CLOPIDOGREL ASPIRIN 75/75 mg PD

SCHEDULING STATUS S3

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

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each film coated tablet contains clopidogrel hydrogen sulphate equivalent to clopidogrel 75 mg, and acetylsalicylic acid (ASA) (aspirin) 75 mg.

Each tablet contains sugar – lactose monohydrate 2,80 mg and mannitol 64 mg (sugar alcohol). For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Film coated tablets.
Yellow coloured, oval shaped, film coated tablets debossed with "I" on one side and plain on the other side.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
CLOPIDOGREL ASPIRIN 75/75 mg PD is indicated for the reduction of atherothrombotic events in adult patients already taking both clopidogrel and acetylsalicylic acid (ASA).
CLOPIDOGREL ASPIRIN 75/75 mg PD is a fixed-dose combination product for continuation of therapy in:

Acute Coronary Syndrome:
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 in combination with ASA has been shown to decrease the rate of a combined endpoint of cardiovascular death, myocardial infarction, or stroke as well as the rate of a combined endpoint of cardiovascular death, MI, stroke, or refractory ischaemia.

For patients with ST-segment elevation acute myocardial infarction, clopidogrel 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
Acute Coronary Syndrome:
CLOPIDOGREL ASPIRIN 75/75 mg PD should be given as a single daily dose (i.e. one tablet daily). CLOPIDOGREL ASPIRIN 75/75 mg PD is used following an initial loading dose of CLOPIDOGREL ASPIRIN 75/75 mg PD in combination with ASA.

In patients with non-ST segment elevation acute coronary syndrome (unstable angina or non-Q-wave myocardial infarction): The optimal duration of treatment has not been formally established. Clinical trial data support use up to 12 months, but the maximum benefit was seen at 3 months.

In patients with ST segment elevation acute myocardial infarction: Therapy should be started as early as possible after symptoms start and continued for at least 4 weeks. The benefit of the combination of clopidogrel with ASA beyond 4 weeks has not been studied in this setting. For patients older than 75 years of age therapy should be initiated without a loading dose of clopidogrel.

Special populations
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 ASPIRIN 75/75 mg PD is not indicated for use in children under the age of 18 years as safety and efficacy have not been established.

Method of administration
For oral use.
CLOPIDOGREL ASPIRIN 75/75 mg PD may be given with or without food.

Missed dose:
Medical practitioners should advise patients who forget to take CLOPIDOGREL ASPIRIN 75/75 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
Due to the presence of clopidogrel and acetylsalicylic acid (aspirin) in the medicine, CLOPIDOGREL ASPIRIN 75/75 mg PD is contraindicated in case of:
- hypersensitivity to clopidogrel, acetylsalicylic acid or to any of the ingredients of CLOPIDOGREL ASPIRIN 75/75 mg PD (see section 6.1)
- active or history of pathological bleeding such as recurrent peptic ulcer/haemorrhage/perforations or intracranial haemorrhage
- safety and efficacy in children below the age of 18 have not been established. ASA has been implicated in Reye's syndrome, a rare but serious illness in children and teenagers with chickenpox and influenza. A medical practitioner should be consulted before aspirin is used in these patients
- safety and efficacy in pregnancy and lactation have not been established (see section 4.6)
- severe hepatic impairment
- thrombocytopenia and platelet dysfunction.

In addition, due to the presence of ASA, CLOPIDOGREL ASPIRIN 75/75 mg PD is also contraindicated in:
- patients with hypersensitivity (allergy) to nonsteroidal anti-inflammatory drugs (NSAIDs) and syndrome of asthma, rhinitis, and nasal polyps. Patients with pre-existing mastocytosis, in whom the use of acetylsalicylic acid may induce severe hypersensitivity reactions (including circulatory shock with flushing, hypotension, tachycardia and vomiting)
- patients with severe renal impairment
- patients with heart failure
- patients with a history of gastrointestinal bleeding, ulceration or perforation (PUBs) related to previous NSAIDs
- pregnancy and lactation (see section 4.6).

4.4 Special warnings and precautions for use

THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP) HAS BEEN REPORTED TO OCCUR WITH CLOPIDOGREL ASPIRIN 75/75 mg PD DURING POST-MARKETING EXPERIENCE. MOST CASES WERE REPORTED IN THE FIRST TWO WEEKS OF TREATMENT. MEDICAL PRESCRIBERS SHOULD ALSO WARN PATIENTS ABOUT THE SIGNS AND SYMPTOMS OF THROMBOTIC THROMBOCYTOPENIC PURPURA. IT IS CHARACTERISED BY THROMBOCYTOPENIA AND MICROANGIOPATHIC HAEMOLYTIC ANAEMIA ASSOCIATED WITH EITHER NEUROLOGICAL FINDINGS, RENAL DYSFUNCTION OR FEVER. TTP IS A POTENTIALLY FATAL CONDITION REQUIRING PROMPT TREATMENT, INCLUDING PLASMAPHERESIS (PLASMA EXCHANGE).

Recent transient ischaemic attack or stroke
In patients with recent transient ischaemic attack or stroke who are at high risk of recurrent ischaemic events, the combination of aspirin and clopidogrel has been shown to increase major bleeding.

Acquired haemophilia
Following use of clopidogrel, acquired haemophilia has been reported. 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 ASPIRIN 75/75 mg PD should be discontinued.

Fluid retention and oedema
In view of the inherent potential of NSAIDs, including ASA, to cause fluid retention, heart failure may be precipitated in some compromised patients. As fluid retention and oedema have been reported in association with CLOPIDOGREL ASPIRIN 75/75 mg PD therapy, caution is required in patients with a history of hypertension and/or heart failure.

Elderly
The elderly have an increased frequency of adverse reactions to NSAIDs, especially gastrointestinal bleeding, ulceration and perforation (PUBs) which may be fatal.

Due to the presence of ASA caution is required in the following:
- patients with a history of asthma or allergic disorders since they are at an increased risk of hypersensitivity reactions
- patients with gout since low doses of ASA increase serum uric acid concentrations
- children: as there is an association between ASA and Reye's syndrome (a very rare disease which can be fatal) when ASA is given to children
- alcohol may increase the risk of gastrointestinal injury when taken with ASA. Alcohol should therefore be used with caution in patients taking CLOPIDOGREL ASPIRIN 75/75 mg PD (see section 4.5). Patients should be counselled about the bleeding risks involved with chronic, heavy alcohol use while taking CLOPIDOGREL ASPIRIN 75/75 mg PD
- in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency, CLOPIDOGREL ASPIRIN 75/75 mg PD must be administered under close medical supervision due to the risk of haemolysis (see section 4.8)
- concomitant treatment with levothyroxine and salicylates, specifically at doses greater than 2,0 g/day, should be avoided (see section 4.5).

Bleeding and haematological disorders
CLOPIDOGREL ASPIRIN 75/75 mg PD produces irreversible inhibition of platelet aggregation for the life of the platelet, which is 7 - 10 days.
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).
As there is a risk of bleeding intensity, concomitant administration of CLOPIDOGREL ASPIRIN 75/75 mg PD with warfarin is not recommended (see section 4.5).

Caution is required when administering CLOPIDOGREL ASPIRIN 75/75 mg PD to patients who may be at risk of increased bleeding from trauma, surgery or other pathological conditions associated with bleeding diathesis as well as in patients receiving treatment with other nonsteroidal anti-inflammatory medicines including COX-2 inhibitors, heparin, glycoprotein IIb/IIIa inhibitors, selective serotonin reuptake inhibitors (SSRIs), or CYP2C19 strong inducers, or thrombolytics (see section 4.5). Patients should be monitored continuously and carefully for any signs of bleeding (including occult bleeding) especially but not limited to during the first weeks of treatment and/or after invasive cardiac procedures or surgery.

CLOPIDOGREL ASPIRIN 75/75 mg PD should be discontinued 7 days prior to surgery in those patients who are to undergo elective surgery where an antiplatelet effect is not desired.

