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

Pharmacology: Lorlatinib is an orally available, ATP-competitive inhibitor of the receptor tyrosine kinases, anaplastic lymphoma kinase (ALK) and C-ros oncogene 1 (Ros1), with potential antineoplastic activity. **Absorption:** The mean absolute bioavailability is 81% after oral administration compared to IV administration. **Elimination:** Following a single oral 100 mg dose of Lorlatinib, 48% of the radioactivity was recovered in urine and 41% in feces. **Distribution:** The mean steady-state volume of distribution was 305 L following a single IVdose. **Clearance:** The mean oral clearance was 11 L/h following a single oral 100 mg dose and increased to 18 L/h at steady state. **Metabolism:** In vitro, Lorlatinib is metabolized primarily by CYP3A4 and UGT1A4, with minor contribution from CYP2C8, CYP2C19, CYP3A5, and UGT1A3. **Half- life:** The mean plasma half-life (t½) was 24 hours (40%) after a single oral 100 mg dose of Lorlatinib.

Indications : It is indicated for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic Non-small Cell Lung Cancer (NSCLC) whose disease has progressed on

- Crizotinib and at least one other ALK inhibitor for metastatic disease; or
- Alectinib as the first ALK inhibitor therapy for metastatic disease; or
- Ceritinib as the first ALK inhibitor therapy for metastatic disease.

Dosage and administration : The recommended dosage of Lorlatinib is 100 mg orally once daily, with or without food, until disease progression or unacceptable toxicity. It should be taken at the same time each day. If a dose is missed, then the missed dose should be taken unless the next dose is due within 4 hours. 2 doses should not be taken at the same time to make up for a missed dose. Or, as directed by the registered physicians.

Dose Modification:

- First Dose Reduction: Lorlatinib 75 mg orally once daily.
- Second Dose Reduction: Lorlatinib 50 mg orally once daily.

It should be permanently discontinued in patients who are unable to tolerate 50 mg orally once daily.

Contraindication : It is contraindicated in patients taking strong CYP3A inducers, due to the potential for

Lorlanib-100
Lorlatinib INN

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serious hepatotoxicity.

Precautions : Caution should be exercised when using Lorlatinib in patients with Risk of serious Hepatotoxicity with concomitant use of Strong CYP3A Inducers, Central Nervous System Effects, Hyperlipidemia, Atrioventricular Block, Interstitial Lung Disease/Pneumonitis and Embryo-Fetal Toxicity.

Side effects : The most common side effects are Risk of Serious Hepatotoxicity with concomitant use of Strong CYP3A Inducers, Central Nervous System Effects, Hyperlipidemia, Atrioventricular Block, Interstitial Lung Disease/Pneumonitis.

Use in pregnancy and lactation : It can cause fetal harm when administered to a pregnant woman. Pregnant women should be advised of the potential risk to a fetus. Women should be advised not to breastfeed during treatment with Lorlatinib and for 7 days after the final dose.

Use in child : The safety and effectiveness of Lorlatinib in pediatric patients have not been established.

Drug interactions : Effect of other Drugs on Lorlatinib: Effect of CYP3A Inducers: Concomitant use of Lorlatinib with a strong CYP3A inducer decreased Lorlatinib plasma concentrations, which may decrease the efficacy of Lorlatinib so it should be avoided. **Effect of Strong CYP3A Inhibitors:** Concomitant use with a strong CYP3A inhibitor increased Lorlatinib plasma concentrations, which may increase the incidence and severity of adverse reactions of Lorlatinib so it should be avoided. **Effect of Lorlatinib on other Drugs: CYP3A Substrates:** Concomitant use of Lorlatinib decreases the concentration of CYP3A substrates, which may reduce the efficacy of these substrates so it should be avoided.

Overdose : There is no data available.

Storage : Store below 30°C in a dry place.

Packing : Each container contains 30 capsules in a box.