Item Code : 204xxx draft 01 Sep 2022

LOVASTIN TABLET

Lovastatin, the active ingredient of Lovastin Tablets, is a cholesterol-lowering agent. It is converted in vivo by esterases to the corresponding open hydroxyacid which is a potent inhibitor of endogenous cholesterol synthesis.

Ingredient(s):
Each tablet contains:
Lovastatin 20mg

Pharmacology (Summary of Pharmacodynamic and Pharmacokinetics):
1. Lovastatin is a cholesterol-lowering agent isolated from a strain of *A. terreus*. After oral ingestion, lovastatin which is an inactive lactone, is hydrolyzed to the corresponding β-hydroxyacid form. This principal metabolite is a specific inhibitor of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase. This enzyme catalyses the conversion of HMG-CoA to mevalonate which is an early and rate limiting step in the biosynthesis of cholesterol.
2. Lovastatin reduces cholesterol production by the liver and induces some changes in cholesterol transport and disposition in the blood and tissues. The mechanism of this effects is believed to involve both reduction of the synthesis of low density lipoprotein (LDL), and in increases in LDL catabolism as a result of induction of the hepatic LDL receptors. The mechanism of the LDL lowering effects of lovastatin may also involve reduction of the very low density lipoprotein cholesterol concentration.
3. Following an oral dose of ^{14}C-labeled lovastatin in man, 10% of the dose was excreted in the urine and 83% in the feces. The latter represents the absorbed as well as any unabsorbed drug that is excreted in the bile. As a consequence of extensive hepatic extraction of lovastatin, the availability of drug to the general circulation is low and variable.
4. Both lovastatin and β-hydroxyacid metabolite are highly bound (>95%) to human plasma proteins. The major active metabolites present in human are the β-hydroxyacid of lovastatin, its 6'-hydroxy derivative, and 2 unidentified metabolites. Peak plasma concentrations of both active and total inhibitors were attained within 2 to 4 hours of dose administration.
5. With a once-a-day dosing regimen, plasma concentrations of total inhibitors over a dosing interval achieved a steady state between the second and third days of therapy and were about 1.5 times those following a single dose.

Indication(s):
For the reduction of elevated total and LDL Cholesterol levels in patients with primary hypercholesterolemia) (Type IIa and IIb), when the response to diet and other nonpharmacological measures alone has been inadequate. Lovastin may be useful to reduce elevated LDL cholesterol levels in patients with combined hypercholesterolemia and hypertriglyceridemia.
Before instituting therapy with Lovastin, an attempt should be made to control hypercholesterolemia with appropriate diet, exercise, weight reduction in obese patients.

Dosage and Administration:
The patient should be placed on a Standard cholesterol-lowering diet before receiving lovastatin and should continue on this diet during treatment with the drug. The usual starting dose is 20mg per day given as a single dose with the evening meal. Adjustment of dosage, if required, should be made at intervals of not less than 4 weeks, to a maximum of 80mg daily given in single doses or divided doses with morning and evening meals.
Concomitant therapy: Preliminary evidence suggests that the cholesterol-lowering effects of lovastatin and the bile acid sequestrant, cholestyramine, are additive.
Dosage in patients with renal insufficiency: In patient with severe renal insufficiency (creatinine clearance <30mL/min) dosage increases above 20mg/day should be carefully considered and, if deemed necessary, implemented cautiously.
To be dispensed on physician's prescription.

Contraindication(s):
1. Hypersensitivity to any component of this medication.
2. Active disease or unexplained persistent elevations of serum transaminases.
3. Pregnancy and lactation.

