CLOPIDOGREL 75 mg PD

SCHEDULING STATUS S3

1. NAME OF THE MEDICINE
CLOPIDOGREL 75 mg PD film coated tablets.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each film coated tablet contains clopidogrel hydrogen sulphate equivalent to clopidogrel 75 mg.

Each tablet contains sugar (lactose – 108,125 mg).
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Film coated tablets.
Pink, round, biconvex, film coated tablets.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
CLOPIDOGREL 75 mg PD is indicated for the following:

- reduction of atherosclerotic events (myocardial infarction, stroke, death due to vascular causes) in patients with a history of symptomatic atherosclerotic disease defined by ischaemic stroke (from 7 days until less than 6 months), myocardial infarction (from a few days until less than 35 days) or established peripheral arterial disease
- for patients with non-ST-segment elevation acute coronary syndrome (unstable angina/non-Q-wave myocardial infarction (MI) including patients who are to be managed medically and those who are to be managed with percutaneous coronary intervention (with or without stent) or CABG (coronary artery bypass graft). CLOPIDOGREL 75 mg PD in combination with acetylsalicylic acid (aspirin (ASA) has been shown to decrease the rate of a combined endpoint of cardiovascular death, myocardial infarction (MI), stroke or refractory ischaemia
- for patients with ST-segment elevation acute myocardial infarction. CLOPIDOGREL 75 mg PD in combination with ASA has been shown to reduce the rate of death from any cause and the rate of a combined endpoint of death, re-infarction or stroke.

4.2 Posology and method of administration
Posology
Adults:
Recent myocardial infarction (MI), recent stroke, or established peripheral arterial disease:
CLOPIDOGREL 75 mg PD should be given as a single daily dose of 75 mg.

Acute coronary syndrome:
For patients with non-ST-segment elevation acute coronary syndrome (unstable angina/non-Q-wave MI), CLOPIDOGREL 75 mg PD should be initiated with a single 300 mg loading dose and then continued at 75 mg once daily. Aspirin (75 mg - 325 mg once daily) should be initiated and continued in combination with CLOPIDOGREL 75 mg PD.

For patients with ST-segment elevation acute myocardial infarction, the recommended dose of CLOPIDOGREL 75 mg PD is one tablet, once daily, administered in combination with aspirin, with or without thrombolytics. CLOPIDOGREL 75 mg PD may be initiated with or without a loading dose.

Special populations
Elderly:
No dosage adjustment is necessary for elderly patients.

Renal disease:
No dosage adjustment is necessary for patients with renal disease.

Pharmacogenetics:
CYP2C19 poor metaboliser status is associated with diminished antiplatelet response to clopidogrel. An appropriate dose regimen for this patient population has not been established in clinical outcome trials.

Paediatric population
CLOPIDOGREL 75 mg PD should not be used in children below the age of 18 years because of efficacy concerns.

Method of administration
For oral use.
CLOPIDOGREL 75 mg PD can be taken with or without food.

Missed dose:
Medical practitioners should advise patients who forget to take CLOPIDOGREL 75 mg PD to take a dose as soon as possible and then continue with the normal dose. Patients should not take a double dose to compensate for the missed dose.

4.3 Contraindications
CLOPIDOGREL 75 mg PD is contraindicated in:

- hypersensitivity to clopidogrel or to any of the ingredients of CLOPIDOGREL 75 mg PD (see section 6.1)
- active bleeding such as peptic ulcer and intracranial haemorrhage
- safety and efficacy in patients below the age of 18 have not been established
- pregnancy and lactation
- severe liver impairment
- thrombocytopenia
- platelet dysfunction
- haemophilia, congenital or acquired, or history of acquired haemophilia related to clopidogrel.

4.4 Special warnings and precautions for use

THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP) HAS BEEN REPORTED TO OCCUR WITH CLOPIDOGREL 75 mg PD DURING POST-MARKETING EXPERIENCE. MOST CASES WERE REPORTED IN THE FIRST TWO WEEKS OF TREATMENT. PRESCRIBERS SHOULD WARN PATIENTS ABOUT THE SIGNS AND SYMPTOMS OF THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP).

Thrombotic thrombocytopenic purpura (TTP):
The clinical diagnosis of TTP is characterised by the presence of thrombocytopenia, haemolytic anaemia, neurological symptoms, renal dysfunction and fever.
Due to the risk of fatal outcome, in the event of suspected thrombotic thrombocytopenic purpura, CLOPIDOGREL 75 mg PD should be stopped. The management of a patient with thrombotic thrombocytopenic purpura is complex. Early treatment with plasmapheresis is indicated in TTP.

Recent ischemic stroke:
In patients with recent transient ischaemic attack (TIA) or stroke, who are at high risk of recurrent ischaemic events, the combination of aspirin and CLOPIDOGREL 75 mg PD has not been shown to be more effective than CLOPIDOGREL 75 mg PD alone, but the combination has been shown to increase major bleeding. It is therefore recommended that such addition should be undertaken with caution outside of clinical situations where the combination has proven to be beneficial.

In view of the lack of data, CLOPIDOGREL 75 mg PD cannot be recommended in acute ischaemic stroke (less than 7 days).

Bleeding and haematological disorders:
Due to the risk of bleeding and haematological undesirable effects, blood cell count determination and/or other appropriate testing should be promptly considered whenever such suspected clinical symptoms arise during the course of treatment (see section 4.8).

CLOPIDOGREL 75 mg PD should be used with caution in patients who may be at risk of increased bleeding including active bleeding such as peptic ulcer and inter-cranial haemorrhage and from trauma, dental and surgical procedures or other pathological conditions and in patients receiving treatment with acetylsalicylic acid (aspirin), nonsteroidal anti-inflammatory drugs (NSAIDs) (including COX-2 inhibitors), and anticoagulants such as heparin or glycoprotein IIb/IIIa inhibitors, selective serotonin reuptake inhibitors (SSRIs) or thrombolytics or CYP2C19 strong inducers (see section 4.5).
Due to the increased risk of haemorrhage, triple antiplatelet therapy (clopidogrel + ASA + dipyridamole) for stroke secondary prevention is not recommended in patients with acute non-cardioembolic ischemic stroke or transient ischaemic attack (TIA) (see sections 4.3 and 4.8).

Clopidogrel produces irreversible inhibition of platelet aggregation for the life of the platelet, which is 7 - 10 days.
If a patient is to undergo elective surgery and an antiplatelet effect is not desired, CLOPIDOGREL 75 mg PD should be discontinued 7 days prior to surgery.
Spinal and epidural anaesthesia should not be administered to a patient taking clopidogrel or for 7 days thereafter. No lumber puncture should be done during these 7 days due to risk of haematoma formation following lumber puncture or spinal and epidural anaesthesia.

Patients should be monitored carefully for any signs of bleeding, including occult bleeding, especially but not limited to during the first week of treatment and/or after invasive cardiac procedures or surgery. The concomitant administration of CLOPIDOGREL 75 mg PD with warfarin is not recommended since it may increase the intensity of bleedings.
CLOPIDOGREL 75 mg PD prolongs bleeding time and should be used with caution in patients who have lesions with a propensity to bleed such as gastrointestinal ulcers and intra-ocular bleeding. Medicines that might induce lesions (such as acetylsalicylic acid and NSAIDs) should be used with caution in patients taking CLOPIDOGREL 75 mg PD.

Patients should be told that it may take longer than usual to stop bleeding when they take CLOPIDOGREL 75 mg PD, and that they should report any unusual bleeding to their medical practitioner. Patients should inform medical practitioners and dentists that they are taking CLOPIDOGREL 75 mg PD before any surgery is scheduled and before any new medicine is taken. In view of the possible increased risk of bleeding, the concomitant administration of CLOPIDOGREL 75 mg PD with acetylsalicylic acid, heparin, warfarin or thrombolytics should be undertaken with caution (see section 4.5).

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. Patients with a confirmed diagnosis of acquired haemophilia should be managed and treated by specialists, and CLOPIDOGREL 75 mg PD should be discontinued (see section 4.3).

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; these tests can be used as an aid in determining therapeutic strategy (see section 4.2 - Pharmacogenetics).

Poor metabolisers with acute coronary syndrome or undergoing percutaneous coronary intervention treated with clopidogrel at recommended doses may exhibit higher cardiovascular event rates than patients with normal CYP2C19 function (see section 5.2).

Use of medicines that induce the activity of CYP2C19 would be expected to result in increased medicine levels of the active metabolite of clopidogrel and might potentiate the bleeding risk. As a precaution, concomitant use of strong CYP2C19 inducers should be discouraged (see section 4.5).

