Tasso™

Osimertinib Mesylate INN

Jenphar Bangladesh | جنفار بنغلاديش

Composition:
Tasso 80 Tablet: Each film coated tablet contains Osimertinib Mesylate INN equivalent to Osimertinib 80 mg.

Clinical Pharmacology:
Osimertinib is 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 9-fold lower concentrations than wild-type. In-vitro, Osimertinib also inhibits the activity of HER2, HER3, HER4, ACK1, and BLK at clinically relevant concentrations.

Indications:
Osimertinib is a kinase inhibitor indicated for:

- Adjuvant therapy after tumor resection in adult patients with non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.
- The first-line treatment of adult patients with metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.
- In combination with pemetrexed and platinum-based chemotherapy, the first-line treatment of adult patients with locally advanced or metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.
- The treatment of adult patients with metastatic EGFR T790M mutation-positive NSCLC, as detected by an FDA-approved test, whose disease has progressed on or after EGFR TKI therapy.

Dosage and Administration:
Adjuvant treatment of early-stage NSCLC: 80 mg orally once daily, with or without food, until disease recurrence, or unacceptable toxicity, or for up to 3 years.

Metastatic NSCLC: 80 mg orally once daily, with or without food, until disease progression or unacceptable toxicity. Locally advanced or metastatic NSCLC: 80 mg orally once daily administered in combination with pemetrexed and platinum-based chemotherapy, with or without food, until disease progression or unacceptable toxicity due to Osimertinib.
Disperse tablet in 60 ml (2 ounces) of non-carbonated water only. Stir until tablet is dispersed into small pieces (the tablet will not completely dissolve) and swallow immediately. Do not crush, heat, or ultrasonicate during preparation. Rinse the container with 120 ml to 240 ml (4 to 8 ounces) of water and immediately drink.
If administration via nasogastric tube is required, disperse the tablet as above in 15 ml of non-carbonated water, and then use an additional 15 ml of water to transfer any residues to the syringe.

Dose Modification:

Target Organ	Adverse Reaction	Dose Modification
Pulmonary	Interstitial lung disease (ILD) / Pneumonitis	Permanently discontinue Osimertinib.
Cardiac	QTc interval greater than 500 msec on at least 2 separate ECGs	Withhold Osimertinib until QTc interval is less than 481 msec or recovery to baseline if baseline QTc is greater than or equal to 481 msec, then resume at 40 mg dose.
	QTc interval prolongation with signs/symptoms of life threatening arrhythmia	Permanently discontinue Osimertinib.
	Symptomatic congestive heart failure	
	Grade 3 or higher adverse reaction	Withhold Osimertinib for up to 3 weeks.
Cutaneous	Erythema Multiforme Major (EMM), Stevens-Johnson syndrome (SJS), and Toxic Epidermal Necrolysis (TEN)	Withhold Osimertinib if suspected and permanently discontinue if confirmed.
Blood & bone marrow	Aplastic anemia	Withhold Osimertinib if aplastic anemia is suspected & permanently discontinue if confirmed.
Other	If improvement to Grade 0-2 within 3 weeks	Resume at 80 mg or 40 mg daily.
	If no improvement within 3 weeks	Permanently discontinue Osimertinib.

Contraindication:
None

Warning and Precaution:

- ***Interstitial Lung Disease (ILD)/Pneumonitis:*** Occurred in 3.7% of patients. Permanently discontinue Osimertinib in patients diagnosed with ILD/Pneumonitis.)
- ***QTc Interval Prolongation:*** Monitor electrocardiograms and electrolytes 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. Withhold then restart at a reduced dose or permanently discontinue Osimertinib.
- ***Cardiomyopathy:*** Occurred in 3% of patients. Monitor left ventricular ejection fraction (LVEF) in patients with cardiac risk factors.
- ***Keratitis:*** Promptly refer patients with signs and symptoms of keratitis to an ophthalmologist for evaluation.
- ***Erythema Multiforme & Stevens-Johnson Syndrome:*** Withhold Osimertinib if erythema multiforme major (EMM) or Stevens-Johnson syndrome (SJS) is suspected and permanently discontinue if confirmed.
- ***Cutaneous Vasculitis:*** Withhold Osimertinib if cutaneous vasculitis is suspected, evaluate for systemic involvement, & consider dermatology consultation. If no other etiology can be identified, consider permanent discontinuation based on severity.
- ***Aplastic Anemia:*** Withhold Osimertinib if aplastic anemia is suspected & permanently discontinue Osimertinib if confirmed.
- ***Embryo-Fetal Toxicity:*** Osimertinib can cause fetal harm. Advise females of potential risk to the fetus and to use effective contraception during treatment with Osimertinib and for 6 weeks after final dose. Advise males to use effective contraception for 4 months, after the last dose of Osimertinib.

