Indication	Monotherapy treatment for moderately to severely anaemic patients with myelofibrosis (intermediate-2 or high risk) and disease-related splenomegaly or symptoms. NB: the patient has not previously received momelotinib unless the patient has received momelotinib via a company early access scheme.
Treatment Intent	Disease modification
Frequency and number of cycles	Every 28 days, continuous treatment. Continue until loss of clinical benefit, unmanageable toxicity or patient choice to discontinue. A formal medical review should be scheduled to occur at least by the start of the third 4-weekly cycle of treatment.
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. • FBC, LFT's and U&Es baseline and at each cycle, for haematological guidance see table 1. • **Hepatic impairment:** no recommended dose adjustment in mild or moderate disease. In severe impairment (child-pugh class c) the recommended starting dose is 150mg OD. • **Renal impairment:** no recommended dose adjustment in renal impairment, CrCl >15ml/min. No available data in end stage renal disease. • Use with caution in patients with pre-existing cardiovascular disease or other cardiovascular risk factors. • Events of DVT and PE have been reported in patients receiving momelotinib, patients with symptoms of thrombosis should be promptly evaluated and treated appropriately. • **Management of adverse reactions and dose adjustments: see table 1** • Treatment should be discontinued in patients unable to tolerate 100mg once a daily. • **Common drug interactions (for comprehensive list refer to BNF/SPC):** o Avoid concomitant treatment with potent CYP3A4 inducers (e.g. phenytoin, St. John's Wort, carbamazepine). o Caution and monitoring for adverse reactions is advised with concomitant use of OATP1B1/1B3 inhibitors, including ciclosporin. o Momelotinib may increase exposure to sensitive BCRP substrates and P-gp substrates, caution is advised when administered with substrates with a narrow therapeutic range. o Caution is advised when administering momelotinib with sensitive substrates of OCT1, MATE1 and MATE2-K (e.g. metformin). o Momelotinib may induce CYP1A2 and CYP2B6 and may inhibit CYP2B6. Therefore, narrow therapeutic index or sensitive substrate products of CYP1A2 (e.g., theophylline, tizanidine) or CYP2B6 (e.g., cyclophosphamide) should be co-administered with momelotinib with caution. • **Missed dose:** If a dose is missed, then do not take the missed dose and continue with the next scheduled daily dose, do not double the dose. • **Driving:** Dizziness or blurred vision has been reported in patients taking momelotinib patients should be advised to be cautious when driving or using machines. • For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet.

References	SPC accessed online 16.02.2024 CDF list V1.298 accessed online 27.03.2024 ARIA regimen MOMELOTINIB compassionate use only. Blueteq form accessed online 26.03.2024

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

Table 1: Dose modifications for adverse reactions

Haematologic toxicities		
Thrombocytopenia		**Dose modification[a]**
Baseline platelet count	**Platelet count**	
>/=100 × 10^9/L	20 × 10^9/L to <50 × 10^9/L	Reduce daily dose by 50 mg from the last given dose
	<20 × 10^9/L	Interrupt treatment until platelets recover to 50 × 10^9/L Restart momelotinib at a daily dose of 50 mg below the last given dose[b]
>/=50 × 10^9/L to <100 × 10^9/L	<20 × 10^9/L	Interrupt treatment until platelets recover to 50 × 10^9/L Restart momelotinib at a daily dose of 50 mg below the last given dose[b]
<50 × 10^9/L	<20 × 10^9/L	Interrupt treatment until platelets recover to baseline Restart momelotinib at a daily dose of 50 mg below the last given dose[b]
Neutropenia		**Dose modification[a]**
ANC <0.5 × 10^9/L		Interrupt treatment until ANC >/=0.75 × 10^9/L Restart momelotinib at a daily dose of 50 mg below the last given dose[b]
Non-haematologic toxicities		
Hepatotoxicity (unless other apparent causes)		**Dose modification[a]**
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
Other non-haematologic toxicities		**Dose modification**
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).

Repeat every 28 days

TTO	Drug	Dose	Route	Directions
Day 1	**MOMELOTINIB**	**200mg**	PO	OD taken at the same time each day with a glass of water. Swallow whole. Do not split, chew or crush. Available as 100mg, 150mg and 200mg tablets
	Loperamide	2mg-4mg	PO	Take TWO capsules at ONCE and then ONE capsule after each loose motion, up to a maximum of 8 capsules in 24 hours if required. Dispense with cycle 1 only.