CYP2C8 substrates
Caution is required in patients treated concomitantly with clopidogrel and CYP2C8 substrate medicines (see section 4.5).

Acute myocardial infarction
In patients with acute myocardial infarction, CLOPIDOGREL 75 mg PD therapy should not be initiated within the first few days following myocardial infarction. In view of the lack of data, CLOPIDOGREL 75 mg PD cannot be recommended in coronary artery bypass graft (CABG) and acute ischaemic stroke (less than 7 days). Clinical experience is limited in patients with renal impairment and moderate hepatic disease with bleeding diatheses. CLOPIDOGREL 75 mg PD should be used with caution in these patients.

Cross-reactivity among thienopyridines:
Thrombocytopenia, neutropenia, ipsilatic anaemia and pancytopenia have been reported in patients taking CLOPIDOGREL 75 mg PD (see section 4.8).

Patients should be evaluated for history of hypersensitivity to another thienopyridine (such as ticlopidine, prasugrel) since cross-reactivity among thienopyridines has been reported (see section 4.8). Thienopyridines may cause mild to severe allergic reactions such as rash, angioedema or haematological reactions such as thrombocytopenia and neutropenia. Patients who had developed a previous allergic reaction and/or haematological reaction to one thienopyridine may have an increased risk of developing the same or another reaction to another thienopyridine. Monitoring for cross-reactivity is advised.

Insulin autoimmune syndrome (IAS)
Insulin autoimmune syndrome (IAS) is characterized by hyperinsulinemic hypoglycaemia with elevated anti-insulin antibodies. The suffrydryl group of clopidogrel metabolite could induce insulin autoimmune syndrome (IAS) as a rare side effect. Insulin, most commonly observed in the Japanese population, have a genetic predisposition for IAS carrying HLA-DRB1*04:06, HLA-DQA1*03:01 and HLA-DQB1*03:02 haplotypes, and are more likely to develop IAS. Clopidogrel induced IAS may also cause hypoglycaemia in Caucasian populations, with the HLADRB1*04:03 haplotypes.

Hepatic impairment:
Experience is limited in patients with moderate hepatic disease who may have bleeding diatheses. CLOPIDOGREL 75 mg PD should therefore be used with caution in this population.

Renal impairment:
Therapeutic experience with clopidogrel is limited in patients with severe renal impairment. Therefore, CLOPIDOGREL 75 mg PD should be used with caution in these patients.

Information on excipients of CLOPIDOGREL 75 mg PD:
CLOPIDOGREL 75 mg PD contains lactose. Patients with rare hereditary problems of fructose intolerance, galactose intolerance, galactosaemia or glucose-galactose malabsorption should not take CLOPIDOGREL 75 mg PD.

CLOPIDOGREL 75 mg PD contains hydrogenated castor oil which may cause stomach upset or diarrhoea.

4.5 Interaction with other medicines and other forms of interaction
Medicines associated with bleeding risk:
There is an increased risk of bleeding due to the potential additive effect. The concomitant administration of medicines associated with bleeding risk should be undertaken with caution.

Acetylsalicylic acid (aspirin):
Acetylsalicylic acid (ASA) did not modify the clopidogrel-mediated inhibition of adenosine diphosphate (ADP)-induced platelet aggregation. Concomitant administration of 500 mg of acetylsalicylic acid twice a day for one day did not significantly increase the prolongation of bleeding time induced by clopidogrel intake.
CLOPIDOGREL 75 mg PD potentiates the effects of acetylsalicylic acid on collagen-induced platelet aggregation. A pharmacodynamic interaction between clopidogrel and acetylsalicylic acid (aspirin) is possible, leading to increased risk of bleeding.
Therefore, concomitant use should be undertaken with caution.
However, clopidogrel and ASA (75 - 325 mg once daily) have been administered together for up to one year.

Heparin:
In healthy subjects, clopidogrel did not necessitate modification of the heparin dose or alter the effect of heparin on coagulation. Co-administration of heparin had no effect on the inhibition of platelet aggregation induced by clopidogrel.
A pharmacodynamic interaction between clopidogrel and heparin is possible, leading to increased risk of bleeding, concomitant use should be undertaken with caution.

Thrombolytics:
The safety of the concomitant administration of clopidogrel, as in CLOPIDOGREL 75 mg PD, fibrin or non-fibrin specific thrombolytic medicines and heparins was assessed in patients with acute myocardial infarction. The incidence of clinically significant bleeding was similar to that observed when thrombolytic medicines and heparins are co-administered with acetylsalicylic acid. However, the concomitant use of CLOPIDOGREL 75 mg PD with thrombolytic medicines should be undertaken with caution.

Warfarin:
The concomitant administration of clopidogrel with oral anticoagulants, including warfarin, is not recommended since it may increase the intensity of bleedings (see section 4.4).
The safety of the co-administration of CLOPIDOGREL 75 mg PD with warfarin has not been established.
Consequently, concomitant administration of these two medicines should be undertaken with caution.

Nonsteroidal anti-inflammatory medicines (NSAIDs) including aspirin:
There is a potential risk of gastrointestinal bleeding, and NSAIDs, including aspirin, and CLOPIDOGREL 75 mg PD should be co-administered with caution (see section 4.4). In healthy volunteers, the concomitant administration of clopidogrel and naproxen increased occult gastrointestinal blood loss.
However, due to the lack of interaction studies with other NSAIDs, it is presently unclear whether there is an increased risk of gastrointestinal bleeding with all NSAIDs.
NSAIDs, including COX-2 inhibitors, and CLOPIDOGREL 75 mg PD should be co-administered with caution.

Glycoprotein IIb/IIIa inhibitors:
CLOPIDOGREL 75 mg PD should be used with caution in patients who may be at risk of increased bleeding from trauma, surgery or other conditions/disorders that may require concomitant glycoprotein IIb/IIIa inhibitors intake.

Selective serotonin reuptake inhibitors (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:
No clinically significant pharmacodynamic interactions were observed when CLOPIDOGREL 75 mg PD was co-administered with atenolol, nifedipine, or both atenolol and nifedipine. The pharmacodynamic activity of CLOPIDOGREL 75 mg PD was not significantly influenced by the co-administration of phenobarbital, cimetidine, or oestrogen.

CLOPIDOGREL 75 mg PD inhibits the activity of cytochrome P450 enzyme: CYP2C9. This leads to increased plasma levels of medicines such as phenytoin, tolbutamide, warfarin, tamoxifen, fluvastatin and many NSAIDs which are metabolised by CYP2C9.

Inducers of CYP2C19:
Since clopidogrel is metabolised to its active metabolite partly by CYP2C19, use of medicines that induce the activity of this enzyme would be expected to result in increased medicine levels of the active metabolite of clopidogrel.
Rifampicin strongly induces CYP2C19, resulting in both an increased level of clopidogrel active metabolite and platelet inhibition, which might potentiate the risk of bleeding. As a precaution, concomitant use of strong CYP2C19 inducers should be discouraged (see section 4.4).

Inhibitors of CYP2C19:
Since clopidogrel is metabolised to its active metabolite partly by CYP2C19, use of medicine that inhibit the activity of this enzyme would be expected to result in reduced medicine levels of the active metabolite of clopidogrel and a reduction in clinical efficacy. Concomitant use of strong or moderate CYP2C19 inhibitors (e.g. omeprazole, esomeprazole, fluvoxamine, fluoxetine, moclobemide, voriconazole, fluconazole, carbamazepine, and efavirenz) should be discouraged (see sections 4.2 and 4.4 – Pharmacogenetics). If a proton pump inhibitor is to be used concomitantly with CLOPIDOGREL 75 mg PD, consider using one with less CYP2C19 inhibitory activity.

The pharmacokinetics of digoxin or theophylline were not modified by the co-administration of clopidogrel, as in CLOPIDOGREL 75 mg PD. Antacids did not modify the extent of clopidogrel absorption.

CYP2C8 substrate medicines:
Due to the risk of increased plasma concentrations, concomitant administration of CLOPIDOGREL 75 mg PD and medicines primarily cleared by CYP2C8 metabolism (e.g. repaglinide, paclitaxel) should be undertaken with caution.

Results of additional clinical studies in which patients received a variety of concomitant medications including diuretics, beta-blocking medicines, angiotensin converting enzyme inhibitors, calcium antagonists, cholesterol lowering medicines, coronary vasodilators, antidiabetic medicines, anti-epileptic medicines and hormone replacement therapy, showed no evidence of clinically significant adverse interactions.

