Indication	Ruxolitinib for treating disease-related splenomegaly or symptoms in adults with intermediate-2 or high-risk myelofibrosis who have not received any therapy with a JAK inhibitor or have been previously treated only with momelotinib or received previous ruxolitinib before subsequently being treated with momelotinib and treatment has failed or the patient was intolerant of momelotinib and a re-start of ruxolitinb is being requested. For the treatment of high-risk polycythaemia vera (PV) in patients who are resistant to treatment with hydroxycarbamide or who cannot tolerate treatment with hydroxycarbamide. Patients must have not received previous treatment with ruxolitinib unless via a company access scheme or within the MAJIC-PV trial and the benefit-risk ratio for continuing treatment is positive. **Note: there are 2 dosing schedules one for myelofibrosis and one for PV**
Treatment Intent	Curative/ Non-curative/Remission
Frequency and number of cycles	Repeat every 28 days **Schedule 1** for the treatment of myelofibrosis **Schedule 2** for the treatment of PV Continue until disease progression, unacceptable toxicity or patient choice. NB Treatment for both indications should be discontinued after 6 months if there has been no reduction in spleen size or improvement in symptoms.
Monitoring Parameters pre-treatment	• **Virology screening:** All new patients referred for systemic anti-cancer treatment should be screened for hepatitis B and C and the result reviewed prior to the start of treatment. Patients not previously tested who are starting a new line of treatment, should also be screened for hepatitis B and C. Further virology screening will be performed following individual risk assessment and clinician discretion. • BP should be checked at baseline and before each cycle. • FBC, Cr, U&E and LFTs should be monitored each cycle. • *Patients diagnosed with hepatic impairment while receiving ruxolitinib should have FBC, including a white blood cell count differential, at least every 1 to 2 weeks for the first 6 weeks after initiation of treatment and as clinically indicated thereafter once their liver function and blood counts have been stabilised. • **Starting dose:** o **Myelofibrosis** o For patients with platelet count of > 200x10^9/l the recommended starting dose is 20mg BD. o For patients with platelet count between 100 x10^9/l and 200 x10^9/l the starting dose is 15mg BD. o For patients with platelet count between 75 x10^9/l and <100 x10^9/l the starting dose is 10mg BD. o The maximum starting dose for patients with platelet count between 50 x10^9/l and <75 x10^9/l is 5mg BD and the patients should be titrated cautiously. o **PV** o 10 mg given orally twice daily. • **Dose modification for Myelofibrosis and PV:** o Treatment should be reviewed by consultant if platelet count less than 50x10^9/l or neutrophil count less than 0.5 x10^9/l.

	○ 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 during treatment see **table 1,** to avoid interruption of treatment. ○ 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. ○ Dose titration can be considered if efficacy insufficient and blood counts are adequate after the first 4 weeks of treatment and no more frequently than every 2 weeks thereafter. The patient's dose can be increased by a **maximum** of 5 mg twice daily, up to the maximum dose of 25 mg twice daily. • **Renal Impairment:** ○ **Myelofibrosis:** ○ No specific dose adjustment is needed in patients with mild or moderate renal impairment. ○ In patients with severe renal impairment (CrCl<30ml/min) starting dose based on platelet count should be reduced by approximately 50%. ○ For patients with end-stage renal disease (ESRD) on haemodialysis the starting dose is a single dose of 15-20mg 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 patients with platelet count between $100x10^9$/l and $200x10^9$/l. A single dose of 20 mg or two doses of 10 mg given 12 hours apart is recommended for patients with platelet count of $>200x10^9$/l. 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. ○ **PV:** ○ No specific dose adjustment is needed in patients with mild or moderate renal impairment. ○ In patients with severe renal impairment (CrCl<30ml/min) recommended starting dose is 5mg BD. Patients should be closely monitored. ○ For patients with end-stage renal disease (ESRD) on haemodialysis the starting dose is 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. This recommendation is based on simulation only, patients should be closely monitored for safety and efficacy. ○ No data is available for dosing patients who are undergoing peritoneal dialysis or continuous venovenous haemofiltration. • **Hepatic Impairment:** (see * above) ○ **Myelofibrosis**: In patients with any hepatic impairment the recommended starting dose based on platelet count should be reduced by approximately 50%. ○ **PV:** In patients with any hepatic impairment the recommended starting dose is 5mg BD. • **Infections:** ○ Serious bacterial, mycobacterial, fungal and viral infections have occurred in patients treated with ruxolitinib. Patients should be monitored for signs and symptoms of infection. ○ Tuberculosis - patients should be evaluated for active and latent tuberculosis due to reports of tuberculosis during treatment. ○ Clinicians should educate patients about early signs and symptoms of herpes zoster, advising that treatment should be sought as early as possible.

