Livadox (Obeticholic Acid INN) Innerleaf design

Pantone Metallic Coated 8483 C **W- 195 mm X H - 255 mm**

Livadox™
Obeticholic Acid

Jenphar Bangladesh | جنفار بنغلاديش

Composition:
Livadox 5 : Each film coated tablet contains Obeticholic Acid INN 5 mg.
Livadox 10 : Each film coated tablet contains Obeticholic Acid INN 10 mg.

Pharmacology:
Obeticholic acid is a selective and potent agonist for the farnesoid X receptor (FXR), a nuclear receptor expressed at high levels in the liver and intestine. FXR is thought to be a key regulator of bile acid, inflammatory, fibrotic and metabolic pathways. FXR activation decreases the intracellular hepatocyte concentrations of bile acids by suppressing de novo synthesis from cholesterol, as well as, by increasing transport of bile acids out of the hepatocytes. These mechanisms limit the overall size of the circulating bile acid pool while promoting choleresis, thus reducing hepatic exposure to bile acids.

Indications:
Livadox is indicated for the treatment of primary biliary cholangitis (also known as primary biliary cirrhosis) in combination with Ursodeoxycholic acid in adults with an inadequate response to Ursodeoxycholic acid or as monotherapy in adults unable to tolerate Ursodeoxycholic acid.

Dose & administration:
Starting dose: 5 mg once daily in adult

Dosage Titration: If adequate reduction in ALP and/or total bilirubin has not been achieved after 3 months of treatment with Obeticholic acid 5 mg once daily and the patient is tolerating it, increase dosage to 10 mg once daily.

Maximum Dosage: 10 mg once daily

Management of Patients with Intolerable Pruritus:
- Add an antihistamine or bile acid binding resin.
- Reduce the dosage to 5 mg every other day, for patients intolerant to 5 mg once daily.
- 5 mg once daily, for patients intolerant to 10 mg once daily.
- Temporarily interrupt dosing for up to 2 weeks followed by restarting at a reduced dosage. Increase the dosage to 10 mg once daily, as tolerated, to achieve optimal response.

Dosage for Hepatic Impairment Patients:
The recommended starting dosage for moderate (Child-Pugh Class B) and severe (ChildPugh Class C) hepatic impairment is 5 mg once weekly. If an adequate reduction in ALP and/or total bilirubin has not been achieved after 3 months increase the dosage to 5 mg twice weekly (at least three days apart) and subsequently to 10 mg twice weekly (at least three days apart) depending on response and tolerability.

Route of Administration: The tablet should be taken orally with or without food.

Contra-indication:
Hypersensitivity to the active substance or to any of the excipients. It is also contraindicated in patients with complete biliary obstruction.

Warning and Precaution:
Elevations in Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST) have been observed in patients taking Obeticholic Acid. Clinical signs and symptoms of hepatic decompensation have also been observed. These events have occurred as early as within the first month of treatment. After initiation of therapy, all patients should be monitored for progression of PBC disease with laboratory and clinical assessment to determine whether dosage adjustment is needed. Dosing frequency should be reduced for patients with progress to advanced disease (i.e. from Child-Pugh Class A to Child-Pugh Class B or C).

Side effects:
Common: The most commonly reported adverse reactions were pruritus (63%) and fatigue (22%).The most common adverse reaction leading to discontinuation was pruritus. The majority of pruritus occurred within the first month of treatment and tended to resolve over time with continued dosing.

Uncommon: Abdominal pain and discomfort, rash, oropharyngeal pain, dizziness, constipation, arthralgia, thyroid function abnormality, and eczema.

Use in Pregnancy & Lactation:
Pregnancy:
There are no data on the use of Obeticholic acid in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity as a precautionary measure, it is preferable to avoid the use of Obeticholic acid during pregnancy.

Lactation:
It is unknown whether Obeticholic acid is excreted in human milk. Based on animal studies and intended pharmacology, Obeticholic acid is not expected to interfere with breast-feeding or the growth or development of a breast-fed child.

Use in children & adolescents:
The safety and effectiveness of Obeticholic Acid have not been established.

Drug interactions:
Warfarin:
International normalized ratio (INR) (Prothrombin time) is decreased following co-administration of warfarin and Obeticholic acid. INR should be monitored and the dose of warfarin adjusted, if needed, to maintain the target INR range when co-administering Obeticholic acid and warfarin.

Bile acid binding resins:
Bile acid binding resins such as Cholestyramine, Colestipol, or Colesevelam adsorb and reduce bile acid absorption and may reduce efficacy of Obeticholic acid. For patients taking bile acid binding resins, Obeticholic acid should be administered at least 4-6 hours before or 4-6 hours after taking the bile acid binding resin, or at an interval as great as possible.

CYP1A2 Substrates with Narrow Therapeutic index:
Obeticholic acid may increase the exposure to concomitant drugs that are CYP1A2 substrates. Therapeutic monitoring of CYP1A2 substrates with a narrow therapeutic index (e.g. Theophylline and Tizanidine) is recommended when co-administered with Obeticholic Acid.

Overdose:
In PBC patients who received Obeticholic Acid 25 mg once daily (2.5 times the highest recommended dosage) or 50 mg once daily (5 times the highest recommended dosage), a dose-dependent increase in the incidence of liver-related adverse reactions, including elevations in liver biochemical tests, ascites, jaundice, portal hypertension, and primary biliary cholangitis flare was reported. In the case of over dosage, patients should be carefully observed and supportive care administered, as appropriate.

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

Packing:
Livadox 5: Each box contains 3 x 10's tablets in Alu-Alu blister pack.
Livadox 10: Each box contains 3 x 10's tablets in Alu-Alu blister pack.

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

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