Opioid agonists:
Co-administration of opioid agonists has the potential to delay and reduce the absorption of an oral $P2Y_{12}$ antagonist such as clopidogrel, presumably because of slowed gastric emptying. The clinical relevance is unknown. Consider the use of a parenteral antiplatelet medicine in acute coronary syndrome patients requiring co-administration of morphine or other opioid agonists.

Rosuvastatin:
Clopidogrel has been shown to increase rosuvastatin exposure in patients by 2-fold (AUC) and 1.3-fold (C_{max}) after administration of a 300 mg clopidogrel dose and by 1.4-fold (AUC) without effect on C_{max} after repeated administration of a CLOPIDOGREL 75 mg PD dose.

Boosted antiretroviral therapy (ART):
Human immunodeficiency virus (HIV) patients treated with boosted antiretroviral therapies (ART) are at high-risk of vascular events.
A significantly reduced platelet inhibition has been shown in HIV patients treated with ritonavir-or cobicistat-boosted ART. Although the clinical relevance of these findings is uncertain, there have been spontaneous reports of HIV-infected patients treated with ritonavir boosted ART, who have experienced re-occlusive events after de-obstruction or have suffered thrombotic events under a clopidogrel loading treatment schedule. Average platelet inhibition can be decreased with concomitant use of clopidogrel and ritonavir. Therefore, concomitant use of clopidogrel with ART boosted therapies should be discouraged.

4.6 Fertility, pregnancy and lactation
Pregnancy
The use of CLOPIDOGREL 75 mg PD during pregnancy is not recommended as safety and efficacy have not been established (see section 4.3).

Breastfeeding
The use of CLOPIDOGREL 75 mg PD during lactation is not recommended as safety and efficacy have not been established (see section 4.3).
Studies in rats have shown that clopidogrel and/or its metabolites are excreted in the milk. It is not known whether clopidogrel is excreted in human breast milk.

Fertility
Clopidogrel was not shown to alter fertility in animal studies.

4.7 Effects on ability to drive and use machines
No impairment of driving or psychomotric performance was observed following CLOPIDOGREL 75 mg PD administration.
CLOPIDOGREL 75 mg PD has no, or negligible, effect on the ability to drive and use machines.

4.8 Undesirable effects
a. Summary of the safety profile
Bleeding is the most common reaction reported both in clinical studies where frequencies varied from common to very common, as well as in post-marketing experience.

b. Tabulated list of adverse reactions

System Organ Class	Frequency	Side effects
Blood and lymphatic system disorders	*Frequent*	Purpura, haematoma
	Less frequent	Severe neutropenia (including agranulocytosis), severe thrombocytopenia (including thrombotic thrombocytopenic purpura), increased bleeding time, eosinophilia, leucopenia
	Frequency unknown	Bruising, haematoma*, ocular bleeding* (mainly conjunctival, but also ocular and retinal), respiratory tract bleeding* and aplastic anaemia (pancytopenia), musculoskeletal bleeding (including haemarthrosis), haemorrhagic ulcer, haemothorax, haemorrhage of operative wound* and retroperitoneal haemorrhage* with fatal outcome, serum sickness, gastrointestinal haemorrhage*, intracranial haemorrhage*
Immune system disorders	*Frequency unknown*	Hypersensitivity reactions such as bronchospasm, angioedema or anaphylactoid reactions, insulin autoimmune syndrome, which can lead to severe hypoglycaemia, particularly in patients with human leukocyte antigen (HLA) DRB4 subtype (more frequent in the Japanese population), serum sickness, cross-reactive drug hypersensitivity among thienopyridines (such as ticlopidine, prasugrel) (see section 4.4)
Psychiatric disorders	*Less frequent*	Mental depression
	Frequency unknown	Confusion, hallucinations
Nervous system disorders	*Frequent*	Headache, dizziness
	Less frequent	Paraesthesia, intracranial bleeding, syncope, anxiety, hypoaesthesia, insomnia, intracranial bleeding (fatal outcome in some cases)
	Frequency unknown	Taste disorders, ageusia*
Eye disorders	*Less frequent*	Eye bleeding (conjunctival, ocular, retinal)
Ear and labyrinth disorders	*Frequency unknown*	Vertigo*
Cardiac disorders	*Frequent*	Chest pain
	Less frequent	Atrial fibrillation or palpitations
	Frequency unknown	Kounis syndrome* (vasospastic allergic angina)
Vascular disorders	*Less frequent*	Hypertension
	Frequency unknown	Hypotension, vasculitis, serious haemorrhage, haemorrhage of operative wound*
Respiratory, thoracic and mediastinal disorders	*Frequent*	Upper respiratory tract infections, epistaxis
	Less frequent	Bronchitis, dyspnoea, cough, rhinitis
	Frequency unknown	Interstitial pneumonitis*, bronchospasm*, eosinophilic pneumonia*, respiratory tract bleeding (haemoptysis, pulmonary haemorrhage)
Gastrointestinal disorders	*Frequent*	Abdominal pain, dyspepsia, diarrhoea
	Less frequent	Gastrointestinal haemorrhage, nausea, constipation, vomiting, peptic, gastric or duodenal ulcer, flatulence, gastritis
	Frequency unknown	Colitis* (including ulcerative or lymphocytic colitis), pancreatitis*, stomatitis*
Hepatobiliary disorders	*Frequency unknown*	Abnormal liver function tests*, hepatitis*, acute liver failure*
Skin and subcutaneous tissue disorders	*Frequent*	Bruising
	Less frequent	Rash, pruritus, purpura
	Frequency unknown	Severe skin reactions (including bullous eruption*, erythema multiforme*, Stevens-Johnson syndrome*, toxic epidermal necrolysis*, lichen planus*, urticaria*, eczema*, maculopapular, erythematous or exfoliative rash*, urticaria*, angioedema*, bullous dermatitis*, acute generalised exanthematous pustulosis (AGEP*), drug-induced hypersensitivity syndrome*, drug rash with eosinophilia*, systemic symptoms (DRESS)*
Musculoskeletal, connective tissue and bone disorders	*Frequent*	Back pain
	Less frequent	Gout, leg cramps
	Frequency unknown	Myalgia*, arthritis*, arthralgia*
Renal and urinary disorders	*Less frequent*	Urinary tract infection, haematuria
	Frequency unknown	Glomerulopathy*, increased creatinine levels*
Reproductive system and breast disorders	*Frequency unknown*	Gynaecomastia*
General disorders and administrative site conditions	*Frequent*	Bleeding at injection site
	Frequency unknown	Fever*
Investigations	*Less frequent*	Bleeding time prolonged, neutrophil count decreased, platelet count decreased

*Post marketing.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Mediafinity X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za, to ensure safety of the product.

4.9 Overdose
Signs and symptoms:
Overdose following CLOPIDOGREL 75 mg PD administration may lead to prolonged bleeding time and subsequent bleeding complications.

Management of overdose:
No antidote to the pharmacological activity of clopidogrel has been found. If prompt correction of prolonged bleeding time is required, platelet transfusion may reverse the effects of clopidogrel. Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Platelet aggregation inhibitors excl. heparin.
ATC code: B01AC24.
Pharmacological classification: A 8.2 Anticoagulants.

Mechanism of action
Clopidogrel is a specific and potent inhibitor of platelet aggregation. It acts by irreversibly modifying the platelet ADP receptors. It inhibits the binding of adenosine diphosphate (ADP) to its platelet receptor, and subsequent ADP-mediated activation of the glycoprotein GPIIb/IIIa complex, thereby inhibiting platelet aggregation. Consequently, platelets exposed to clopidogrel are affected for the remainder of their lifespan and recovery of normal platelet function occurs at a rate consistent with platelet turnover (of about 7 days).
Dose-dependent inhibition of platelet aggregation was noted 2 hours after single oral doses of clopidogrel.
Clopidogrel also inhibits platelet aggregation induced by other agonists by blocking the amplification of platelet activation by released ADP.
Biotransformation of clopidogrel is necessary to produce inhibition of platelet aggregation. Because the active metabolite is formed by CYP450 enzymes, some of which are polymorphic or subject to inhibition by other medicines, not all patients will have adequate platelet inhibition. Repeated doses of 75 mg per day may produce inhibition of ADP-induced platelet aggregation from the first day; the may increase progressively and reach steady state between day 3 and day 7. At steady state, the average inhibition level observed with a dose of 75 mg per day may be between 40 % and 60 %. Platelet aggregation and bleeding time gradually returns to baseline values, generally within 7 days after treatment has been discontinued.

