Giltela™
Gilteritinib

Jenphar
Bangladesh

جنفار
بنغلاديش

Composition:
Giltela™ 40 mg Tablet: Each film coated tablet contains Gilteritinib Hemifumarate INN equivalent to Gilteritinib 40 mg.

Pharmacology:
Mechanism of Action:
Gilteritinib is a small molecule that inhibits multiple receptor tyrosine kinases, including FMS-like tyrosine kinase 3 (FLT3). Gilteritinib demonstrated the ability to inhibit FLT3 receptor signaling and proliferation in cells exogenously expressing FLT3 including FLT3-ITD, tyrosine kinase domain mutations (TKD) FLT3-D835Y and FLT3-ITD-D835Y, & it induced apoptosis in leukemic cells expressing FLT3-ITD. Pharmacodynamics in patients with relapsed or refractory AML administered Gilteritinib 120 mg, substantial (>90%) inhibition of FLT3 phosphorylation was rapid (within 24 hours after first dose) and sustained, as characterized by an ex vivo plasma inhibitory activity (PIA) assay.

Indications:
Gilteritinib is a kinase inhibitor indicated for the treatment of adult patients who have relapsed or refractory acute myeloid leukemia (AML) with a FLT3 mutation as detected by an FDA-approved test.

Dosage and Administration:
Dosage:
The recommended starting dose of Gilteritinib is 120 mg orally once daily with or without food. In the absence of disease progression or unacceptable toxicity, treatment for a minimum of 6 months is recommended to allow time for a clinical response.
Do not break or crush Gilteritinib tablets. Administer Gilteritinib tablets orally about the same time each day. If a dose of Gilteritinib is missed or not taken at the usual time, administer the dose as soon as possible on the same day, and at least 12 hours prior to the next scheduled dose. Return to the normal schedule the following day. Do not administer 2 doses within 12 hours.
Dose Modification:
Interrupt dosing or reduce dose for toxicities

Adverse Reaction	Recommended Action
Differentiation Syndrome	If differentiation syndrome is suspected, administer systemic corticosteroids & initiate hemodynamic monitoring until symptom resolution and for a minimum of 3 days. Interrupt Gilteritinib if severe signs or symptoms persist for more than 48 hours after initiation of corticosteroids. Resume Gilteritinib when signs & symptoms improve to Grade 2 or lower.
Posterior Reversible Encephalopathy Syndrome	Discontinue Gilteritinib.
QTc interval greater than 500 msec	Interrupt Gilteritinib. Resume Gilteritinib at 80 mg when QTc interval returns to within 30 msec of baseline or less than or equal to 480 msec.
QTc interval increased by >30 msec on ECG on day 8 of cycle 1	Confirm with ECG on day 9. If confirmed, consider dose reduction to 80 mg.
Pancreatitis	Interrupt Gilteritinib until pancreatitis is resolved. Resume Gilteritinib at 80 mg.
Other Grade 3 or higher toxicity considered related to treatment	Interrupt Gilteritinib until toxicity resolves or improves to Grade 1. Resume Gilteritinib at 80 mg.

Contraindications:
Hypersensitivity to gilteritinib or any of the excipients. Anaphylactic reactions have been observed in clinical trials.

Adverse Reactions:
The most common adverse reactions (≥20%) are transaminase increased, myalgia/arthralgia, fatigue/malaise, fever, mucositis, edema, rash, noninfectious diarrhea, dyspnea, nausea, cough, constipation, eye disorders, headache, dizziness, hypotension, vomiting, & renal impairment.

Warning and Precautions:

Posterior reversible encephalopathy syndrome (PRES): Discontinue Gilteritinib in patients who develop PRES.

Prolonged QT Interval: Interrupt and reduce Gilteritinib dosage in patients who have a QTcF >500 msec. Correct hypokalemia or hypomagnesemia prior to and during Gilteritinib administration.

Pancreatitis: Interrupt and reduce the dose in patients who develop pancreatitis.

Embryo-Fetal Toxicity: Gilteritinib can cause fetal harm when administered to a pregnant woman. Advise of the potential risk to a fetus and to use effective contraception.

Use in Specific Populations:

Pregnancy: Based on findings from animal studies and its mechanism of action, Gilteritinib can cause fetal harm when administered to a pregnant woman. There are no available data on Gilteritinib use in pregnant women to inform a drug-associated risk of adverse developmental outcomes.

Nursing Mothers: There are no data on the presence of Gilteritinib and/or its metabolites in human milk, the effects on the breastfed child, or the effects on milk production. Advise a lactating woman not to breastfeed during treatment with Gilteritinib and for 2 months after the last dose.

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

Geriatric Use: Of the 319 patients in clinical studies of Gilteritinib, 43% were age 65 years or older, & 13% were 75 years or older. No overall differences in effectiveness or safety were observed between patients age 65 years or older & younger patients.

Hepatic impairment: No dose adjustment is required for patients with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment. Gilteritinib is not recommended for use in patients with severe (Child-Pugh Class C) hepatic impairment, as safety and efficacy have not been evaluated in this population.

Renal impairment: No dose adjustment is necessary in patients with mild, moderate or severe renal impairment.

Drug Interactions:

Effect of Other Drugs on Gilteritinib:

Combined P-gp and Strong CYP3A Inducers: Concomitant use of Gilteritinib with a combined P-gp and strong CYP3A inducer decreases Gilteritinib exposure which may decrease Gilteritinib efficacy. Avoid concomitant use of Gilteritinib with combined P-gp and strong CYP3A inducers.

Strong CYP3A Inhibitors: Concomitant use of Gilteritinib with a strong CYP3A inhibitor increases Gilteritinib exposure. Consider alternative therapies that are not strong CYP3A inhibitors. If the concomitant use of these inhibitors is considered essential for the care of the patient, monitor patient more frequently for Gilteritinib adverse reactions. Interrupt and reduce Gilteritinib dosage in patients with serious or life-threatening toxicity.

Effect of Gilteritinib on Other Drugs:

Drugs that Target 5HT2B Receptor or Sigma Nonspecific Receptor: Concomitant use of Gilteritinib may reduce the effects of drugs that target the 5HT2B receptor or the sigma nonspecific receptor (e.g., escitalopram, fluoxetine, sertraline). Avoid concomitant use of these drugs with Gilteritinib unless their use is considered essential for the care of the patient.

Overdose:

There is no known specific antidote for Gilteritinib. In the event of an overdose, treatment with Gilteritinib should be stopped. Patients must be closely monitored for signs or symptoms of adverse reactions, and appropriate symptomatic and supportive treatment initiated, taking into consideration the long half-life estimated at 113 hours.

Storage Condition:

Store in a cool and dry place below 30° C, protect from light. Keep out of the reach of children.

Packaging:

Giltela™ 40 mg Tablet: Each box contains 21 tablets and one packet silica gel in a sealed HDPE container.

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

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