SELPERCATINIB (Retsevmo)

IINDICATIONS (ICD10) C34, C73

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (SEL1) (SEL2) (SEL3) (SEL4) (SEL5) (SEL6)

1. Selpercatinib monotherapy for the treatment of patients with previously treated RET fusion positive **non-medullary thyroid** cancer. Either has differentiated thyroid cancer (papillary/follicular/Hurtle cell) and has therefore been treated with lenvatinib or sorafenib or the patient has anaplastic thyroid cancer in which case no previous TKI treatment requirement is necessary. PS 0, 1 or 2. (TA1038)
2. Selpercatinib monotherapy for the treatment of patients with previously treated with cabozantinib or vandetanib RET mutant **medullary thyroid** cancer. PS 0, 1 or 2. (TA1038)
3. Selpercatinib monotherapy for the treatment of adult patients with locally advanced or metastatic non-small cell **lung** cancer (NSCLC) exhibiting a RET gene fusion and who have previously received immunotherapy and/or platinum-based chemotherapy. Either has no known brain/CNS metastases or if the patient does have brain/ CNS metastases then the patient is symptomatically stable before starting selpercatinib. PS 0, 1 or 2. (TA1042)
4. Selpercatinib monotherapy for the 1st line treatment of adult patients with previously untreated locally advanced or metastatic non-small cell **lung** cancer (NSCLC) exhibiting a RET gene fusion. Either has no known brain/CNS metastases or if the patient does have brain/CNS metastases then the patient is symptomatically stable before starting selpercatinib. PS 0, 1 or 2.
5. Selpercatinib monotherapy for the treatment of adults and adolescents aged 12 years and older with RET fusion positive **non-medullary thyroid** cancer previously UNTREATED with any kinase inhibitor therapy, either refractory to radioactive iodine or that treatment with radioactive iodine is inapprorpriate. PS 0, 1 or 2. (TA1039)
6. Selpercatinib monotherapy for the treatment of adults or adolescents aged 12 years and older with RET mutant **medullary thyroid** cancer previously UNTREATED with any kinase inhibitor therapy. PS 0, 1 or 2. (TA1039)

REGIMEN

<50kg: SELPERCATINIB 120mg oral twice daily
≥50kg: SELPERCATINIB 160mg oral twice daily

CYCLE FREQUENCY AND NUMBER OF CYCLES

Continuously until disease progression.
A formal medical review as to how selpercatinib is being tolerated and whether treatment with selpercatinib should continue or not will be scheduled to occur at least by the start of the third 4- weekly cycle of treatment.

ADMINISTRATION

Available as 40mg and 80mg capsules
Swallowed whole with or without food. Selpercatinib must be accompanied by a meal if used concomitantly with a proton pump inhibitor, or administered 2 hours before or 10 hours after H_2 receptor antagonists.

ANTI-EMETICS

Minimal risk

CONCURRENT MEDICATION REQUIRED

Selpercatinib	None required

EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

INVESTIGATIONS

Blood results required before SACT
administration FBC and U&E every cycle
LFTs every 2 weeks for first 3 cycles then every cycle
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Creatinine every cycle
Blood pressure every cycle
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Selpercatinib	Haemorrhagic events Hypersensitivity Hypertension Increased ALT or AST QT interval prolongation

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS

(not exhaustive list check SPC/BNF/Stockleys)

Selpercatinib	Many drug interactions check carefully. Reduce the current selpercatinib dose should be reduced by 50% if co- administering with a strong CYP3A inhibitor. If the CYP3A inhibitor is discontinued, the selpercatinib dose should be increased (after 3-5 half- lives of the inhibitor) to the dose that was used before starting the inhibitor.

DOSE MODIFICATIONS

Recommended dose modifications for adverse reactions based on body weight

Dose modification	Adults and adolescents ≥50Kg	Adults and adolescents <50Kg
Starting dose	160mg orally twice daily	120mg orally twice daily
First dose reduction	120mg orally twice daily	80mg orally twice daily
Second dose reduction	80mg orally twice daily	40mg orally twice daily
Third dose reduction	40mg orally twice daily	Not applicable

Non-haematological

Recommended dose modifications for adverse reactions

Adverse drug reaction (ADR)		Dose modification
Haemorrhagic events	Grade 3 or grade 4	• Selpercatinib should be suspended until recovery to baseline. Resume at reduced dose. • If grade 3 events reoccur following dose modification, permanently discontinue selpercatinib.
	Grade 4	• Permanently discontinue

Hypersensitivity	All grades	• Suspend dose until toxicity resolves and begin corticosteroids at a dose of 1mg/kg. Resume selpercatinib at 40mg twice daily while continuing steroid treatment. Discontinue selpercatinib for recurrent hypersensitivity. • If after at least 7 days, selpercatinib is tolerated without recurrent hypersensitivity, incrementally increase the selpercatinib dose by 1 dose level each week, until the dose taken prior to the onset of hypersensitivity is reached. Taper steroid dose after selpercatinib has been tolerated for at least 7 days at the final dose.
Hypertension	Grade 3	• Patient blood pressure should be controlled before starting treatment. • Selpercatinib should be suspended temporarily for medically significant hypertension until controlled with antihypertensive therapy. Dosing should be resumed at the next lower dose if clinically indicated
	Grade 4	• Selpercatinib should be discontinued permanently if medically significant hypertension cannot be controlled.
Increased ALT or AST	Grade 3 or grade 4	• Suspend dose until toxicity resolves to baseline. Resume at a dose reduced by 2 levels. • If after at least 2 weeks selpercatinib is tolerated without recurrent increased ALT or AST, increase dosing by 1 dose level. • If selpercatinib is tolerated without recurrence for at least 4 weeks, increase to dose taken prior to the onset of grade 3 or 4 increased AST or ALT. • Permanently discontinue selpercatinib if grade 3 or 4 ALT or AST increases recur despite dose modifications.
Interstitial lung disease (ILD) / pneumonitis	Grade 2	• Withhold selpercatinib until resolution. • Resume at a reduced dose. • Discontinue selpercatinib for recurrent ILD / pneumonitis
	Grade 3 or 4	• Discontinue selpercatinib
QT interval prolongation	Grade 3	• Suspend dose for QTcF intervals >500ms until the QTcF returns to <470ms or baseline. • Resume selpercatinib treatment at the next lower dose level.
	Grade 4	• Permanently discontinue selpercatinib if QT prolongation remains uncontrolled after two dose reductions or if the patient has signs or symptoms of serious arrhythmia.
Other adverse reactions	Grade 3 or grade 4	• Selpercatinib should be suspended until recovery to baseline. • Resume at reduced dose. • If grade 4 events reoccur following dose modification permanently discontinue selpercatinib.

Hepatic impairment
Close monitoring with impaired hepatic function is important.
No dose adjustment is required with mild (Child-Pugh class A) or moderate (Child-Pugh class B) hepatic impairment.
Child-Pugh class C hepatic impairment should be dosed with 80mg selpercatinib twice daily.

Renal impairment
Dose adjustment is not necessary with mild, moderate or severe renal impairment. There are no data with end stage renal disease, or in patients on dialysis.

REFERENCES

1. SPC