DEPLATT

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

abbreviated prescribing information for DEPLATT (Clopidogrel Tablets I.P.) [Please refer the complete prescribing information available at www.torrentpharma.com]

PHARMACOLOGICAL PROPERTIES: 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. Because the active metabolite is formed by CYP450 enzymes, some of which are polymorphic or subject to inhibition by other medicinal products, not all patients will have adequate platelet inhibition.

INDICATION: For treament of atherosclerosis events (myocardial infarction, stroke & vascular death).

DOSAGE AND ADMINISTRATION: *Dosage:* Clopidogrel should be given as a single daily dose of 75 mg. 300 mg tablet of clopidogrel is intended for use as a loading dose. In patients suffering from acute coronary syndrome: *Administration:* To be taken orally. It may be given with or without food.

CONTRAINDICATION: Hypersensitivity to the active substance or to any of the excipients listed.Severe hepatic impairment, and Active pathological bleeding such as peptic ulcer or intracranial haemorrhage.

WARNINGS & PRECAUTIONS:*Bleeding and haematological disorders:* Due to the risk of bleeding and haematological adverse reactions, blood cell count determination and/or other appropriate testing should be promptly considered whenever clinical symptoms suggestive of bleeding arise during the course of treatment. The concomitant administration of clopidogrel with oral anticoagulants is not recommended. *Thrombotic Thrombocytopenic Purpura (TTP):* it has been reported very rarely following the use of clopidogrel, sometimes after a short exposure. *Acquired haemophilia:* 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:* In view of the lack of data, clopidogrel cannot be recommended during the first 7 days after acute ischaemic stroke. *Cytochrome P450 2C19 (CYP2C19):*Pharmacogenetics: In patients who are poor CYP2C19 metabolisers, clopidogrel at recommended doses forms less of the active metabolite of clopidogrel and has a smaller effect on platelet function. Tests are available to identify a patient's CYP2C19 genotype. Since clopidogrel is metabolised to its active metabolite partly by CYP2C19, use of medicinal products that inhibit the activity of this enzyme would be expected to result in reduced drug levels of the active metabolite of clopidogrel. *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 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 and *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 INTERACTIONS: *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. *Acetylsalicylic acid (ASA):* ASA did not modify the clopidogrel-mediated inhibition of ADPinduced platelet aggregation, but clopidogrel potentiated the effect of ASA on collageninduced platelet aggregation. *Heparin*: Co-administration of heparin had no effect on the inhibition of platelet aggregation induced by clopidogrel. *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*: concomitant administration of clopidogrel and naproxen increases occult gastrointestinal blood loss. *SSRIs*: since SSRIs affect platelet activation and increase the risk of bleeding, the concomitant administration of SSRIs with clopidogrel should be undertaken with caution. *Other concomitant therapy*: Since clopidogrel is metabolised to its active metabolite partly by CYP2C19, use of medicinal products that inhibit the activity of this enzyme would be expected to result in reduced drug levels of the active metabolite of clopidogrel. *Proton Pump Inhibitors (PPI)*: Omeprazole 80 mg once daily administered either at the same time as clopidogrel or with 12 hours between the administrations of the two drugs decreased the exposure of the active metabolite by 45% (loading dose) and 40% (maintenance dose).

ADVERSE REACTIONS: *Common:* Haematoma Epistaxis,Gastrointestinal haemorrhage, diarrhoea, abdominal pain, dyspepsia, Bruising, Bleeding at puncture site Uncommon Thrombocytopenia, leucopenia, eosinophilia, Intracranial, bleeding (some cases were reported with fatal outcome), headache, paraesthesia,, dizziness, Eye bleeding, (conjunctival, ocular, retinal), Gastric ulcer and duodenal ulcer, gastritis, vomiting, nausea, constipation, flatulence, Rash, pruritus, skin bleeding (purpura), Haematuria, Bleeding time prolonged, neutrophil count decreased, platelet count decreased *Rare* Neutropenia, including severe neutropenia. Vertigo, Retroperitoneal haemorrhage, Gynaecomastia *Very rare, not known** Thrombotic thrombocytopenic purpura (TTP), aplastic anaemia, pancytopenia, agranulocytosis, severe thrombocytopenia, acquired Kounis syndrome (vasospastic allergic angina / allergic myocardial infarction) in the context of a hypersensitivity reaction due to clopidogrel, Serum sickness, anaphylactoin, reactions, cross-reactive drug, hypersensitivity among, thienopyridines (such as ticlopidine, prasugrel), insulin autoimmune syndrome, which can lead to severe hypoglycemia, particularly in patients with HLA DRA4 subtype (more frequent in the Japanese population), Hallucinations, confusion Taste disturbances, ageusia, Serious haemorrhage, haemorrhage of operative wound, vasculitis, hypotension Respiratory tract, Bleeding (haemoptysis, pulmonary haemorrhage), bronchospasm, interstitial, pneumonitis, eosinophilic pneumonia, Gastrointestinal and retroperitoneal, haemorrhage with fatal outcome, pancreatitis, colitis (including ulcerative or lymphocytic colitis), stomatitis Acute liver failure, hepatitis, abnormal liver function test Bullous dermatitis (toxic epidermal necrolysis, Stevens Johnson Syndrome, erythema multiforme, acute generalised exanthematous pustulosis (AGEP)), angioedema, druginduced hypersensitivity syndrome, drug rash with eosinophilia and systemic symptoms (DRESS), rash erythematous or exfoliative, urticaria, eczema, lichen planus, Musculo-skeletal bleeding (haemarthrosis), arthritis, arthralgia, myalgia, Glomerulonephritis, blood creatinine increase and Fever.

MARKETED BY:

TORRENT PHARMACEUTICALS LTD.

IN/DEPLATT 75mg, 150mg/JUN 2022/09/ABPI

(Additional information is available on request)