Solung
Tablet

DRUG INTERNATIONAL LTD.

Composition : Each film coated tablet contains Sotorasib INN 120mg.

Pharmacology : Sotorasib is an inhibitor of KRASG12C, a tumor-restricted, mutant-oncogenic form of the RAS GTPase, KRAS. Sotorasib forms an irreversible, covalent bond with the unique cysteine of KRASG12C, locking the protein in an inactive state that prevents downstream signaling without affecting wild-type KRAS. Sotorasib blocked KRAS signaling, inhibited cell growth, and promoted apoptosis only in KRAS G12C tumor cell lines. Sotorasib inhibited KRASG12C in vitro and in vivo with minimal detectable off-target activity. Absorption:The median time to Sotorasib peak plasma concentration is 1 hour. Distribution: The Sotorasib mean volume of distribution (Vd) at steady state is 211 L (CV: 135%). In vitro, Sotorasib plasma protein binding is 89%. Elimination: The Sotorasib mean terminal elimination half-life is 5 hours (standard deviation (SD): 2). At 960mg Sotorasib once daily, the Sotorasib steady state apparent clearance is 26.2 L/hr (CV: 76%). Metabolism: The main metabolic pathways of Sotorasib are non-enzymatic conjugation and oxidative metabolism with CYP3As. Excretion: After a single dose of radiolabeled Sotorasib, 74% of the dose was recovered in feces (53% unchanged) and 6% (1% unchanged) in urine.

Indications : It is an inhibitor of the RAS GTPase family indicated for the treatment of adult patients with KRAS G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC), as determined by an FDA-approved test, who have received at least one prior systemic therapy. This indication is approved under accelerated approval based on overall response rate (ORR) and duration of response (DOR).

Dosage & Administration : The recommended dosage of Sotorasib is 960 mg (eight 120 mg tablets) orally once daily until disease progression or unacceptable toxicity. Sotorasib should be taken at the same time each day with or with out food. Whole tablet should be swallowed. It should not bechewed, or crushed. If a dose of Sotorasib is missed by more than 6 hours, The next dose should take as prescribed the next day. 2 doses should not be taken at the same time to make up for the missed dose. If vomiting occurs after taking Sotorasib, do not take an additional dose. Take the next dose as prescribed the next day.

Recommended Sotorasib Dosage Modifications for Adverse Reactions

Adverse Reaction	Severity[a]	Dosage Modification
Hepatotoxicity	Grade 2 AST or ALT with symptoms or Grade 3 to 4 AST or ALT	• Withhold Sotorasib until recovery to ≤ Grade 1 or baseline. • Resume Sotorasib at the next lower dose level.
	AST or ALT > 3 × ULN with total bilirubin > 2 × ULN in the absence of alternative causes	• Permanently discontinue Sotorasib.
Interstitial Lung Disease pneumonitis	Any Grade	•Withhold Sotorasib if ILD/pneumonitis is suspected. • Permanently discontinue Sotorasib if ILD/pneumonitis is confirmed.
Nausea or vomiting despite appropriate supportive care (including anti-emetic therapy)	Grade 3 to 4	• Withhold Sotorasib until recovery to ≤ Grade 1 or baseline. • Resume Sotorasib at the next lower dose level.
Diarrhea despite appropriate supportive care (including anti-diarrheal therapy)	Grade 3 to 4	• Withhold Sotorasib until recovery to ≤ Grade 1 or baseline. • Resume Sotorasib at the next lower dose level.
Other Adverse Reaction	Grade 3 to 4	• Withhold Sotorasib until recovery to ≤ Grade 1 or baseline. • Resume Sotorasib at the next lower dose 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)

Recommended Sotorasib Dose Reduction Levels for Adverse Reactions

Dose Reduction Level	Dose
First dose reduction	480 mg (4 tablets) once daily
Second dose reduction	240 mg (2 tablets) once daily

Or, as directed by the registered physicians.

Contraindications : It is contraindicated in patients with hypersensitivity to Sotorasib or any component of the product.

Precautions : • Hepatotoxicity: Sotorasib can cause hepatotoxicity, which may lead to drug-induced liver injury and hepatitis. Liver function tests (ALT, AST, and total bilirubin) should be monitored prior to the start of Sotorasib, every 3 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. Sotorasib dose should be reduced, Withheld, or permanently discontinued based on severity of adverse reaction. • Interstitial Lung Disease (ILD)/Pneumonitis: Sotorasib can cause ILD/pneumonitis that can be fatal. New or worsening pulmonary symptoms should be monitored. Immediately withhold Sotorasib for suspected ILD/pneumonitis and permanently discontinue if no other potential causes of ILD/pneumonitis are identified.

Side Effects : • Hepatotoxicity • Interstitial Lung Disease (ILD) • Pneumonitis

Use in pregnancy and lactation : There are no available data on Sotorasib use in pregnant women. Lactation: There are no data on the presence of Sotorasib or its metabolites in human milk, the effects on the breastfed child or on milk production. Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment with Sotorasib and for 1 week after the final dose.

Use in child : The safety and effectiveness of Sotorasib have not been established in pediatric patients.

Drug interactions : • Effects of Other Drugs on Sotorasib: Acid-Reducing Agents: Coadministration of Sotorasib with gastric acid reducing agents decreased Sotorasib concentrations which may reduce the efficacy of Sotorasib. Coadministration of Sotorasib should be avoided with proton pump inhibitors (PPIs), H2 receptor antagonists, and locally acting antacids. If coadministration with an acid-reducing agent can't be avoided, administer Sotorasib 4 hours before or 10 hours after administration of a locally acting antacid. Strong CYP3A4 Inducers : Coadministration of Sotorasib with a strong CYP3A4 inducer decreased Sotorasib concentrations, which may reduce the efficacy of Sotorasib. Coadministration of Sotorasib should be avoided with strong CYP3A4 inducers. • Effects of Sotorasib on Other Drugs: CYP3A4 Substrates : Coadministration of Sotorasib with a CYP3A4 substrate decreased its plasma concentrations, which may reduce the efficacy of the substrate. Coadministration of Sotorasib should be avoided with CYP3A4 sensitive substrates, for which minimal concentration changes may lead to therapeutic failures of the substrate. If coadministration cannot be avoided, increase the sensitive CYP3A4 substrate dosage in accordance with its Prescribing Information. P-glycoprotein (P-gp) Substrates: Coadministration of Sotorasib with a P-gp substrate (Digoxin) increased Digoxin plasma concentrations, which may increase the adverse reactions of Digoxin. Coadministration of Sotorasib should be avoided with P-gp substrates for which minimal concentration changes may lead to serious toxicities. If coadministration cannot be avoided, decrease the P-gp substrate dosage in accordance with its Prescribing Information. Breast Cancer Resistance Protein (BCRP) Substrates: Sotorasib is a BCRP-inhibitor. Coadministration of Sotorasib with a BCRP substrate increased its plasma concentrations, which may increase the risk of adverse reactions of the substrate. When coadministered with Sotorasib, adverse reactions should be monitored of the BCRP substrate and decrease the BCRP substrate dosage in accordance with its Prescribing Information.

Overdose : No data available.

Storage : Store below 30° C in a dry place, away from sunlight & keep out of reach of children.

Packing : Each box contains 240 tablets in a container.