VEMURAFENIB (Zelboraf)

INDICATION (ICD10) C43
1. BRAF V600 mutation-positive unresectable or metastatic malignant melanoma (TA269).

REGIMEN
Day 1 VEMURAFENIB 960mg orally twice daily continuously

CYCLE FREQUENCY AND NUMBER OF CYCLES
Every 28 days until disease progression

ADMINISTRATION
Available as 240mg tablets
Swallow whole with water, taken with or without food, but consistent intake of both daily doses on an empty stomach should be avoided.

ANTI-EMETICS
Low emetic risk

CONCURRENT MEDICATION REQUIRED

Vemurafenib	None required

INVESTIGATIONS
Blood results required before SACT administration
FBC, U&E, Mg^{++} and LFTs every cycle
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Serum creatinine - GFR each cycle
ECG baseline, 1 month then every 3 months

MAIN TOXICITES AND ADVERSE REACTIONS

Vemurafenib	Mild to moderate photosensitivity. Diarrhoea and vomiting. Arthralgia and musculoskeletal pain. Hypersensitivity reactions, including anaphylaxis. QT prolongation and ventricular arrhythmias. Cutaneous squamous cell carcinoma (keratoacanthoma).

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS
(not exhaustive list check SPC/BNF/Stockleys)

Vemurafenib	Many interactions check carefully

DOSE MODIFICATIONS

Vemurafenib

Other toxicities

Grade 1 or grade 2 (tolerable)	Maintain vemurafenib at a dose of 960mg twice daily.
Grade 2 (intolerable) or grade 3 1st occurrence of any grade 2 or 3 AE	Interrupt treatment until grade 0–1. Resume dosing at 720mg twice daily (or 480mg twice daily if the dose has already been lowered).
Grade 2 (intolerable) or grade 3 2nd occurrence of any grade 2 or 3 AE or persistence after treatment interruption	Interrupt treatment until grade 0–1. Resume dosing at 480mg twice daily (or discontinue permanently if the dose has already been lowered to 480mg twice daily).
Grade 2 (intolerable) or grade 3 3rd occurrence of any grade 2 or 3 AE or persistence after 2nd dose reduction	Discontinue permanently.
Grade 4 1st occurrence of any grade 4 AE	Discontinue permanently or interrupt vemurafenib treatment until grade 0–1. Resume dosing at 480mg twice daily (or discontinue permanently if the dose has already been lowered to 480mg twice daily).
Grade 4 2nd occurrence of any grade 4 AE or persistence of any grade 4 AE after 1st dose reduction	Discontinue permanently.

QTc interval

QTc>500ms at baseline	Treatment not recommended.
QTc increase meets values of both >500ms and >60ms change from pre-treatment values	Discontinue permanently.
1st occurrence of QTc>500ms during treatment and change from pre-treatment value remains <60ms	Temporarily interrupt treatment until QTc decreases below 500ms. Resume dosing at 720mg twice daily (or 480mg twice daily if the dose has already been lowered).
2nd occurrence of QTc>500ms during treatment and change from pre-treatment value remains <60ms	Temporarily interrupt treatment until QTc decreases below 500ms. Resume dosing at 480mg twice daily (or discontinue permanently if the dose has already been lowered to 480mg twice daily).
3rd occurrence of QTc>500ms during treatment and change from pre-treatment value remains <60ms	Discontinue permanently.

Hepatic impairment

Vemurafenib

Moderate to severe hepatic impairment should be closely monitored.

Renal impairment

Vemurafenib

Severe renal impairment should be monitored.

REFERENCES

1. SPC