Anib- 40

Afatinib Dimaleate INN 40 mg Tablet

Composition: Each film coated tablet contains Afatinib 40 mg as Afatinib Dimaleate INN.

Mechanism of Action: Afatinib covalently binds to the kinase domains of EGFR (ErbB1), HER2 (ErbB2), and HER4 (ErbB4) and irreversibly inhibits tyrosine kinase autophosphorylation, resulting in downregulation of ErbB signaling.

Pharmacokinetics:

Absorption and Distribution: Following oral administration of Anib tablets, time to peak Afatinib plasma concentrations (Tmax) is 2 to 5 hours. Maximum concentration (Cmax) and area under the concentration-time curve from time zero to infinity (AUC0-∞) values increased slightly more than dose proportional in the range of 20 to 50 mg. The geometric mean relative bioavailability of 20 mg Anib tablets was 92% as compared to an oral solution. In vitro binding of Afatinib to human plasma proteins is approximately 95%. A high-fat meal decreased Cmax by 50% and AUC0-∞ by 39% relative to the fasted condition.

Metabolism and Elimination: Covalent adducts to proteins are the major circulating metabolites of Afatinib and enzymatic metabolism of Afatinib is minimal. In humans, excretion of Afatinib is primarily via the feces (85%) with 4% recovered in the urine following a single oral dose of [14C]-labeled Afatinib solution. The parent compound accounted for 88% of the recovered dose. The elimination half-life of Afatinib is 37 hours after repeat dosing in cancer patients. Steady-state plasma concentrations are achieved within 8 days of repeat dosing of Anib resulting in an accumulation of 2.8-fold for AUC and 2.1-fold for Cmax.

Indications:

EGFR Mutation-Positive, Metastatic Non-Small Cell Lung Cancer: Anib is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test.

Limitation of Use: The safety and efficacy of Anib have not been established in patients whose tumors have other EGFR mutations.

Previously Treated, Metastatic Squamous NSCLC: Anib is indicated for the treatment of patients with metastatic squamous NSCLC progressing after platinum-based chemotherapy.

Dosage and Administration:

Patient Selection for EGFR Mutation-Positive Metastatic NSCLC: Patients should be selected for first-line treatment of metastatic NSCLC with GILOTRIF based on the presence of EGFR exon 19 deletions or exon 21 (L858R) substitution mutations in tumor specimens.

Recommended Dose: The recommended dose of Anib is 40 mg orally, once daily until disease progression or no longer tolerated by the patient.

Severe Renal Impairment: The recommended dose of Anib in patients with severe renal impairment (estimated glomerular filtration rate [eGFR *] 15 to 29 mL/min /1.73 m^2) is 30 mg orally, once daily.

Anib should be taken at least 1 hour before or 2 hours after a meal. A missed dose should not be taken within 12 hours of the next dose. Or, as directed by the registered physicians.

Dose Modifications for Adverse Reactions: Anib should be withheld for any adverse reactions of:

- NCI CTCAE* Grade 3 or higher
- Diarrhea of Grade 2 or higher persisting for 2 or more consecutive days while taking anti-diarrheal medication
- Cutaneous reactions of Grade 2 that are prolonged (lasting more than 7 days) or intolerable
- Renal impairment of Grade 2 or higher

Side Effects:

- Diarrhea
- Bullous and Exfoliative Skin Disorders
- Interstitial Lung Disease
- Hepatic Toxicity
- Keratitis

Contraindications: It is contraindicated in patients with known hypersensitivity to Afatinib or any other components of this product.

Recommended Dose For Metastatic High-Risk CSPC: The recommended dose of Abiraterone Acetate is 1,000mg (two 500mg tablets or four 250mg tablets) orally once daily with Prednisone 5mg administered orally once daily.

Important Administration Instructions :

Patients receiving Abiraterone Acetate should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had bilateral orchiectomy. Abiraterone Acetate must be taken on an empty stomach, at least one hour before or at least two hours after a meal. The tablets should be swallowed whole with water. Do not crush or chew tablets.

Dose Modification:

• For patients with baseline moderate hepatic impairment (Child-Pugh Class B), reduce the Abiraterone Acetate starting dose to 250mg once daily.

