Osinib
Tablet

Composition: Osinib: Each film coated tablet contains Osimertinib 80 mg as Osimertinib Mesylate INN.

Clinical Pharmacology: Osimertinib is a kinase inhibitor of the epidermal growth factor receptor (EGFR), which binds irreversibly to certain mutant forms of EGFR (T790M, L858R, and exon 19 deletion) at approximately 9fold lower concentrations than wild-type. Two pharmacologically-active metabolites (AZ7550 and AZ5104 circulating at approximately 10% of the parent) with similar inhibitory profiles to Osimertinib have been identified in the plasma after oral administration of Osimertinib. AZ7550 showed a similar potency to Osimertinib, while AZ5104 showed greater potency against exon 19 deletion and T790M mutants (approximately 8-fold) and wild-type (approximately 15-fold) EGFR.

Pharmacodynamics/Kinetics:

Absorption: The median time to Cmax of Osimertinib was 6 hours (range 3-24 hours).

Following administration of a 20 mg Osinib tablet with a high-fat, high-calorie meal (containing approximately 58 grams of fat and 1000 calories), the Cmax and AUC of Osimertinib were comparable to that under fasting conditions.

Distribution: The mean volume of distribution at steady-state (Vss/F) of Osimertinib was 997 L. Plasma protein binding of Osimertinib was 95%.

Elimination: Plasma concentrations decreased with time and a population estimated mean half-life of Osimertinib was 48 hours, and oral clearance (CL/F) was 14.2 (L/h).

Metabolism: The main metabolic pathways were oxidation (predominantly CYP3A) and dealkylation in vitro. Two pharmacologically active metabolites (AZ7550 and AZ5104) have been identified in the plasma after Osinib oral administration. The geometric mean exposure (AUC) of each metabolite (AZ5104 and AZ7550) was approximately 10% of the exposure of Osimertinib at steady-state.

Indications: Osinib is indicated for the treatment of patients with metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive non-small cell lung cancer (NSCLC), as detected by an FDA-approved test, whose disease has progressed on or after EGFR tyrosine kinase inhibitor (TKI) therapy.

Dosage and Administration: The recommended dose of Osinib is 80 mg tablet once a day until disease progression or unacceptable toxicity. It can be taken with or without food. If a dose is missed, one should not make up the missed dose and take the next dose as scheduled. Or, as directed by the registered physician.

Renal Impairment: No dose adjustment is recommended in patients with mild, [creatinine clearance (CLcr) 60-89 mL/min, as estimated by the Cockcroft Gault method (C-G)] moderate, (CLcr 30-59 mL/min, as estimated by C-G) or severe (CLcr 15-29 mL/min) renal impairment. There is no recommended dose of Osinib for patients with end-stage renal disease.

Hepatic Impairment No dose adjustment is recommended in patients with mild hepatic impairment [total bilirubin less than or equal to upper limit of normal (ULN) and AST greater than ULN or total bilirubin between 1.0 to 1.5 times ULN and any AST] or moderate hepatic impairment (total bilirubin between 1.5 to 3 times ULN and any AST). There is no recommended dose for Osinib for patients with severe hepatic impairment.

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

Side Effects: The most common side effects of this tablet are- Interstitial Lung Disease/Pneumonitis, QTc Interval Prolongation, Cardiomyopathy and Keratitis.

Contraindicatios: Osimertinib is contraindicated in patients with known hypersensitivity to it or any other components of this drug.

Use in pregnancy and lactation: There are no adequate and well-controlled studies in pregnant women using Osimertinib. If it is used during pregnancy or if the patient becomes pregnant while receiving this drug, she should be apprised of the potential hazard to the fetus or potential risk for loss of the pregnancy.

Lactation: There are no data on the presence of Osimertinib in human milk, the effects of Osimertinib on the breastfed infant or on milk production. Because of the potential for serious adverse reactions in breastfed infants from Osimertinib, a lactating woman should be advised not to breastfeed during treatment with Osinib and for 2 weeks after the final dose.

Females and Males of Reproductive Potential:

Females of reproductive potential are advised to use effective contraception during treatment with Osinib and for 6 weeks after the final dose.

Males are advised to use effective contraception during treatment and for 4 months after the final dose of Osinib.

Drug Interactions:

Effect of other drugs on Osimertinib: Strong CYP3A Inducers: Coadministering Osinib with a strong CYP3A4 inducer decreased the exposure of it compared to administering Osinib alone. Decreased Osimertinib exposure may lead to reduced efficacy. Osinib administration should be avoided with strong CYP3A inducers (e.g., phenytoin, rifampin, carbamazepine, St. John's Wort). Osinib dosage should be increased when coadministering with a strong CYP3A4 inducer if concurrent use is unavoidable. No dose adjustments are required when it is used with moderate or weak CYP3A inducers.

Effect of Osimertinib on other drugs: Coadministering Osinib with a BCRP substrate increased the exposure of the BCRP substrate compared to administering the BCRP substrate alone. Increased BCRP substrate exposure may increase the risk of exposure-related toxicity.

Precautions: Interstitial Lung Disease (ILD)/Pneumonitis: Occurred in 3.3% of patients. Osimertinib should be permanently discontinued in patients diagnosed with ILD/Pneumonitis. **QTc Interval Prolongation:** Electrocardiograms and electrolytes should be monitored in patients who have a history or predisposition for QTc prolongation, or those who are taking medications that are known to prolong the QTc interval. Osimertinib should be withheld then restarted at a reduced dose or permanently discontinued. **Cardiomyopathy:** Occurred in 1.4% of patients. Left ventricular ejection fraction (LVEF) should be assessed before treatment and then every 3 months thereafter. **Embryo-Fetal Toxicity:** Osimertinib can cause fetal harm. Females should be advised of potential risk to the fetus and to use effective contraception during treatment with Osimertinib and for 6 weeks after final dose. Males should be advised to use effective contraception for 4 months, after the last dose of Osimertinib.

Overdose: No information provided.

Storage: Store at 25^{o} C in a cool and dry place, away from sunlight. Keep out of the reach of children.

Packaging: Each box contains 3x10's tablets in Alu- Alu blister pack.