NOVARTIS

JAKAVI - Dose optimisation - HCP

Prescribing information

Image

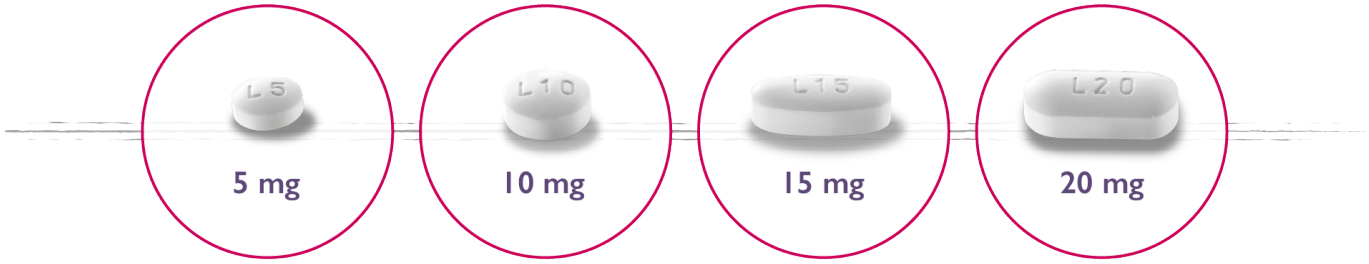
Image

Dose optimisation

JAKAVI® (ruxolitinib) 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]

JAKAVI® is available in four tablet strengths to enable dose optimisation for each patient[1]

Image



Tablets shown are not actual size.

The recommended starting dose for JAKAVI® in myelofibrosis is based on a patient's platelet count at treatment initiation.[1]

- 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
- 20 mg twice daily for patients with a platelet count of >200,000/mm^3

The recommended starting dose of JAKAVI® in polycythaemia vera (PV) is 10 mg given orally twice daily.[1] For more information about JAKAVI® in PV, click here.

Optimise your patients' response to therapy with dose titration that's based on efficacy and safety data[1]

JAKAVI® treatment should only be initiated by a physician experienced in the administration of anti-cancer medicinal products. A complete blood cell count, including a white blood cell count differential, must be performed before initiating therapy with JAKAVI®.

For further information, please refer to the SmPC.

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Initiation

Starting dose[1]

Based on platelet count:

>200,000/mm³
20 mg orally twice daily

100,000 to 200,000/mm³
15 mg orally twice daily

75,000 to <100,000/mm³
10 mg orally twice daily

50,000 to <75,000/mm³
5 mg orally 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 the recommendations below this diagram and section 4.2 of the SmPC for full information.

Monitoring[1]

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.

Approx 4 weeks

Improvement in spleen size[2,3]

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 titration[1]

Doses should not be increased during the **first 4 weeks** of therapy.

Thereafter, doses should not be increased more frequently than at **2-week intervals**.

Doses may be increased by a maximum of 5 mg twice daily, up to the maximum dose of 25 mg twice daily.

Dose should be titrated based on safety and efficacy, per SmPC.

Approx 8 weeks

Symptom improvement[1–3]

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

Anaemia[1,4]

Anaemia was generally transient, reaching a nadir of approximately 10g/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.

Management: Patients with anaemia may require blood transfusions.

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

Approx 8–12 weeks

Thrombocytopenia[1]

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.

Restart at 5 mg twice daily once recovered. Consider dose reduction to avoid dose interruption due to thrombocytopenia.

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

24 weeks

Stabilisation of platelet and haemoglobin levels[1]

Continue to monitor complete blood count (including a white blood cell count differential) as clinically indicated.

6 months

Efficacy[1]

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

Dosing in special populations

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.

There are limited data to determine the best dosing options for patients with end-stage renal disease (ESRD) on haemodialysis. Pharmacokinetic/pharmacodynamic simulations based on available data in this population suggest that the starting dose for MF patients with ESRD on haemodialysis is a single dose of 15-20 mg or two doses of 10 mg given 12 hours apart, to be administered post-dialysis and only on the day of haemodialysis. A single dose of 15 mg is recommended for MF patients with platelet count between 100,000/mm^3 and 200,000/mm^3. A single dose of 20 mg or two doses of 10 mg given 12 hours apart is recommended for MF patients with platelet count of >200,000/mm^3. Subsequent doses (single administration or two doses of 10 mg given 12 hours apart) should be administered only on haemodialysis days following each dialysis session.

In MF patients with any hepatic impairment, the recommended starting dose based on platelet count should be reduced by approximately 50% to be administered twice daily. Subsequent doses should be adjusted based on careful monitoring of safety and efficacy.

If JAKAVI® is to be co-administered with strong CYP3A4 inhibitors in MF and PV patients or dual inhibitors of CYP3A4 and CYP2C9 enzymes (e.g., fluconazole), the unit dose of JAKAVI® should be reduced by approximately 50%, to be administered twice daily (for monitoring frequency, see sections 4.2 and 4.5 of the SmPC).[1]

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. Refer to the full Summary of Product Characteristics for further management guidance.[1]

Please refer to the SmPC for full dosing information before prescribing.

Active monitoring can help you find a patient's optimal JAKAVI® dose[1]

Footnotes & references

*For the full list of AEs, please refer to the SmPC.[1]

AE, adverse event; MF, myelofibrosis; PV, polycythaemia vera; SmPC, summary of product characteristics.

References

1. JAKAVI® (ruxolitinib) Summary of Product Characteristics.

2. Polverelli N, et al. EHA 2016, 9–12 June; Copenhagen, Denmark. Abstract P672.

3. Harrison C, et al. *N Engl J Med* 2012;366:787–798.

4. Verstovsek S, et al. *Haematologica* 2013;98:1865–1871.

Learn more about a generally manageable safety profile for your patients

Find out more

UK | November 2024 | FA-11210096
