Lornatib 100

Lorlatinib 100 mg

Composition:
Lornatib 100 Tablet: Each film coated tablet contains Lorlatinib INN 100 mg.

Pharmacology:
Lorlatinib is an inhibitor of poly (ADP-ribose) polymerase (PARP) enzymes, including PARP1, PARP2, and PARP3. PARP enzymes are involved in normal cellular homeostasis, such as DNA transcription, cell cycle regulation, and DNA repair. Lorlatinib has been shown to inhibit growth of select tumor cell lines in vitro and decrease tumor growth in mouse xenograft models of human cancer both as monotherapy or following platinum-based chemotherapy. Increased cytotoxicity and anti-tumor activity following treatment with Lorlatinib were noted in cell lines and mouse tumor models with deficiencies in BRCA. In vitro studies have shown that Lorlatinib-induced cytotoxicity may involve inhibition of PARP enzymatic activity and increased formation of PARP-DNA complex, resulting in disruption of cellular homeostasis and cell death.

Indications:
Ovarian cancer:
- Lorlatinib is indicated for the maintenance treatment of adult patients with deleterious or suspected deleterious germline or somatic BRCA-mutated advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy.
- In combination with Bevacizumab for the maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy and whose cancer is associated with homologous recombination deficiency (HRD)-positive status defined by either a deleterious or suspected deleterious BRCA mutation, and/or genomic instability.
- Lorlatinib is indicated for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, who are in complete or partial response to platinum-based chemotherapy.
- Lorlatinib is indicated for the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy.

Breast cancer:
- Lorlatinib is indicated for the treatment of adult patients with deleterious or suspected deleterious gBRCAm, HER2-negative metastatic breast cancer who have been treated with chemotherapy in the neoadjuvant, adjuvant or metastatic setting. Patients with hormone receptor (HR)-positive breast cancer should have been treated with a prior endocrine therapy or be considered inappropriate for endocrine therapy.

Pancreatic cancer:
- Lorlatinib is indicated for the maintenance treatment of adult patients with deleterious or suspected deleterious gBRCAm metastatic pancreatic adenocarcinoma whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen.

Prostate cancer:
- Lorlatinib is indicated for the treatment of adult patients with deleterious or suspected deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC) who have progressed following prior treatment with enzalutamide or abiraterone.

Dose & administration:
The recommended dosage of Lorlatinib is 100 mg taken orally twice daily, with or without food.

If a patient misses a dose of Lorlatinib, instruct patient to take their next dose at its scheduled time. Instruct patients to swallow tablets whole. Do not chew, crush, dissolve, or divide tablet.

Continue treatment until disease progression, unacceptable toxicity, or completion of 2 years of treatment. Patients with a complete response (no radiological evidence of disease) at 2 years should stop treatment. Patients with evidence of disease at 2 years, who in the opinion of the treating healthcare provider can derive further benefit from continuous treatment, can be treated beyond 2 years.

For First-Line Maintenance Treatment of HRD-positive Advanced Ovarian Cancer in Combination with Bevacizumab, the recommended dose of bevacizumab is 15 mg/kg every three weeks. Bevacizumab should be given for a total of 15 months including the period given with chemotherapy and given as maintenance.

Patients receiving Lorlatinib for mCRPC should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had bilateral orchiectomy.

Dosage Modifications for Adverse Reactions:

To manage adverse reactions, consider interruption of treatment or dose reduction. The recommended dose reduction is 250 mg taken twice daily. If a further dose reduction is required, then reduce to 200 mg taken twice daily.

Dosage Modifications for Concomitant Use with Strong or Moderate CYP3A Inhibitors: Reduce Lorlatinib dosage to 100 mg twice daily when used concomitantly with a strong CYP3A inhibitor and reduce to 150 mg twice daily when used concomitantly with a moderate CYP3A inhibitor.

Dosage Modifications for Renal Impairment: In patients with moderate renal impairment (CLcr 31-50 mL/min), reduce the Lorlatinib dosage to 200 mg orally twice daily.

Contra-indications:
Lorlatinib is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation.