• For patients who develop hepatotoxicity during treatment, hold Abiraterone Acetate until recovery. Retreatment may be initated at a reduced dose. Abiraterone Acetate should be discontinued if patients develop severe hepatotoxicity.

• Avoid concomitant strong CYP3A4 inducers (e.g., Phenytoin, Carbamazepine, Rifampin, Rifabutin, Rifapentine, Phenobarbital) during Abiraterone Acetate treatment. If a strong CYP3A4 inducer must be co-administered, increase the Abiraterone Acetate dosing frequency to twice a day only during the co-administration period (e.g., from 1,000mg once daily to 1,000mg twice a day). Reduce the dose back to the previous dose and frequency, if the concomitant strong CYP3A4 inducer is discontinued. Or, as directed by the registered physician.

ADVERSE EFFECTS

The most common adverse reactions are fatigue, arthalgia, hypertension, nausea, edema, hypokalemia, hot flush, diarrhea, vomiting, upper respiratory infection, cough, and headache.

CONTRAINDICATIONS

It is contraindicated in any patient who has shown a hypersensitivity reaction to the drug or to any of the excipients.

DRUG INTERACTIONS

Drugs That Inhibit Or Induce CYP3A4 Enzymes

Based on in vitro data, Abiraterone Acetate is a substrate of CYP3A4. In a dedicated drug interaction trial, co-administration of Rifampin, a strong CYP3A4 inducer, decreased exposure of Abiraterone by 55%. Avoid concomitant strong CYP3A4 inducers during Abiraterone Acetate treatment. If a strong CYP3A4 inducer must be co-administered, increase the Abiraterone Acetate dosing frequency. In a dedicated drug interaction trial, co-administration of ketoconazole, a strong inhibitor of CYP3A4, had no clinically meaningful effect on the pharmacokinetics of Abiraterone.

Effects Of Abiraterone On Drug Metabolizing Enzymes

Abiraterone Acetate is an inhibitor of the hepatic drug-metabolizing enzymes CYP2D6 and CYP2C8. In a CYP2D6 drug-drug interaction trial, the Cmax and AUC of Dextromethorphan (CYP2D6 substrate) were increased 2.8- and 2.9-fold, respectively, when Dextromethorphan was given with Abiraterone Acetate 1,000mg daily and Prednisone 5 mg twice daily. Avoid co-administration of Abiraterone Acetate with substrates of CYP2D6 with a narrow therapeutic index (e.g., Thioridazine). If alternative treatments cannot be used, consider a dose reduction of the concomitant CYP2D6 substrate drug. In a CYP2C8 drug-drug interaction trial in healthy subjects, the AUC of Pioglitazone (CYP2C8 substrate) was increased by 46% when Pioglitazone was given together with a single dose of 1,000mg Abiraterone Acetate. Therefore, patients should be monitored closely for signs of toxicity related to a CYP2C8 substrate with a narrow therapeutic index if used concomitantly with Abiraterone Acetate.

PRECAUTIONS

Abiraterone Acetate may cause hypertension, hypokalemia, and fluid retention as a consequence of increased mineralocorticoid levels resulting from CYP17 inhibition. Patients should be monitored for hypertension, hypokalemia, and fluid retention at least once a month. Hypertension and hypokalemia should be controlled and corrected before and during treatment with Abiraterone. Patients should be monitored for symptoms and signs of adrenocortical insufficiency. Serum transaminases (ALT and AST) and bilirubin levels should be measured prior to starting treatment with Abiraterone, every two weeks for the first three months of treatment and monthly thereafter.

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

Use in Pregnancy: The safety and efficacy of Abiraterone Acetate have not been established in females. The drug can cause fetal harm and potential loss of pregnancy.

Use in Lactation: There is no information available on the presence of Abiraterone Acetate in human milk, or on the effects on the breastfed child or milk production.

OVERDOSE

There is no specific antidote. In the event of an overdose, Abiraterone Acetate should be stopped, general supportive measures are undertaken, including monitoring for arrhythmias and cardiac failure and assess liver function.

PHARMACEUTICAL INFORMATION

Storage: Store below 30° C in a dry place. Protect from light. Keep out of the reach of children.

Packing: Abiret: Each box contains 7 tablets in Alu-Alu blister pack.

DRUG INTERNATIONAL LTD.
UNIT-2
13A & 14A,TONGI I/A, GAZIPUR