The concomitant administration of CLOPIDOGREL ASPIRIN 75/75 mg PD with oral anticoagulants is not recommended since it may increase the intensity of bleeding (see section 4.5).

CLOPIDOGREL ASPIRIN 75/75 mg PD prolongs bleeding time and should therefore be used with caution in patients who have lesions with a propensity to bleed (particularly gastrointestinal and intra-ocular).

Spinal and epidural anaesthesia should not be administered to a patient taking CLOPIDOGREL ASPIRIN 75/75 mg PD or for 7 days thereafter. No lumbar puncture should be done during these 7 days due to risk of haematoma formation following lumbar puncture or spinal and epidural anaesthesia.

Patients should be told that it may take longer than usual to stop bleeding whilst on CLOPIDOGREL ASPIRIN 75/75 mg PD therapy, and that they should report any unusual bleeding (site or duration) to their medical practitioner.

Patients should inform medical practitioners and dentists that they are taking CLOPIDOGREL ASPIRIN 75/75 mg PD before any surgery is scheduled and before any new medicine is taken.

Gastrointestinal
In patients with a history of gastrointestinal disease (GI) (e.g. ulcerative colitis, Crohn's disease, hiatus hernia, gastro-oesophageal reflux disease, angiodysplasia), peptic ulcer, gastroduodenal haemorrhage or minor upper gastrointestinal symptoms, CLOPIDOGREL ASPIRIN 75/75 mg PD should be used with caution as the condition may be exacerbated or may be due to gastric ulceration which in turn may lead to gastric bleeding.

In patients with a history of ulcers, and the elderly the risk of gastrointestinal bleeding, ulceration or perforation (PUBs) is higher with increasing doses of CLOPIDOGREL ASPIRIN 75/75 mg PD. Should gastrointestinal bleeding, perforation or ulceration occur in patients receiving CLOPIDOGREL ASPIRIN 75/75 mg PD, therapy should be stopped.
Gastrointestinal side effects including stomach pain, heartburn, nausea, vomiting, and GI bleeding may occur. Although minor upper GI symptoms (such as dyspepsia) are common and can occur anytime during therapy, medical practitioners should remain alert for signs of ulceration and bleeding, even in the absence of previous GI symptoms. Patients should be told about signs and symptoms of GI side effects and what steps to take if they occur.

In patients concomitantly receiving nicorandil and NSAIDs including acetylsalicylic acid (ASA) and lysine acetylsalicylate (LAS), there is an increased risk for severe complications such as gastrointestinal ulceration, perforation and haemorrhage (see section 4.5).

Skin reactions
Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported. CLOPIDOGREL ASPIRIN 75/75 mg PD should be discontinued at the first appearance of a skin rash, mucosal lesions, or any other sign of hypersensitivity.

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. 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 CY2C19 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 5.2: Pharmacogenetics and section 4.2).
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 medicinal products (see section 4.5).

Cross-reactivity among thienopyridines
As cross-reactivity among thienopyridines has been reported, patients should be evaluated for history of hypersensitivity to another thienopyridine (such as ticlopidine, prasugrel) (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.

Hepatic impairment
CLOPIDOGREL ASPIRIN 75/75 mg PD is contraindicated in patients with severe hepatic impairment (see section 4.3).
Caution is advised in patients with mild to moderate hepatic impairment.
Therapeutic experience is limited in patients with moderate hepatic disease who may have bleeding diatheses. Therefore CLOPIDOGREL ASPIRIN 75/75 mg PD should be used with caution in this population.

Renal impairment
CLOPIDOGREL ASPIRIN 75/75 mg PD is contraindicated in patients with severe renal impairment (see section 4.3).
Therapeutic experience with CLOPIDOGREL ASPIRIN 75/75 mg PD is limited in patients with mild to moderate renal impairment.
CLOPIDOGREL ASPIRIN 75/75 mg PD should therefore be used with caution in this population.

Excipients with known effect:
CLOPIDOGREL ASPIRIN 75/75 mg PD contains lactose. Patients with the rare hereditary conditions of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take CLOPIDOGREL ASPIRIN 75/75 mg PD.
CLOPIDOGREL ASPIRIN 75/75 mg PD contains hydrogenated castor oil which may cause stomach upset and diarrhoea.

4.5 Interaction with other medicines and other forms of interaction
There are no studies on the concomitant use of clopidogrel and acetylsalicylic acid with other medicines. The information below was obtained with clopidogrel or ASA alone. Safety of CLOPIDOGREL ASPIRIN 75/75 mg PD and the concomitant use with the medicines mentioned below have not been established.

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 (see section 4.4).

Nicorandil
In patients concomitantly receiving nicorandil and NSAIDs including acetylsalicylic acid (ASA) and lysine acetylsalicylate (LAS), there is an increased risk for severe complications such as gastrointestinal ulceration, perforation and haemorrhage (see section 4.4).

Injectable anticoagulants
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, however, as a pharmacodynamic interaction between CLOPIDOGREL ASPIRIN 75/75 mg PD and heparin is possible, concomitant use should be undertaken with caution.

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 with the incidence of clinically significant bleeding being similar to that as observed when thrombolytic medicines and heparins are co-administered with acetylsalicylic acid. However, the concomitant use of CLOPIDOGREL ASPIRIN 75/75 mg PD with thrombolytic medicines should be undertaken with caution.

Oral anticoagulants
Concomitant administration of warfarin with CLOPIDOGREL ASPIRIN 75/75 mg PD is not recommended due to the increased risk of bleeding (see section 4.4).

Glycoprotein IIb/IIIa inhibitors
CLOPIDOGREL ASPIRIN 75/75 mg PD should be used with caution in patients who may be at risk of increased bleeding from trauma, surgery or other pathological conditions and who receive concomitant glycoprotein IIb/IIIa inhibitors.

Nonsteroidal anti-inflammatory drugs (NSAIDs)
In healthy volunteers, the concomitant administration of clopidogrel and naproxen increased occult gastrointestinal blood loss. Consequently, the concomitant use of NSAIDs, including COX-2 inhibitors, is not recommended with CLOPIDOGREL ASPIRIN 75/75 mg PD (see section 4.4).

When they are dosed concomitantly, experimental data suggests that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation (see section 5.1). However, the limitations of these data and the uncertainties regarding extrapolation of *ex vivo* data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional ibuprofen use.

Selective serotonin reuptake inhibitors (SSRIs)
The concomitant administration of SSRIs with clopidogrel should be undertaken with caution as SSRIs affect platelet activation and increase the risk of bleeding.

Other concomitant therapy with CLOPIDOGREL ASPIRIN 75/75 mg PD:
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 in particular 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 and esomeprazole) should be discouraged (see section 4.4 and section 5.2; Pharmacogenetics). If a proton pump inhibitor is to be used concomitantly with CLOPIDOGREL ASPIRIN 75/75 mg PD, consider using one with less CYP2C19 inhibitory activity.

Other medicinal products
No clinically significant pharmacodynamic interactions were observed when clopidogrel was co-administered with atenolol, nifedipine, or both atenolol and nifedipine. The pharmacodynamic activity of clopidogrel was not significantly influenced by the co-administration of phenobarbital or estrogen.

The pharmacokinetics of digoxin or theophylline were not modified by the co-administration of clopidogrel. Antacids did not modify the extent of clopidogrel absorption.

Data from studies with human liver microsomes indicated that CLOPIDOGREL ASPIRIN 75/75 mg PD could inhibit the activity of one of the Cytochrome P450 (CYP) enzymes (CYP2C9). This could potentially lead to increased plasma levels of medicines such as phenytoin, tolbutamide, torsemide, tamoxifen, fluvastatin and NSAIDs which are metabolised by CYP2C9. Data indicates that phenytoin and tolbutamide can be safely co-administered with clopidogrel.

