165mm

155mm

• you have a history of eye problems
If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist or nurse before taking this medicine.

DRUG INTERACTIONS
• Co-administration of cytochrome P450 inhibitors, such as ketoconazole, may alter serum levels of calcifediol.
• Co-administration of thiazides may cause hypercalcemia.
• Cholestyramine may impair the absorption of calcifediol.
• The half-life of calcifediol is reduced by drugs stimulating microsomal hydroxylation, such as phenobarbital or other anticonvulsants.

HOW SUPPLIED
Osimernib Film Coated Tablet 80mg available in blister pack of 1x10's 2x10's, 3x10's and 4x7's.

Instructions: Store at 25°C (Excursions permitted between 15°C to 30°C).
Protect from sunlight & moisture.
Keep out of the reach of children.
To be dispensed on the prescription of a registered medical practitioner only.

خوراک : ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
ہدایات : دوا کو ۲۵ ڈگری سینٹی گریڈ درجہ حرارت پر رکھیں
(درجہ حرارت کی حد ۱۵ سے ۳۰ ڈگری سینٹی گریڈ ہے)۔
دھوپ اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔

Manufactured by:
Kaizen Pharmaceuticals (Pvt) Ltd.,
E-127, E-128 & E-129, North Western Industrial Zone,
Port Qasim Authority, Karachi-75020, Pakistan.

Art no. 1393

Osimernib Tablet

(Osimertinib Mesylate)

Film coated tablet 80mg

اوسیمرنِب گولی

(اوسیمرٹینب میسلائیٹ)

۸۰ ملی گرام

Description:
Osimernib (Osimertinib) is Film coated tablet, for oral use.

Composition:
Each film coated tablet contains:
Osimertinib Mesylate 95.4mg Eq. to Osimertinib.....80mg

CLINICAL PHARMACOLOGY

Mechanism of Action:
Osimernib is a type of medicine called a kinase inhibitor. It attaches itself to the mutant EGFR protein and turns the protein off. When EGFR is turned off, it quits sending the signal to cells to grow and multiply. This causes the cells to die and can cause tumors to shrink in size.

PHARMACOKINETICS

Absorption
Following oral administration of OSIMERNIB, peak plasma concentrations of Osimertinib were achieved with a median (min-max) tmax of 6 (3-24) hours, with several peaks observed over the first 24 hours in some patients. The absolute bioavailability of OSIMERNIB is 70% (90% CI 67, 73). Based on a clinical pharmacokinetic study in patients at 80 mg, food does not alter Osimertinib bioavailability to a clinically meaningful extent (AUC increase by 6% (90% CI -5, 19) and Cmax decrease by 7% (90% CI -19, 6)). In healthy volunteers administered an 80 mg tablet where gastric pH was elevated by dosing of omeprazole for 5 days, Osimertinib exposure was not affected (AUC and Cmax increase by 7% and 2%, respectively) with the 90% CI for exposure ratio contained within the 80-125% limit.

Distribution
Population estimated mean volume of distribution at steady-state (Vss/F) of Osimertinib is 918 L indicating extensive distribution into tissue. In vitro plasma protein binding of Osimertinib is 94.7% (5.3% free). Osimertinib has also been demonstrated to bind covalently to rat and human plasma proteins, human serum albumin and rat and human hepatocytes.

Metabolism
In vitro studies indicate that Osimertinib is metabolized predominantly by CYP3A4, and CYP3A5. However, with current available data, alternative metabolic pathways cannot be fully ruled out. Based on in vitro studies, 2 pharmacologically active metabolites (AZ7550 and AZ5104) have subsequently been identified in the plasma of preclinical species and in humans after oral dosing with Osimertinib; AZ7550 showed

a similar pharmacological profile to OSIMERNIB while AZ5104 showed greater potency across both mutant and wild-type EGFR. Both metabolites appeared slowly in plasma after administration of OSIMERNIB to patients, with a median (minmax) tmax of 24 (4-72) and 24 (6-72) hours, respectively. In human plasma, parent Osimertinib accounted for 0.8%, with the 2 metabolites contributing 0.08% and 0.07% of the total radioactivity with the majority of the radioactivity being covalently bound to plasma proteins. The geometric mean exposure of both AZ5104 and AZ7550, based on AUC, was approximately 10% each of the exposure of Osimertinib at steady-state. The main metabolic pathway of Osimertinib was oxidation and dealkylation. At least 12 components were observed in the pooled urine and faecal samples in humans with 5 components accounting for >1% of the dose of which unchanged Osimertinib, AZ5104 and AZ7550, accounted for approximately 1.9, 6.6 and 2.7% of the dose while a cysteinyl adduct (M21) and an unknown metabolite (M25) accounted for 1.5% and 1.9% of the dose, respectively.
Based on in vitro studies, Osimertinib is a competitive inhibitor of CYP 3A4/5 but not CYP1A2, 2A6, 2B6, 2C8, 2C9, 2C19, 2D6 and 2E1 at clinically relevant concentrations. Based on in vitro studies, Osimertinib is not an inhibitor of UGT1A1 and UGT2B7 at clinically relevant concentrations hepatically. Intestinal inhibition of UGT1A1 is possible but the clinical impact is unknown.

