MODLIP-AM

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory Only

Abbreviated Prescribing information for MODLIP-AM

(Atorvastatin and S-Amlodipine Tablets)

[Please refer the complete prescribing information for details].

PHARMACOLOGICAL PROPERTIES:

Mechanism of Action: Atorvastatin: is a selective, competitive inhibitor of HMG-CoA reductase, the rate-limiting enzyme responsible for the conversion of 3-hydroxy-3-methyl-glutaryl-coenzyme A to mevalonate, a precursor of sterols, including cholesterol. Triglycerides and cholesterol in the liver are incorporated into very low-density lipoproteins (VLDL) and released into the plasma for delivery to peripheral tissues. Low-density lipoprotein (LDL) is formed from VLDL and is catabolised primarily through the receptor with high affinity to LDL (LDL receptor). Atorvastatin reduces LDL production and the number of LDL particles. Atorvastatin produces a profound and sustained increase in LDL receptor activity coupled with a beneficial change in the quality of circulating LDL particles. Atorvastatin is effective in reducing LDL-C in patients with homozygous familial hypercholesterolaemia, a population that has not usually responded to lipid-lowering medicinal products.
Amlodipine Besylate: Amlodipine is a calcium ion influx inhibitor of the dihydropyridine group (slow channel blocker or calcium ion antagonist) and inhibits the transmembrane influx of calcium ions into cardiac and vascular smooth muscle. The mechanism of the antihypertensive action of amlodipine is due to a direct relaxant effect on vascular smooth muscle. Amlodipine dilates peripheral arterioles and thus, reduces the total peripheral resistance (afterload) against which the heart works. Since the heart rate remains stable, this unloading of the heart reduces myocardial energy consumption and oxygen requirements.The mechanism of action of amlodipine also probably involves dilatation of the main coronary arteries and coronary arterioles, both in normal and ischaemic regions. This dilatation increases myocardial oxygen delivery in patients with coronary artery spasm (Prinzmetal's or variant angina).
INDICATION: For the treatment of co-existing essential hypertension and hyperlipidemia in adults.
DOSAGE AND ADMINISTRATION: Dosage of Modlip-AM must be individualized on the basis of both effectiveness and tolerance for each individual component in the treatment of hypertension and hyperlipidaemia.
CONTRAINDICATION: ***Atorvastatin:*** in patients With hypersensitivity to the active substance or to any of the excipients, With active liver disease or unexplained persistent elevations of serum transaminases exceeding 3 times the upper limit of normal, During pregnancy, while breast-feeding and in women of child-bearing potential not using appropriate contraceptive measures, treated with the hepatitis C antivirals glecaprevir/pibrentasvir.***Amlodipine:*** Hypersensitivity to dihydropyridine derivatives, amlodipine or to any of the excipients, Severe hypotension. Shock (including cardiogenic shock), Obstruction of the outflow tract of the left ventricle (e.g., high grade aortic stenosis), Haemodynamically unstable heart failure after acute myocardial infarction.

WARNINGS & PRECAUTIONS: Atorvastatin: *Liver effects***:** Liver function tests should be performed before the initiation of treatment and periodically thereafter. Increase in transaminases of greater than 3 times the upper limit of normal (ULN) persist, reduction of dose or withdrawal of Atorvastatin is recommended. *Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL)***:** In a post-hoc analysis of stroke subtypes in patients without coronary heart disease (CHD) who had a recent stroke or transient ischemic attack (TIA) there was a higher incidence of haemorrhagic stroke in patients initiated on atorvastatin 80 mg compared to placebo**.** *Skeletal muscle effects***:** Atorvastatin, like other HMG-CoA reductase inhibitors, may in rare occasions affect the skeletal muscle and cause myalgia, myositis, and myopathy that may progress to rhabdomyolysis, a potentially life-threatening condition characterised by markedly elevated creatine kinase (CK) levels (> 10 times ULN),

myoglobinaemia and myoglobinuria which may lead to renal failure. ***Amlodipine Besylate***: The safety and efficacy of amlodipine in hypertensive crisis has not been established.Patients with cardiac failure, Patients with heart failure should be treated with caution. In a long-term, placebo controlled study in patients with severe heart failure (NYHA class III and IV) the reported incidence of pulmonary oedema was higher in the amlodipine treated group than in the placebo group. Calcium channel blockers, including amlodipine, should be used with caution in patients with congestive heart failure, as they may increase the risk of future cardiovascular events and mortality.

DRUG INTERACTIONS: ***Atorvastatin***: Atorvastatin is metabolised by cytochrome P450 3A4 (CYP3A4) and is a substrate of the hepatic transporters, organic anion-transporting polypeptide 1B1 (OATP1B1) and 1B3 (OATP1B3) transporter. Metabolites of atorvastatin are substrates of OATP1B1. Atorvastatin is also identified as a substrate of the multi-drug resistance protein 1 (MDR1) and breast cancer resistance protein (BCRP), which may limit the intestinal absorption and biliary clearance of atorvastatin. Concomitant administration of medicinal products that are inhibitors of CYP3A4 or transport proteins may lead to increased plasma concentrations of atorvastatin and an increased risk of myopathy. The risk might also be increased at concomitant administration of atorvastatin with other medicinal products that have a potential to induce myopathy, such as fibric acid derivates and ezetimibe. ***Amlodipine Besylat:*** Concomitant use of amlodipine with strong or moderate CYP3A4 inhibitors (protease inhibitors, azole antifungals, macrolides like erythromycin or clarithromycin, verapamil or diltiazem) may give rise to significant increase in amlodipine exposure resulting in an increased risk of hypotension. The clinical translation of these PK variations may be more pronounced in the elderly. Clinical monitoring and dose adjustment may thus be required.

ADVERSE REACTIONS: Serious allergic reaction which causes swelling of the face, tongue and throat that can cause great difficulty in breathing. Peeling and swelling of the skin, blistering of the skin, mouth, eyes, genitals and fever. Skin rash with pink-red blotches especially on palms of hands or soles of feet which may blister. Muscle weakness, tenderness or pain, sudden wheeziness, chest pain, shortness of breath or difficulty in breathing, swelling of eyelids, Heart attack, abnormal heart beat Inflamed pancreas which may cause severe abdominal and back pain accompanied with feeling very unwell. Oedema (fluid retention), inflammation of the nasal passages, pain in the throat, nose bleed, allergic reactions, increase in blood creatine kinase, headache, nausea, constipation, wind, indigestion, diarrhoea, joint pain, muscle pain and back pain, Headache, dizziness, sleepiness, Palpitations, flushing abdominal pain, feeling sick, Altered bowel habits, Tiredness, weakness, Visual disturbances, double vision, Ankle swelling, Cold hands and feet, Feeling tired, anorexia having nightmares, insomnia, dizziness, numbness or tingling in the fingers and toes, reductions of sensation to pain or touch, change in sense of taste, loss of memory, ringing in the ears and/or head, hepatitis (liver inflammation), hair loss.

MARKETED BY:

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TORRENT PHARMACEUTICALS LTD.

IN/MODLIP-AM 10,2.5mg/Jan-22/02/ABPI

(Additional information is available on request)