CYP2C8 substrate medicines
Clopidogrel has been shown to increase repaglinide exposure in healthy volunteers. *In vitro* studies have shown the increase in repaglinide exposure is due to inhibition of CYP2C8 by the glucuronide metabolite of clopidogrel. Due to the risk of increased plasma concentrations, concomitant administration of clopidogrel and medicines primarily cleared by CYP2C8 metabolism (e.g. repaglinide, paclitaxel) should be undertaken with caution.

Rosuvastatin
Clopidogrel has been shown to increase rosuvastatin exposure in patients by 1,4-fold (AUC) without effect on C_{max}, after repeated administration of a 75 mg clopidogrel dose.

Other concomitant therapy with ASA
Interactions with the following medicinal products have been reported with ASA:

Uricosurics
Caution is required because ASA may inhibit the effect of uricosuric agents through competitive elimination of uric acid.

Methotrexate
Due to the presence of ASA, methotrexate used at doses higher than 20 mg/week should be used with caution with CLOPIDOGREL ASPIRIN 75/75 mg PD as it can inhibit renal clearance of methotrexate, which may lead to bone marrow toxicity.

Metamizole
Metamizole may reduce the effect of ASA on platelet aggregation when taken concomitantly. Therefore, this combination should be used with caution in patients taking low-dose ASA for cardio-protection.

NSAIDs
Use of two or more NSAIDs concomitantly could result in an increase in side effects.

Corticosteroids
Increased risk of gastrointestinal perforation, ulceration or bleeding (PUBs).

Selective serotonin reuptake inhibitors (SSRIs)
Increased risk of gastrointestinal bleeding.

Acetazolamide
Due to the increased risk of metabolic acidosis, caution is recommended when co-administering salicylates with acetazolamide.

Varicella vaccine
Cases of Reye's syndrome have occurred following the use of salicylates during varicella infections. It is therefore recommended that patients not be given salicylates for an interval of six weeks after receiving the varicella vaccine. (see section 4.4).

Levothyroxine
Thyroid hormone levels should be monitored as salicylates, specifically at doses greater than 2,0 g/day, may inhibit binding of thyroid hormones to carrier proteins and thereby lead to an initial transient increase in free thyroid hormones, followed by an overall decrease in total thyroid hormone levels.

Valproic acid
The concomitant administration of salicylates and valproic acid may result in decreased valproic acid protein binding and inhibition of valproic acid metabolism resulting in increased serum levels of total and free valproic acid.

Tenofovir
Concomitant administration of tenofovir disoproxil fumarate and NSAIDs may increase the risk of renal failure.

Other interactions with ASA
Interactions with the following medicinal products with higher (anti-inflammatory) doses of ASA have also been reported: angiotensin converting enzyme (ACE) inhibitors, acetazolamide, anticonvulsants (phenytoin and valproic acid), beta blockers, diuretics, and oral hypoglycaemic medicines.

Alcohol
Alcohol, when taken with ASA, may increase the risk of gastrointestinal injury. Therefore, alcohol should be used with caution in patients taking CLOPIDOGREL ASPIRIN 75/75 mg PD (see section 4.4).

Other interactions with CLOPIDOGREL ASPIRIN 75/75 mg PD
More than 30 000 patients who entered into clinical trials with clopidogrel and ASA, at maintenance doses lower than or equal to 325 mg, received a variety of concomitant medications including diuretics, beta blockers, ACE inhibitors, calcium antagonists, cholesterol lowering medicines, coronary vasodilators, antidiabetic medicines (including insulin), antiepileptic agents and GPIIb/IIIa antagonists without evidence of clinically significant adverse interactions.

Apart from the specific medicine interaction information described above, interaction studies with CLOPIDOGREL ASPIRIN 75/75 mg PD and some medicines commonly administered in patients with atherothrombotic disease have not been performed.

Opioid agonists
Co-administration of opioid agonists have the potential to delay and reduce the absorption of an oral P2Y12 inhibitor such as clopidogrel, presumably because of slowed gastric emptying. The clinical relevance is unknown. Consider the use of a parenteral antiplatelet medicines in acute coronary syndrome patients requiring co-administration of morphine or other opioid agonists.

4.6 Fertility, pregnancy and lactation
Pregnancy
CLOPIDOGREL ASPIRIN 75/75 mg PD is contraindicated during pregnancy (see section 4.3).

Breastfeeding
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. ASA is known to be excreted in human breast milk.
CLOPIDOGREL ASPIRIN 75/75 mg PD is contraindicated whilst breastfeeding (see section 4.3).

Fertility
There are no fertility data with clopidogrel/acetylsalicylic acid.

4.7 Effects on ability to drive and use machines
CLOPIDOGREL ASPIRIN 75/75 mg PD has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects
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.

Tabulated summary of adverse reactions: CLOPIDOGREL ASPIRIN 75/75 mg PD
The frequencies of adverse events are ranked according to the following:
Frequent = (≥ 1/100 to < 1/10).
Less frequent = Infrequent (≥ 1/1 000 to < 1/100); Rare (≥ 1/10 000 to < 1/1 000);
Very rare (<1/10 000).
Frequency not known = cannot be estimated from the available data.

System organ class	Frequency	Side effects
Blood and lymphatic system disorders	*Less frequent*	Thrombocytopenia (sometimes severe), increased bleeding time, leucopenia, eosinophilia, neutropenia (sometimes severe), platelets decreased, aplastic anaemia
	Frequency unknown	Bleeding*
Nervous system disorders	*Less frequent*	Intracranial bleeding, headache, dizziness, paraesthesia
Eye disorders	*Less frequent*	Eye bleeding (mainly conjunctival), ocular, retinal
Ear and labyrinth disorders	*Less frequent*	Vertigo
Vascular disorders	*Frequent*	Haematoma
Respiratory, thoracic and mediastinal disorders	*Frequent*	Epistaxis
Gastrointestinal disorders	*Frequent*	Dyspepsia, abdominal pain, diarrhoea, gastrointestinal haemorrhage
	Less frequent	Nausea, gastritis, flatulence, constipation, vomiting, gastric ulcer, duodenal ulcer
Skin and subcutaneous tissue disorders	*Frequent*	Bruising
	Less frequent	Rash, pruritus, purpura
Renal and urinary disorders	*Less frequent*	Haematuria
General disorders and administrative site conditions	*Frequent*	Bleeding at the puncture site

*Post marketing events.

Tabulated summary of adverse reactions: CLOPIDOGREL

System organ class	Frequency	Side effects
Blood and lymphatic system disorders	*Frequency unknown*	Serious cases of bleeding, mainly skin, musculoskeletal (haemarthrosis), eye (conjunctival, ocular, retinal) and respiratory tract bleeding (haemoptysis, pulmonary haemorrhage), epistaxis, haematuria and haemorrhage of operative wound; cases of bleeding with fatal outcome (especially intracranial, gastrointestinal and retroperitoneal haemorrhage), acquired haemophilia A, serious haemorrhage in patients taking CLOPIDOGREL ASPIRIN 75/75 mg PD with or without heparin, thrombotic thrombocytopenic purpura (TTP), aplastic anaemia/pancytopenia, agranulocytosis, severe thrombocytopenia, granulocytopenia, anaemia
Immune system disorders	*Frequency unknown*	Anaphylactoid reactions, serum sickness, cross-reactive medicine hypersensitivity among thienopyridines, such as ticlopidine or prasugrel, insulin autoimmune syndrome, which can lead to severe hypoglycaemia, particularly in patients with HLA DRA4 subtype (more frequent in the Japanese population)
Cardiac disorders	*Frequency unknown*	Kounis syndrome (vasospastic allergic angina/allergic myocardial infarction) in the context of a hypersensitivity reaction due to clopidogrel
Psychiatric disorders	*Frequency unknown*	Confusion, hallucinations
Nervous system disorders	*Frequency unknown*	Taste disturbances, ageusia
Vascular disorders	*Frequency unknown*	Vasculitis, hypotension
Respiratory, thoracic and mediastinal disorders	*Frequency unknown*	Bronchospasm, interstitial pneumonitis, eosinophilic pneumonia
Gastrointestinal disorders	*Frequency unknown*	Colitis (including ulcerative or lymphocytic colitis), stomatitis, pancreatitis
Hepatobiliary disorders	*Frequency unknown*	Acute liver failure, hepatitis, abnormal liver function test
Skin and subcutaneous tissue disorders	*Frequency unknown*	Maculopapular, erythematous or exfoliative rash; urticaria; pruritus; angioedema; bullous dermatitis (erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, acute generalised exanthematous pustulosis (AGEP)); drug-induced hypersensitivity syndrome (DiHS), drug rash with eosinophilia and systemic symptoms (DRESS), eczema; lichen planus
Musculoskeletal, connective tissue and bone disorders	*Frequency unknown*	Arthritis, arthralgia, myalgia
Renal and urinary disorders	*Frequency unknown*	Glomerulonephritis, increased blood creatinine
Reproductive system and breast disorders	*Frequency unknown*	Gynaecomastia
General disorders and administrative site conditions	*Frequency unknown*	Fever

