

# Plagrin®

Clopidogrel Bisulfate USP

**Composition :**

Each Plagrin® tablet contains 75mg Clopidogrel as Clopidogrel Bisulfate.

**Category :**

Anti-thrombotic platelet aggregation inhibitor.

**Indications :**

Myocardial infarction (prophylaxis) or stroke, thromboembolic (prophylaxis) or vascular death (prophylaxis). Clopidogrel is indicated for reducing the risk of arteriosclerosis documented by recent myocardial infarction, recent stroke or established peripheral arterial disease.

**Mechanism of Action:**

Clopidogrel is an inhibitor of platelet aggregation; doses of 75mg per day inhibit platelet aggregation by 40 to 60% at steady state, which occurs within 3 to 7 days. Clopidogrel inhibits adenosine diphosphate (ADP) binding to its platelet receptor and subsequent ADP-mediated activation of the glycoprotein GPIIb/IIIa complex, thus inhibiting platelet aggregation. Because Clopidogrel irreversibly modifies the ADP receptor, platelets are affected for the remainder of their lifespan. An active metabolite, not yet isolated, is responsible for the medication's activity. Platelet aggregation induced by agonists other than ADP is also inhibited by blocking the amplification of platelet activation by released ADP. Clopidogrel does not inhibit phosphodiesterase activity.

**Absorption :**

Rapid, at least 50% Bioavailability has not been found to be affected by food.

**Protein Binding :**

Very high for Clopidogrel and its main circulating metabolite (98% and 94% respectively). Binding is nonsaturable in vitro up to a concentration of 100 micrograms per ml.

**Elimination :**

Carboxylic acid derivative : 8 hours (after single and multiple doses).

**Time to peak concentration :**

Approximately 1 hour for the carboxylic acid derivative.

**Peak plasma concentration :**

Approximately 3mg per liter (Carboxylic acid derivative) after repeated doses of 75mg. Pharmacokinetics of the main circulating metabolite are linear (increased in proportion to dose) in a dose range of 50 to 150mg.

**Time to peak effect :**

Steady State inhibition of platelet aggregation with repeated doses of 75mg per day usually occurs between day 3 and 7 day.

**Duration of Action :**

Platelet aggregation and bleeding time gradually return to base-line levels within about 5 days after treatment is withdrawn.

**Elimination :**

Renal, approximately 50%, five days after dosing with radio labeled clopidogrel.

**Geriatrics :**

Plasma concentrations of the main circulating metabolite have been found to be significantly higher in elderly individuals (75 year of age) than in young healthy volunteers, but these higher concentrations have not been found to be associated with differences in platelet aggregation and bleeding time. No dosage adjustment is recommended for elderly patients.

**Drug Interaction :**

Aspirin did not modify the Clopidogrel mediated inhibition of ADP induced

platelet aggregation. Concomitant administration of 500mg of aspirin twice a day for 1 day did not significantly increase the prolongation of bleeding time induced by Clopidogrel. Clopidogrel potentiated the effect of aspirin on collagen induced platelet aggregation. Co-administration of heparin had no effect on inhibition of platelet aggregation induced by Clopidogrel. In healthy volunteers receiving naproxen, concomitant administration of Clopidogrel was associated with increased gastrointestinal blood loss. Clopidogrel may interfere with the metabolism of phenytoin, tamoxifen, tolbutamide, torsemide, fluvastatin & many non-steroidal anti-inflammatory agents but there are no data with which to predict the magnitude of these interactions. At high concentrations in the blood, Clopidogrel inhibits the activity of the enzyme, which metabolizes warfarin, a blood thinner. This could lead to an increase in levels of warfarin and increase the risk of bleeding due to over thinning of the blood. Blood tests to measure the degree to which the blood is anticoagulated or thinned may be ordered to assess the degree of blood thinning when warfarin & Clopidogrel are used together. Risk-Benefit should be considered when the following medical.

**Problems exist:**

Any condition in which there is a significant risk of bleeding, such as: Gastrointestinal ulceration, Surgery, Trauma, Hepatic function impairment.

**Side/adverse effects :**

Signs of potential side effects, especially chest pain, generalized pain, purpura, upper respiratory infection, atrial fibrillation or palpitations, bronchitis, edema, epistaxis, gastrointestinal hemorrhage, gout, hypertension, syncope, urinary tract infection, intracranial hemorrhage, neutropenia, agranulocytosis, gastrointestinal ulcers, severe skin reactions, thrombocytopenia.

**Clinical effects of overdose :**

No adverse effects have been reported after ingestion of up to fourteen 75mg tablets, bleeding time after six 75mg tablets was prolonged by about the same amount as with the usual therapeutic dose of one 75mg tablet.

**Treatment of overdose :**

If quick reversal of pharmacological effects is required, platelet transfusions may be useful.

**Contra-Indication :**

The use of Clopidogrel is contraindicated in the following conditions :

- Hypersensitivity to the drug substance or any component of the product.
- Active pathological bleeding such as peptic ulcer or intracranial hemorrhage.

**General dosing information :**

It is recommended that clopidogrel should be discontinued 7 days prior to elective surgery because of the risk of increased blood loss.

**Usual adult dose :**

75mg once a day be taken with or without food.

**Pregnancy Category: B****Nursing Mother:**

Decision of discontinuing drug or nursing should be made taking into account the importance of the drug to the mother.

**Storage condition:**

Store in a cool and dry place, away from light and children.

**Packing :**

Each box contains 3x10's flim coated tablets in blister pack.  
Each box contains 2x10's flim coated tablets in blister pack.

 <sup>®</sup>Trade Mark  
Manufactured by  
**Renata Limited**  
Dhaka, Bangladesh  
Updated : June' 2014

C Code : 5462/V03

Size : H-180mm W- 80mm