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NØCLOT-EA®

(CLOPIDOGREL / ENTERIC COATED ASPIRIN)

75/75 tablet

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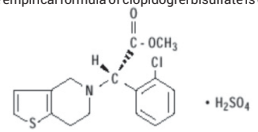
COMPOSITION:
Each film coated tablet contains:
Clopidogrel Bisulfate USP equivalent to
Clopidogrel ..... 75 mg.
Aspirin USP ..... 75 mg.

Products Specs.: CCL Pharmaceuticals

DESCRIPTION:
NOCLOT-EA is the combination of Clopidogrel and enteric coated aspirin.
Clopidogrel: Clopidogrel bisulfate is a thienopyridine class inhibitor of P2Y12 ADP platelet receptors. Chemically it is methyl (+)-(S)-α-(2-chlorophenyl)-6,7-dihydrothieno[3,2-c] pyridine-5(4H)¬acetate sulfate (1:1).The empirical formula of clopidogrel bisulfate is $C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ and its molecular weight is 419.9.
The structural formula is as follow:



CLINICAL PHARMACOLOGY:
Mechanism of Action:
Clopidogrel: Clopidogrel is an inhibitor of platelet aggregation. Clopidogrel selectively inhibits the binding of adenosine diphosphate (ADP) to its platelet receptor and the subsequent ADP-mediated activation of the glycoprotein GPIIb/IIIa complex, thereby inhibiting platelet aggregation. Clopidogrel also inhibits platelet aggregation induced by agonists other than ADP by blocking the amplification of platelet activation by released ADP.
Asprin: Aspirin is also an antiplatelet agent. Aspirin acts by causing irreversible inhibition of the cyclooxygenase enzyme, which leads to decreased formation of thromboxane A2. Since platelets do not synthesize new enzyme, the action of aspirin on platelet cyclooxygenase is permanent, lasting for the life of the platelets (7-10 days). Enteric Coated Aspirin is indicated when prolonged dosage of Aspirin is required. The special Enteric Coating resists dissolution in Gastric juice, but will dissolve readily in the relatively less acidic environment of duodenum, avoiding gastric irritation.
Pharmacokinetics:
Absorption:
Clopidogrel is rapidly absorbed after oral administration of repeated doses of 75 mg Clopidogrel, with peak plasma levels (3 mg/l) occurring approximately 1 hour after dosing.
Asprin: After absorption salicylic acid achieves peak plasma levels within 1-2 hours.
Distribution:
Clopidogrel: and the main circulating metabolite bind reversibly, in vitro, to human plasma proteins (98% and 94% respectively).
Asprin: Salicylate has a concentration dependent protein binding. Approximately 90 percent of plasma salicylate is protein bound at concentrations lower than 100mcg/ml while at concentrations higher than 400 mcg/ml the protein binding is about 75 percent.
Metabolism: Clopidogrel is extensively metabolized by the liver. Aspirin, after absorption, is hydrolyzed and converted to salicylic acid, whose rate of elimination is constant in relation to plasma concentration.
Elimination:
Clopidogrel: Excretion is through urine and feces. The elimination half-life is 8 hours after single and repeated administration. Meals do not significantly modify the bioavailability of Clopidogrel.
Asprin: Renal excretion of free salicylate is dependent upon urine pH. As urinary pH rises above 6.5, the renal clearance increases from <5 percent to >80 percent.

INDICATIONS AND USAGE:
NOCLOT-EA is indicated for the prevention of ischemic events, myocardial infarction, stroke and cardiovascular death in patients with
Acute Coronary Syndrome (ACS).

DOSAGE AND ADMINISTRATION:
The recommended dose is one tablet once daily, or as directed by Physician.

CONTRAINDICATIONS:
- Hypersensitivity to Clopidogrel.
- Hypersensitivity to Enteric Coated Aspirin and/or non-steroidal anti-inflammatory agents.
- Recent history of gastrointestinal bleeding.
- Active pathological bleeding such as peptic ulcer or intracranial haemorrhage, or bleeding disorders like haemophilia.

WARNINGS AND PRECAUTIONS:
General: Clopidogrel should be used with caution in patients who may be at risk of increased bleeding from trauma, surgery, or other pathological conditions. If a patient is to undergo elective surgery and an antiplatelet effect is not desired, NOCLOT-EA should be discontinued 7 days prior to surgery.
Thrombotic thrombocytopenic purpura (TTP): TTP has been reported rarely following use of Clopidogrel, sometimes after a short exposure (<2weeks). TTP is a serious condition requiring prompt treatment. It is characterized by thrombocytopenia, microangiopathic haemolytic anemia, neurological findings, renal dysfunction and fever. TTP has been reported at a rate of about four cases per million patients exposed, or about 11 cases per million patients.
GI Bleeding: NOCLOT-EA prolongs the bleeding time. NOCLOT-EA should be used with caution in patients who have lesions with a propensity to bleed (such as ulcers). Drugs that might induce such lesions (such as non steroidal anti-inflammatory drugs) should be used with caution in patients taking NOCLOT-EA.Reye's syndrome: Reye's syndrome may develop in individuals who have chicken pox, influenza or flu symptoms. NOCLOT-EA is not recommended for use in patients with chicken pox, Influenza or flu symptoms.
Nasal polyps or nasal allergies: NOCLOT-EA should be administered with caution to patients with nasal polyps or nasal allergies. In patients receiving large doses of Aspirin and/or prolonged therapy, mild salicylate intoxication (salicylism) may develop that may be reversed by reduction in dosage.
Hepatic or Renal Impairment: NOCLOT-EA should be avoided in patients with impaired hepatic and renal function.
Recommended Laboratory Tests.

