Indication	For the treatment of newly diagnosed FLT3-ITD mutation positive acute myeloid leukaemia. NB: quizartinib is not commissioned for use in patients with AML bearing a FLT3-TKD mutation.
Treatment Intent	Disease modification
Frequency and number of cycles	**Induction:** Cycle 1 and 2 repeat every 28 days. **Consolidation**: Cycle 3 to 6 repeat every 28 days (for patients with complete remission or complete remission with incomplete haematologic recovery). **Maintenance:** repeat every 28 days to a maximum of 36 cycles (cycle 7 to 42) for patients in complete remission of their AML.
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. • **Cardiac monitoring:** o **Baseline:** ECG and Echo. o **Induction and consolidation chemotherapy: ECG** once weekly and more frequently if clinically indicated. o **Maintenance quizartinib:** ECG once weekly during the 1st month of maintenance quizartinib and thereafter if clinically indicated. o Do not start treatment if the QTcF interval is greater than 450 ms. • **FBC, U&Es** and **LFTs** baseline and at each cycle. • Correction of hypokalaemia and hypomagnesaemia should be performed prior to and during treatment. More frequent monitoring of electrolytes and ECGs should be performed in patients who experience diarrhoea or vomiting. • **Haematological parameters** o During induction and consolidation, blood parameters must meet those required for chemotherapy. o During maintenance: neuts > 0.5 and PLT > 50 without transfusion support. Discuss dose modification with the consultant for persistent Grade 4 neutropenia or thrombocytopenia without active bone marrow disease. • **Renal impairment:** No dose adjustment is recommended for patients with mild or moderate renal impairment. not recommended for use in patients with severe renal impairment (CrCl < 30 mL/min). • **Hepatic impairment:** No dose adjustment is recommended for patients with mild or moderate hepatic impairment. Not recommended in severe impairment (Child-Pugh Class C). • **QT interval prolongation:** Quizartinib must not be used in patients with congenital long QT syndrome and should be used with caution in patients who are at significant risk of developing QT interval prolongation. • **Management of adverse reactions and dose adjustments: See table 1 and table 2.** • **Dose Modification:** For dose modification of quizartinib for adverse reactions see table 1 and table 2. • **Haematopoietic stem cell transplantation** o For patients who proceed to haematopoietic stem cell transplantation (HSCT), quizartinib should be stopped 7 days before the start of a conditioning regimen. It may be resumed after completion of the transplant based on white blood cell count (WBC)

	and at the discretion of the treating physician for patients with sufficient haematologic recovery and with </= Grade 2 graft-versus-host disease (GVHD), not requiring the initiation of new systemic GVHD therapy within 21 days. • **Common drug interactions (for comprehensive list refer to BNF/SPC):** o Concurrent use of strong CYP3A and P-gp inhibitors (ritonavir, itraconazole, clarithromycin, telithromycin, posaconazole, grapefruit juice) during treatment with quizartinib should be avoided. *If concurrent use is unavoidable the recommended dose of quizartinib should be reduced (see table 2). **The required dose reduction has been applied to this protocol for both the induction and consolidation phase as posaconazole is to be prescribed as standard of care. If posaconazole is contraindicated and not prescribed it is the clinicians' responsibility to prescribe the recommended full dose of quizartinib.** o Co-administration of quizartinib with strong or moderate CYP3A inducers should be avoided (e.g. apalutamide, carbamazepine, enzalutamide, phenytoin, rifampicin, St John's Wort, efavirena, phenobarbital and primidone). o Caution should be used when co-administering medicinal products that prolong the QT interval with quizartinib and ECG monitoring should be performed more frequently. o Caution should be used when quizartinib is co-administered with medicinal products that are substrates of BCRP. • **Missed dose:** If a dose of quizartinib is missed the patient should take the dose as soon as possible on the same day and return to the usual schedule the following day. The patient should not take 2 doses on the same day. If a patient vomits an additional dose should not be taken and they should resume treatment the next day**.** • **Contraception and pregnancy**: Women of childbearing potential should use effective contraception during treatment and for at least 7 months after the last dose. Male patients should use effective contraception during treatment and for at least 4 months after the last dose. • **For oral self-administration:** refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet and Macmillan information sheet. • Each patient should be given a copy of the **Vanflyta®** patient alert card at the start of treatment.
References	SPC accessed online 25.09.2024 and 27.11.2024 CDF list accessed online 25.09.2024 https://ashpublications.org/blood/article/132/6/598/39411/Phase-2b-study-of-2-dosing-regimens-of-quizartinib

