REGIMEN NAME : RUXOLITINIB

INDICATIONS: : **Primary myelofibrosis**

Post polcythaemia myelofibrosis

Post essential thrombocythaemia myelofibrosis

Symptomatic splenomegaly

Constitutional symptoms

Not eligible for stem cell transplantation

Prior to a course of treatment

- Physical examination with documentation of spleen size
- Full Blood Count
- Biochemical profile to include hepatic and renal function.
- Consent for course

Prior to each prescription

- Medical review of fitness for chemotherapy – exclude active infection, major changes in organ function
- Full Blood Count
- Biochemical profile

Ruxolitinib

Starting dose 5-20mg bd po

Depending on platelet count as below

Titrate in max of 5mg bd increments according to response .Starting dose should not be increased within the first four weeks of treatment and therafter no more frequently than 2 week intervals

For dose reductions due to toxicity see below

Maximum dose 25mg bd

Starting dose

The recommended starting dose of Ruxolitinib is 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. There is limited information to recommend a starting dose for patients with platelet counts between 50,000/mm^3 and <100,000/mm^3. The maximum recommended starting dose in these patients is 5 mg twice daily and the patients should be titrated cautiously

If efficacy is considered insufficient and platelet and neutrophil counts are adequate, doses may be increased by a maximum of 5 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.

Titrate according to response continuous treatment

Prophylaxis for acute & delayed emesis N/A

Other medications

Dose modification for haematological toxicity

Dose modification for neutropenia and infection

In the phase 3 clinical studies, in patients who developed grade 3 or 4 neutropenia, the median time to onset was 12 weeks. Dose holding or reductions due to neutropenia were reported in 1.0% of patients, and 0.3% of patients discontinued treatment because of neutropenia.

Discontinue if neutrophil count less than 0.5

After recovery of neutrophil 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 modification for thrombocytopenia

Doses may be titrated based on safety and efficacy. Treatment should be discontinued for platelet counts less than 50,000/mm^3. After recovery of platelet 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

Dose modification for hepatic dysfunction

In patients with any hepatic impairment the recommended starting dose based on platelet count should be reduced by approximately 50% to be administered twice daily

Patients diagnosed with hepatic impairment while receiving Ruxolitinib should have complete blood counts, including a white blood cell count differential, monitored at least every one to two weeks for the first 6 weeks after initiation of therapy

Dose modification for renal failure

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 should be reduced by approximately 50% to be administered twice daily. Patients should be carefully monitored with regard to safety and efficacy during Ruxolitinib treatment.

There are limited data to determine the best dosing options for patients with end-stage renal disease (ESRD) on haemodialysis

Dose modification for 'other toxicities'

Ruxolitinib Toxicities

Anaemia, neutropaenia, thrombocytopaenia	Weight gain
Hepatotoxicity-raised liver function tests	Hypercholesterolaemia
Bruising	
Dizziness	
Headache	

Drug Interactions:

When Ruxolitinib is administered with strong CYP3A4 inhibitors or dual inhibitors of CYP2C9 and CYP3A4 enzymes (e.g. fluconazole) the unit dose of Ruxolitinib should be reduced by approximately 50%, to be administered twice daily

More frequent monitoring (e.g. twice a week) of haematology parameters and of clinical signs and symptoms of Ruxolitinib-related adverse drug reactions is recommended while on strong CYP3A4 inhibitors or dual inhibitors of CYP2C9 and CYP3A4 enzymes

Written by Dr P Kelsey, Consultant Haematologist

Date

Review date