Precaution(s) / Warning(s):
1. In controlled clinical trials, marked persistent increases (to more than 3 times the upper limit of normal) in serum transaminases occurred in 1.6% of adult patient who received lovastatin for at least 1 year. The increase usually appeared 3-12 months after the start of therapy. It is recommended that liver function tests be performed at baseline and every 4-6 weeks during the first 15 months of therapy with lovastatin and periodically there after in all patients. The drug should be used with caution in patients with past history of liver disease.
2. Rhabdomyolysis has occurred rarely and should be considered in any patient with diffuse myalgias, muscle tenderness and/or marked elevation of creatine phosphokinase (10 times the upper limit of normal).
3. Most of the patients who have developed myopathy were receiving concomitant therapy with immunosuppressive drugs included cyclosporine, gemfibrozil or lipid-lowering doses of niacin.
4. Patients should be advised to report promptly unexplained muscle pain, tenderness, weakness particularly if accompanied by malaise or fever.
5. Pediatric use: Safety and effectiveness in children have not been established. Treatment of children with lovastatin is not recommended.
6. Homozygous familial hypercholesterolemia: Lovastatin is less effective in patients with the rare homozygous familial hypercholesterolemia and appears to be more likely to raise serum transaminase in this group of patients.

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7. Eye: It is recommended that patients placed on lovastatin therapy be examined with a slit lamp before or shortly after initiation of treatment, and annually thereafter as new opacities was noted during clinical trial. However, this finding is inconclusive at the moment.

Drug Interaction(s):
Immunosuppressive drugs, gemfibrozil, niacin (nicotinic acid) erythromycin and itraconazole.
When lovastatin and coumarin anticoagulants are administered concomitantly, prothrombin time may be increased in some patients. In patients taking anticoagulants, prothrombin time should be determined prior to starting therapy with lovastatin and thereafter, monitored at the intervals usually recommended for patients on coumarin anticoagulants. Myopathy or rhabdomyolysis has occurred in transplant and non-transplant patients receiving lovastatin following the initiation of treatment with the antifungal agent itraconazole. This is probably related to metabolism of both drugs by the same P-450 isoform. Therapy with lovastatin should be temporarily interrupted if itraconazole therapy is required.

Side Effect(s) / Adverse Reaction(s):

Gastrointestinal:	Constipation, diarrhea, dyspepsia, flatus, abdominal pain/cramps, nausea, heartburn.
Musculoskeletal:	Muscle cramps, myalgia, myopathy, rhabdomyolysis.
CNS:	Dizziness, headache, fatigue, sleep disorders, insomnia.
Skin:	Rash, pruritus.
Special senses:	Blurred vision, dysgeusia.
Laboratory test:	Marked persistent increases of serum transaminases have been noted.

- There have been rare post-marketing reports of cognitive impairment (e.g., memory loss, forgetfulness, amnesia, memory impairment, confusion) associated with statin use. These cognitive issues have been reported for all statins. The reports are generally non-serious, and reversible upon statin discontinuation, with variable times to symptom onset (1 day to years) and symptoms resolution (median of 3 weeks).
- Increases in HbA1c and fasting serum glucose levels have been reported with statins.

Symptoms and Treatment for Overdosage and Antidote(s):
No specific symptoms and all patients recovered without sequelae in a few reported cases of accidental overdosage. The maximum dosage taken was fifty-two 20mg tablets (1.04g).
In the event of overdosage, treatment should be symptomatic and supportive, liver function should be monitored, and appropriate therapy should be instituted. Until further experience is obtained, no specific therapy of overdosage can be recommended.

Shelf-Life:
2 years from the date of manufacture.

Storage Condition(s):
Keep in a tight container. Store at temperature below 30°C. Protect from light and moisture.

Product Description & Packing(s):
A light blue octagonal tablet, one side impressed with the mark “YUNG SHIN”.
Plastic bottle of 1000’s.
Blister packing of 10’s x 10 and 10’s x 50.

(Not all presentations may be available locally)

Manufacturer and Product Registration Holder:
Y.S.P. INDUSTRIES (M) SDN. BHD. (199001001034)
Lot 3, 5 & 7, Jalan P/7, Section 13,
Kawasan Perindustrian Bandar Baru Bangi,
43000 Kajang, Selangor Darul Ehsan, Malaysia.

Product Registrant and Importer:
YUNG SHIN PHARMACEUTICAL (S) PTE. LTD.
10 Ubi Crescent, #06-57/58 Ubi Techpark,
Singapore 408564.

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