Tabulated summary of adverse reactions: ASA

System organ class	Frequency	Side effects
Blood and lymphatic system disorders	*Frequency unknown*	Thrombocytopenia, haemolytic anaemia in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency, pancytopenia, bicytopenia, aplastic anaemia, bone marrow failure, agranulocytosis, neutropenia, leukopenia
Immune system disorders	*Frequency unknown*	Anaphylactic shock, aggravation of allergic symptoms of food allergy
Cardiac disorders	*Frequency unknown*	Kounis syndrome in the context of a hypersensitivity reaction due to ASA
Metabolism and nutrition disorders	*Frequency unknown*	Hypoglycaemia, gout
Nervous system disorders	*Frequency unknown*	Intracranial haemorrhage (may be fatal, especially in the elderly)
Ear and labyrinth disorders	*Frequency unknown*	Hearing loss or tinnitus
Vascular disorders	*Frequency unknown*	Hypertension, cardiac failure, vasculitis including Henoch-Schönlein purpura
Respiratory, thoracic and mediastinal disorders	*Frequency unknown*	Non-cardiogenic pulmonary oedema with chronic use and in the context of a hypersensitivity reaction due to ASA
Gastrointestinal disorders	*Frequent*	Gastro-duodenal ulcer/perforations, upper gastrointestinal symptoms such as gastralgia, peptic ulcers, small (jejunum and ileum) and large (colon and rectum) intestinal ulcers, perforation or gastrointestinal bleeding, sometimes fatal, oesophagitis, oesophageal ulceration, perforation, erosive gastritis, erosive duodenitis, colitis, (these reactions may or may not be associated with haemorrhage, and may occur at any dose of ASA and in patients with or without warning symptoms or a previous history of serious gastrointestinal events), nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease, gastritis, acute pancreatitis in the context of a hypersensitivity reaction due to ASA
Hepatobiliary disorders	*Frequency unknown*	Elevation of hepatic enzymes, liver injury, mainly hepatocellular, chronic hepatitis
Skin and subcutaneous tissue disorders	*Frequency unknown*	Bullous reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis; fixed eruption
Renal and urinary disorders	*Frequency unknown*	Renal failure, acute renal impairment (especially in patients with existing renal impairment, heart decompensation, nephritic syndrome, or concomitant treatment with diuretics)
General disorders and administrative site conditions	*Frequency unknown*	Oedema

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 (Medsafety 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:
There is no information concerning overdosage with CLOPIDOGREL ASPIRIN 75/75 mg PD – the fixed-dose combination tablets, however due to the pharmacological activity of both clopidogrel and ASA individually, overdose may be associated with increased bleeding and subsequent bleeding complications.

Symptoms of the individual active ingredients are as follows:
Clopidogrel:
Overdose following clopidogrel administration may lead to prolonged bleeding time and subsequent bleeding complications.

Acetylsalicylic acid (ASA):
Moderate overdose: dizziness, ringing in the ears, sensation of reduced hearing, headaches, vertigo and gastrointestinal symptoms (nausea, vomiting and gastric pain).

Severe overdose: fever, hyperventilation, ketosis, respiratory alkalosis, metabolic acidosis, coma, cardiovascular collapse, respiratory failure, severe hypoglycaemia, hyperthermia and perspiration, leading to dehydration.
Non-cardiogenic pulmonary oedema can occur with acute and chronic acetylsalicylic acid overdose (see section 4.8).

Management of overdose:
Clopidogrel:
Appropriate therapy should be considered if bleedings are observed. 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.
Further treatment is symptomatic and supportive.

Acetylsalicylic acid (ASA):
If a toxic dose has been ingested, admission to hospital is necessary. With moderate intoxication, an attempt can be made to induce vomiting. Activated charcoal (adsorbent) and sodium sulphate (laxative) are then administered. Alkalising of the urine (250 mmol sodium bicarbonate for 3 hours), while monitoring the urine pH, is indicated. Haemodialysis is the preferred treatment for severe intoxication. Treat other signs of intoxication symptomatically.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Antithrombotic agents, platelet aggregation inhibitors excl. heparin.
ATC code: B01AC30.
Pharmacological classification: A 8.2 Anticoagulants

Mechanism of action
Clopidogrel:
Clopidogrel is a specific and potent inhibitor of platelet aggregation.
Clopidogrel is a promedicine, 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 the 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 medicines, not all patients will have adequate platelet inhibition.

Dose-dependent inhibition of platelet aggregation was noted 2 hours after single oral doses of clopidogrel.

Repeated doses of 75 mg per day produced substantial inhibition of ADP-induced platelet aggregation from the first day; this increased progressively and reached steady state between Day 3 and Day 7. At steady state, the average inhibition level observed with a dose of 75 mg per day was between 40 % and 60 %. Platelet aggregation and bleeding time gradually returned to baseline values, generally within 5 days after treatment was discontinued.

Acetylsalicylic acid (ASA):
Acetylsalicylic acid inhibits platelet aggregation by irreversible inhibition of prostaglandin cyclo-oxygenase and thus inhibits the generation of thromboxane A2, an inducer of platelet aggregation and vasoconstriction. This effect lasts for the life of the platelet.

5.2 Pharmacokinetic properties
CLOPIDOGREL ASPIRIN 75/75 mg PD:
Absorption:
After single and repeated oral doses of 75 mg per day, clopidogrel is rapidly absorbed. Mean peak plasma levels of unchanged clopidogrel (approximately 2,2 - 2,5 ng/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 circulating (inactive) metabolite bind reversibly *in vitro* 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. *In vitro* and *in vivo*, clopidogrel is metabolised according to two main metabolic pathways: one mediated by esterases and leading to hydrolysis into its inactive carboxylic acid derivative (85 % of circulating metabolites), 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. The active metabolite is formed mostly by CYP2C19 with contributions from several other CYP enzymes, including CYP1A2, CYP2B6 and CYP3A4. The active thiol metabolite which has been isolated *in vitro*, binds rapidly and irreversibly to platelet receptors, thus inhibiting platelet aggregation.

Elimination:
Following an oral dose of ^{14}C-labelled clopidogrel in man, approximately 50 % was excreted in the urine and approximately 46 % in the faeces in the 120-hour interval after dosing. 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 (inactive) metabolite was 8 hours after single and repeated administration.

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 whites, 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 micromolar 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 micromolar 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.

Acetylsalicylic acid (ASA):
Absorption:
Following absorption, the ASA in the fixed dose combination tablet is hydrolised to salicylic acid with peak plasma levels of salicylic acid occurring within 1 hour of dosing, such that plasma levels of ASA are essentially undetectable 1,5 - 3 hours after dosing.

Distribution:
ASA is poorly bound to plasma proteins and its apparent volume of distribution is low (10 L). Its metabolite, salicylic acid, is highly bound to plasma proteins, but its binding is concentration dependent (nonlinear). At low concentrations (< 100 microgram/mL), approximately 90 % of salicylic acid is bound to albumin. Salicylic acid is widely distributed to all tissues and fluids in the body, including the central nervous system, breast milk, and foetal tissues.