5.2 Pharmacokinetic properties
Absorption:
After single and repeated oral doses, clopidogrel is rapidly absorbed. Absorption is at least 50 %. Mean peak plasma levels of unchanged clopidogrel (approximately 2.2 - 2.5 mg/ml after a single 75 mg oral dose) occurred approximately 45 minutes after dosing. Absorption is at least 50 %, based on urinary excretion of clopidogrel metabolites.

Distribution:
Clopidogrel and the main metabolite bind, *in vitro*, reversibly to human plasma proteins (98 % and 94 % respectively).
The binding is non-saturable *in vitro* over a wide concentration range.

Biotransformation:
Clopidogrel is extensively metabolised by the liver and is metabolised according to two main metabolic pathways: the main metabolite, which is inactive, is the carboxylic acid derivative which represents about 85 % of the circulating compound in the plasma and one mediated by multiple cytochromes P450. Clopidogrel is first metabolised to a 2-oxo-clopidogrel intermediate metabolite. Subsequent metabolism of the 2-oxo-clopidogrel intermediate metabolite results in formation of the active metabolite, a thiol derivative of clopidogrel. *In vitro*, this metabolic pathway is mediated by CYP3A4, CYP2C19, CYP2B6, CYP1A2 and CYP2B6. The active thiol metabolite which has isolated *in vitro*, binds rapidly and irreversibly to platelet receptors, thus inhibiting platelet aggregation.

Elimination:
After a single oral dose of 75 mg, clopidogrel has a half-life of approximately 6 hours. The elimination half-life of the main circulating metabolite is up to 8 hours after administration.
Clopidogrel and the main metabolite are excreted in urine (50 %) and faeces (46 %) in the 120-hour interval after dosing.

Pharmacogenetics:
CYP2C19 is involved in the formation of both the active metabolite and the 2-oxo-clopidogrel intermediate metabolite. Clopidogrel active metabolite pharmacokinetics and antiplatelet effects, as measured by *ex vivo* aggregation assays, differ according to CYP2C19 genotype.

The CYP2C19*1 allele corresponds to fully functional metabolism while the CYP2C19*2 and CYP2C19*3 alleles are non-functional. The CYP2C19*2 and CYP2C19*3 alleles account for the majority of reduced function alleles in white (85 %) and Asian (99 %) poor metabolisers. Other alleles associated with absent or reduced metabolism are less frequent, and include, but are not limited to, CYP2C19*4, *5, *6, *7, and *8. A patient with poor metaboliser status will possess two loss-of-function alleles as defined above. Published frequencies for poor CYP2C19 metaboliser genotypes are approximately 2 % for white, 4 % for blacks and 14 % for Chinese.
Tests are available to determine a patient's CYP2C19 genotype.

No substantial differences in active metabolite exposure and mean inhibition of platelet aggregation (IPA) were observed between ultra-rapid, extensive and intermediate metabolisers. In poor metabolisers, active metabolite exposure was decreased by 63 - 71 % compared to extensive metabolisers. At steady state, platelet aggregation inhibition (5 µM ADP) was decreased in poor metabolisers with mean IPA of 37 % compared to 58 % in the extensive metabolisers and 60 % in the intermediate metabolisers. An appropriate dose regimen for this patient population has not been established in clinical outcome trials.
In a meta-analysis including 6 studies of 335 clopidogrel-treated subjects at steady state, it was shown that active metabolite exposure was decreased by 28 % for intermediate metabolisers, and 72 % for poor metabolisers while platelet aggregation inhibition (5 µM ADP) was decreased with differences in IPA of 5.9 % and 21.4 %, respectively, when compared to extensive metabolisers.

There is some evidence that patients who are either intermediate or poor metabolisers may have a higher rate of cardiovascular events (death, myocardial infarction, stroke or stent thrombosis) compared to extensive metabolisers.

Pharmacokinetics in special patient groups
The pharmacokinetics of the active metabolite of clopidogrel is not known in these special populations.

Elderly
In elderly (> 75 years) volunteers compared to young healthy volunteers, there were no differences in platelet aggregation and bleeding time. No dosage adjustment is needed for the elderly.

Renal impairment
After repeated administration of 75 mg clopidogrel/day in subjects with severe renal impairment (creatinine clearance from 5 - 15 mL/min) ADP-induced platelet aggregation was lower (25 %) than that observed in healthy subjects, however, the prolongation of bleeding was similar to that seen in healthy subjects receiving 75 mg clopidogrel per day.

Ethnicity
The prevalence of CYP2C19 alleles that result in intermediate and poor CYP2C19 metabolism differs according to ethnicity (see section 5.2, Pharmacogenetics). From literature, limited data in Asian populations are available to assess the clinical implication of genotyping of this CYP on clinical outcome events.

5.3 Preclinical safety data
Not applicable.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Lactose
Castor oil (hydrogenated)
Hypromellose
Iron oxide red
Macrogol
Microcrystalline cellulose
Pregelatinised starch
Propylene glycol
Talc
Titanium dioxide.

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
3 years.

6.4 Special precautions for storage
Store at or below 30 °C.

6.5 Nature and contents of container
CLOPIDOGREL 75 mg PD tablets are packed in OPA/AL/PVC film and heat sealing aluminium blister strips. The blister strips are packed in an outer carton in packs of 28 or 30.
Not all pack sizes are marketed.

6.6 Special precautions for disposal
No special requirements.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION
Pharma Dynamics (Pty) Ltd.
1st Floor Grayevine House, Steenberg Office Park
Silverwood Close
Westlake, 7945
Cape Town, South Africa
Tel.: +27 21 707 7000
or 0860-PHARMA (742 762).

8. REGISTRATION NUMBER
A42/8.2/0128

9. DATE OF FIRST AUTHORISATION
Date of registration: 04 December 2009

10. DATE OF REVISION OF THE TEXT
24 October 2025

NAM(NS) 10/7.1/0377
JIM 2021/10.5/6132 Category for distribution: P/P10.
ZAM(PDM) ZAMRA-HM-23-13

Manufactured by:
Krka, d.d., Novo Mesto
Šmarješka cesta 6
8501, Novo Mesto, Slovenia

pharma dynamics

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS S3

CLOPIDOGREL 75 mg PD film coated tablets
Clopidogrel
CLOPIDOGREL 75 mg PD contains sugar (each tablet contains lactose – 108,125 mg)

Read all of this leaflet carefully before you start taking CLOPIDOGREL 75 mg PD
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist, nurse or other healthcare provider.
- CLOPIDOGREL 75 mg PD has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What CLOPIDOGREL 75 mg PD is and what it is used for
2. What you need to know before you take CLOPIDOGREL 75 mg PD
3. How to take CLOPIDOGREL 75 mg PD
4. Possible side effects
5. How to store CLOPIDOGREL 75 mg PD
6. Contents of the pack and other information

1. What CLOPIDOGREL 75 mg PD is and what it is used for

CLOPIDOGREL 75 mg PD belongs to a group of medicines called antiplatelet medicinal products.
Platelets are very small structures in the blood which clump together during blood clotting.

CLOPIDOGREL 75 mg PD is used:
- to lessen the chance of heart attack or stroke. It is given to adults who have already had a heart attack or stroke or to those with other blood circulation problems, (including hardening of the arteries) that could lead to a stroke or heart attack
- if you have experienced a severe type of chest pain known as 'unstable angina' or 'myocardial infarction' (heart attack). For the treatment of this condition your doctor may have placed a stent in the blocked or narrowed artery to restore effective blood flow. You may also be given acetylsalicylic acid (aspirin to prevent blood clotting) by your doctor.

A heart attack or stroke may occur when a blood vessel in the heart or brain is blocked by a blood clot.
CLOPIDOGREL 75 mg PD reduces the chance that a harmful blood clot will form by preventing certain cells in the blood from clumping together.

2. What you need to know before you take CLOPIDOGREL 75 mg PD

Do not take CLOPIDOGREL 75 mg PD:
- if you are hypersensitive (allergic) to clopidogrel, or to any of the ingredients of CLOPIDOGREL 75 mg PD (see section 6)
- if you have bleeding problems (such as bleeding stomach ulcer or increased bleeding tendency that characterise platelet dysfunction- reduction in blood platelets which increases risk of bleeding and bruising)
- CLOPIDOGREL 75 mg PD should not be given to patients younger than 18 years
- if you are pregnant or breastfeeding your baby (see Pregnancy and breastfeeding)
- if you have liver problems
- if you have been diagnosed with haemophilia (a medical condition in which the ability of the blood to clot is severely reduced, causing you to bleed severely from even a slight injury), either hereditary or as a result of previously taking this medicine.

