

RUXOLITINIB

For management of disease-related splenomegaly or constitutional symptoms in patients with intermediate-2 or high risk primary myelofibrosis, post PV myelofibrosis or post ET myelofibrosis
NICE approved March 2016

Drug/Dosage:

Platelet Count (x 10 ⁹ /l)	Ruxolitinib Start Dose
>200	20mg twice daily
100 – 200	15mg twice daily
50 – 99	5mg twice daily
< 50	Not recommended

If efficacy is considered insufficient and platelet and neutrophil counts are adequate, ruxolitinib doses may be increased in 5mg once or twice daily increments, to a maximum of 25mg twice daily.

The starting dose should not be increased for the first 4 weeks of treatment, and then no more frequently than at 2-weekly intervals.

The maximum dose increase at any one time is an additional 5mg twice daily.

The maximum daily dose is 25mg twice daily.

Administration: ruxolitinib is available as 5mg, 15mg and 20mg tablets, to be swallowed whole with or without food.

Frequency: continuous therapy
Treatment should be discontinued after 6 months if there has been no reduction in spleen size or improvement in symptoms since initiation of therapy.

Main Toxicities: myelosuppression; raised transaminases; hypercholesterolaemia;
dizziness; headache; bruising / bleeding

Anti- emetics: none usually needed

Regular Investigations: FBC every 2 – 4 weeks until the dose is stabilised, then every 2 – 3 months
LFTs monthly initially, then every 3 – 6 months
U&Es monthly initially, then every 3 – 6 months

Drug Interactions: Ruxolitinib is metabolised via CYP3A4 enzymes.

When a strong CYP3A4 inhibitor (e.g. clarithromycin, itraconazole, posaconazole) or fluconazole is co-prescribed with ruxolitinib, the ruxolitinib dose should be reduced by approximately 50%.

FBC should be monitored more frequently e.g. twice weekly, and the dose titrated according to efficacy.

Potent CYP3A4 inducers (e.g. rifampicin) are thought to have minimal effect on the ruxolitinib active metabolites.

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Version: 3	Date: 7.6.16
Supersedes: Version 2	Review date: July 2019
Prepared by: S Taylor	Checked by: C Tucker

Dose Modifications

Haematological Toxicity:

SPC advice is for a dose reduction to be considered if the platelet count falls to $< 100 \times 10^9/l$, with the goal of avoiding dose interruptions for thrombocytopenia.

However, advice on file from Novartis is to consider titrating the ruxolitinib dose according to the platelet count, as advised for the start dose, e.g. if the platelet count falls to $< 200 \times 10^9/l$, consider reducing the ruxolitinib dose to 15mg bd.

Treatment should definitely be interrupted if platelets $< 50 \times 10^9/l$ or neutrophils $< 0.5 \times 10^9/l$. Once the counts have recovered to above these thresholds, ruxolitinib can be re-started at 5mg twice daily, then gradually increased based on FBC monitoring.

Renal Impairment:

CrCl (ml/min)	Ruxolitinib Dose
< 30	The starting dose based on platelet count should be reduced by approximately 50%
On haemodialysis and platelet count $100 - 200 \times 10^9/l$	15mg as a single dose after each haemodialysis session (dosing only on dialysis days)
On haemodialysis and platelet count $>200 \times 10^9/l$	20mg as a single dose after each haemodialysis session (dosing only on dialysis days)

Hepatic Impairment:

In patients with any hepatic impairment, the starting dose based on platelet count should be reduced by approximately 50%.

FBC should be monitored more frequently: every 1-2 weeks for the first 6 weeks, then as clinically indicated.

Patient Information:

No Macmillan leaflet available

References:

Harrison, C et al; NEJM 2012; 366 (9): 787 – 798
Verstovsek, S et al; NEJM 2012; 366 (9): 799 - 807

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