Biotransformation and elimination:
The ASA in the fixed dose combination tablet is rapidly hydrolised in plasma to salicylic acid, with a half-life of 0,3 - 0,4 hours for ASA doses from 75 - 100 mg. Salicylic acid is primarily conjugated in the liver to form salicyluric acid, a phenolic glucuronide, an acyl glucuronide, and a number of minor metabolites. Salicylic acid in the fixed dose combination tablet has a plasma half-life of approximately 2 hours.
Salicylate metabolism is saturable and total body clearance decreases at higher serum concentrations due to the limited ability of the liver to form both salicyluric acid and phenolic glucuronide. Following toxic doses (10 - 20 g), the plasma half-life may be increased to over 20 hours. At high ASA doses, the elimination of salicylic acid follows zero-order kinetics (i.e. the rate of elimination is constant in relation to plasma concentration), with an apparent half-life of 6 hours or higher.
Renal excretion of unchanged medicine depends upon urinary pH. As urinary pH rises above 6,5, the renal clearance of free salicylate increases from < 5 % - > 80 %. Following therapeutic doses, approximately 10 % is found excreted in the urine as salicylic acid, 75 % as salicyluric acid, 10 % phenolic- and 5 % acyl-glucuronides of salicylic acid.
Based on the pharmacokinetic and metabolic characteristics of both compounds, clinically significant pharmacokinetic interactions are unlikely.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Core tablet:
Castor oil, hydrogenated
Cellulose, microcrystalline
Hydroxypropyl cellulose
Iron oxide yellow
Mannitol
Polyethylene glycol
Silica, colloidal hydrated
Stearic acid

Film coating (Opadry II yellow):
Hypromellose
Iron oxide yellow
Lactose monohydrate
Titanium dioxide
Triacetin

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
2 years

6.4 Special precautions for storage
Store below at or below 25 °C, in a cool, dry place.
Keep blisters in the carton until required for use.

6.5 Nature and contents of container
Alu-Alu blister packed in a printed outer carton.
Pack size: 30.

6.6 Special precautions for disposal
No special requirements.

7. HOLDER OF THE 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)

8. REGISTRATION NUMBER
A58/8.2/0137

9. DATE OF FIRST AUTHORISATION
30 September 2025

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS S3

CLOPIDOGREL ASPIRIN 75/75 mg PD film coated tablets
Clopidogrel and acetylsalicylic acid (ASA) (aspirin)
CLOPIDOGREL ASPIRIN 75/75 mg PD contains sugar – lactose monohydrate 2,80 mg and mannitol 64 mg (sugar alcohol).

Read all of this leaflet carefully before you start taking CLOPIDOGREL ASPIRIN 75/75 mg PD

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- CLOPIDOGREL ASPIRIN 75/75 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 ASPIRIN 75/75 mg PD is and what it is used for
2. What you need to know before you take CLOPIDOGREL ASPIRIN 75/75 mg PD
3. How to take CLOPIDOGREL ASPIRIN 75/75 mg PD
4. Possible side effects
5. How to store CLOPIDOGREL ASPIRIN 75/75 mg PD
6. Contents of the pack and other information

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

CLOPIDOGREL ASPIRIN 75/75 mg PD contains the active substances clopidogrel and acetylsalicylic acid (aspirin), which belongs to a group of medicines called antiplatelet medicines.
Platelets are very small structures in the blood which clump together during blood clotting. By preventing this clumping in some types of blood vessels, antiplatelet medicines reduce the chances of blood clots forming (a process called atherothrombosis).

CLOPIDOGREL ASPIRIN 75/75 mg PD is used to treat adult patients who have suffered with angina (a severe type of chest pain), or who have had a heart attack, by preventing blood clots, forming and reducing the risk of further atherothrombotic events (such as stroke, heart attack, or death).

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

Do not take CLOPIDOGREL ASPIRIN 75/75 mg PD:

- if you are hypersensitive (allergic) to clopidogrel, acetylsalicylic acid (aspirin) or to any of the ingredients of CLOPIDOGREL ASPIRIN 75/75 mg PD (see section 6)
- if you are allergic to other medicines called nonsteroidal anti-inflammatory drugs (NSAIDs) usually used to treat painful and/or inflammatory conditions of muscles and joints
- if you have been diagnosed with mastocytosis (a condition where certain immune cells, called mast cells, build up under the skin and/or in the bones) as taking CLOPIDOGREL ASPIRIN 75/75 mg PD may cause a severe hypersensitivity (allergic) reaction
- if you have a history of gastrointestinal bleeding, gastrointestinal ulcer or gastrointestinal perforation related to previous use of an NSAID
- if you have a medical condition that is currently causing bleeding such as a stomach ulcer, haemophilia or bleeding within the brain or bowel or a history of such a condition
- if you are under the age of 18 years
- if you have a medical condition that includes the combination of asthma, nasal discharge (runny nose) and polyps (a type of growth in the nose)
- if you have a medical condition that is currently causing bleeding such as a stomach ulcer, haemophilia or bleeding within the brain or bowel or a history of such a condition
- if you have heart problems which can cause shortness of breath or ankle swelling (heart failure)
- if you suffer from severe liver disease
- if you suffer from severe kidney disease
- if you suffer from a dysfunction of, or reduction in, blood platelets which increases risk of bleeding and bruising (thrombocytopenia)
- if you are pregnant or breastfeeding your baby.

Warnings and precautions
Take special care with CLOPIDOGREL ASPIRIN 75/75 mg PD:
Inform your doctor or healthcare provider before taking CLOPIDOGREL ASPIRIN 75/75 mg PD if any of the following apply to you, if:

- you develop a medical condition (also known as thrombotic thrombocytopenic purpura or TTP) that includes 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) (see section 4)
- you start retaining fluid (symptoms include swelling of feet, ankles and hands, stiff joints, rapid weight gain over a few days or weeks, unexplained weight fluctuations, when pressed, the skin may hold the indent for a few seconds
- you have had a clot in an artery of your brain (ischaemic stroke) which occurred in the last seven days
- you have a history of asthma or allergic reactions including allergy to any medicine used to treat your disease
- if you have a history of heart problems which can cause shortness of breath or ankle swelling (heart failure) or high blood pressure
- you at risk of bleeding, including:
  - 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 tissues, organs or joints of your body)
  - a recent serious injury
  - a recent surgery (including dental)
  - a planned surgery (including dental) in the next 7 days
  - a planned spinal, epidural anaesthetic or lumbar puncture in the next 7 days
- you have gout
- you drink alcohol, because of the increased risk of bleeding or gastrointestinal injury
- you have a condition known as glucose-6-phosphate dehydrogenase (G6PD) deficiency because of the risk of a particular form of anaemia (low number of red blood cells)
- you have a history of inflammation of the colon which causes abdominal pain or diarrhoea or any other gastrointestinal conditions
- you are taking any other type of medication (see Other medicines with CLOPIDOGREL ASPIRIN 75/75 mg PD)
- you are a CYP2C19 poor metaboliser (you have very little or no function of the CYP2C19 enzyme, used to break down medicines, in your body)
- you are taking water tablets (used to treat high blood pressure and swelling associated with heart failure, renal failure, or liver disease)
- you are hypersensitive (allergic) to other antiplatelet medicines used to prevent clots (such as ticlopidine or prasugrel)
- you have kidney or liver disease.

Before surgery is planned (including dental), inform your doctor and anaesthetist that you are taking CLOPIDOGREL ASPIRIN 75/75 mg PD.

Inform your doctor immediately should you develop any stomach or abdominal pain or bleeding in the stomach or bowels (red stools or black stools) whilst taking CLOPIDOGREL ASPIRIN 75/75 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 or shaving, this is usually of no concern. However, if you are concerned by your bleeding, you should contact your doctor straightaway (see section 4).

Your doctor may order blood tests before or during treatment.

