SOTORASIB (Lumykras)

INDICATION (ICD10) C34

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (SOT1)

1. Sotorasib monotherapy for the treatment of adult patients with advanced non-small cell lung cancer (NSCLC) exhibiting a KRAS G12C mutation and who have been previously treated with at least 1 prior systemic therapy (a platinum doublet chemotherapy and/or PD-1/PD-L1 targeted immunotherapy) for advanced NSCLC. No known brain metastases or if the patient does have brain metastases then the patient is symptomatically stable before staring sotorasib. PS 0 or 1.

REGIMEN

SOTORASIB 960mg orally once daily continuously

CYCLE FREQUENCY AND NUMBER OF CYCLES

Until disease progression.
A formal medical review as to how sotorasib is being tolerated will be done before the start of the second month of treatment and the next review to determine whether treatment with sotorasib should continue or not will be scheduled to occur at least by the end of the second month of therapy.

ADMINISTRATION

Available as 120mg tablets
Swallowed whole with water once daily.
Patients who have difficulty swallowing tablets should disperse tablets in 120mL of non-carbonated, room-temperature water without crushing. Other liquids must not be used. Stir until tablets are dispersed into small pieces (the tablet will not completely dissolve) and drink immediately. The appearance of the mixture may range from pale to bright yellow. The container must be rinsed with an additional 120mL of water, which should be drunk immediately. If it is not drunk immediately, it must be stirred again to ensure that the tablets are dispersed. The dispersion must be discarded if it is not drunk within 2 hours.

ANTI-EMETICS

Low risk

CONCURRENT MEDICATION REQUIRED

Sotorasib	Loperamide

EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E every cycle for 6 cycles then may be increased to every 3 cycles
LFTs every 2 weeks for 3 cycles then every cycle
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Baseline weight

MAIN TOXICITES AND ADVERSE REACTIONS

Sotorasib	Interstitial lung disease Hepatotoxicity

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

Sotorasib	Lots of interactions check carefully. Co-administration of proton pump inhibitors or H_2 antagonists with sotorasib is not recommended. If treatment with an acid-reducing agent is required, take sotorasib 4 hours before or 10 hours after administration of a local antacid. Co-administration of strong CYP3A4 inducers (e.g. phenytoin, carbamazepine, rifampicin) with sotorasib is not recommended because the impact on sotorasib efficacy is unknown. Sotorasib is a moderate CYP3A4 inducer. Co-administration of sotorasib with CYP3A4 substrates led to a decrease in their plasma concentrations, which may reduce the efficacy of these substrates. Avoid co-administration of sotorasib with CYP3A4 substrates with narrow therapeutic indices. If co-administration cannot be avoided, adjust the CYP3A4 substrate dosage accordingly.

DOSE MODIFICATIONS
Non-haematological

Sotorasib

Recommended dose	960mg once daily
First dose adjustment	480mg once daily
Second dose adjustment	240mg once daily

Diarrhoea despite appropriate ant-diarrhoeal therapy

Grade 3 to 4	• Stop treatment until recovered to ≤grade 1 or to baseline grade • After recovery, resume treatment at the next dose reduction level

Hepatoxicity

Grade 2 AST or ALT with symptoms or Grade ≥3 AST or ALT	• Stop treatment until recovered to ≤grade 1 or to baseline grade • After recovery, resume treatment at the next dose reduction level
AST or ALT >3×ULN with total bilirubin >2×ULN, in the absence of alternative causes	Permanently discontinue.

Interstitial lung disease (ILD)

Any grade	Stop treatment if ILD is suspected. Permanently discontinue if ILD is confirmed.

Nausea or vomiting despite appropriate antiemetic therapy

Grade 3 to 4	• Stop treatment until recovered to ≤grade 1 or to baseline grade • After recovery, resume treatment at the next dose reduction level

Other adverse reactions

Grade 3 to 4	• Stop treatment until recovered to ≤grade 1 or to baseline grade • After recovery, resume treatment at the next dose reduction level

Hepatic impairment
Sotorasib
No dose adjustment is required for patients with mild hepatic impairment (AST or ALT <2.5×ULN or bilirubin <1.5×ULN).
Sotorasib has not been studied in patients with moderate or severe hepatic impairment.

Renal impairment
Sotorasib
Dose adjustment is not necessary in patients with CrCl ≥60ml/min.
There are no data in patients with CrCl <60ml/min.

REFERENCES
1. SPC