Adverse Reactions:
Most common (>20%) adverse reactions, including laboratory abnormalities, were:
Osimertinib monotherapy: leukopenia, lymphopenia, thrombocytopenia, anemia, diarrhea, rash, musculoskeletal pain, neutropenia, nail toxicity, dry skin, stomatitis, and fatigue.
Osimertinib in combination with pemetrexed and platinum-based chemotherapy: leukopenia, thrombocytopenia, neutropenia, lymphopenia, rash, diarrhea, stomatitis, nail toxicity, dry skin, and increased blood creatinine.

Use In Special Population:
Pregnancy
Osimertinib can cause fetal harm when administered to a pregnant woman. There are no available data on Osimertinib use in pregnant women.
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.
Contraception
Females: Advise females of reproductive potential to use effective contraception during treatment with Osimertinib and for 6 weeks after the final dose.
Males: Advise male patients with female partners of reproductive potential to use effective contraception during and for 4 months following the final dose of Osimertinib.
Infertility
Based on animal studies, Osimertinib may impair fertility in females and males of reproductive potential. The effects on female fertility showed a trend toward reversibility. It is not known whether the effects on male fertility are reversible.
Pediatric Use
The safety and effectiveness of Osimertinib in pediatric patients have not been established.
Geriatric Use
Monotherapy: No overall differences in safety or effectiveness were observed between patients 65 years or older and younger patients.
Combination with Pemetrexed and Platinum-based Chemotherapy: Clinical studies of Osimertinib in combination with pemetrexed and platinum-based chemotherapy did not include sufficient numbers of patients age 65 and over to determine whether they respond differently from younger patients.
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) or severe (CLcr 15- 29 ml/min) renal impairment. There is no recommended dose of Osimertinib for patients with end-stage renal disease.
Hepatic Impairment
No dose adjustment is recommended in patients with mild to moderate hepatic impairment (Child-Pugh A and B or total bilirubin ≤ ULN and AST > ULN or total bilirubin 1 to 3 times ULN and any AST). There is no recommended dose for Osimertinib for patients with severe hepatic impairment (total bilirubin between 3 to 10 times ULN and any AST).

Drug Interaction:
Strong CYP3A Inhibitors
Avoid concomitant administration of Osimertinib with strong CYP3A inhibitors, including macrolide antibiotics (e.g., Telithromycin), antifungals (e.g., Itraconazole), antivirals (e.g., Ritonavir), Nefazodone, as concomitant use of strong CYP3A inhibitors may increase Osimertinib plasma concentrations. If no other alternative exists, monitor patients more closely for adverse reactions of Osimertinib.
Strong CYP3A Inducers
Avoid concomitant administration of Osimertinib with strong CYP3A inducers (e.g., Phenytoin, Rifampicin, Carbamazepine, St. John's Wort) as strong CYP3A inducers may decrease Osimertinib plasma concentrations.
Effect on other drugs

- *Strong CYP3A Inducers:* Co-administering Osimertinib with a strong CYP3A4 inducer decreased the exposure of Osimertinib compared to administering Osimertinib alone. Decreased Osimertinib exposure may lead to reduced efficacy. Avoid co-administering Osimertinib with strong CYP3A inducers. Increase the Osimertinib dosage when co-administering with a strong CYP3A4 inducer if concurrent use is unavoidable. No dose adjustments are required when Osimertinib is used with moderate and/or weak CYP3A inducers.
- *Effect of Osimertinib on Other Drugs:* Co-administering Osimertinib with a breast cancer resistant protein (BCRP) or P-glycoprotein (P-gp) substrate increased the exposure of the substrate compared to administering it alone. Increased BCRP or P-gp substrate exposure may increase the risk of exposure-related toxicity. Monitor for adverse reactions of the BCRP or P-gp substrate, unless otherwise instructed in its approved labeling, when co-administered with Osimertinib.
- *Drugs That Prolong the QTc Interval:* The effect of co-administering medicinal products known to prolong the QTc interval with Osimertinib is unknown. When feasible, avoid concomitant administration of drugs known to prolong the QTc interval with known risk of Torsades de pointes. If not feasible to avoid concomitant administration of such drugs, conduct periodic ECG monitoring.

Overdose:
No Information provided.

Storage:
Store in a cool & dry place below 30^0 C, protect from light. Keep out of the reach of children.

Packaging:
Tasso 80 Tablet: Each box contains 30 Film Coated Tablets and one packet silica gel in a sealed HDPE container.

Manufactured by:
Jenphar Bangladesh Ltd.
Sreepur, Gazipur, Bangladesh.

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