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DRUG INTERACTIONS:
NOCLOT-EA should be used with caution when anticoagulants are prescribed concurrently, since both Aspirin and Clopidogrel may depress the concentration of prothrombin in plasma and thereby increase bleeding time.
Hypoglycemic agents: Large doses of salicylates have hypoglycemic action and may enhance the effect of the oral hypoglycemics. Consequently, they should not be given concomitantly; if however this is necessary, the dosage of the hypoglycemic agent must be reduced while the salicylate is given.
Non-steroidal Anti-Inflammatory Drugs (NSAIDs): Concomitant administration of Clopidogrel with Naproxen was associated with increased occult gastrointestinal blood loss. NSAIDs and Clopidogrel should be coadministered with caution.
NOCLOT-EA is contra-indicated in patients who are hypersensitive to NSAIDs.
Spironolactone:
Sodium excretion produced by spironolactone may be decreased in the presence of salicylates. Salicylates can produce changes in thyroid function tests, Salicylates should be used with caution in patients with severe hepatic damage, preexisting hypoprothrombinemia or Vitamin K deficiency and in those undergoing surgery.
Alcohol: Alcohol has a synergistic effect with Aspirin in causing gastrointestinal bleeding.
Corticosteroids: Concomitant administration of Aspirin with corticosteroids may increase the risk of gastrointestinal ulceration and may reduce serum salicylate levels.
Pyrazolone derivatives: (phenylbutazone, Oxyphenbutazone and possibly dipyrone), Concomitant administration may increase the risk of gastrointestinal ulceration.
Urinary alkalinizers; Decreases Aspirin effectiveness by increasing the risk of salicylate renal excretion. Phenobarbital; Decreases Aspirin effectiveness by enzyme induction. Phenytoin, tamoxifen, tolbutamide, torsemide, fluvastatin; At high concentrations in vitro, Clopidogrel inhibits P450 (2C9). Accordingly, Clopidogrel may interfere with the metabolism of phenytoin, tamoxifen, tolbutamide, torsemide and fluvastatin, but there are no data with which to predict the magnitude of these interactions. Caution should be observed when any of these drugs is co-administered with Clopidogrel. Aspirin may also increase serum levels of phenytoin. Propranolol; May decrease Aspirin's anti-inflammatory action by competing for the same receptors.

USE IN SPECIFIC POPULATIONS:
Pregnancy:
There are no adequate and well controlled studies in pregnant women. So, NOCLOT-EA should be used during pregnancy only if clearly needed.
Lactation:
NOCLOT-EA should be avoided in nursing mothers because of the possible risk of developing Reye's syndrome. Regular use of high doses of Aspirin could impair platelet function and produce hypo-prothrombinemia in infants if neonatal vitamin K levels are low.
Hepatic or Renal Impairment: NOCLOT-EA should be avoided in patients with impaired hepatic and renal function.
Pediatric Use: Safety and effectiveness of NOCLOT-EA in the pediatric population have not been established.

ADVERSE REACTIONS:
The drug is generally well tolerated. Side effects that have been reported include abdominal pain, dyspepsia, gastritis, diarrhea, nausea, vomiting, constipation, gastrointestinal hemorrhage, ulceration, neutropenia, rash, palpitation, syncope, drowsiness, asthenia, neuralgia, paresthesia and vertigo.

OVERDOSAGE:
Over dosage produce dizziness, tinnitus, sweating, nausea, vomiting, confusion and hyperventilation. In case of over dosage, symptomatic treatment is advised. Platelet transfusion may be appropriate to reverse the pharmacological effects of NOCLOT-EA if quick reversal is required.

INSTRUCTIONS:
- Store below 30°C.
- Protect from heat, sunlight & moisture.
- Keep out of the reach of children.
- To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:
NOCLOT-EA 75/75 Tablet : Pack of 1 x 10 tablets.

ہدایات:
۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گرمی، دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف ڈاکٹر کے نسخہ پر فروخت کریں۔

FOR FURTHER INFORMATION PLEASE CONTACT:

CCL
Manufactured by:
CCL Pharmaceuticals (Pvt.) Ltd.
62 Industrial Estate, Kot Lakhpat, Lahore, Pakistan.

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