Vixo™
Larotrectinib

Jenphar
Bangladesh

جنفار
بنغلاديش

Composition:
Vixo™ 100 Capsule: Each capsule contains Larotrectinib Sulfate INN equivalent to Larotrectinib 100 mg.

Clinical Pharmacology:
Larotrectinib is an orally bioavailable, adenosine triphosphate (ATP)-competitive & highly selective Tropomyosin Receptor Kinase (TRK) inhibitor. Larotrectinib targets the TRK family of proteins inclusive of TRKA, TRKB & TRKC that are encoded by NTRK1, NTRK2 & NTRK3 genes, respectively. Larotrectinib demonstrated inhibition of TRK proteins and inhibition of proliferation of cell lines containing NTRK gene fusions in a concentration -dependent manner.

Indications:
Larotrectinib is indicated for the treatment of adult and pediatric patients with solid tumors that:
- Have a Neurotrophic Tyrosine Receptor Kinase (NTRK) gene fusion without a known acquired resistance mutation,
- Are metastatic or where surgical resection is likely to result in severe morbidity, and
- Have no satisfactory treatment options.

Dosage and Administration:
Recommended Dose
Adults: The recommended dose of larotrectinib in adults is 100 mg taken orally, twice daily (total dose of 200 mg) until the patient is no longer clinically benefiting from therapy or until unacceptable toxicity occurs.
Pediatrics: Dosing in pediatric patients is based on body surface area (BSA). The recommended dose of larotrectinib in pediatric patients (1 month to 18 years) is 100 mg/m^2 taken orally, twice daily with a maximum of 100 mg per dose (maximum total dose of 200 mg) until the patient is no longer clinically benefiting from therapy or until unacceptable toxicity occurs.
Recommended Dose Modification for Adverse Reactions:

Dose Modification	Adult and Pediatric Patients with Body Surface Area of at Least 1.0 m^2	Pediatric Patients with Body Surface Area Less Than 1.0 m^2
1st Dose Modification	75 mg orally twice daily	75 mg/m^2 orally twice daily
2nd Dose Modification	50 mg orally twice daily	50 mg/m^2 orally twice daily
3rd Dose Modification	100 mg orally once daily	25 mg/m^2 orally twice daily[a]

[a] Pediatric patients on 25 mg/m^2 orally twice daily should remain on this dosage even if body surface area becomes greater than 1.0 m^2 during the treatment. Maximum dose should be 25 mg orally twice daily at the third dosage modification.

Contraindication:
Larotrectinib is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient or component of the container.

Warning and Precaution:
Driving and Operating Machinery: Neurologic adverse events and fatigue have very commonly been reported in patients receiving larotrectinib and may influence the patient's ability to drive and use machines. Caution patients and caretakers about driving and operating potentially hazardous machinery, until they are reasonably certain larotrectinib therapy does not affect them adversely.
Hepatic/Biliary/Pancreatic: Monitor for liver function including ALT, AST, ALP and bilirubin assessments. Consider baseline assessment of liver function, including transaminase levels, before the first dose, then every 2 weeks during the first month of treatment, then monthly for the first 6 months of treatment, then periodically during treatment. In patients who develop transaminase elevations, more frequent testing is needed.

Neurologic/Psychiatric: Withholding, reducing or permanently discontinuing larotrectinib dosing should be considered, depending on the severity and persistence of these symptoms- Grade 4 encephalopathy, brain edema, seizure and cerebrovascular accident and Grade 3 delirium (1%), dizziness (1%), mental status change (1%), gait disturbance (1%), paresthesia (1%), and syncope (1%).
Embryo-Fetal Toxicity: Can cause fetal harm. Females with reproductive potential should be advised about the potential risk to the fetus and to use effective contraception.

Adverse Reactions:
The most commonly reported (≥ 20%) adverse reactions with larotrectinib are fatigue, cough, increased ALT, constipation, diarrhea, dizziness, anemia, increased AST, vomiting nausea, and pyrexia.

Use In Special Population:
Pregnancy: There are no clinical data on the use of larotrectinib in pregnant women.
Lactation: There are no data on the presence of larotrectinib in human milk, the effects of larotrectinib on the breastfed child, or the effects of larotrectinib on milk production. Because of the unknown risk of larotrectinib in nursing infants, advise a nursing woman to discontinue breastfeeding during treatment with larotrectinib and for 1 week following the final dose.
Pediatric Use: Pediatric patients from 1 to 3 months of age, the drug exposure was 3-fold higher than in adults when using recommended doses. The clinical relevance is unknown.
Geriatric Use: Clinical studies of larotrectinib did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.
Renal impairment: No dose adjustment is required for patients with renal impairment of any severity.
Hepatic Impairment: Larotrectinib exposure was increased in patients with hepatic impairment up to 3.2-fold. Reduce the starting dose of larotrectinib by 50% in patients with moderate (Child-Pugh B) to severe (Child-Pugh C) hepatic impairment. No dose adjustment is recommended for patients with mild (Child-Pugh A) hepatic impairment.

Drug Interaction:
Strong CYP3A4 Inhibitors: Avoid co-administration of strong CYP3A4 inhibitors with larotrectinib, including grapefruit or grapefruit juice. If co-administration of a strong CYP3A4 inhibitor cannot be avoided, reduce the larotrectinib dose by 50%.
Strong or Moderate CYP3A4 Inducers: Avoid co-administration of strong CYP3A4 inducers with larotrectinib. If co-administration of a strong CYP3A4 inducer cannot be avoided, double the larotrectinib dose. Additionally, for co-administration with a moderate CYP3A4 inducer, double the larotrectinib dose. After the inducer has been discontinued for 3 to 5 elimination half-lives, resume the larotrectinib dose that was used prior to initiating the CYP3A4 inducer.

Overdose:
There is no known antidote for larotrectinib. The treatment of overdose with larotrectinib should consist of general supportive measures.

Storage:
Store in a cool & dry place below 30^0 C, protect from light. Keep out of the reach of children.

Packaging:
Vixo™ 100 Capsule: Each box contains 14 Capsules & one packet silica gel in a sealed HDPE container.

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

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