Mobonib

Mobocertinib Succinate INN

Composition:
Mobonib 40 Capsule: Each capsule contains Mobocertinib Succinate INN eqv. to Mobocertinib 40 mg.

Pharmacology:
Mobocertinib is a kinase inhibitor of the epidermal growth factor receptor (EGFR) that irreversibly binds to and inhibits EGFR exon 20 insertion mutations at lower concentrations than wild type (WT) EGFR. Two pharmacologically-active metabolites (AP32960 and AP32914) with similar inhibitory profiles to Mobocertinib have been identified in the plasma after oral administration of Mobocertinib. In vitro, Mobocertinib also inhibited the activity of other EGFR family members (HER2 and HER4) and one additional kinase (BLK) at clinically relevant concentrations.

Indication:
Mobocertinib is indicated for the treatment of adult patients with locally advanced or metastatic non small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy. This indication is approved under accelerated approval based on overall response rate and duration of response.

Dosage and Administration:
The recommended dosage of Mobocertinib is 160 mg orally once daily until disease progression or unacceptable toxicity. Take Mobocertinib with or without food, at the same time each day. Swallow Mobocertinib capsules whole. Do not open, chew or dissolve the contents of the capsules. If a dose is missed by more than 6 hours, skip the dose and take the next dose the following day at its regularly scheduled time

Contraindications:
None

Precaution:
QTc Prolongation and Torsades de Pointes
MOBOCERTINIB can cause life-threatening heart rate-corrected QT (QTc) prolongation, including Torsades de Pointes, which can be fatal. In the 250 patient subset of the pooled MOBOCERTINIB safety population who had scheduled and unscheduled electrocardiograms (ECGs), Clinical Pharmacology , 1.2% of patients had a QTc interval >500 msec and 11% of patients had a change-from-baseline QTc interval >60 msec. Grade 4 Torsades de Pointes occurred in 1 patient (0.4%). Clinical trials of MOBOCERTINIB did not enroll patients with baseline QTc greater than 470 msec. Assess QTc and electrolytes at baseline and correct abnormalities in sodium, potassium, calcium, and magnesium prior to initiating MOBOCERTINIB. Monitor QTc and electrolytes periodically during treatment. Increase monitoring frequency in patients with risk factors for QTc prolongation, such as patients with congenital long QT syndrome, heart disease, or electrolyte abnormalities. Avoid use of concomitant drugs which are known to prolong the QTc interval. Avoid concomitant use of strong or moderate CYP3A inhibitors with MOBOCERTINIB, which may further prolong the QTc. Withhold, reduce the dose, or permanently discontinue MOBOCERTINIB based on the severity of the QTc prolongation.

Interstitial Lung Disease (ILD)/Pneumonitis
MOBOCERTINIB can cause ILD/pneumonitis, which can be fatal. In the pooled MOBOCERTINIB safety population [see Adverse Reactions (6.1)], ILD/pneumonitis occurred in 4.3% of patients including 0.8% Grade 3 events and 1.2% fatal events. Monitor patients for new or worsening pulmonary symptoms indicative of ILD/pneumonitis. Immediately withhold MOBOCERTINIB in patients with suspected ILD/pneumonitis and permanently discontinue MOBOCERTINIB if ILD/pneumonitis is confirmed.

Cardiac Toxicity
MOBOCERTINIB can cause cardiac toxicity (including decreased ejection fraction, cardiomyopathy, and congestive heart failure) resulting in heart failure which can be fatal. In the pooled MOBOCERTINIB safety population heart failure occurred in 2.7% of patients including 1.2% Grade 3 reactions, 0.4% Grade 4 reactions, and one (0.4%) fatal case of heart failure. MOBOCERTINIB can cause QTc prolongation resulting in Torsades de Pointes. Atrial fibrillation (1.6%), ventricular tachycardia (0.4%), first degree atrioventricular block (0.4%), second degree atrioventricular block (0.4%), left bundle branch block (0.4%), supraventricular extrasystoles (0.4%) and ventricular extrasystoles (0.4%) also occurred in patients receiving MOBOCERTINIB. Monitor cardiac function, including assessment of left ventricular ejection fraction at baseline and during treatment. Withhold, reduce the dose, or permanently discontinue MOBOCERTINIB based on the severity