Children and adolescents
CLOPIDOGREL ASPIRIN 75/75 mg PD is not intended for use in children or adolescents younger than 18 years of age. There is a possible association between acetylsalicylic acid (ASA) and Reye's Syndrome when products containing ASA are given to children or adolescents with a viral infection. Reye's Syndrome is a very rare disease which can be fatal.

Other medicines and CLOPIDOGREL ASPIRIN 75/75 mg PD
Always tell your healthcare provider if you are taking any other medicine. (This includes complementary or traditional medicines.)
Some other medicines may influence the use of CLOPIDOGREL ASPIRIN 75/75 mg PD or vice versa.

Inform your doctor if you take any of the following:

- medicine that may increase your risk of bleeding such as:
  - oral anticoagulants, thrombolytics, medicines used to reduce blood clotting
  - aspirin or another nonsteroidal anti-inflammatory medicine usually used to treat painful and/or inflammatory conditions of muscle or joints
  - heparin or any other injectable medicine used to reduce blood clotting
  - ticlopidine or prasugrel or other antiplatelet medicines used to reduce blood clotting
  - a selective serotonin reuptake inhibitor (SSRI) (e.g. fluoxetine or fluvoxamine), medicines usually used to treat depression
  - rifampicin (used to treat severe infections)
- omeprazole, esomeprazole or cimetidine, medicines to treat upset stomach or to prevent gastric reflux (heartburn)
- methotrexate, a medicine used to treat severe joint disease (rheumatoid arthritis) or skin disease (psoriasis)
- probenecid, benzbromarone, or sulfinpyrazone, medicines used to treat gout
- fluconazole, voriconazole, ciprofloxacin or chloramphenicol, medicines to treat bacterial and fungal infections
- moclobemide, a medicine to treat depression
- nicorandil, a medicine to treat cardiac chest pain
- repaglinide, a medicine to treat diabetes
- paclitaxel, a medicine to treat cancer
- metamizole, a medicine to treat pain, muscle spasms and fever
- corticosteroids, used to treat inflammation (such a cortisone, prednisolone, hydrocortisone)
- acetazolamide, a medicine to treat glaucoma
- the varicella vaccine, a medicine to prevent chickenpox or shingles, within 6 weeks of taking CLOPIDOGREL ASPIRIN 75/75 mg PD, or if you have an active chickenpox or shingles infection
- levothyroxine, a medicine to treat low thyroid activity
- valproic acid, valproate and carbamazepine, medicines to treat some forms of epilepsy
- tenofovir, an antiretroviral medicine used in the treatment of human immunodeficiency virus (HIV)
- rosuvastatin (used to lower your cholesterol level)
- opioids: while you are treated with clopidogrel, you should inform your doctor before being prescribed any opioids (used to treat severe pain, e.g. morphine).

Alcohol: The consumption of alcohol may affect how well CLOPIDOGREL ASPIRIN 75/75 mg PD works; it may increase blood loss and stomach irritation. Please ask your doctor for more information. Alcohol should be used with caution if you are taking CLOPIDOGREL ASPIRIN 75/75 mg PD.

You should stop other clopidogrel treatments and talk to your doctor before taking any other aspirin containing medicines while you are taking CLOPIDOGREL ASPIRIN 75/75 mg PD.

CLOPIDOGREL ASPIRIN 75/75 mg PD with food and drink
CLOPIDOGREL ASPIRIN 75/75 mg PD can be taken with or without food.
Alcohol should be used with caution if you are taking CLOPIDOGREL ASPIRIN 75/75 mg PD (see Other medicine with CLOPIDOGREL ASPIRIN 75/75 mg PD).

Pregnancy, breastfeeding and fertility
Pregnancy and breastfeeding:
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 ASPIRIN 75/75 mg PD.

You should not take CLOPIDOGREL ASPIRIN 75/75 mg PD if you are pregnant or breastfeeding your baby (see section 2).

Fertility:
There are no fertility data with clopidogrel/acetylsalicylic acid.

Driving and using machines
CLOPIDOGREL ASPIRIN 75/75 mg PD should not affect your ability to drive or to use machines. It is not always possible to predict to what extent CLOPIDOGREL ASPIRIN 75/75 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 ASPIRIN 75/75 mg PD affects them.

CLOPIDOGREL ASPIRIN 75/75 mg PD contains lactose and castor oil
CLOPIDOGREL ASPIRIN 75/75 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 ASPIRIN 75/75 mg PD.

CLOPIDOGREL ASPIRIN 75/75 mg PD contains hydrogenated castor oil which may cause stomach upset and diarrhoea.

3. How to take CLOPIDOGREL ASPIRIN 75/75 mg PD

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

Adults:
The usual dose is 1 tablet of CLOPIDOGREL ASPIRIN 75/75 mg PD per day to be taken orally with a glass of water, with or without food.

You should take your medicines at the same time each day.
You should take CLOPIDOGREL ASPIRIN 75/75 mg PD for as long as your doctor continues to prescribe it.

Children:
CLOPIDOGREL ASPIRIN 75/75 mg PD is not prescribed for children.

Your doctor will tell you how long your treatment with CLOPIDOGREL ASPIRIN 75/75 mg PD will last. Do not stop treatment early.

If you have the impression that the effect of CLOPIDOGREL ASPIRIN 75/75 mg PD is too strong or too weak, tell your doctor or pharmacist.

If you take more CLOPIDOGREL ASPIRIN 75/75 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.

If you forget to take CLOPIDOGREL ASPIRIN 75/75 mg PD
If you forget to take CLOPIDOGREL ASPIRIN 75/75 mg PD, but remember within 12 hours of your usual time, take your tablet straight away and then take your next tablet at the usual time. If you forget for more than 12 hours, simply take the next single dose at the usual time. Do not take a double dose to make up for forgotten individual doses.

If you stop taking CLOPIDOGREL ASPIRIN 75/75 mg PD
Do not stop the treatment unless your doctor tells you so. Contact your doctor before stopping or restarting your treatment.
If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

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

The most frequent side effect which has been seen with CLOPIDOGREL ASPIRIN 75/75 mg PD is bleeding. Bleeding may occur as bleeding in the stomach or bowels, bruising, haematoma (unusual bleeding or bruising under the skin), nosebleed, blood in the urine. In a small number of cases, bleeding in the eye, inside the head, the lung or the joints has also been reported.

If you experience prolonged bleeding when taking CLOPIDOGREL ASPIRIN 75/75 mg PD:
If you cut or injure yourself, it may take slightly longer than usual for bleeding to stop. This is linked to the way CLOPIDOGREL ASPIRIN 75/75 mg PD works as it prevents the ability of blood clots to form. For minor cuts and injuries e.g. cutting yourself or shaving, this is usually of no concern. However, if you are concerned by your bleeding, you should contact your doctor straight away (see section 2).

If any of the following happens, stop using CLOPIDOGREL ASPIRIN 75/75 mg PD and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing
- rash or itching
- fainting
- if you develop a medical condition known as thrombotic thrombocytopenic purpura (also known as TTP) – the symptoms may include fever, 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) – see section 2
- chest pain that may radiate to the neck or left arm, pallor, sweatiness, nausea, breathlessness, low blood pressure. These symptoms may be signs of heart problems due to an allergy to clopidogrel or aspirin (Kounis syndrome)
- sudden severe headache, seizures with no previous history of seizures, weakness in your arm or leg, nausea or vomiting (severe and continuing), sudden tiredness, difficulty speaking or understanding speech, loss of balance, hand tremors or loss of consciousness. These symptoms may be signs of life-threatening bleeding within your skull
- tightness in the chest, wheezing, coughing or difficulty breathing, fatigue
- blistering, peeling or bleeding on any part of your skin (including your lips, eyes, mouth, nose, genitals, hands or feet) with or without a rash. You may also have flu-like symptoms at the same time, such as fever, chills or aching muscles, rash, facial swelling, enlarged lymph nodes and kidney or liver injury. These may be signs of serious skin disorders such as Stevens-Johnson syndrome, toxic epidermal necrolysis (TEN) and drug reaction with eosinophilia and systemic symptoms (DRESS).

