SELPERCATINIB (Retsevmo)

INDICATIONS (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/)

For the treatment of patients with previously treated RET fusion positive non-medullary thyroid cancer where the following criteria have been met:

2. An adult with a proven histological or cytological diagnosis of non-medullary thyroid cancer (there is a separate form SEL02 for selpercatinib in medullary thyroid cancer) - papillary thyroid cancer or- follicular thyroid cancer or- Hurtle cell thyroid cancer or- anaplastic thyroid cancer
3. Thyroid cancer has been documented as having a RET fusion as determined by a validated genomic test, CCDC6 or NCOA4 or- another fusion partner.
4. 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.
5. ECOG performance status (PS) of 0 or 1 or 2.
6. Selpercatinib is being given as monotherapy.
7. Not previously received selpercatinib or any other TKI which targets the RET receptor unless the patient has received selpercatinib via a company early access scheme and the patient meets all the other criteria listed here.
8. Selpercatinib is to be continued until disease progression or unacceptable toxicity or patient choice to stop treatment.
9. The prescribing clinician is aware of the following issues as regards the administration of selpercatinib as detailed in its Summary of Product Characteristics (SPC):- the dosage of selpercatinib is according to body weight- selpercatinib has reduced solubility at a higher pH and hence precautions are necessary with the co-administration of proton pump inhibitors or H2 antagonists - selpercatinib has clinically important interactions with CYP3A inhibitors or CYP3A inducers
10. 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.
11. When a treatment break of more than 6 weeks beyond the expected 4-weekly cycle length is needed, I will complete a treatment break approval form to restart treatment, including indicating as appropriate if the patient had an extended break because of COVID 19.
12. Selpercatinib is to be otherwise used as set out in its Summary of product characteristics

For the treatment of patients with previously treated RET mutant medullary thyroid cancer where the following criteria have been met:

2. An adult or an adolescent aged 12 years and older with a proven histological or cytological diagnosis of medullary thyroid cancer (there is a separate form SEL01 for selpercatinib in non-medullary thyroid cancer).
3. Thyroid cancer has been documented as having a RET mutation as determined by a validated genomic test. M918T mutation or an extracellular cysteine mutation or V804M/L mutation or another mutation
4. Has been previously treated with cabozantinib or vandetanib.Please enter below as to the previous TKI therapy that the patient has received:- cabozantinib or- vandetanib
5. ECOG performance status (PS) of 0 or 1 or 2.
6. Selpercatinib is being given as monotherapy.
7. Not previously received selpercatinib or any other TKI which targets the RET receptor unless the patient has received selpercatinib via a company early access scheme and the patient meets all the other criteria listed here.
8. Selpercatinib is to be continued until disease progression or unacceptable toxicity or patient choice to stop treatment.
9. The prescribing clinician is aware of the following issues as regards the administration of

selpercatinib as detailed in its Summary of Product Characteristics (SPC):- the dosage of selpercatinib is according to body weight- selpercatinib has reduced solubility at a higher pH and hence precautions are necessary with the co-administration of proton pump inhibitors or H2 antagonists - selpercatinib has clinically important interactions with CYP3A inhibitors or CYP3A inducers
10. 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.
11. When a treatment break of more than 6 weeks beyond the expected 4-weekly cycle length is needed, I will complete a treatment break approval form to restart treatment, including indicating as appropriate if the patient had an extended break because of COVID 19.
12. Selpercatinib is to be otherwise used as set out in its Summary of Product Characteristics.