Diarrhea
MOBOCERTINIB can cause diarrhea, which can be severe. In the pooled MOBOCERTINIB safety population , diarrhea occurred in 93% of patients, including 20% Grade 3 and 0.4% Grade 4. The median time to first onset of diarrhea was 5 days but diarrhea has occurred within 24 hours after administration of MOBOCERTINIB. In the 48% of patients whose diarrhea resolved, the median time to resolution was 3 days. Diarrhea may lead to dehydration or electrolyte imbalance, with or without renal impairment. Treat diarrhea promptly. Advise patients to start an antidiarrheal agent (e.g., loperamide) at first sign of diarrhea or increased bowel movement frequency and to increase fluid and electrolyte intake. Monitor electrolytes and withhold, reduce the dose or permanently discontinue MOBOCERTINIB based on the severity.

Embryo-Fetal Toxicity
Based on findings from animal studies and its mechanism of action, MOBOCERTINIB can cause fetal harm when administered to a pregnant woman. Oral administration of Mobocertinib to pregnant rats during the period of organogenesis resulted in embryolethality at maternal exposures approximately 1.7 times the human exposure based on area under the curve (AUC) at the 160 mg once daily clinical dose. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective non-hormonal contraception during treatment with MOBOCERTINIB and for 1 month after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with MOBOCERTINIB and for 1 week after the last dose of MOBOCERTINIB.

Side Effect:
Serious adverse reactions occurred in 46% of patients who received MOBOCERTINIB. Serious adverse reactions in ≥ 2% of patients included diarrhea, dyspnea, vomiting, pyrexia, acute kidney injury, nausea, pleural effusion, and cardiac failure. Fatal adverse reactions occurred in 1.8% of patients who received MOBOCERTINIB, including cardiac failure (0.9%), and pneumonitis (0.9%).
Permanent discontinuation occurred in 17% of patients who received MOBOCERTINIB. Adverse reactions requiring permanent discontinuation of MOBOCERTINIB in at least ≥2% of patients were diarrhea and nausea. Dose reductions of MOBOCERTINIB due to an adverse reaction occurred in 25% of patients. The adverse reaction requiring dose reduction in >5% of patients was diarrhea.

Use in Specific Population:
Pregnancy
MOBOCERTINIB can cause fetal harm when administered to a pregnant woman. There are no available data on MOBOCERTINIB use in pregnant women. Advise pregnant women of the potential risk to a fetus.

Lactation
There are no data on the presence of Mobocertinib or its metabolites in human milk or their 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 MOBOCERTINIB and for 1 week after the last dose.

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

Geriatric Use
No overall difference in effectiveness was observed between patients aged 65 and older and younger patients

Drug Interactions
Coadministration of MOBOCERTINIB with strong or moderate CYP3A inhibitors increased Mobocertinib plasma concentrations, which may increase the risk of adverse reactions, including QTc interval prolongation.
Coadministration of MOBOCERTINIB with strong or moderate CYP3A inducers decreased Mobocertinib plasma concentrations, which may reduce MOBOCERTINIB anti-tumor activity.
Coadministration of MOBOCERTINIB with CYP3A substrates may decrease plasma concentrations of CYP3A substrates, which may reduce the efficacy of these substrates.
Coadministration of MOBOCERTINIB with drugs known to prolong the QTc interval may increase the risk of QTc interval prolongation.

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

Storage
Do not Store above 25°C. Protect from light. Keep out of the reach of children.

Packing:
Mobonib 40 Capsule: Each HDPE container of Mobonib 40 contains 60 capsules, a silica gel desiccant and polyester coil with a child resistant closure.

Manufactured by:
ZISKA PHARMA **Ziska Pharmaceuticals Ltd.**
Kaliakoir, Gazipur, Bangladesh
Version: 00
P-3313