
Dose should be titrated based on efficacy and safety, per SmPC.

Approximately 8 weeks

Symptom improvement^{1–3}

In patients with symptom improvement, symptom responses generally occurred rapidly – **usually within the first 8 weeks**.

Thrombocytopenia¹

In the phase 3 clinical studies, median onset of Grade 3 or 4 thrombocytopenia was **8 weeks**.*

Management: Interrupt treatment if platelet count <50,000/mm³ or absolute neutrophil count reduced to <500/mm³.

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.

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.

Please refer to the dosing recommendation in section 4.2 of the SmPC for information on specific dose reductions in patients with thrombocytopenia.

Approximately 8–12 weeks

Anaemia^{1,4}

Anaemia was generally transient, reaching a nadir of approximately 10 g/L below baseline after **8 to 12 weeks** of therapy and gradually recovering to reach a new steady state (approximately 5 g/L below baseline) by Week 24.

Management: Patients with anaemia may require blood transfusions.

Dose modifications or interruption for patients developing anaemia may also be considered.

24 weeks

Efficacy¹

Discontinue JAKAVI® after 6 months if there is no spleen size reduction or symptom improvement.



* Grade 3 or 4 thrombocytopenia is defined as absolute platelet counts below 50,000/mm³.¹

Proactively monitor all your patients' myelofibrosis-related symptoms to treat as early as possible in those who are eligible for JAKAVI®.^{5–8}

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Treatment may continue as long as benefit-risk balance remains positive. After interruption or discontinuation of JAKAVI® dosing, symptoms of myelofibrosis may return over a period of approximately 1 week. Unless abrupt discontinuation is required, gradual tapering of the dose may be considered, although the utility of tapering is unproven. 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

Adverse events should be reported. Reporting forms and information can be found 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 a question about the product, please contact Medical Information on 01276 698370 or by email at medinfo.uk@novartis.com.

JAKAVI®
ruxolitinib

Prescribing information
can be found on the next page.

References

1. Novartis Pharmaceuticals UK Ltd. JAKAVI® summary of product characteristics. Last accessed April 2024. 2. Harrison C, et al. N Engl J Med. 2012;366:787–798. 3. Verstovsek S, et al. N Engl J Med. 2012;366:799–807. 4. Cervantes F. Blood. 2014;124:2635–2642. 5. Mesa R, et al. Blood. 2012;120:1727. 6. McLornan DP, et al. Br J Haematol 2024;204:136–150. 7. NICE. Ruxolitinib for treating disease-related splenomegaly or symptoms in adults with myelofibrosis. TA386, 2016. Available at: <https://www.nice.org.uk/guidance/ta386>. Last accessed April 2024. 8. Scottish Medicines Consortium. Available at: <https://www.scottishmedicines.org.uk/medicines-advice/ruxolitinib-jakavi-fullsubmission-86713/>. Last accessed April 2024.

GREAT BRITAIN 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 5mg twice daily for patients with a platelet count between 50,000/mm³ and < 75,000/mm³, 10 mg twice daily for patients with a platelet count between 75,000/mm³ and < 100,000/mm³, 15 mg twice daily for patients with a platelet count between 100,000/mm³ and 200,000/mm³ and 20 mg twice daily for patients with a platelet count of >200,000/mm³. 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/mm³ or absolute neutrophil counts less than 500/mm³. 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/mm³, 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/mm³ or absolute neutrophil

count less than 500/mm³. It has been observed that patients with low platelet counts (<200,000/mm³) 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 as 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. **Non-melanoma skin cancer:** 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. A causal relationship to ruxolitinib has not been established. 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. **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, 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 products: 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. Avoid the concomitant use of Jakavi with fluconazole doses greater than 200 mg 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:** On the basis of in silico modelling, 50% dose reduction may be considered when using fluconazole, a medicinal product which is a dual CYP3A4 and CYP2C9 inhibitor. **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 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: PLGB 00101/1098. Basic NHS price: £1,428, Jakavi 10mg x 56 tablets - MA Number PLGB 00101/1095. Basic NHS price: £2,856; Jakavi 15mg x 56 tablets - MA Number: PLGB 00101/1096. Basic NHS price: £2,856; Jakavi 20mg x 56 tablets - MA Number: PLGB 00101/1097. 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:** January 2022

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Adverse events should also be reported to Novartis
via uk.patientsafety@novartis.com or online through
the pharmacovigilance intake (PVI) tool
at www.report.novartis.com
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