# Sotakras

Sotorasib INN

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

**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. In mouse tumor xenograft models, sotorasib-treatment led to tumor regressions and prolonged survival, and was associated with anti-tumor immunity in KRAS G12C models

**Indication**
Sotorasib is 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.

**Dosage and Administration**
The recommended dosage of SOTORASIB is 960 mg (eight 120 mg tablets) orally once daily until disease progression or unacceptable toxicity. Take SOTORASIB at the same time each day with or without food. Swallow tablets whole. Do not chew, crush or split tablets. If a dose of SOTORASIB is missed by more than 6 hours, take the next dose as prescribed the next day. Do not take 2 doses at the same time to make up for the missed dose.

**Contraindications**
None

**Precaution**
Hepatotoxicity
SOTORASIB can cause hepatotoxicity, which may lead to drug-induced liver injury and hepatitis. Among 357 patients who received SOTORASIB in CodeBreaK, hepatotoxicity occurred in 1.7% (all grades) and 1.4% (Grade 3). A total of 18% of patients who received SOTORASIB had increased alanine aminotransferase (ALT)/increased aspartate aminotransferase (AST); 6% were Grade 3 and 0.6% were Grade 4. The median time to first onset of increased ALT/AST was 9 weeks (range: 0.3 to 42). Increased ALT/AST leading to dose interruption or reduction occurred in 7% of patients. SOTORASIB was discontinued due to increased ALT/AST in 2.0% of patients. In addition to dose interruption or reduction, 5% of patients received corticosteroids for the treatment of hepatotoxicity. Monitor liver function tests (ALT, AST, and total bilirubin) 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. Withhold, dose reduce or permanently discontinue SOTORASIB based on severity of adverse reaction.

Interstitial Lung Disease (ILD)/Pneumonitis
SOTORASIB can cause ILD/pneumonitis that can be fatal. Among 357 patients who received SOTORASIB in CodeBreaK 100, ILD/pneumonitis occurred in 0.8% of patients, all cases were Grade 3 or 4 at onset, and 1 case was fatal. The median time to first onset for ILD/pneumonitis was 2 weeks (range: 2 to 18 weeks). SOTORASIB was discontinued due to ILD/pneumonitis in 0.6% of patients. Monitor patients for new or worsening pulmonary symptoms indicative of ILD/pneumonitis (e.g., dyspnea, cough, fever). Immediately withhold SOTORASIB in patients with suspected ILD/pneumonitis and permanently discontinue SOTORASIB if no other potential causes of ILD/pneumonitis are identified

**Side Effect**

The following clinically significant adverse reactions are discussed in greater detail in other sections of the labeling:
• Hepatotoxicity
• Interstitial Lung Disease (ILD)/Pneumonitis

**Use in Specific Population**
Pregnancy
There are no available data on SOTORASIB use in pregnant women. In rat and rabbit embryo-fetal development studies, oral sotorasib did not cause adverse developmental effects or embryo-lethality at exposures up to 4.6 times the human exposure at the 960 mg clinical dose . In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

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.

Pediatric Use
The safety and effectiveness of SOTORASIB have not been established in pediatric patients.

Geriatric Use
Of the 357 patients with any tumor type who received SOTORASIB 960 mg orally once daily in CodeBreaK 100, 46% were 65 and over, and 10% were 75 and over. No overall differences in safety or effectiveness were observed between older patients and younger patients

**Drug Interactions**
Acid-Reducing Agents
Coadministration of SOTORASIB with gastric acid-reducing agents decreased sotorasib concentrations, which may reduce the efficacy of sotorasib. Avoid coadministration of SOTORASIB with proton pump inhibitors (PPIs), H2 receptor antagonists, and locally acting antacids. If coadministration with an acid-reducing agent cannot 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. Avoid coadministration of SOTORASIB with strong CYP3A4 inducers.

CYP3A4 Substrates
Coadministration of SOTORASIB with a CYP3A4 substrate decreased its plasma concentrations, which may reduce the efficacy of the substrate. Avoid coadministration of SOTORASIB with CYP3A4 sensitive substrates, for which minimal concentration changes may lead to therapeutic 7 failures of the substrate.

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. Avoid coadministration of SOTORASIB 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

**Overdose**
There is no known antidote for Sotorasib. The treatment of overdose should consist of general supportive measures.

**Storage**
Do not store above 25$^{0}$C. Protect from light. Keep out of the reach of children.

**Packaging**
**Sotakras 120 Tablet:** Each HDPE container of Sotakras 120 contains 56 tablets, a silica gel desiccant and polyester coil with a child-resistant closure.

*Manufactured by:*
ZISKA PHARMA **Ziska Pharmaceuticals Ltd.**
Kaliakoir, Gazipur, Bangladesh

Version: 00

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