Warnings and precautions
Take special care with CLOPIDOGREL 75 mg PD:
- if you have had a clot in an artery of your brain (ischaemic stroke) which occurred in the last seven days
- if you are going to have surgery or have dental work done. CLOPIDOGREL 75 mg PD may increase the risk of serious bleeding during surgery or some kind of dental work. Therefore, treatment may have to be stopped about 7 days before the operation or dental work is done
- if you have a risk of haemorrhage (bleeding) such as:
  - a medical condition that puts you at risk of internal bleeding (such as a stomach ulcer)
  - a blood disorder that makes you prone to internal bleeding (bleeding inside any tissue, organs or joints of your body)
  - a recent serious injury
  - a recent surgery (including dental)
  - a planned surgery (including dental) in the next seven days
  - a planned spinal, epidural anaesthetic or a lumbar puncture in the next seven days
- if you have thrombotic thrombocytopenic purpura (TTP) - a serious blood disorder (that includes symptoms such as fever and bruising under the skin that may appear as red pinpoint dots, with or without unexplained extreme tiredness, confusion, yellowing of the skin or eyes (jaundice))
- if you develop a condition called acquired haemophilia (causing you to bleed severely from even a slight injury) your doctor may discontinue this medicine
- if you are hypersensitive (allergic) to other antiplatelet medicines called thienopyridine (such as ticlopidine, prasugrel), used to prevent blood clots
- if you have insulin autoimmune syndrome (a rare condition that causes low blood sugar)
- if you have kidney or liver disease
- tell all medical doctors, dentists, nurses and pharmacists you go to that you are taking CLOPIDOGREL 75 mg PD.

If you cut or injure yourself, it may take longer than usual for bleeding to stop. This is linked to the way your medicine works as it prevents the ability of blood clots to form. For minor cuts and injuries e.g. cutting yourself shaving, this is usually of no concern. However, if you are concerned by your bleeding, you should contact your doctor straightaway. Your doctor may order blood tests.

Other medicines and CLOPIDOGREL 75 mg PD
Always tell your healthcare provider if you are taking any other medicine. (This includes complementary or traditional medicines.)

Please consult your doctor, pharmacist or other healthcare professional for advice if you are using any of the following medicines:
- Nonsteroidal anti-inflammatory agents (such as aspirin, ibuprofen, indomethacin, diclofenac, etc.)
- blood clotting medication such as heparin or warfarin
- selective serotonin reuptake inhibitors (medicines that are typically used as antidepressants in the treatment of major depressive disorder, anxiety disorders, and other psychological conditions)
- phenytoin (antiepileptic medicine)
- rifampicin (used to treat severe infections such as tuberculosis (TB))
- tolbutamide and repaglinide (medicine for type-2 diabetes)
- tamoxifen and paclitaxel (medicine used for breast cancer)
- fluvastatin (medicine used to treat high cholesterol)
- omeprazole and esomeprazole (used in the treatment of acid reflux, ulcers)
- fluconazole or voriconazole, medicines to treat fungal infections
- efavirenz or other antiretroviral medicines (used to treat human immunodeficiency virus (HIV) infections)
- carbamazepine, a medicine to treat some forms of epilepsy
- mocibemide, medicine to treat depression
- opioids: while you are treated with CLOPIDOGREL 75 mg PD, you should inform your doctor before being prescribed any opioid (used to treat severe pain, e.g. morphine).

CLOPIDOGREL 75 mg PD with food and drink
CLOPIDOGREL 75 mg PD tablets may be taken with food or on an empty stomach. CLOPIDOGREL 75 mg PD tablets should be swallowed whole with water, do not chew or crush the tablets (see How to take CLOPIDOGREL 75 mg PD).

Pregnancy, breastfeeding and fertility
If you are pregnant or breastfeeding your baby, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before using CLOPIDOGREL 75 mg PD.

Safety in pregnancy and breastfeeding has not been established. This medicine should not be taken during pregnancy or breastfeeding (see Do not take CLOPIDOGREL 75 mg PD).

Driving and using machines
CLOPIDOGREL 75 mg PD is not expected to affect your ability to drive or use machines.
It is not always possible to predict to what extent CLOPIDOGREL 75 mg PD may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which CLOPIDOGREL 75 mg PD affects them.

CLOPIDOGREL 75 mg PD contains lactose
CLOPIDOGREL 75 mg PD contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking CLOPIDOGREL 75 mg PD.

Hydrogenated castor oil
CLOPIDOGREL 75 mg PD contains hydrogenated castor oil which may cause stomach upset or diarrhoea.

3. How to take CLOPIDOGREL 75 mg PD

Do not share medicines prescribed for you with any other person. Always take CLOPIDOGREL 75 mg PD exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

The usual dose is one CLOPIDOGREL 75 mg PD tablet daily, with or without food.

CLOPIDOGREL 75 mg PD tablets should be swallowed whole with water. Do not crush or chew the tablets.

Your doctor will tell you how long your treatment with CLOPIDOGREL 75 mg PD will last.
If you have the impression that the effect of CLOPIDOGREL 75 mg PD is too strong or too weak, tell your doctor or pharmacist.

If you take more CLOPIDOGREL 75 mg PD than you should
In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre because of the increased risk of bleeding. Take this leaflet and any remaining tablets with you, so that the doctor knows what you have taken.

If you forget to take CLOPIDOGREL 75 mg PD
If you missed a dose, take it as soon as you remember. If it is almost time for your next dose, skip the missed dose and continue to take the tablet at the usual time. Do not take a double or larger dose to make up for the forgotten individual doses.

If you stop taking CLOPIDOGREL 75 mg PD
Do not stop the treatment unless your doctor tells you so. Contact your doctor or pharmacist before stopping.

4. Possible side effects

CLOPIDOGREL 75 mg PD can have side effects.
Not all side effects reported for CLOPIDOGREL 75 mg PD are included in this leaflet. Should your general health worsen, or if you experience any untoward effects while using CLOPIDOGREL 75 mg PD, please consult your doctor, pharmacist or other healthcare professional for advice.

If any of the following happens, stop using CLOPIDOGREL 75 mg PD and tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:
- swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing
- rash or itching
- fainting.

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to CLOPIDOGREL 75 mg PD. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:
- yellowing of the skin and eyes, also called jaundice
- CLOPIDOGREL 75 mg PD may reduce the number of white cells in your blood or general blood count, which may decrease your ability to fight infections. If you experience any infection with symptoms such as fever or a serious deterioration in your general health, or a fever with symptoms such as sore throat/mouth, or bladder problems, you should see your doctor immediately
- unusual bleeding including nose bleeds, bruising or sudden weakness, vomiting of blood or material that looks like ground coffee, black tarry stools and blood in urine or stools, serium sickness with symptoms including joint pain and swollen lymph nodes
- blood disorders which may make you more likely to get infections, get tired very easily, or bruise very frequently
- depression, confusion, hallucinations (hearing, feeling or seeing things that are not there)
- chest pain, changes in the way your heart beats, for example, if you notice it is beating faster
- serious skin disorders including Stevens-Johnson syndrome/ toxic epidermal necrolysis (TEN) with flu-like symptoms, followed by a painful red or purplish rash that spreads and blisters, skin scores and peeling of the skin, which could be fatal
- skin rash or skin lesions with a pink/red ring and a pale centre which may be itchy, scaly or filled with fluid. The rash may appear especially on the palms or soles of your feet. These could be signs of a serious skin allergy called 'erythema multiforme'
- a serious reaction (drug reaction with eosinophilia and systemic symptoms (DRESS) with flu-like symptoms, a widespread rash with a high body temperature and enlarged lymph nodes. Abnormal blood test results may include increased levels of liver enzymes and an increase in a type of white blood cell (eosinophilia)
- hepatitis (symptoms include loss of appetite, nausea or vomiting, unusual tiredness or weakness, yellow eyes or skin), liver failure
- bleeding in the brain (symptoms include increasing headache, vomiting, drowsiness and progressive loss of consciousness, dizziness, confusion, unequal pupil size, slurred speech)
- pancreatitis (inflammation of the pancreas) (symptoms may include upper abdominal pain that radiates into the back; swollen and tender abdomen; nausea and vomiting, fever and increased heart rate)
- lung diseases like bronchospasm, eosinophilic pneumonia or interstitial pneumonitis (cough, difficulty breathing, noisy breathing, shortness of breath, tightness in chest, wheezing, night sweats, fever)
- serum sickness (a hypersensitivity reaction with symptoms that may include general ill feeling, skin rash, joint stiffness, joint pain, facial and extremity swelling, and fever)
- blood in your urine, foamy or bubbly urine.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:
Frequent side effects:
- red or purple discoloured spots on the skin, haematoma (a solid swelling of clotted blood within the tissues)
- headache, dizziness
- abdominal or stomach pain, indigestion, diarrhoea
- bruising
- back pain
- fever, chills, or sore throat, difficulty breathing, cough, runny nose or sneezing, nose bleeds
- bleeding at injection site.

