Momelotinib Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
For the treatment of disease-related splenomegaly or symptoms in adult patients with: Moderate to severe anaemia who have primary myelofibrosis, Post polycythaemia vera myelofibrosis or Post essential thrombocythaemia myelofibrosis and who are Janus Kinase (JAK) inhibitor naïve or have been treated with ruxolitinib.	 D47 D45 D46	00867a	CDS 01/09/2024

* This applies to post 2012 indications

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Momelotinib is administered orally once daily on a continuous basis until disease progression or unacceptable toxicity develops.

Drug	Dose	Route	Cycle
Momelotinib	200mg once daily	PO with or without food	Continuous
If a dose is missed, the next scheduled dose should be taken the following day. Two doses should not be taken at the same time to make up for the missed dose.			

ELIGIBILITY:

- Indications as above
- ≥ 18 years
- ECOG 0-2
- Adequate organ function

CAUTIONS:

- Patients with pre-existing cardiovascular disease or other cardiovascular risk factors
- Active infection

EXCLUSIONS:

- Hypersensitivity to momelotinib or to any of the excipients
- Pregnancy/breastfeeding

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Haematologist working in the area of haematological malignancies.

TESTS:

Baseline tests:

- FBC, renal and liver profile, LDH
- Physical exam including splenic measurement by palpation
- Weight
- Cardiac assessment including history and physical exam if clinically indicated
- Virology screen - Hepatitis B (HBsAg, HBcoreAb) & C
  *See Regimen Specific Complications re Hepatitis B Reactivation

Regular tests:

- FBC weekly for the first month the prior to each cycle
- Renal and liver profile, LDH
- Physical exam including splenic measurement by palpation if clinically indicated
- Weight

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant
- Dose modifications should be considered for haematologic and non-haematologic toxicities as shown in Tables 1, 2 and 3
- Treatment should be discontinued in patients unable to tolerate 100 mg once daily

Haematological:

Table 1: Dose modification of momelotinib in haematological toxicity

ANC (x10^9/L)	Dose	Thrombocytopenia		Dose Modification[a]
		Baseline Platelets (x10^9/L)	Platelets (x10^9/L)	
<0.5	Interrupt treatment until ANC ≥0.75 × 10^9 /L. Restart momelotinib at a daily dose of 50 mg below the last given dose [b]	≥100	20 to <50	Reduce daily dose by 50 mg from the last given dose.
			<20	Interrupt treatment until platelets recover to 50 × 10^9 /L. Restart at a daily dose of 50 mg below the last given dose[b]
		≥50 to <100	<20	Interrupt treatment until platelets recover to 50 × 10^9 /L. Restart at a daily dose of 50 mg below the last given dose [b]
		<50	<20	Interrupt treatment until platelets recover to baseline Restart at a daily dose of 50 mg below the last given dose [b]
[a] Reinitiate or escalate treatment up to starting dosage as clinically appropriate				
[b] May reinitiate treatment at 100 mg if previously dosed at 100 mg				

Renal and Hepatic Impairment:

Table 2: Dose modification of momelotinib in renal and hepatic impairment

Renal Impairment	Hepatic Impairment	
No dose adjustment is required for patients with renal impairment (CrCl>15 mL/min). Momelotinib has not been studied in patients with end-stage renal disease.	**Mild/Moderate**	No dose adjustment is recommended
	Severe (Child –Pugh C)	The recommended starting dose is 150 mg once daily.
Recommendations from SmPC		

Management of adverse events:

Table 3: Dose modifications of momelotinib for non-haematologic toxicities

Toxicity	Recommended dose modification[a]
Hepatotoxicity (unless other apparent causes). ALT and/or AST >5 × ULN (or >5 × baseline, if baseline is abnormal) and/or total bilirubin >2 × ULN (or >2 × baseline, if baseline is abnormal).	Interrupt treatment until AST and ALT ≤2 × ULN or baseline and total bilirubin ≤1.5 × ULN or baseline. Restart at a daily dose of 50 mg below the last given dose [b] If reoccurrence of ALT or AST elevations >5 × ULN, permanently discontinue momelotinib.
Other non-haematologic toxicities Grade 3 or higher[c] Grade 2 or higher[c] bleeding.	Interrupt treatment until the toxicity resolves to Grade 1 or lower (or baseline) Restart at a daily dose of 50 mg below the last given dose[b].
[a] Reinitiate or escalate treatment up to starting dosage as clinically appropriate	
[b] May reinitiate treatment at 100 mg if previously dosed at 100 mg	
[c] Graded using the National Cancer Institute Common Terminology Criteria for Adverse Events per (CTCAE).	

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

- As outlined in NCCP Classification Document for Systemic AntiCancer Therapy (SACT) Induced Nausea and Vomiting linked here

Momelotinib: Minimal to low (**Refer to local policy).**

For information:
Within NCIS regimens, antiemetics have been standardised by the Medical Oncologists and Haemato-oncologists and information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) - link here
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) - link here

PREMEDICATIONS:

None required

OTHER SUPPORTIVE CARE:

Anti-diarrhoeal treatment as clinically indicated **(Refer to local policy).**

ADVERSE EFFECTS:

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details
- **Momelotinib is subject to additional monitoring. Healthcare professionals are asked to report any suspected adverse reactions**

REGIMEN SPECIFIC COMPLICATIONS

- **Hepatitis B Reactivation**: Patients should be tested for both HBsAg and HBcoreAb as per local policy. If either test is positive, such patients should be treated with anti-viral therapy (Refer to local infectious disease policy). These patients should be considered for assessment by hepatology.
- **Diarrhoea:** In clinical trials diarrhoea was reported in 23% of patients treated with momelotinib.

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for information.

REFERENCES:

1. Mesa R A t al. SIMPLIFY-1: A Phase III Randomized Trial of Momelotinib Versus Ruxolitinib in Janus Kinase Inhibitor–Na¨ıve Patients With Myelofibrosis. J Clin Onc: 2017:34 (34)3844- 3850. Available here https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6553796/pdf/JCO.2017.73.4418.pdf
2. Harrison C Net al. Momelotinib versus best available therapy in patients with myelofibrosis previously treated with ruxolitinib (SIMPLIFY 2): a randomised, open-label, phase 3 trial. Lancet Haem: 2018 Feb;5(2):e73-e81. doi: 10.1016/S2352-3026(17)30237-5. Available here https://pubmed.ncbi.nlm.nih.gov/29275119/
3. Gerds A t et al. Momelotinib versus danazol in symptomatic patients with anaemia and myelofibrosis previously treated with a JAK inhibitor (MOMENTUM): an updated analysis of an international, double-blind, randomised phase 3 study. Lancet Haem: 2023-09-01, Vol10, Issue 9, Pages e735-e746. Available here https://www.clinicalkey.com/#!/content/journal/1-s2.0-S2352302623001746
4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Antiemesis Version 1.2024 – December 13, 2023. Accessed June 2024. Available at https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf
5. Momelotinib (Omjjara®) Summary of Product Characteristics. Accessed August 2024. Available here: https://www.ema.europa.eu/en/documents/product-information/omjjara-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	16/09/2024		Dr Claire Andrews

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