Selpercatinib as monotherapy for the treatment of adult patients with advanced non-small cell lung cancer (NSCLC) exhibiting a RET gene fusion and who have previously received immunotherapy and/or platinum-based chemotherapy where the following criteria have been met:
2. Locally advanced or metastatic non-small cell lung cancer.
3. A histologically or cytologically confirmed diagnosis of non-small cell lung cancer.
4. This patient's NSCLC has been shown to harbour a RET gene fusion as determined on a tumour tissue biopsy or a plasma specimen (liquid biopsy) or both.
5. This patient's RET fusion partner has been determined to be in one of the categories: KIF5B, CCDC6, NCOA4, RELCH, another fusion partner, unknown fusion partner
6. Has previously received immunotherapy and/or platinum-based chemotherapy for this locally advanced or metastatic NSCLC indication.
- only treatment received is 1st line platinum-based cytotoxic chemotherapy for locally advanced or metastatic NSCLC or
- only treatment received is 1st line immunotherapy monotherapy for locally advanced or metastatic NSCLC or
- has received 1st line combination treatment of platinum-based chemotherapy with immunotherapy for locally advanced or metastatic NSCLC with or without 2nd line cytotoxic chemotherapy or
- has received 1st line immunotherapy monotherapy for locally advanced or metastatic NSCLC followed by 2nd line cytotoxic chemotherapy with or without further cytotoxic chemotherapy or
- has received 1st line cytotoxic chemotherapy for locally advanced or metastatic NSCLC followed by 2nd line immunotherapy monotherapy with or without further cytotoxic chemotherapy
7. Has not previously received selpercatinib or any other TKI which targets the RET receptor unless the patient has received selpercatinib via a company early access scheme and the patient meets all the other criteria listed here.
8. ECOG performance status (PS) score of 0 or 1 or 2.
9. 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.
- has never had known brain/CNS metastases
- has had brain/CNS metastases treated before with surgery/radiotherapy and is currently symptomatically stable
- has brain secondaries which have not been treated with surgery/radiotherapy and is currently symptomatically stable
10. Selpercatinib will be used as monotherapy.
11. The prescribing clinician is aware of the following issues as regards the administration of selpercatinib as detailed in its Summary of Product Characteristics (SPC):
- the dosage of selpercatinib is according to body weight
- selpercatinib has reduced solubility at a higher pH and hence precautions are necessary with the co-administration of proton pump inhibitors or H_2 antagonists
- selpercatinib has clinically important interactions with CYP3A inhibitors or CYP3A inducers

12. Will be treated until loss of clinical benefit or excessive toxicity or patient choice to discontinue treatment whichever is the sooner.
13. 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.
14. When a treatment break of more than 6 weeks beyond the expected 4-weekly cycle length is needed, I will complete a treatment break approval form to restart treatment, including as appropriate if the patient has had an extended break on account of Covid-19.
15. Selpercatinib is to be otherwise used as set out in its Summary of Product Characteristics.

Selpercatinib as monotherapy for the 1st line treatment of adult patients with previously untreated advanced non-small cell lung cancer (NSCLC) exhibiting a RET gene fusion where the following criteria have been met:
2. Locally advanced or metastatic non-small cell lung cancer.
3. Has a histologically or cytologically confirmed diagnosis of non-small cell lung cancer.
4. This NSCLC has been shown to harbour a RET gene fusion as determined on a tumour tissue biopsy or a plasma specimen (liquid biopsy) or both.
5. The RET fusion partner KIF5B, CCDC6, NCOA4, RELCH, another or unknown fusion partner
6. Has NOT received any prior systemic therapy for this locally advanced or metastatic NSCLC indication.
7. Has not previously received selpercatinib or any other TKI which targets the RET receptor unless the patient has received selpercatinib via a company early access scheme and the patient meets all the other criteria listed here.
8. ECOG performance status (PS) score of 0 or 1 or 2.
9. 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.
10. Selpercatinib will be used as monotherapy.
11. The dosage of selpercatinib is according to body weight, has reduced solubility at a higher pH and hence precautions are necessary with the co-administration of proton pump inhibitors or H2 antagonists, has clinically important interactions with CYP3A inhibitors or CYP3A inducers.
12. Will be treated until loss of clinical benefit or excessive toxicity or patient choice to discontinue treatment whichever is the sooner.
13. 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.
14. When a treatment break of more than 6 weeks beyond the expected 4-weekly cycle length is needed, the prescribing clinician will complete a treatment break approval form to restart treatment.
15. Selpercatinib is to be otherwise used as set out in its Summary of Product Characteristics.

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

CYCLE FREQUENCY AND NUMBER OF CYCLES
Continuously until disease progression. Formal review before the start of 3rd 28 day cycle.

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. Teduce 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. • Discontinue selpercatinib for severe or life-threatening haemorrhagic events.
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.

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. • Discontinue selpercatinib for severe or life-threatening events

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