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to CLOPIDOGREL ASPIRIN 75/75 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:

- fever, signs of infection or extreme tiredness. These may be due to rare decrease of some blood cells (agranulocytosis, granulocytopenia)
- signs of liver problems such as yellowing of the skin and/or the eyes (jaundice, liver failure, hepatitis, liver injury)
- hallucinations (seeing and hearing things that are not there), confusion
- shortness of breath, fatigue, swollen legs and rapid heartbeat (symptoms of cardiac failure)
- reduction in the number of your red blood cells (anaemia) – symptoms may include that you feel weak and tired, and looking pale and that you are more susceptible to infections and uncontrolled bleeding (aplastic anaemia)
- bleeding (including nose bleeds) or bruising more easily than normal. Signs of bleeding may include unusually heavy bleeding from cuts and wounds, coughing up blood, blood in the urine, vomiting of blood or vomit that looks like coffee grounds, bloody or black bowel motions, unusually heavy or unexpected menstrual bleeding, bleeding in the eyes
- reduction in your red and white blood cells and blood platelets (aplastic anaemia) – symptoms may include that you feel weak and tired, and that you are more susceptible to infections and uncontrolled bleeding
- a serious skin reaction called acute generalized exanthematous pustulosis (AGEP) – symptoms may include a red, scaly widespread rash with bumps under the skin (including your skin folds, trunk, and upper extremities) and blisters filled with white/yellow fluid accompanied by fever
- inflammation of the pancreas with symptoms such as severe upper abdominal pain, the abdominal pain may radiate to your back, nausea, vomiting, diarrhoea, tenderness when touching your abdomen, fever
- lung problems called non-cardiogenic pulmonary oedema causing a fluid build-up in the lung – symptoms may include dry cough, fever, difficulty breathing when lying down, chest pain, shortness of breath
- a condition where a certain type of white blood cell called eosinophils accumulates in your lungs (eosinophilic pneumonia) – symptoms may include fever, chest pain worsened by deep breathing, shortness of breath, cough and generally feeling unwell
- low blood sugar (hypoglycaemia) – symptoms may include feeling shaky, anxious or nervous, light-headed, dizzy, chills, sweating or clammy skin, fast heartbeat
- insulin autoimmune syndrome a condition which can cause persistent low blood sugar levels
- increase in blood pressure (hypertension)
- decrease in blood pressure (hypotension)
- severe abdominal pain, with or without back pain, worsening of inflammation of the colon (colitis) which causes abdominal pain and diarrhoea
- ulcer perforation (where an ulcer burns through the stomach or duodenal wall, causing severe, sharp abdominal pain)
- inflammation of your blood vessels with symptoms such as fever, headache, tiredness, weight loss, general aches and pains, night sweats, rash or nerve problems such as numbness or weakness
- presence of blood in urine, kidney failure or inflammation of the kidneys – symptoms may include swelling of legs, ankles, feet or face due to fluid retention, reduction in your urine output, shortness of breath, fatigue, confusion
- fever.

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:

- abdominal pain, indigestion, diarrhoea
- bleeding in the digestive tract (mouth to anus)
- bruising
- bleeding at puncture site
- vomiting, nausea, constipation, excessive gas in stomach or intestines, gastritis (inflammation of the stomach lining).

Less frequent side effects:

- eye bleeding, broken blood vessels in the eye, bleeding in the retina
- vertigo (loss of balance, spinning sensation)
- rash, itching, rash of purple spots on the skin caused by internal bleeding from small blood vessels.

The following side effects have been reported but the frequency for them to occur is not known:

- taste disturbances, loss of taste
- hives, eczema, purplish, itchy, flat-topped bumps or lacy, white patches, sometimes with painful sores in the mouth
- arthritis, joint pain, muscle pain
- abnormal urine test results
- enlarged breasts in men
- gout
- hearing loss, ringing in the ears
- oedema – swelling caused by fluid trapped in your body's tissues (mainly in the feet, legs and ankles).

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 or 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.
An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za to ensure safety of the product.
By reporting side effects, you can help provide more information on the safety of CLOPIDOGREL ASPIRIN 75/75 mg PD.

5. How to store CLOPIDOGREL ASPIRIN 75/75 mg PD

Store all medicines out of reach of children.
Store at or below 25 °C, in a cool, dry place.
Keep blisters in carton until required for use.
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 ASPIRIN 75/75 mg PD contains:
The active ingredients are clopidogrel hydrogen sulphate equivalent to clopidogrel 75 mg and and acetylsalicylic acid (ASA) (aspirin) 75 mg.

The other ingredients are:
Tablet core:
Colloidal hydrated silica, hydrogenated castor oil, hydroxypropyl cellulose, iron oxide yellow, mannitol, microcrystalline cellulose, polyethylene glycol, stearic acid.

Film coating (Opadry II yellow):
Hypromellose, iron oxide yellow, lactose monohydrate, titanium dioxide, triacetin.

What CLOPIDOGREL ASPIRIN 75/75 mg PD looks like and contents of the pack
Yellow coloured, oval shaped, film coated tablets debossed with "I" on one side and plain on the other side.

CLOPIDOGREL ASPIRIN 75/75 mg PD tablets are available in:
Alu-Alu blister packs packed in a printed outer carton.
Pack sizes: 30

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
Registration date: 30 September 2025

Registration number
A58/8.2/0137

A6222

PASIËNTINLIGTINGSBLAD

SKEDULERINGSTATUS S3

CLOPIDOGREL ASPIRIN 75/75 mg PD filmbedekte tablet
Klopidogrel en asetielsalisielsuur (ASA) (aspirien)
CLOPIDOGREL ASPIRIN 75/75 mg PD bevat suiker – laktosemonohidraat 2,80 mg en mannitol 64 mg (suikeralkohol).

Lees hierdie hele inligtingsblad deeglik deur, voordat u begin om CLOPIDOGREL ASPIRIN 75/75 mg PD te gebruik

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

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

CLOPIDOGREL ASPIRIN 75/75 mg PD bevat die aktiewe bestanddeel klopidogrel en asetielsalisielsuur (aspirien), wat aan 'n groep medisyne behoort wat antiplaatjie medisyne genoem word.
Plaatjies is baie klein strukture in die bloed, wat saam klomp tydens bloedstolling. Antiplaatjie medisyne verlaag die moontlikheid van bloedklonte om te vorm ('n proses wat aterotrombose genoem word), deur hierdie klompvorming te verhoed in sommige tipe bloedvate.

CLOPIDOGREL ASPIRIN 75/75 mg PD word gebruik om volwasse pasiënte, wie aan angina gely het ('n erge tipe borspyn), of die wie 'n hartaanval gehad het, te behandel, deur die vorming van bloedklonte te voorkom en die risiko vir verdere aterotrombotiese gevalle (soos beroerte, hartaanval, of sterfte), te verlaag.