Less frequent side effects:
- high blood pressure (severe headaches, vision problems, blurred vision, irregular heartbeat)
- bronchitis, shortness of breath
- anxiety, trouble in sleeping, decreased sense of touch or a tingling, numb feeling on the skin
- bleeding in the eye
- bleeding, constipation, vomiting or nausea, stomach ulcer, flatulence, mild abdominal or stomach pain
- dry, itchy and flaky skin
- leg cramps, gout
- bladder infection
- abnormal blood test results.

The following side effects have been reported but the frequency for them to occur is not known:
- an inflammation of the blood vessels that causes changes in the blood vessel walls (vasculitis with symptoms including fever, fatigue, weight loss and muscle and joint pain)
- low blood pressure (light-headedness, dizziness, blurred vision, feeling sick, weakness)
- loss of taste, taste disorders, feeling of spinning while being still
- muscle pain, rigidness or stiffness, leg cramps, joint pain and discomfort, arthritis
- frequent, painful or difficult urination, abnormal urine test results
- colitis (inflammation of the bowel with symptoms including diarrhoea, weight loss, abdominal cramping, anemia, and blood or pus in bowel movements)
- inflammation of the mucous membrane of the mouth (causing ulcers, sores, or white spots in mouth)
- enlarged breasts in men
- bleeding in the eye, the lung or the joints
- insulin autoimmune syndrome (condition that causes low blood sugar that manifest in involuntary hunger, tremors, anxiety, irritability, confusion, seizures or loss of consciousness).

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects
If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.
By reporting side effects, you can help provide more information on the safety of CLOPIDOGREL 75 mg PD. You can also send an email directly to the company, pharmacovigilance@pharmadynamics.co.za, to ensure safety of the product.

5. How to store CLOPIDOGREL 75 mg PD

Store all medicines out of reach of children.
Store at or below 30 °C.
Do not use after the expiry date stated on the carton.
Return all unused medicine to your pharmacist.
Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What CLOPIDOGREL 75 mg PD contains:
The active substance is clopidogrel.
Each CLOPIDOGREL 75 mg PD tablet contains clopidogrel hydrogen sulphate equivalent to clopidogrel 75 mg.

The other ingredients are
Castor oil (hydrogenated), hypromellose, iron oxide red, lactose, macrogol, microcrystalline cellulose, pregelatinised starch, propylene glycol, talc and titanium dioxide.

What CLOPIDOGREL 75 mg PD looks like and contents of the pack
Pink, round, biconvex, film coated tablets.

CLOPIDOGREL 75 mg PD tablets are packed in OPA/Al/PVC film and heat sealing aluminium blister strips. The blister strips are packed in an outer carton in packs of 28 or 30.
Not all pack sizes are marketed

Holder of Certificate of Registration
Pharma Dynamics (Pty) Ltd
1st Floor Grapevine House, Steenberg Office Park
Silverwood Close
Westlake, 7945
Cape Town, South Africa
Tel: + 27 21 707 7000
or 0860-PHARMA (742 762)

This leaflet was last revised in
24 October 2025

Registration number
A42/8.2/0128

NAMRSA 10/7.1/0377
ZIM 2021/10.56132 Category for distribution: P.P.10.
ZAMPCMB ZAMRA-HM-23-13

Manufactured by;
Krka, d.d., Novo Mesto
Šmarješka cesta 6
8501, Novo Mesto, Slovenia

E6544

pharma dynamics

PASIËNTINLIGTINGSBLAD

SKEDULERINGSTATUS S3

CLOPIDOGREL 75 mg PD filmbedekte tablette
Klopidogrel
CLOPIDOGREL 75 mg PD bevat suiker (elke tablet bevat laktose – 108,125 mg)

Lees hierdie hele inlig tingsblad deeglik deur, voordat u begin om CLOPIDOGREL 75 mg PD te neem
- Hou hierdie inligtingsblad. Dit mag nodig wees vir u om dit weer te lees.
- Indien u verdere vrae het, vra asseblief u dokter, apteker, verpleegkundige, of ander gesondheidsorgwerkaffer.
- CLOPIDOGREL 75 mg PD is vir u persoonlik voorgeskryf en u moet nie u medisyne met ander mense deel nie. Dit mag skadelik wees vir hulle, selfs al is hulle simptome dieselfde as u eie.

Inhoud van hierdie inligtingsblad

1. Wat CLOPIDOGREL 75 mg PD is en waarvoor dit gebruik word
2. Wat u nodig het om te weet, voordat u CLOPIDOGREL 75 mg PD neem
3. Hoe om CLOPIDOGREL 75 mg PD te neem
4. Moontlike newe-effekte
5. Hoe om CLOPIDOGREL 75 mg PD te bewaar
6. Verpakkingsinhoud en ander inligting

1. Wat CLOPIDOGREL 75 mg PD is en waarvoor dit gebruik word

CLOPIDOGREL 75 mg PD behoort aan 'n groep medisyne wat antiplaatjie mediksie genoem word.
Plaatjies is baie klein strukture in die bloed, wat saamkoek tydens bloedstolling.

CLOPIDOGREL 75 mg PD word gebruik:
- om die moontlikheid vir 'n hartaanval of bereerte te verminder Dit word aan volwassenes gegee wie alreeds 'n hartaanval of bereerte gehad het, of die wie ander bloedsirkulasieprobleme ondervind (insluitend verhanding van die arteries), wat tot 'n bereerte of hartaanval mag lei.
- indien u 'n erge type borspyn, bekend as "onstabiele angina", of "miokardiale infarksie" (hartaanval), ervaar het. Vir die behandeling van hierdie toestand, kon u dokter reeds 'n stent in die versperde of vernoude arterie geplaas het, om doeltreffende bloedvloei te herstel. U dokter mag ook asetielsalisilesuur vir u voorskryf (aspirien – om bloedstolling te verhoed).

'n Hartaanval of bereerte mag voorkom, wanneer 'n bloedvat in die hart of brein, deur 'n boeklkort versper word.
CLOPIDOGREL 75 mg PD verminder die moontlikheid dat 'n skadelike bloeklkort vorm, deur te verhoed dat sekere selle in die bloed, saamkoek.

2. Wat u nodig het om te weet, voordat u CLOPIDOGREL 75 mg PD neem

Moet nie CLOPIDOGREL 75 mg PD neem:
- indien u hipersensitief (allergies) is vir klopidogrel, of vir enige van die bestanddele van CLOPIDOGREL 75 mg PD nie (sien afdeling 6)
- indien u bloedingsprobleme het nie (soos bloeiende maageseer of 'n toenemende geneigdheid tot bloeding, wat 'n kenmerk van plaatjiesvanfunksie is)
- CLOPIDOGREL 75 mg PD moet nie aan pasiënte jonger as 18 jaar oud gegee word nie
- indien u swanger is of u baba borsvoed nie (sien Swangerskap en borsvoeding)
- indien u lewersprobleme het nie
- indien u gediagnoseer is met hemofilie nie ('n mediese toestand waar die vermoë van bloed kom te skort, erg afneem en veroorsaak dat u emstig bloei van selfs 'n ligte besering), of oorerflik, of as gevolg van die vorige gebruik van hierdie medisyne.

Waarskuwings en voorsorgmaatreels
Neem spesiale sorg met CLOPIDOGREL 75 mg PD:
- indien u onlord in 'n aar van u brein gehad het (iskemiese beroerte), wat tydens die vorige seven dae voorgekom het
- indien u 'n operasie of tandheelkundige prosedure beplan. CLOPIDOGREL 75 mg PD mag die risiko vir emstige bloeding tydens 'n operasie of sommige tandheelkundige prosedures, verhoog. Behandeling moet dus gestaak word, ongeveer 7 dae voor die operasie, of tandheelkundige prosedure uitgevoer word
- indien u 'n risiko vir hemorrasie (bloeding) het, soos:
  - 'n mediese toestand wat lei tot 'n risiko vir interne bloeding (soos 'n maageseer)
  - 'n bloedversteuring wat u geneig maak tot interne bloeding (bloeding binne-in enige weefsel, orgaan of gewrigte van u liggaam)
  - 'n onlangse ernstige besering
  - 'n onlangse operasie (insluitend tandheelkundige prosedure)
  - 'n beplande operasie (insluitend tandheelkundige prosedure) in die volgende 7 dae
  - 'n beplande spinale, epidurale verdowing, of 'n lumbale punktuur in die volgende swee dae
- indien u trombotiese trombosiopenese purpura (TTP) het – 'n ernstige bloedversteuring (sluit simptome soos koors en kneusing onder die vel in, wat mag verskyn as rooi spotpuntkeltjies, met, of sonder onverklaarbare, uiterste moegheid, verwarring en vergeling van die vel of oë (geelsug), in)
- u dokter mag hierdie medisyne onttrek, indien u 'n toestand, wat vervorme hemofilie genoem word, ontwikkel (veroorsaak dat u erg bloei, selfs van 'n ligte besering)
- indien u hipersensitief (allergies) is vir ander antiplaatjie mediksie, wat tiënopiridien genoem word (soos tiklopidien, prasugrel) en gebruik word om bloedklontje te verhoed
- indien u insulien outo-immuun sindroom het ('n skaars toestand, wat lae bloedsuiker veroorsaak)
- indien u niier-, of lewersiekte het
- vertel alle mediese dokters, tandarte, verpleegkundiges en aptekers wat u besoek, dat u CLOPIDOGREL 75 mg PD neem.

