**ROZUCOR CV 20**

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

Abbreviated Prescribing information for Rozucor CV 20 (Rosuvastatin And Clopidogrel Capsules (10 mg/ 20 mg) [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.

**Clopidogrel** is a prodrug, one of whose metabolites is an inhibitor of platelet aggregation. Clopidogrel must be metabolised by CYP450 enzymes to produce the active metabolite that inhibits platelet aggregation. The active metabolite of clopidogrel selectively inhibits the binding of adenosine diphosphate (ADP) to its platelet P2Y12 receptor and the subsequent ADP-mediated activation of the glycoprotein GPIIb/IIIa complex, thereby inhibiting platelet aggregation. Due to the irreversible binding, platelets exposed are affected for the remainder of their lifespan (approximately 7-10 days) and recovery of normal platelet function occurs at a rate consistent with platelet turnover. Platelet aggregation induced by agonists other than ADP is also inhibited by blocking the amplification of platelet activation by released ADP.

**INDICATIONS:** For the treatment of acute coronary syndrome, myocardial infarction, stroke and angina.

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

**CONTRAINDICATION:** *Known hypersensitivity to Rosuvastatin or Clopidogrel 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 ciclosporin, During pregnancy and lactation and in women of childbearing potential not using appropriate contraceptive measures. *Contraindicated in patients with pre-disposing factors for myopathy/rhabdomyolysis. Such factors include*: Moderate renal impairment (creatinine clearance < 60 ml/min), Hypothyroidism, Personal or family history of hereditary muscular disorders, Previous history of muscular toxicity with another HMG-CoA reductase inhibitor or fibrate, Alcohol abuse, Situations where an increase in plasma levels may occur, Asian patients, Concomitant use of fibrates, Active pathological bleeding such as peptic ulcer or intracranial haemorrhage.

**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. **Clopidogrel:** Due to the risk of bleeding and haematological adverse reactions, blood cell count determination and/or other appropriate testing should be promptly considered. *Thrombotic Thrombocytopenic Purpura (TTP):* has been reported very rarely following the use of clopidogrel, sometimes after a short exposure. It is characterised by thrombocytopenia and microangiopathic haemolytic anaemia

associated with either neurological findings, renal dysfunction or fever. *Acquired haemophilia:* has been reported following use of clopidogrel. In cases of confirmed isolated activated Partial Thromboplastin Time (aPTT) prolongation with or without bleeding, acquired haemophilia should be considered. *Recent ischaemic stroke:* clopidogrel cannot be recommended during the first 7 days after acute ischaemic stroke. *Cytochrome P450 2C19 (CYP2C19):* clopidogrel at recommended doses forms less of the active metabolite of clopidogrel and has a smaller effect on platelet function. *CYP2C8 substrates:* Caution is required in patients treated concomitantly with clopidogrel and CYP2C8 substrate medicinal products. Cross-reactions among thienopyridines: Patients should be evaluated for history of hypersensitivity to thienopyridines (such as clopidogrel, ticlopidine, prasugrel) since cross-reactivity among thienopyridines has been reported. *Renal impairment:* Therapeutic experience with clopidogrel is limited in patients with renal impairment. Therefore clopidogrel should be used with caution in these patients. *Hepatic impairment:* Experience is limited in patients with moderate hepatic disease who may have bleeding diatheses. Clopidogrel should therefore be used with caution in this population.

**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:** Concomitant use of 10 mg Rosuvastatin and 10 mg ezetimibe resulted in a 1.2-fold increase in AUC of rosuvastatin in hypercholesterolaemic subjects, ***Antacid***: The simultaneous dosing of Rosuvastatin with an antacid suspension containing aluminium and magnesium hydroxide resulted in a decrease in rosuvastatin plasma concentration of approximately 50%, ***Erythromycin*****:** Concomitant use of Rosuvastatin and erythromycin resulted in a 20% decrease in AUC and a 30% decrease in $C_{max}$ of rosuvastatin, *Cytochrome P450 enzymes*. ***Clopidogrel*****:** *Medicinal products associated with bleeding risk*: There is an increased risk of bleeding due to the potential additive effect, *Oral anticoagulants:* the concomitant administration of clopidogrel with oral anticoagulants is not recommended since it may increase the intensity of bleedings, *Glycoprotein IIb/IIIa inhibitors:* clopidogrel should be used with caution in patients who receive concomitant glycoprotein IIb/IIIa inhibitors, *Heparin*: in a reported clinical study conducted in healthy subjects, clopidogrel did not necessitate modification of the heparin dose or alter the effect of heparin on coagulation, *Thrombolytics*: the safety of the concomitant administration of clopidogrel, fibrin or non-fibrin specific thrombolytic agents and heparins was assessed in patients with acute myocardial infarction, *NSAIDs*: in a reported clinical study conducted in healthy volunteers, the concomitant administration of clopidogrel and naproxen increased occult gastrointestinal blood loss,

**ADVERSE REACTIONS:** *Blood and the lymphatic system disorders*: Thrombocytopenia, *Immune system disorders:* Hypersensitivity reactions including angioedema, *Endocrine disorders:* Diabetes mellitus, *Psychiatric disorders:* Depression, *Nervous system disorders:* Headache, Dizziness, Polyneuropathy, Memory loss, *Respiratory, thoracic and mediastinal disorders:* Cough Dyspnoea, *Gastro-intestinal disorders:* Constipation, Nausea, Abdominal pain, Pancreatitis, *Hepatobiliary disorders:* Jaundice, Hepatitis, Increased hepatic transaminases, *Skin and subcutaneous tissue disorders:* Pruritus, Rash, Urticaria, *Musculo-skeletal and connective tissue:* Myalgia, Myopathy (including myositis), Rhabdomyolysis, *Renal and urinary disorders:* Haematuria, *Reproductive system and breast disorders:* Gynaecomastia, *General disorders and administration site conditions:* Asthenia, Oedema.

**MARKETED BY:**

TORRENT PHARMACEUTICALS LTD.

**IN/ROZUCOR CV 20/SEP-2023/01/ABPI**

(Additional information is available on request)