Indication	Monotherapy for the treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC), with KRAS G12C-mutation who have progressed on, or are intolerant to, platinum-based chemotherapy and/or anti PD-1/PD-L1 immunotherapy. NB the patient must have had no previous treatment with a drug specifically targeting the KRAS G12C mutation unless the patient has received sotorasib via a company early access scheme.
Treatment Intent	Palliative
Frequency and number of cycles	Repeat every 28 days continuously. Continue until disease progression, unacceptable toxicity or patient choice. A formal medical review must be done before the second month of treatment to assess tolerability, a second review must take place by the end of the second month of treatment to decide if treatment should continue.
Monitoring Parameters pre-treatment	• **Virology screening:** All new patients referred for systemic anti-cancer treatment should be screened for hepatitis B and C and the result reviewed prior to the start of treatment. Patients not previously tested who are starting a new line of treatment, should also be screened for hepatitis B and C. Further virology screening will be performed following individual risk assessment and clinician discretion. • Monitor FBC and U&Es baseline and every month. • LFTs (ALT, AST, and total bilirubin) at baseline, **every 2 weeks for the first 3 months of treatment**, then once a month or as clinically indicated, with more frequent testing in patients who develop transaminase and/or bilirubin elevations. • The patient should either have no known brain metastases or if the patient does have brain metastases then the patient should be symptomatically stable before starting sotorasib. • **Hepatic impairment:** No dose adjustment required in mild or moderate hepatic impairment (Child-Pugh class A and B). The safety and efficacy of multiple doses has not been studied in severe hepatic impairment (Child-Pugh C). Sotorasib should be used with caution in severe impairment and a dose adjustment considered. • **Renal impairment:** No dose adjustment required in mild renal impairment (CrCL >/= 60ml/min). The safety and efficacy have not been studied in moderate or severe renal impairment (<60ml/min). • **Dose Modification:** Dosing interruption and/or dose reduction may be required based on individual safety and tolerability. If dose reduction is necessary, then the 1st dose reduction should be to 480mg taken once daily, the 2nd dose reduction to 240mg once daily. No further dose reduction is permitted, if the patient cannot tolerate 240mg once daily treatment should be stopped. • **Management of adverse reactions and dose adjustments:** • Refer to table 1 for dose modifications in the event of adverse reaction. • Assessment of all patients with an acute onset and/or unexplained worsening of pulmonary symptoms (dyspnoea, cough, fever) should be performed to exclude interstitial lung disease (ILD)/Pneumonitis. Treatment should be suspended whilst symptoms are investigated. If ILD or pneumonitis is confirmed – permanently discontinue sotorasib. • **<u>Common drug interactions (for comprehensive list refer to BNF/SPC)</u>:** • Co-administration of proton pump inhibitors or H2 antagonists with sotorasib may reduce sotorasib concentrations. If treatment with an acid-reducing agent is required, sotorasib should be taken with an acidic beverage (such as cola), alternatively take 4 hours before or 10 hours after administration of a local antacid, e.g. Gaviscon.

	• Co-administration of strong CYP3A4 inducers (e.g. phenytoin, carbamazepine, rifampicin) is not recommended. • 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. Caution with concomitant use of CYP3A substrates with narrow therapeutic range (e.g. alfentanil, ciclosporin, dihydroergotamine, ergotamine, fentanyl, pimozide, quinidine, sirolimus, or tacrolimus) dose modification of the CYP3A substrate may be required. • Avoid coadministration of sotorasib with P-gp substrates with a narrow therapeutic index, e.g. digoxin. If coadministration cannot be avoided, decrease the P-gp substrate dosage as appropriate. • Sotorasib is a weak BCRP inhibitor, if co-administration with a BCRP substrate (e.g. rosuvastatin) cannot be avoided, monitor for adverse reactions of the BCRP substrate and decrease the BCRP substrate dosage as required. • **Missed dose:** If less than 6 hours has passed since the scheduled dose, patients should take the dose, if more than 6 hours have passed, the dose should be omitted. If vomiting occurs after taking a dose the patient must not take an additional dose on the same day, and treatment must be continued as prescribed the next day. • For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet and Macmillan information sheet.
References	SPC accessed online 28.07.2025 KMCC protocol LUN-047 V2

NB For funding information, refer to CDF and NICE Drugs Funding List

Table 1. Recommended dose modifications for sotorasib

Adverse reaction	**Severity**[a]	**Dose modification**
Hepatotoxicity	Grade 2 AST or ALT with symptoms (> 3.0 - 5.0 x ULN if baseline was normal; > 3.0 - 5.0 x baseline if baseline was abnormal) or Grade ≥ 3 AST or ALT (>5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal)	• 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 treatment
Interstitial Lung Disease/(ILD)/pneumonitis	Any Grade	• Stop treatment if ILD/pneumonitis is suspected • Permanently discontinue if ILD/pneumonitis is confirmed
Nausea or vomiting despite appropriate supportive care (including anti-emetic 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
Diarrhoea despite appropriate supportive care (including anti-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
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

ALT = alanine aminotransferase; AST = aspartate aminotransferase; ULN = upper limit of normal

[a] Grading defined by National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 5.0

Repeat every 28 days

TTO	Drug	Dose	Route	Directions
Day 1	**SOTORASIB**	**960mg**	PO	OD. Swallow whole at the same time each day, with or without food. Available as 240mg tablets Administration for patients with swallowing difficulties: Disperse tablets in 120 ml of non-carbonated, room-temperature water without crushing. Do not use other liquids. Stir until tablets are dispersed into small pieces (the tablets will not completely dissolve) and drink immediately. The appearance of the mixture may range from pale yellow to bright yellow. Rinse the container with an additional 120 ml of water and drink immediately. If the mixture is not consumed immediately, stir the mixture again to ensure that tablets are dispersed. Consume within two hours of preparation. Dispense 30 days supply.
	Metoclopramide	10mg	PO	10mg up to 3 times a day as required. Do not take for more than 5 days continuously. Dispense on cycle 1 then only if required.
	Loperamide	2-4mg	PO	Take 4mg (2 capsules) initially, then 2mg (1 capsule) after each loose stool when required. Maximum 16mg (8 capsules) a day. Dispense 30 capsules on cycle 1 then only if required.