Ruxolitinib

Indication
Management of disease related splenomegaly.
Symptomatic patients with primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis.

ICD-10 codes
Codes with a pre fix D45, D47, C94

Regimen details

Day	Drug	Platelet count (x 10^9/L)	Dose	Route
1-28*	Ruxolitinib	≥ 200	20mg BD	PO
1-28*	Ruxolitinib	100 - < 200	15mg BD	PO
1-28*	Ruxolitinib	50 - < 100	5mg BD (maximum starting dose, titrate carefully)	PO

* continuously

Ruxolitinib is not recommended if platelet count < 50 x 10^9/L.

The dose may be increased by 5mg BD after 4 weeks of treatment and not more frequently than 2 weekly.
Maximum dose 25mg BD.

Cycle frequency
Continuous – treatment should not be interrupted (unless neutrophil or platelet count necessitates- see below).

Number of cycles
Treatment may be continued as long as the benefit-risk remains positive. However the treatment should be discontinued after 6 months if there has been no reduction in spleen size or improvement in symptoms since initiation of therapy.

Administration
Ruxolitinib is available as 5mg, 10mg, 15mg and 20mg tablets. Tablets should be swallowed whole, with or without food.

Pre-medication
Nil

Emetogenicity
This regimen has low emetic potential

Additional supportive medication
Antiemetics if required.

Extravasation
N/A

Investigations – pre first cycle

Investigation	Validity period
FBC	72 hours
U + E (including creatinine)	72 hours
LFTs	72 hours

Investigations – pre subsequent cycles

Investigation	Validity period (or as per local policy)
FBC	2-4 weekly until stable then 2-3 monthly
U+E (including creatinine)	2-4 weekly until stable then 2-3 monthly
LFTs	2-4 weekly until stable then 2-3 monthly

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	Limit
Neutrophils	≥ 0.5 x 10^9/L
Platelets	≥ 50 x 10^9/L
Creatinine clearance (CrCl)	≥ 30mL/min
Bilirubin	≤ ULN
AST/ALT	≤ ULN

Dose modifications

- **Haematological toxicity**

Treatment should be interrupted if neutrophils < 0.5 x 10^9/L and/or platelets < 50 x 10^9/L. After recovery above these levels treatment may be recommenced at 5mg BD and titrated upwards with close monitoring of FBC.

- **Renal impairment**

No specific dose adjustment is required in mild-moderate renal impairment.

In severe renal impairment (CrCl <30mL/min) the starting dose according to platelet count should be reduced to 50% with close monitoring.

Haemodialysis:

Platelet count (x 10^9/L)	Ruxolitinib dose
100-200	15mg as a single dose after each haemodialysis session (i.e. dose only on dialysis days)
≥ 200	20mg as a single dose (or 10mg 12 hours apart) after each haemodialysis session (i.e. dose only on dialysis days)

- **Hepatic impairment**

In hepatic impairment (any degree) the starting dose according to platelet count should be reduced to 50% with close monitoring. FBC should be monitored 1-2 weekly for the first 6 weeks. Subsequent doses should be adjusted with careful monitoring.

If hepatic impairment develops during treatment FBC should be monitored closely.

- **Other toxicities**

No dose adjustments required.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Bleeding

- **Commonly occurring side effects**

Myelosuppression
Diarrhoea
Abdominal pain
Headache
Dizziness
Bruising, bleeding
Raised transaminases
Raised blood pressure

- **Other side effects**

Hypercholesterolaemia
Weight gain

Significant drug interactions – for full details consult product literature/ reference texts

Ruxolitinib is metabolised by CYP3A4 enzymes

Potent CYP3A4 inhibitors (e.g. ketoconazole, clarithromycin, itraconazole, voriconazole): avoid co-administration these may increase plasma concentrations of ruxolitinib, increasing the risk of toxicity. If co-administration is necessary reduce dose of ruxolitinib to 50% and monitor FBC twice weekly.

Dual CYP3A4 and CYP2C9 inhibitors (e.g fluconazole): If co-administration is necessary reduce dose of ruxolitinib to 50% and monitor FBC twice weekly.

Weak-moderate CYP3A4 inhibitors (e.g. erythromycin, ciprofloxacin, dilatiazem): avoid co-administration if possible. No dose adjustments required.

Inducers of CYP3A4 (e.g. rifampicin, phenytoin, carbamazepine, St Johns Wort): may reduce exposure to ruxolitinib, but studies have shown little effect on active metabolites. If co-administration required, monitor closely, dose increase may be required.

Additional comments

Nil

References

- Summary of Product Characteristics Ruxolitinib (Novartis), accessed 28 January 2015 via http://www.medicines.org.uk
- Harrison, C et al; JAK inhibition with ruxolitinib versus best available therapy for myelofibrosis NEJM 2012; 366 (9): 787 – 798
- Verstovsek, S et al; A double-blind, placebo-controlled trial of ruxolitinib for myelofibrosis NEJM 2012; 366 (9): 799 - 807

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