Dose modification schedule & management of adverse reactions to Vandetanib

Adverse reactions based on grade (except for prolongation of QT interval).

Grade	Recommended dose modification
Grade 3 or higher toxicity	Vandetanib should be stopped and resumed at a reduced dose when toxicity has resolved or improved to grade 1 (see SpC section 4.2). The 300 mg daily dose can be reduced to 200 mg (two 100 mg tablets), and then to 100 mg if necessary. The patient must be monitored appropriately. **Due to the 19-day half-life, adverse reactions including a prolonged QTc interval may not resolve quickly (see SpC section 4.2).**

Dose modification schedule based on prolongation of QT interval

QT c value	Recommended dose modification
QTc > 480ms at baseline	Treatment not recommended
QTc increases markedly but remains<500ms	Seek cardiologist advice Electrolyte abnormalities (including magnesium) should be corrected, and cardiac risk factors for QT prolongation (e.g. congestive heart failure, bradyarrhythmias) should be controlled
1st occurrence of QTc≥500ms during treatment	Temporarily interrupt treatment until QTc decreases to pre-treatment levels. Resume dosing at 200 mg daily. ECG and electrolyte monitoring should be carried out at a minimum of prior to each cycle for 3 months and every 3 months after re-starting
2nd occurrence of QTc≥500 ms	Temporarily interrupt treatment until QTc decreases to pre-treatment levels. Resume dosing at 100 mg daily. ECG and electrolyte monitoring should be carried out at a minimum of prior to each cycle for 3 months and every 3 months after re-starting

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N.B. Version numbers re-started from 1 when adverse reaction information separated from proforma