Warning and precaution:
Interactions with other medicinal products: Co-administration of Lorlatinib with strong or moderate CYP3A inhibitors is not recommended. If a strong or moderate CYP3A inhibitor must be co-administered, the dose of Lorlatinib should be reduced. Co-administration of Lorlatinib with strong or moderate CYP3A inducers is not recommended. In the event that a patient already receiving Olakin requires treatment with a strong or moderate CYP3A inducer, the prescriber should be aware that the efficacy of Lorlatinib may be substantially reduced.

Hematologic: Hematological toxicity has been reported in patients treated with Lorlatinib, including clinical diagnoses and/or laboratory findings of generally mild or moderate (Common Terminology Criteria for Adverse Events [CTCAE] grade 1 or 2) anemia, neutropenia, thrombocytopenia and lymphopenia. Patients should not start treatment with Olakin until they have recovered from hematological toxicity caused by previous anti-cancer therapy (hemoglobin, platelet, and neutrophil levels should be ≤CTCAE grade 1). Baseline testing, followed by monthly monitoring of complete blood counts, is recommended for the first 12 months of treatment and periodically after this time to monitor for clinically significant changes in any parameter during treatment.

Pneumonitis: Pneumonitis, including fatal cases, occurred in <1% of patients treated with Lorlatinib. If patients present with new or worsening respiratory symptoms such as dyspnea, fever, cough, wheezing, or a radiological abnormality occurs, interrupt treatment with Lorlatinib and initiate prompt investigation. If pneumonitis is confirmed, discontinue Lorlatinib.

Embryo-Fetal Toxicity: Lorlatinib can cause fetal harm when administered to a pregnant woman based on its mechanism of action and findings in animals. Lorlatinib was teratogenic and caused embryo-fetal toxicity in rats at exposures below those in patients receiving the recommended human dose of 400 mg twice daily. If the patient becomes pregnant while taking this drug, apprise the patient of the potential hazard to a fetus. Advise females of reproductive potential to avoid becoming pregnant while taking Lorlatinib. If contraceptive methods are being considered, use effective contraception during treatment and for at least one month after receiving the last dose of Lorlatinib.

Side Effects:
The most common serious adverse reaction reported was anemia (2.4% Lorlatinib vs 2.2% chemotherapy). The following serious ADRs were reported in one patient each: dermatitis allergic, neutrophil count decreased and platelet count decreased. The proportion of patients who permanently discontinued Lorlatinib due to adverse events was 4.9% in the Olakin group compared with 7.7% in the chemotherapy group. Anemia and platelet count decrease were the only adverse reactions leading to discontinuation of Olakin in more than one patient.

Use in specific population:
Pregnancy: Lorlatinib can cause fetal harm when administered to a pregnant woman based on its mechanism of action and findings in animals. Lorlatinib was teratogenic and caused embryo-fetal toxicity in rats at exposures below those in patients receiving the recommended human dose of 400 mg twice daily. If this drug is used during pregnancy, or if a patient becomes pregnant while taking this drug, apprise the patient of the potential hazard to the fetus and the potential risk for loss of the pregnancy.

Nursing Mothers: It is not known whether Lorlatinib is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Lorlatinib, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric population: The safety and efficacy of Lorlatinib in children have not been established.

Drug interaction:
Clinical studies of Lorlatinib in combination with other anti-cancer agents, including DNA damaging agents, indicate a potentiation and prolongation of myelosuppressive toxicity. The recommended Lorlatinib monotherapy dose is not suitable for combination with myelosuppressive anti-cancer agents. Lorlatinib is predominantly metabolised by CYP3A. Co-administered CYP3A inhibitors or inducers may respectively increase or decrease Lorlatinib plasma concentration.

Overdose:
There is no specific treatment in the event of Lorlatinib overdose, and symptoms of overdose are not established. In the event of an overdose, physicians should follow general supportive measures and should treat symptomatically.

Storage:
Do not store above 30°C. Protect from light. Keep out of the reach of children.

Packing:
Lornatib 100 Tablet: Each HDPE container of Lornatib 100 contains 30 tablets, a silica gel desiccant and polyester coil with a child resistant closure.

Manufactured by:
Ziska Pharmaceuticals Ltd.
Kaliakoir, Gazipur, Bangladesh

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