DABRAFENIB (Tafinlar)

INDICATION (ICD10) C43

1. The treatment of advanced unresectable or metastatic **melanoma** (PS 0 or 1) with a BRAF V600 mutation and intolerance to vemurafenib (severe intolerance necessitating discontinuation, without disease progression whilst on full dose, within 2 months of initiating vemurafenib) No other previous systemic treatment other than vemurafenib (TA321).

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/)

2. Dabrafenib monotherapy for BRAFV600E mutation positive **histiocytic neoplasms** (eg Langerhans Cell Histiocytosis (LCH), Erdheim Chester Disease (ECD), Juvenile Xanthogranuloma (JXG), Rosai Dorman Disease (RDD), Other histiocytic neoplasms within the ICD11 code (eg 2B31.1, 2B31.Y, 2B31.Z)) where standard systematic treatments (but no other BRAF inhibitors) have failed or there is no alternative current standard of care treatment (eg for neurodegenerative LCH or LCH with life-threatening pulmonary involvement) and treatment with dabrafenib has also been approved by the National Histiocytic Advisory Panel. (unlicensed)

REGIMEN

Day 1 DABRAFENIB 150mg orally twice daily (12 hourly) continuously

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 28 days until disease progression

ADMINISTRATION

Available as 50mg and 75mg capsules
Swallow whole with water, at least 1 hour before or at least 2 hours after a meal.
Grapefruit and grapefruit juice should be avoided.

ANTI-EMETICS

Low emetic risk

CONCURRENT MEDICATION REQUIRED

Dabrafenib	-

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
Hba1c baseline
Random glucose every cycle
ECG at baseline, 1 month then every 3 months
Blood pressure every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Dabrafenib	Cutaneous squamous cell carcinoma Hepatic toxicity New primary melanoma Non-cutaneous secondary / recurrent malignancy Renal failure Uveitis Pancreatitis QT prolongation Pyrexia

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

Dabrafenib	Effect of anticoagulants many be decreased. Antiviral exposure may be decreased. CYP3A4, CYP2C and CYP2B6 inducers should be avoided. Many interactions check carefully. Grapefruit and grapefruit juice should be avoided

DOSE MODIFICATIONS
Dabrafenib

Dose level	Dose
Full dose	150mg twice daily
First reduction	100mg twice daily
Second reduction	75mg twice daily
Third reduction	50mg twice daily

Grade (CTCAE)	Recommended dabrafenib dose modifications
Grade 1 or grade 2 (tolerable)	Continue treatment and monitor as clinically indicated.
Grade 2 (intolerable) or grade 3	Interrupt therapy until toxicity is grade 0-1 and reduce by one dose level when resuming therapy.
Grade 4	Discontinue permanently, or interrupt therapy until grade 0-1 and reduce by one dose level when resuming therapy.

Hepatic impairment
Dabrafenib
No dose adjustment for patients with mild or moderate renal impairment.
Use in caution with severe impairment.

Renal impairment
Dabrafenib
No dose adjustment for patients with mild hepatic impairment.
Use with caution in moderate or severe impairment.

REFERENCES
1. SPC