Indien u uself sny, of beser, mag dit langer as gewoonlik neem vir die bloeding om op te hou. Dit hou verband met die manier waarop u medisyne werk, aangesien dit die vermoë vir bloeklklonte om te vorm, verhoed. Vir minder ernstige snye en besenings, bv. indien u uself sou raakskiet wanneer u skeer, is daar gewoonlik geen rede tot kommer nie. Indien u egter bekommerd is oor u bloeding, raadpleeg u dokter onmiddellik. U dokter mag bloedtoetse aanwa.

Ander medisyne en CLOPIDOGREL 75 mg PD
Vertel altyd u gesondheidsorgwerkaffer indien u enige ander medisyne neem (Dit sluit aanvullende of tradisionele medisyne in).

Raadpleeg asseblief u dokter, apteker, of ander gesondheidsorgdeskundige vir advies, indien u enige van die volgende medisyne neem:
- niesteroïdale anti-inflammatoriese middels (soos aspirien, ibuprofen, indometasien, diklofenak, ens.)
- bloedstollingsmediksie, soos heparien, of warfarien
- selektiewe serotoniemheropname remmers (medisyne wat tipies gebruik word as antidepressante, vir die behandeling van major depressiewe steuring, angoversteurings en ander psigologiese toestande)
- fenitoïen (anti-epileptiese medisyne)
- tolbutamid en repaglinid (medisyne vir tipe-2 diabetes)
- tamoksifen en paklitaksel (medisyne wat gebruik word vir borskanker)
- fluvastatien (medisyne wat gebruik word om hoë cholesterol te behandel)
- omeprasool en esomeprasool (gebruik vir die behandeling van suurrefleks, ulkuse)
- flukonasol of vorkonasool (medisyne wat gebruik word om swaminfeksies te behandel)
- efavirens of ander antiretrovirale medisyne (gebruik om menslike immuntekortsindroomvirus (MIV)-infeksies te behandel)
- karbamasepien ('n mediese wat gebruik word om sommige vorms van epilepsie te behandel)
- mokibemied (medisyne om depressie te behandel)
- opioïede: terwyl u met CLOPIDOGREL 75 mg PD behandel word, moet u dokter ingelig word, voordat enige opioïede oorgeskryf word (gebruik om erge pyn te behandel bv. morfien).

CLOPIDOGREL 75 mg PD saam met kos en drinkgoed
CLOPIDOGREL 75 mg PD tablette mag saam met, of sonder kos, op 'n leë maag geneem word. CLOPIDOGREL 75 mg PD tablette moet heel, saam met water geslyk word. Moet nie tablette kou of verkrummel nie (sien Hoe om CLOPIDOGREL 75 mg PD te neem).

Swangerskap, borsvoeding en fertiliteit
Indien u swanger is, of u baba borsvoed, vermoed dat u swanger is, of 'n baba beplan, raadpleeg asseblief u dokter, apteker, of ander gesondheidsorgverskaffer vir advies, voordat u CLOPIDOGREL 75 mg PD neem.

Veiligheid tydens swangerskap en borsvoeding, is nie vasgestel nie.
Hierdie medisyne moet nie tydens swangerskap of borsvoeding geneem word nie (sien Moet nie CLOPIDOGREL 75 mg PD neem).

Bestuur en die hantering van masjiene
Daar word nie verwag dat CLOPIDOGREL 75 mg PD, met u vermoë om te bestuur of masjiene te hanteer, sal inmeng nie. Dit is nie altyd moontlik om te voorspel, tot watter mate CLOPIDOGREL 75 mg PD met die daagliikse aktiwiteite van 'n pasiënt sal inmeng nie. Pasiente moet verseker dat hulle nie by bogenoemde aktiwiteite betrokke raak, totdat hulle weet hoe CLOPIDOGREL 75 mg PD hulle beïnvloed nie.

CLOPIDOGREL 75 mg PD bevat Laktose
CLOPIDOGREL 75 mg PD bevat laktose. Indien u dokter vir u gesê het dat u 'n onverdraagsaamheid teenoor sommige suikers het, kontak u dokter voordat u CLOPIDOGREL 75 mg PD neem.

Gehydrogeneerde kasterolie
CLOPIDOGREL 75 mg PD bevat gehidrogeneerde kasterolie, wat maagongesteldheid of diarree mag veroorsaak.

3. Hoe om CLOPIDOGREL 75 mg PD te neem

Moet nie medisyne wat vir u voorgeskryf is met enige ander persoon deel nie. Gebruik CLOPIDOGREL 75 mg PD altyd presies soos deur u dokter aanbeveel word. U moet u dokter of apteker raadpleeg, indien u onseker is.

Die gewone dosis is een CLOPIDOGREL 75 mg PD tablet daagliks, saam met, of sonder kos.

CLOPIDOGREL 75 mg PD tablette moet heel, saam met water, geslyk word. Moet nie die tablette verkrummel of kou nie.

U dokter sal u vertel vir hoe lank u behandeling met CLOPIDOGREL 75 mg PD sal duur. Indien u onder die indruk is dat die effek van CLOPIDOGREL 75 mg PD te sterk, of te swak is, vertel u dokter of apteker.

Indien u meer CLOPIDOGREL 75 mg PD neem as wat u behoort
In die geval van oordosering, raadpleeg u dokter of apteker. Indien beide nie beskikbaar is nie, kontak die naaste hospitaal, of giftoebeheersentrum, weens die verhoogde risiko vir bloeding. Neem hierdie inligtingsblad en enige oortbywende tablette saam met u, sodat die dokter weet wat u geneem het.

Indien u vergeet om CLOPIDOGREL 75 mg PD te neem
Indien u 'n dosis oorgeslaan het, neem dit so gou as wat u ontho. Indien dit amper tyd is vir u volgende dosis, los die vergete dosis en gaan voort om die tablet op die gewone tyd te neem. Moet nie 'n dubbel, of hoër dosis neem, om op te maak vir die vergete, individuele doserings nie.

Indien u die gebruik van CLOPIDOGREL 75 mg PD staak
Moet nie die behandeling staak, tensy u dokter so aanbeveel nie. Raadpleeg u dokter of apteker, voordat u die gebruik hiervan staak.

4. Moontlike newe-effekte

CLOPIDOGREL 75 mg PD kan newe-effekte hê.
Nie alle newe-effekte wat vir CLOPIDOGREL 75 mg PD aangemeld is, word in hierdie inligtingsblad ingesluit nie. Sou u algemene gesondheid verslig, of indien u enige ongunstige effekte ervaar, terwyl u CLOPIDOGREL 75 mg PD gebruik, raadpleeg asseblief u dokter, apteker, of ander gesondheidsorgdeskundige vir advies.

Indien enige van die volgende gebeur, staak die gebruik van CLOPIDOGREL 75 mg PD en vertel u dokter onmiddellik, of gaan na die ongevalle-afdeling by u naaste hospitaal:
- swelling van die hande, voete, enkels, gesig, lippe, mond of keel, wat sluk of asemhaling mag bemoeilik
- uitslag of geiseuk
- floute.

Hierdie is alles baie emstige newe-effekte. Indien u dit ondervind, kon u 'n emstige allergiese reaksie teenoor CLOPIDOGREL 75 mg PD ervaar het. U mag dringende mediese aandag of hospitalisasie benodig.

