TG TOR

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

Abbreviated Prescribing information for TG TOR

(Atorvastatin Film Coated Tablets I.P.)

[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 lowers plasma cholesterol and lipoprotein serum concentrations by inhibiting HMG-CoA reductase and subsequently cholesterol biosynthesis in the liver and increases the number of hepatic LDL receptors on the cell surface for enhanced uptake and catabolism of LDL.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.

INDICATIONS: 1) As an Adjunct to Diet to Reduce Elevated Total Cholesterol and Triglyceride Levels in Patients with Primary Hypercholesterolemia and Mixed Dyslipidemia (Type IIa and IIIb). 2) In adult patients with type II diabetes and without clinically evident coronary heart disease to reduce the risk of myocardial infarction and stroke.

DOSAGE AND ADMINISTRATION: The usual starting dose is 10 mg once a day. Adjustment of dose should be made at intervals of 4 weeks or more. The maximum dose is 80 mg once a day. Atorvastatin is for oral administration. Each daily dose of atorvastatin is given all at once and may be given at any time of day with or without food.

CONTRAINDICATION: Atorvastatin is contraindicated in patients: With hypersensitivity to the active substance or to any of the excipients, 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. And in people Treated with the hepatitis C antivirals glecaprevir/pibrentasvir.

WARNINGS & PRECAUTIONS: *Liver effects* Patients who develop any signs or symptoms suggestive of liver injury should have liver function tests performed. *Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL*) There was a higher incidence of haemorrhagic stroke in patients initiated on atorvastatin 80 mg compared to placebo. *Skeletal muscle effects* 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. Atorvastatin should be prescribed with caution in patients with pre-disposing factors for rhabdomyolysis.*Concomitant treatment with other medicinal* products Potent inhibitors of CYP3A4 or transport proteins (e.g. ciclosporin, telithromycin, clarithromycin, delavirdine, stiripentol, ketoconazole, voriconazole, itraconazole, posaconazole and HIV protease inhibitors including ritonavir, lopinavir, atazanavir, indinavir, darunavir, tipranavir/ritonavir, etc.). The risk of myopathy may also be increased with the concomitant use of gemfibrozil and other fibric acid derivates, antivirals for the treatment of hepatitis C (HCV) (boceprevir, telaprevir, and elbasvir/grazoprevir), erythromycin, niacin, or ezetimibe. I*nterstitial lung disease* Exceptional cases of interstitial lung disease have been reported with some

statins, especially with long term therapy. *Diabetes Mellitus*Some evidence suggests that statins as a class raise blood glucose and in some patients, at high risk of future diabetes, may produce a level of hyperglycaemia where formal diabetes care is appropriate. **DRUG INTERACTIONS:** *Effect of co-administered medicinal products on 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. *CYP3A4 inhibitors*
Co-administration of potent CYP3A4 inhibitors (e.g. ciclosporin, telithromycin, clarithromycin, delavirdine, stiripentol, ketoconazole, voriconazole, itraconazole, posaconazole, some antivirals used in the treatment of HCV (e.g., elbasvir/grazoprevir), and HIV protease inhibitors including ritonavir, lopinavir, atazanavir, indinavir, darunavir, etc.) should be avoided if possible. *CYP3A4 inducers* Concomitant administration of atorvastatin with inducers of cytochrome P450 3A (e.g. efavirenz, rifampin, St. John's Wort) can lead to variable reductions in plasma concentrations of atorvastatin. *Transport inhibitors* Inhibitors of transport proteins (e.g. ciclosporin) can increase the systemic exposure of atorvastatin. The effect of inhibition of hepatic uptake transporters on atorvastatin concentrations in hepatocytes is unknown. *Gemfibrozil / fibric acid derivatives* The use of fibrates alone is occasionally associated with muscle related events, including rhabdomyolysis. *Ezetimibe* The use of ezetimibe alone is associated with muscle related events, including rhabdomyolysis. *Colestipol* Reportedly, plasma concentrations of atorvastatin and its active metabolites were lower (ratio of atorvastatin concentration: 0.74) when colestipol was co-administered with Atorvastatin. *Fusidic acid* The risk of myopathy including rhabdomyolysis may be increased by the concomitant administration of systemic fusidic acid with statins.*Colchicine* cases of myopathy have been reported with atorvastatin co-administered with colchicine, *Effect of atorvastatin on co-administered medicinal products : Digoxin* When multiple doses of digoxin and 10 mg atorvastatin were co-administered, steady-state digoxin concentrations increased slightly. *Oral contraceptives* Co-administration of Atorvastatin with an oral contraceptive produced increases in plasma concentrations of norethindrone and ethinyl oestradiol. *Warfarin* Although only very rare cases of clinically significant anticoagulant interactions have been reported.
ADVERSE REACTIONS: *Common: may affect up to 1 in 10 people:* Inflammation of the nasal passages, pain in the throat, nose bleed, Allergic reactions, Increases in blood sugar levels, Headache, Nausea, constipation, wind, indigestion, diarrhea, Joint pain, muscle pain and back pain, Blood test results that show your liver function can become abnormal. *Uncommon: may affect up to 1 in 100 people* Anorexia (loss of appetite), weight gain, decreases in blood sugar levels (if you have diabetes you should continue careful monitoring of your blood sugar levels),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, blurred vision, ringing in the ears and/or head, Vomiting, belching, abdominal pain upper and lower, pancreatitis , Hepatitis, Rash, skin rash and itching, hives, hair loss, Neck pain, muscle fatigue, Fatigue, feeling unwell, weakness, chest pain, swelling especially in the ankles, Raised temperature, Urine tests that are positive for white blood cells, *Rare: may affect up to 1 in 1,000 people* Visual disturbance, Unexpected bleeding or bruising, Cholestasis Tendon injury, *Very rare: may affect up to 1 in 10,000 people*, an allergic reaction - symptoms may include sudden wheezing and chest pain or tightness, swelling of the eyelids, face, lips, mouth, tongue or throat, difficulty breathing, collapse, hearing loss, Gynecomastia.

MARKETED BY:

TORRENT PHARMACEUTICALS LTD.
IN/TG TOR 5, 10, 20, 40 and 80 mg/JULY- 22/02/PI