Excretion
Following a single oral dose of 20 mg, 67.8% of the dose was recovered in faeces (1.2% as parent) while 14.2% of the administered dose (0.8% as parent) was found in urine by 84 days of sample collection. Unchanged Osimertinib accounted for approximately 2% of the elimination with 0.8% in urine and 1.2% in faeces.

THERAPEUTIC INDICATIONS
Osimernib (Osimertinib) is commonly used for treating different kinds of epidermal growth factor receptor (EGFR) mutated lung cancer. EGFR is a protein on the surface of cells and helps cells to grow and multiply. When there is a mutation in EGFR, cancer cells can grow and multiply nonstop. Osimernib may be used by itself or in combination with other medicines to treat certain EGFR mutated non-small cell lung cancer (NSCLC).

DOSAGE & ADMINISTRATION
Always take this medicine exactly as your doctor or pharmacist has told you.
Check with your doctor or pharmacist if you are not sure.
How much to take
• The recommended dose is one 80 mg tablet each day.
• If necessary, your doctor may reduce your dose to one 40 mg tablet each day.
How to take
• OSIMERNIB is taken by mouth. Swallow the tablet whole with water.
Do not crush, split or chew the tablet.
• Take OSIMERNIB every day at the same time.
• You can take this medicine with or without food.
If you have trouble swallowing the tablet, you can mix it in water:
• Put the tablet in a glass.
• Add 50 mL (about two-thirds of a tumblerful) of still (non-fizzy) water – do not use any other liquids.
• Stir the water until the tablet breaks up into very small pieces - the tablet will not completely dissolve.

• Drink the liquid straight away.
• To make sure you have taken all of the medicine, rinse the glass thoroughly with another 50 mL of water and drink it.

If you take more OSIMERNIB than you should:
If you take more than your normal dose, contact your doctor or nearest hospital straight away.
If you forget to take OSIMERNIB:
If you forget a dose, take it as soon as you remember it. However, if it is less than 12 hours until your next dose is due, skip the missed dose.
Take your next normal dose at its scheduled time.
If you stop taking OSIMERNIB:
Do not stop taking this medicine - talk to your doctor first. It is important to take this medicine every day, for as long as your doctor prescribes it for you.
If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse

METHOD OF ADMINISTRATION
Oral

ADVERSE REACTIONS
If you get any side effects, talk to your doctor, pharmacist or nurse.
This includes any possible side effects not listed in this leaflet.

CONTRAINDICATIONS
Do not take OSIMERNIB if:
• you are allergic (hypersensitive) to Osimertinib or any of the other ingredients of this medicine
• you are taking St. John's Wort (Hypericum perforatum).

If you are not sure, talk to your doctor, pharmacist or nurse before taking OSIMERNIB

Overdose:
In OSIMERNIB clinical trials a limited number of patients were treated with daily doses of up to 240 mg without dose limiting toxicities. In these studies, patients who were treated with OSIMERNIB daily doses of 160 mg and 240 mg experienced an increase in the frequency and severity of a number of typical EGFR TKI-induced AEs (primarily diarrhea and skin rash) compared to the 80 mg dose. There is limited experience with accidental overdoses in humans. All cases were isolated incidents of patients taking an additional daily dose of OSIMERNIB in error, without any resulting clinical consequences.

There is no specific treatment in the event of OSIMERNIB overdose. In case of suspected overdose, OSIMERNIB should be withheld and symptomatic treatment initiated.

WARNINGS AND PRECAUTIONS
Talk to your doctor, pharmacist or nurse before taking OSIMERNIB if:
• you have suffered from inflammation of your lungs (a condition called 'interstitial lung disease').
• you have ever had heart problems – your doctor may want to keep a close eye on you.