	• Progressive multifocal leukoencephalopathy (PML) has been reported in patients treated with ruxolitinib. If PML is suspected treatment should be suspended until PML has been excluded. • **Common drug interactions (for comprehensive list refer to BNF/SPC):** o The dose of ruxolitinib should be reduced by approximately 50% when administered with strong CYP3A4 inhibitors (e.g. ketoconazole, itraconazole, clarithromycin, voriconazole, posaconazole) or dual inhibitor CYP2C9 and CYP3A4 (e.g. fluconazole). Avoid the concomitant use of ruxolitinib with fluconazole doses greater than 200 mg daily. o Increased haematological monitoring is required during concomitant administration of ruxolitinib with strong CYP3A4 inhibitors or dual inhibitors of CYP2C9 and CYP3A4 enzymes. o Consider increasing the dose of ruxolitinib according to response if patient also prescribed a strong CYP 3A4 inducer. o Ruxolitinib may inhibit P-gp and BRCP resulting in increased expose of substrates of these transporters (ciclosporin, digoxin and dabigatran). Therapeutic drug monitoring and clinical monitoring is recommended. Where possible dose administration of ruxolitinib and these transporters substrates should be kept apart for as long as possible. • **Missed dose:** If a dose is missed, the dose should be omitted and the patient should resume with the next dose at the next scheduled time. • **Driving:** Dizziness has been reported as a side effect, if effected patients should refrain from driving or operating machinery. • For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet and Macmillan information sheet**.**
References	SPC accessed online 26.09.2023 KMCC proforma HAEM-AML-020 V3 CDF list V1.277 accessed online 26.09.2023 BlueTeq form accessed online 26.09.2023

NB For funding information, refer to CDF and NICE Drugs Funding List

Table 1 Dose recommendations for thrombocytopenia in Myelofibrosis and PV

Dose at time of platelet decline					
	25 mg BD	20 mg BD	15 mg BD	10 mg BD	5 mg BD
Platelet count	**New dose**				
$100x10^9$/l to $<125x10^9$/l	20 mg BD	15 mg BD	No change	No change	No change
$75x10^9$/l to $<100x10^9$/l	10 mg BD	10 mg BD	10 mg BD	No change	No change
$50 x10^9$/l to $<75x10^9$/l	5 mg BD	5 mg BD	5 mg BD	5 mg BD	No change
Less than $50x10^9$/l	Discuss with consultant	Discuss with consultant	Discuss with consultant	Discuss with consultant	Discuss with consultant

Schedule 1 for the treatment of MYELOFIBROSIS
Repeat every 28 days

TTO	Drug	Dose	Route	Directions
Day 1	**RUXOLITINIB**	**15mg***	PO	Twice a day. (Available as 5mg, 10mg, 15mg and 20mg tablets)
***see notes above: starting dose dependant on PLT count.**				

Schedule 2 for the treatment of PV
Repeat every 28 days

TTO	Drug	Dose	Route	Directions
Day 1	**RUXOLITINIB**	**10mg**	PO	Twice a day. (Available as 5mg, 10mg, 15mg and 20mg tablets)