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

Table 1 Recommended dose modifications of quizartinib for adverse reactions

Adverse reaction	Recommended action
QTcF 450-480 ms (Grade 1)	• Continue dose.
QTcF 481-500 ms (Grade 2)	• Reduce dose (see Table 2) without interruption. • Resume at the previous dose in the next cycle if QTcF has decreased to < 450 ms. Monitor the patient closely for QT prolongation for the first cycle at the increased dose.
QTcF ≥ 501 ms (Grade 3)	• Interrupt treatment. • Resume at a reduced dose (see Table 2) when QTcF returns to < 450 ms. • Do not escalate to 53 mg once daily during maintenance if QTcF > 500 ms was observed during induction and/or consolidation, and it is suspected to be associated with quizartinib. Maintain the 26.5 mg once daily dose.
Recurrent QTcF ≥ 501 ms (Grade 3)	• Permanently discontinue if QTcF > 500 ms recurs despite appropriate dose reduction and correction/elimination of other risk factors (e.g., serum electrolyte abnormalities, concomitant QT prolonging medicinal products).
Torsade de pointes; polymorphic ventricular tachycardia; signs/symptoms of life-threatening arrhythmia (Grade 4)	• Permanently discontinue.
Grade 3 or 4 non-haematologic adverse reactions	• Interrupt treatment. • Resume treatment at the previous dose if adverse reaction improves to ≤ Grade 1. • Resume treatment at a reduced dose (see Table 2) if adverse reaction improves to < Grade 3. • Permanently discontinue if Grade 3 or 4 adverse reaction persists beyond 28 days and is suspected to be associated with quizartinib.
Persistent Grade 4 neutropenia or thrombocytopenia without active bone marrow disease	• Reduce the dose (see Table 2).

Table 2 Dose adjustment of Quizartinib for adverse reactions and/or concomitant use with strong CYP3A inhibitors.

Phase of treatment	Full Dose	Dose reductions		
		Adverse reaction	Concomitant strong CYP3A inhibitors	Adverse reaction and concomitant strong CYP3A inhibitors
Induction or Consolidation	35.4mg	26.5mg	17.7mg	Interrupt
Maintenance (first two weeks)	26.5mg	Interrupt	17.7mg	Interrupt
Maintenance (after two weeks)	53mg	35.4mg	26.5mg	17.7mg

INDUCTION: Commence quizartinib following the completion of chemotherapy.
Cycle 1 and 2 To be prescribed with DA (daunorubicin and cytarabine 28 day cycle.

TTO	Drug	Dose	Route	Directions
Day 1	**QUIZARTINIB**	**17.7mg**	PO	OD for **14 days** only, commencing the day after completion of chemotherapy. Available as 17.7mg and 26.5mg tablets
	Prescribe anti fungal prophylaxis if not already prescribed with chemotherapy regimen. See drug interaction section above*.			

CONSOLIDATION: Commence quizartinib following the completion of chemotherapy.
Cycle 3 to 6: To be prescribed with high dose cytarabine, 28 day cycle.

TTO	Drug	Dose	Route	Directions
Day 1	**QUIZARTINIB**	**17.7mg**	PO	OD for **14 days** only, commencing the day after completion of chemotherapy. Available as 17.7mg and 26.5mg tablets
	Prescribe anti fungal prophylaxis if not already prescribed with chemotherapy regimen. See drug interaction section above*.			

MAINTENANCE:
Cycle 7 onwards to a maximum of 36 cycles: Repeat every 28 days continuously.

TTO	Drug	Dose	Route	Directions
Day 1	**QUIZARTINIB**	**See directions***	PO	OD continuously *26.5mg once daily for two weeks if QTcF is </= 450 ms. After two weeks, if QTcF is </= 450 ms, the dose should be increased to 53mg once daily. Available as 17.7mg and 26.5mg tablets