Livacol™

Obeticholic Acid

COMPOSITION
Livacol™ 5 Tablet: Each film coated tablet contains Obeticholic Acid INN 5 mg.
Livacol™ 10 Tablet: Each film coated tablet contains Obeticholic Acid INN 10 mg.

PHARMACOLOGY
Obeticholic acid is an agonist for Farnesoid X receptor (FXR), a nuclear receptor expressed in the liver and intestine. FXR is 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 increased 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.

INDICATION
Livacol™ is indicated for the treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in adults with an inadequate response to UDCA, or as monotherapy in adults unable to tolerate UDCA.

DOSAGE AND ADMINISTRATION
The starting dose and dosage titration for primary biliary cholangitis patient.

Staging/ Classification	Non-Cirrhotic or Compensated Child Pugh Class A	Child-Pugh Class B or C or Patients with a Prior Decompensation Event
Starting Dosage for first 3 months	5 mg once daily.	5 mg once weekly.
Dosage Titration after first 3 months, for patients who have not achieved an adequate reduction at least in ALP and/or bilirubin and who are tolerating Livacol	10 mg once daily.	5 mg twice weekly (at least 3 days apart). Titrate to 10 mg twice weekly (at least 3 days apart) based on response and tolerability.
Maximum Dosage	10 mg once daily.	10 mg twice weekly (at least 3 days apart)

Management and dose adjustment for severe pruritus
For Non-Cirrhotic or Child-Pugh Class A patients:
●Reducing the dosage of Obeticholic acid 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 interrupting Obeticholic acid dosing for up to 2 weeks followed by restarting at a reduced dosage.
●Continue to increase the dosage to 10 mg once daily, as tolerated, to achieve optimal response.
For Child-Pugh Class B or C or Decompensated Cirrhotic patients:
●Reducing the dosage of Obeticholic acid to:
►5 mg once weekly, for patients intolerant to 5 mg twice weekly
►10 mg once weekly, for patients intolerant to 10 mg twice weekly
●Temporarily interrupting Obeticholic acid dosing for up to 2 weeks followed by restarting at a reduced dosage if applicable.
●Continue to increase the dosage to 10 mg twice weekly, as tolerated, to achieve optimal response.
Consider discontinuing treatment with Obeticholic acid for patients who continue to experience persistent, intolerable pruritus.

CONTRAINDICATIONS
Contraindicated in patients known to have hypersensitivity to the drug or any of its components & in patients with complete biliary obstruction.

WARNING AND PRECAUTION
Special monitoring is essential for patients with the following clinical conditions:
●Liver-Related Adverse Reactions
●Severe Pruritus

SIDE EFFECTS
Most common adverse reactions (≥ 5%) are: pruritus, fatigue, abdominal pain and discomfort, rash, oropharyngeal pain, dizziness, constipation, arthralgia, thyroid function abnormality, and eczema.

USE IN PREGNANCY AND 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.
Breast-feeding
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. A decision should be made whether to discontinue breast-feeding or to discontinue/abstain from Obeticholic acid therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman

DRUG INTERACTION
Bile Acid Binding Resins: Bile acid binding resins such as cholestyramine, colestipol, or colesevelam adsorb and reduce bile acid absorption and may reduce the absorption, systemic exposure, and efficacy of Livacol. If taking a bile acid binding resin, take Livacol at least 4 hours before or 4 hours after taking the bile acid binding resin, or at as great an interval as possible.
Warfarin: The International Normalized Ratio (INR) decreased following coadministration of warfarin and Livacol. Monitor INR and adjust the dose of warfarin, as needed, to maintain the target INR range when coadministering Livacol and warfarin.
CYP1A2 Substrates with Narrow Therapeutic Index: Obeticholic acid, the active ingredient in Livacol, 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 coadministered with Livacol.
Inhibitors of Bile Salt Efflux Pump: Avoid concomitant use of inhibitors of the bile salt efflux pump (BSEP) such as cyclosporine. Concomitant medications that inhibit canalicular membrane bile acid transporters such as the BSEP may exacerbate accumulation of conjugated bile salts including taurine conjugate of Obeticholic acid in the liver and result in clinical symptoms. If concomitant use is deemed necessary, monitor serum transaminases and bilirubin.

STORAGE
Store below 30^0C in a dry place. Keep all medicines out of reach of children.

HOW SUPPLIED
Livacol™ 5 Tablet: Each box contains 20 Tablets in Alu-Alu Blister pack.
Livacol™ 10 Tablet: Each box contains 10 Tablets in Alu-Alu Blister pack.

Manufactured by
SQUARE
PHARMACEUTICALS PLC.
BANGLADESH