

# MF risk stratification:

Myelofibrosis

A guide to using IPSS, DIPSS and DIPSS Plus<sup>1-3</sup>



The day you choose JAKAVI<sup>®</sup> (ruxolitinib)  
is the day you could begin to change their life<sup>4-6</sup>



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JAKAVI<sup>®</sup> 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<sup>®</sup> is also indicated for adult patients with polycythaemia vera who are resistant to or intolerant of hydroxyurea.<sup>4</sup>

Adverse events should be reported. Reporting forms and information can be found at [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard). Adverse events should also be reported to Novartis via [uk.patientsafety@novartis.com](mailto:uk.patientsafety@novartis.com) or online through the pharmacovigilance intake (PVI) tool at [www.novartis.com/report](http://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](mailto:medinfo.uk@novartis.com)

# MF risk stratification: a guide to using IPSS, DIPSS and DIPSS Plus<sup>1-3</sup>

Risk stratifying patients with MF requires the use of a uniform scoring system to ensure accuracy and consistency of predicted prognoses. This information can also be part of helping you determine the most appropriate MF treatment and management pathway for your patients.<sup>1-3</sup>

There are three prognostic scoring systems you can use:<sup>1-3</sup>

IPSS <sup>1</sup>	DIPSS <sup>2</sup>	DIPSS Plus <sup>3</sup>
Can be used to assess a patient's prognosis and predict survival at the point of diagnosis <sup>1</sup>	Can be used to assess a patient's prognosis at any time after diagnosis <sup>2</sup>	Combines prognostic information from DIPSS with information from karyotype, platelet count, and transfusion status to predict overall survival <sup>3</sup>

Choose a scoring system and score for each variable as indicated to calculate a total score:<sup>1-3</sup>

Variable	IPSS <sup>1</sup>	DIPSS <sup>2</sup>	DIPSS Plus <sup>3</sup>
Age >65 years	1 point	1 point	1 point
Constitutional symptoms	1 point	1 point	1 point
Hb <100 g/L	1 point	2 points	1 point
Leukocyte count >25x10 <sup>9</sup> /L	1 point	1 point	1 point
Circulating blastocysts ≥1%	1 point	1 point	1 point
Platelet count <100x10 <sup>9</sup> /L			1 point
Red blood cell transfusion needed			1 point
Unfavourable karyotype*			1 point
<b>TOTAL SCORE</b>	<b>0-5</b>	<b>0-6</b>	<b>0-8</b>

\* Included complex karyotype or single or two abnormalities including +8, -7/7q-, i(17q), inv (3), -5/5q-, 12p- or 11q23 rearrangement.<sup>3</sup>

Using the total score, identify the MF risk group to predict median survival:<sup>1-3</sup>

MF risk group	IPSS <sup>1</sup>		DIPSS <sup>2</sup>		DIPSS Plus <sup>3</sup>	
	IPSS total score	Median survival (years)	DIPSS total score	Median survival (years)	DIPSS Plus total score	Median survival (years)
Low	0	11.3	0	Not reached	0	15.0
Intermediate-1	1	7.9	1-2	14.2	1	6.5
Intermediate-2	2	4.0	3-4	4.0	2-3	2.9
High	≥3	2.3	5-6	1.5	4-6	1.3

## JAKAVI® is:

Recommended by NICE as an option for treating disease-related splenomegaly or symptoms in adults with intermediate-2 or high risk MF.\*<sup>7</sup>

SMC-accepted for the treatment of disease-related splenomegaly or symptoms in adult patients with MF.\*<sup>8</sup>

Recommended within the BSH guidelines as an option for the treatment of myelofibrosis-related splenomegaly or symptoms in eligible adult patients.<sup>9</sup>

\* NICE and SMC also recommend JAKAVI® for patients with post polycythaemia vera MF and post essential thrombocythaemia MF.<sup>7,8</sup>

### Abbreviations:

BSH, British Society for Haematology; DIPSS, Dynamic International Prognostic Scoring System; Hb, haemoglobin; IPSS, International Prognostic Scoring System; JAK2, janus kinase 2; MF, myelofibrosis; NICE, National Institute for Health and Care Excellence; QoL, quality of life; SMC, Scottish Medicines Consortium.

### References:

1. Cervantes F, et al. Blood. 2009;113:2895-2901. 2. Passamonti F, et al. Blood. 2010;115:1703-1708. 3. Gangat N, et al. J Clin Oncol. 2011;29:392-397. 4. Novartis Pharmaceuticals NI Ltd. JAKAVI® summary of product characteristics. Last accessed May 2024. 5. Verstovsek S, et al. N Engl J Med. 2012;366:799-807. 6. Harrison C, et al. N Engl J Med. 2012;366:787-798. 7. National Institute for Health and Care Excellence. Available at: <https://www.nice.org.uk/guidance/ta386>. Last accessed May 2024. 8. Scottish Medicines Consortium. Available from: <https://www.scottishmedicines.org.uk/medicines-advice/ruxolitinib-jakavi-fullsubmission-86713/>. Last accessed May 2024. 9. McLornan DP, et al. Br J Haematol. 2024;204:136-150.

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**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<sup>3</sup> and < 75,000/mm<sup>3</sup>, 10 mg twice daily for patients with a platelet count between 75,000/mm<sup>3</sup> and < 100,000/mm<sup>3</sup>, 15 mg twice daily for patients with a platelet count between 100,000/mm<sup>3</sup> and 200,000/mm<sup>3</sup> and 20 mg twice daily for patients with a platelet count of >200,000/mm<sup>3</sup>. 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<sup>3</sup> or absolute neutrophil counts less than 500/mm<sup>3</sup>. 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<sup>3</sup>, 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<sup>3</sup> or absolute neutrophil count less than 500/mm<sup>3</sup>. It has been observed that patients with low platelet counts (<200,000/mm<sup>3</sup>) 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

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