Vertel u dokter onmiddellik, of gaan na die ongevalle-afdeling by u naaste hospitaal, indien u enige van die volgende opmerk:
- vergeling van die vel en oë (ook geelsug genoem)
- CLOPIDOGREL 75 mg PD mag die hoeveelheid witbloedselle in u bloed, of algemene bloedtelling, verlaag. Dit mag u vermoë om infeksies te beveg verswak. Indien u enige infeksie onder lede het, met simptome soos koors, of 'n ernstige aftreuktyang in u algemene gesondheid, of 'n koors met simptome soos 'n seer keel/mond, of blaasprobleme ervaar, moet u dadelik u dokter besoek
- ongewone bloeding, insluitend neusbloeding, kneusing, of skelike swakheid, braking van bloed, of 'n stof wat soos gemaalde koffie lyk, swart, teeragtige stoelgang en bloed in die urine of stoelgang, serumsieke, met simptome wat gewrigspyn en geswelde limfnode insluit.
- Bloedversteurings, wat u meer geneig maak tot infeksies, word gou moeg, of kneus baie gereld)
- depressie, verwarring, hallusinasies (hoor, voel of sien dinge wat nie daar is nie)
- borspyn, veranderinge in u hartklop byvoorbeeld, indien u opmerk dat dit vinniger klop
- emstige velverseteurings, insluitend Stevens-Johnson-sindroom/toksiese epidermale nekrolise (TEN), met griep-soortige simptome, gevolg deur 'n pynlike rooi, of perserige uitslag, wat verspreë en blase, velsere en velafskilfering veroorsaak, en noodlottig mag wees
- veluitslag, of velletjiestu met 'n pienk/rooi ring en bleek kern, wat jeukerig, skubberig of met vloeistof gevul mag wees. Die uitslag mag verol op u palms, of voetsole verskyn. Hierdie mag tekens van 'n emstige allergie, wat 'erythema multiforme' genoem word, wees
- 'n emstige reaksie (geneesmiddelreaksie met eosinofilie en sistemiese simptome [DRESS], met griep-soortige simptome, 'n wydverspreide uitslag met 'n hoë liggaamstemperatuur en vergrote limfnode. Abnormale bloedtoetsresultate mag verhoogde leweransiemwaklike insluit en 'n verhoging in 'n tipe witbloedsel (eosinofilie)
- hepatitis (simptome sluit aptyverlies, naarheid of braking, ongewone moegheid of swakheid, vergeling van de oë wel, in), leweroversaking
- breinbloeding (simptome sluit hoofpyn wat vererger, braking, lomerigheid en progressiewe bewusynsverlies, duiseligheid, verwarring, onewenstige pupilgrootte, sleperde spraak, in)
- pankreatitis (inflammasie van die pankreas) (simptome mag boonste abdominale pyn, wat uitstraal in die rug; geswelde en gevoelige buik; naarheid en braking, koors en 'n winniger hartklop, insluit)
- longsieke soos brongospasma, eosinofiliese pneumonie, of interstisiële pneumonitis (hoes, moeilike asemhaling, rasenige asemhaling, asemnood, benoude bors, gehyg, nagsweet, koors)
- serumsieke ('n hipersensitiwiteitsreaksie, met simptome soos 'n algemene gevoel van ongesteldheid, veluitslag, gewrigstiwheid, gewrigspyn, gesig- en ledemaatswelling en koors)
- bloed in u urine, skuimerige of borreltige urine.

Hierdie is alles emstige newe-effekte. U mag dringende mediese aandag benodig.

Vertel u dokter indien u enige van die volgende opmerk:
Algemene newe-effekte:
- rooi, of perskleurige koltetjies op die vel, hematoom ('n solieede swelling van gestolde bloed binne-in die weefsels)
- hoofpyn, duiseligheid
- buik-, of maagpyn, sleghte spysvertering, diarree
- kneusing
- ruigsyn
- koors, koue rillings of seer keel, moeilike asemhaling, hoes, loopneus of gemes, neusbloeding
- bloeding by die inspuitingspleek.

Minder algemene newe-effekte:
- hoë bloeddruk (erge hoofpyne, sigroblerne, troebel visie, onreëlmatige hartklop)
- bronqitis, asemnood
- angsigheid, slaapprobleme, vermindering in tassensasie, of 'n tintelende, geveelloosheid op die vel
- oogbloeding
- bloeding, hardwyksheid, braking of naarheid, maageseer, winderigheid, lighte buik-, of maagpyn
- droë, jeukerige en skilferige vel
- beenkrampe, jig
- blaasinfeksie
- abnormale bloedtoetsresultate.

Die volgende newe-effekte is aangemeld, maar die frekwensie van voorkoms is onbekend:
- 'n inflammasie van die bloedvat, wat veranderinge in die bloedvatwande veroorsaak (vaskulitis, met simptome wat koors, uitputting, gewigsverlies en spier- en gewrigspyn insluit)
- lae bloeddruk (lighoofdigheid, duiseligheid, troebel visie, voel naar, swakheid)
- smaakverlies, smaaksteurnisse, draaigevoel wanneer u stilstaanvsit
- spierpyn, stramheid of styfheid, beenkrampe, gewrigspyn en ongemak, artritis
- geneide, pynlike of moeilike urinering, abnormale urientoetsresultate
- kolitis (inflammasie van die ingewande, met simptome wat diarree, gewigsverlies, abdominale krampe, bloedarmoede en bloed of eiter in stoelgang, insluit)
- inflammasie van die mukusmembrane van die mond (veroorsaak uilusse, sere, of wit koltetjies in die mond)
- vergrote borste by mans
- bloeding in die oog, die long, of die gewrigte
- insulien outo-immuun sindroom (toestand wat lae bloedsuiker veroorsaak en manifesteer as onwillekeurige honger, bewing, angstigheid, prikkelbaarheid, verwarring, aanvalle, of bewusynsverlies).

Indien u enige newe-effekte opmerk wat nie in hierdie inligtingsblad genoem word nie, lig asseblief u dokter of apteker in.

Aanmelding van newe-effekte
Indien u newe-effekte ervaar, praat met u dokter, apteker of verpleegkundige. U kan ook newe-effekte aanmeld by SAHPRA via die Med Safety toepassing (Medsafety X SAHPRA) en eReporting platform (who-umc.org), wat op SAHPRA se webtuiste gevind kan word. Deur die aanmelding van newe-effekte kan u help om meer inligting aangaande die veiligheid van CLOPIDOGREL 75 mg PD in te win. U kan ook 'n epos dink aan die maatskappy stuur, pharmacovigilance@pharmadynamics.co.za, om die veiligheid van die produk te verseker.

5. Hoe om CLOPIDOGREL 75 mg PD te bewaar

Bewaar alle medisyne buite die bereik van kinders.
Bewaar teen of bereide 30 °C.
Moet nie gebruik na die vervaldatum wat op die kartonhouer aangedui word nie.
Neem alle ongebruikte medisyne na u apteker terug.
Moet nie ongebruikte medisyne in afvoerpype of riooldestelsels (bv. toilette), weggooi nie.

6. Verpakkingsinhoud en ander inligting

Wat CLOPIDOGREL 75 mg PD bevat:
Die aktiewe bestanddeel is klopidogrel.
Elke CLOPIDOGREL 75 mg PD tablet bevat klopidogrelwaterstofsulfaat, gelykstaande aan klopidogrel 75 mg.

Die ander bestanddele is
Hipromellose, kastorolie (gehidrogeneerd), laktose, makrogol, mikrokristalline sellulose, propileenglikol, rooi ysteroksied, talkum, titaandioksied en voorgel-gegelatiniseerde stysel.

Hoe CLOPIDOGREL 75 mg PD lyk, en die verpakkingsinhoud
Pienk, ronde, bikonvekse filmbedekte tablette.

CLOPIDOGREL 75 mg PD tablette word verpak in OPA/Al/PVC film en hitte-verseëlde aluminium stukpstrokie. Die stukpstrokie word verpak in 'n buitenste kartonhouer in verpakkings van 28 of 30.
Nie alle verpakkingshoeveelhede word bemark nie.

Eienaar van die Registrasiesertifikaat
Pharma Dynamics (Edms.) Bpk.
1ste Vloer Grapevine House, Steenberg Office Park
Silverwood Close
Westlake, 7945
Kaapstad, Suid-Afrika
Tel: +27 21 707 7000
of 0860-PHARMA (742 762)

Hierdie inligtingsblad was voorheen hersien
24 Oktober 2025

Registrasienommer
A42/8.2/0128

NAMRSA 10/7.1/0377
ZIM 2021/10.56132 Verspreidingskategorie: P.P.10
ZAMPCMB ZAMRA-HM-23-13

Manufactured by;
Krka, d.d., Novo Mesto
Šmarješka cesta 6
8501, Novo Mesto, Slovenia