UNISTAR

For the use of a Registered Medical Practitioner or Hospital or a Laboratory only.

Abbreviated Prescribing information for UNISTAR (Aspirin Gastro-resistant and Rosuvastatin capsules I.P.) [Please refer the complete prescribing information for details]

PHARMACOLOGICAL PROPERTIES:

Mechanism of Action:

Rosuvastatin is a selective and competitive inhibitor of HMG-CoA reductase, the rate-limiting enzyme that converts 3-hydroxy-3-methylglutaryl coenzyme A to mevalonate, a precursor for cholesterol. The primary site of action of rosuvastatin is the liver, the target organ for cholesterol lowering. Rosuvastatin increases the number of hepatic LDL receptors on the cell-surface, enhancing uptake and catabolism of LDL and it inhibits the hepatic synthesis of VLDL, thereby reducing the total number of VLDL and LDL particles.

Acetylsalicylic acid

Acetylsalicylic acid inhibits the platelet activation: blocking the platelet cyclooxygenase by acetylation, it inhibits thromboxane A2 synthesis, a physiological activating substance released by the platelets and which would play a role in the complications of the atheromatosic lesions.

Inhibition of TXA2-synthesis is irreversible, because thrombocytes, which have no nucleus, are not capable (due to lack of protein synthesis capability) to synthesise new cyclooxygenase, which had been acetylated by acetylsalicylic acid.

INDICATIONS: For the treatment of dyslipdemia associated with arthersclerotic arterial disease with risk of myocardial infarction, stroke or peripheral vascular disease.

DOSAGE AND ADMINISTRATION: Dosage should be taken as directed by Physician**.**

CONTRAINDICATION: In patients with hypersensitivity to rosuvastatin, salicylic acid compounds or prostaglandin synthetase inhibitors (e.g. certain asthma patients who may suffer an attack or faint and certain patients who may suffer from bronchospasm, rhinitis and urticaria) or to any of the excipients. In patients with active liver disease including unexplained, persistent elevations of serum transaminases and any serum transaminase elevation exceeding 3 times the upper limit of normal (ULN). In patients with severe renal impairment (creatinine clearance <30 ml/min), In patients with myopathy, In patients receiving concomitant combination of sofosbuvir/velpatasvir/voxilaprevir, In patients receiving concomitant ciclosporin, During pregnancy and lactation and in women of childbearing potential not using appropriate contraceptive measures, Active or history of peptic ulceration and/or gastric/intestinal haemorrhage, or other kinds of bleeding such as cerebrovascular haemorrhages, Haemorrhagic diathesis; coagulation disorders such as haemophilia and thrombocytopenia or concurrent anticoagulant therapy, Patients who are suffering from gout, Severe hepatic impairment, Do not give to children aged under 16 years, unless specifically indicated (e.g. for Kawasaki's disease).

WARNINGS & PRECAUTIONS: **Rosuvastatin:** *Renal Effects* Proteinuria, detected by dipstick testing and mostly tubular in origin, has been observed in patients treated with higher doses of Rosuvastatin, in particular 40 mg, *Skeletal Muscle Effects*: Effects on skeletal muscle e.g. myalgia, myopathy and, rarely, rhabdomyolysis have been reported in Rosuvastatin -treated patients with all doses and in particular with doses > 20 mg, *Creatine Kinase Measurement,* CK) should not be measured following strenuous exercise or in the presence of a plausible alternative cause of CK increase which may confound interpretation of the result. Before Treatment Rosuvastatin, as with other HMG-CoA reductase inhibitors, should be prescribed with caution in patients with pre-disposing factors for myopathy/rhabdomyolysis. Such as Renal impairment, Hypothyroidism, Alcohol abuse, Age >70 years, Concomitant use of fibrates. Whilst on Treatment Patients should be asked to report inexplicable muscle pain, weakness or cramps immediately, particularly if associated with malaise or fever. CK levels should be measured in these patients.

Aspirin: Caution should be exercised in patients with allergic disease, impairment of hepatic or renal function (avoid if severe) and dehydration, since the use of NSAIDs may result in deterioration of renal function. Liver function tests should be performed regularly in patients presenting slight or moderate hepatic insufficiency.

Aspirin may also precipitate bronchospasm, induce attacks of asthma in susceptible subjects, or promote other hypersensitivity reactions. Risk factors are existing asthma, hay fever, nasal polyps or chronic respiratory diseases. The same applies for patients who also show allergic reaction to other substances (e.g. with skin reactions, itching or urticaria).
Serious skin reactions, including Steven-Johnsons syndrome, have rarely been reported in association with the use of acetylsalicylic acid. Aspirin should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.
The elderly may be more susceptible to the toxic effects of salicylates. Continuous prolonged use of aspirin should be avoided in the elderly because of the risk of gastrointestinal bleeding and perforation which may be fatal. Where prolonged therapy is required, patients should be reviewed regularly.
Caution should be taken in patients with glucose-6-phosphate dehydrogenase deficiency as haemolytic anaemia may occur.
Aspirin is not recommended during menorrhagia where it may increase menstrual bleeding.

Aspirin prolongs bleeding time, mainly by inhibiting platelet aggregation and therefore it should be discontinued several days before scheduled surgical procedures. Haematological and haemorrhagic effects can occur, and may be severe. Use with caution before surgery, including tooth extraction. Patients should report any unusual bleeding.

DRUG INTERACTION: **Rosuvastatin:** Transporter protein inhibitors: Rosuvastatin is a substrate for certain transporter proteins including the hepatic uptake transporter OATP1B1 and efflux transporter BCRP, *Ciclosporin:* During concomitant treatment with Rosuvastatin and ciclosporin, rosuvastatin AUC values were on average 7 times higher than those observed in healthy volunteers, ***Protease inhibitors****:* Although the exact mechanism of interaction is unknown, concomitant protease inhibitor use may strongly increase rosuvastatin exposure, ***Gemfibrozil and other lipid-lowering products***: Concomitant use of Rosuvastatin and gemfibrozil resulted in a 2-fold increase in rosuvastatin C_{max} and AUC, Ezetimibe**,** Erythromycin**,** **Aspirin*:*** Methotrexate The combined drugs, methotrexate and acetylsalicylic acid, enhance haematological toxicity of methotrexate due to the decreased renal clearance of methotrexate by acetylsalicylic acid, Anticoagulants e.g. coumarin, heparin, warfarin and phenindione: Increased risk of bleeding due to inhibited thrombocyte function, injury of the duodenal mucosa and displacement of oral anticoagulants from their plasma protein binding sites. The bleeding time should be monitored. *Anti-platelet agents (e.g. clopidogrel and dipyridamole) and selective serotonin re-uptake inhibitors. Antidiabetics, e.g. sulphonylureas:* Salicylic may increase the hypoglycaemic effect of sulphonylureas. Digoxin and lithium, Diuretics and antihypertensive

ADVERSE REACTIONS: Thrombocytopenia Granulocytosis, aplastic anaemia, Hypersensitivity reactions including angioedema, Skin rashes, urticarial, asthma, bronchospasm, angio-oedema, allergic oedema, anaphylactic reactions including shock, Increased bleeding tendencies, Asthenia, Myalgia, Constipation, Nausea, Abdominal pain, Dyspepsia, Rhinitis, dyspnoea, Pancreatitis, Severe gastrointestinal haemorrhage, nausea, vomiting, gastritis, Pruritus Rash Urticaria.

MARKETED BY:

TORRENT PHARMACEUTICALS LTD.

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(Additional information is available on request)