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

Moet nie CLOPIDOGREL ASPIRIN 75/75 mg PD neem:

- indien u hipersensitief (allergies) is vir klopidogrel, asetielsalisielsuur (aspirien), of vir enige van die bestanddele van CLOPIDOGREL ASPIRIN 75/75 mg PD nie (sien afdeling 6)
- indien u allergies is vir ander medisyne, wat nie-steroïedale anti-inflammatoriese middels (NSAIM) genoem word nie (word gewoonlik gebruik om pynlike en/of inflammatoriese toestande van die spiere of gewrigte, te behandel)
- indien u met mastositose ('n toestand waar sekere immuunselle, wat masselle genoem word, onder die vel en/of die bene opbou), gediagnoseer is nie, aangesien die gebruik van CLOPIDOGREL ASPIRIN 75/75 mg PD 'n erge hipersensitiwiteit (allergiese) reaksie, mag veroorsaak
- indien u 'n geskiedenis van gastro-intestinale bloeding, gastro-intestinale ulkus, of gastro-intestinale perforasie, verwant aan vorige gebruik van 'n NSAIM, het nie
- indien u 'n mediese toestand wat tans bloeding veroorsaak, soos 'n maagseer, hemofilie, of bloeding in die brein of derms, of 'n geskiedenis van 'n soortgelyke toestand, het nie
- indien u jonger as 18 jaar oud is nie
- indien u 'n mediese toestand, wat 'n kombinasie van asma, neusafskeiding (loopneus) en poliepe ('n tipe gewas in die neus) insluit, het nie
- indien u aan hartprobleme, wat asemnood, of enkelswelling mag veroorsaak (hartversaking), ly nie
- indien u aan erge lewersiekte ly nie
- indien u aan erge niersiekte ly nie
- indien u aan 'n wanfunksie, of vermindering van bloedplaatjies, wat die risiko vir bloeding en kneusing (trombositopenie) verhoog, ly nie
- indien u swanger is, of u baba borsvoed nie.

Waarskuwings en voorsorgmaatreëls
Neem spesiale sorg met CLOPIDOGREL ASPIRIN 75/75 mg PD:
Lig u dokter of gesondheidsorgverskaffer in, voordat u CLOPIDOGREL ASPIRIN 75/75 mg PD neem, indien enige van die volgende op u van toepassing is:

- u ontwikkel 'n mediese toestand (ook bekend as trombotiese, trombositopeniese purpura of TTP), wat koors, kneusing onder die vel (wat mag verskyn as rooi, speldpunt kolletjies), saam met, of sonder onverklaarbare, uiterste moegheid, verwarring, vergeling van die vel of oë (geelsug), insluit (sien afdeling 4)
- u begin om vloeistof terug te hou (simptome sluit swelling van die voete, enkels en hande in, stywe gewrigte, vinnige gewigstoename oor 'n tydperk van etlike dae of weke, onverklaarbare gewigsveranderinge, wanneer daar op die vel gedruk word, mag die inkeping in die vel, vir etlike sekondes, hou
- u het 'n klont in 'n arterie van die brein (iskemiese beroerte), wat in die vorige sewe dae gebeur het
- u het 'n geskiedenis van asma, of allergiese reaksies, insluitend allergie teenoor enige medisyne wat gebruik word om u siekte te behandel
- u het 'n geskiedenis van hartprobleme, wat asemnood, of enkelswelling (hartversaking) insluit, of hoë bloeddruk
- u toon 'n risiko vir bloeding, insluitend:
  - 'n mediese toestand wat u 'n risiko maak vir interne bloeding (soos 'n maagseer)
  - 'n bloedversteuring wat u geneig maak tot interne bloeding (bloeding in enige weefsels, organe, of gewrigte van u liggaam)
  - 'n onlangse ernstige besering
  - 'n onlangse operasie (insluitend dentaal)
  - 'n beplande operasie (insluitend dentaal), in die volgende 7 dae
  - 'n beplande spinale, epidurale narkose, of lumbale punksie in die volgende 7 dae
- u jig het
- u alkohol inneem, aangesien dit die risiko vir bloeding, of gastro-intestinale skade, verhoog
- u 'n aan 'n toestand ly wat bekend staan as glukose-6-fosfaatdehidrogenase (G6PD) tekort, weens die risiko vir 'n spesifieke vorm van anemie (lae hoeveelheid rooibloedselle)
- u 'n geskiedenis van inflammasie van die kolon het, wat buikpyn, of diarree, of enige ander gastro-intestinale toestande tot gevolg het
- u enige ander tipe medikasie neem (sien Ander medisyne saam met CLOPIDOGREL ASPIRIN 75/75 mg PD)
- u 'n swak CYP2C19 metaboliseerder is (u het baie min, of geen funksie van die CYP2C19 ensiem, wat medisyne in u liggaam afbreek)
- u watertablette neem (gebruik om hoë bloeddruk en swelling, wat verband hou met hartversaking, nierversaking, of lewersiekte, te behandel)
- u hipersensitief (allergies) is vir ander antiplaatjie medisyne om bloedklonte te voorkom (soos tiklopidien, of prasugrel)
- u nier-, of lewersiekte het.

A6222

Lig u dokter of narkotiseur in dat u CLOPIDOGREL ASPIRIN 75/75 mg PD neem, voor 'n operasie beplan word (insluitend tandheelkundige operasies).

Lig u dokter onmiddellik in, sou u enige maag-, buikpyn, of bloeding in die maag of derms (rooi, of swart stoelgang) ontwikkel, terwyl u CLOPIDOGREL ASPIRIN 75/75 mg PD neem.

Indien u uself sny, of beseer, mag dit langer as gewoonlik neem vir bloeding om te stop. Dit word gekoppel aan hoe u medisyne werk, aangesien dit die moontlikheid vir bloedklonte om te vorm, voorkom. Daar is gewoonlik geen rede tot kommer vir minder ernstige snye en beserings, soos om uself raak te sny terwyl u skeer nie. Indien u egter bekommerd is oor u bloeding, moet u u dokter dadelik raadpleeg (sien afdeling 4).

U dokter mag bloedtoetse voor, of tydens behandeling aanvra.

Kinders en adolessente
CLOPIDOGREL ASPIRIN 75/75 mg PD word nie aanbeveel vir gebruik deur kinders, of adolessente jonger as 18 jaar oud nie. Daar is 'n moontlike verband tussen asetielsalisielsuur (ASA) en Reye se sindroom, wanneer produkte wat ASA bevat, aan kinders, of adolessente met 'n virusinfeksie, gegee word. Reye se sindroom is 'n baie skaars siekte, wat noodlottig mag wees.

Ander medisyne en CLOPIDOGREL ASPIRIN 75/75 mg PD
Vertel altyd u gesondheidsorgverskaffer, indien u enige ander medisyne neem (Dit sluit aanvullende, of tradisionele medisyne in).
Sommige ander medisyne mag die gebruik van CLOPIDOGREL ASPIRIN 75/75 mg PD beïnvloed, of vice versa.

Lig u dokter in, indien u enige van die volgende neem:

- medisyne wat u risiko vir bloeding verhoog, soos:
  - mondelikse teenstolmiddels, trombolitiese medisyne wat gebruik word om bloedstolling te verminder
  - aspirien of 'n ander nie-steroïedale anti-inflammatoriese medisyne, wat gewoonlik gebruik word om pynlike en/of inflammatoriese toestande van spiere of gewrigte, te behandel
  - heparien of enige ander inspuitbare medisyne wat gebruik word om bloedstolling te verminder
  - tiklopidien, of prasugrel, of ander antiplaatjie medisyne wat gebruik word om bloedstolling te verminder
  - 'n selektiewe serotonien heropname inhibitor (SSHI) (bv. fluoksetien, of fluvoksamien), medisyne wat gewoonlik gebruik word om depressie te behandel
  - rifampisien (gebruik om erge infeksies te behandel)
- omeprasool, esomeprasool, of simetidien (medisyne wat gebruik word om 'n ongestelde maag te behandel, of gastriese refluks te verhoed (sooibrand))
- metotreksaat, 'n medisyne wat gebruik word om erge gewrigsiekte te behandel (rumatoïede artritis), of velsiekte (psoriase)
- probenesied bensbromaroon, of sulfienpirasoon (medisyne om jig te behandel)
- flukonasool, vorikonasool, siprofloksasien, of chlooramfenikol (medisyne wat gebruik word om bakteriële en swaminfeksies te behandel
- moklobemied ('n medisyne wat depressie behandel)
- nikorandiel ('n medisyne wat kardiale borspyn behandel)
- repaglinied ('n medisyne wat diabetes behandel)
- paklitaksel ('n medisyne om kanker te behandel)
- metamisool ('n medisyne om pyn, spierspasma en koors te behandel)
- kortikosteroïede, soos kortisoon, prednisoloon, hidrokortisoon (gebruik om inflammasie te behandel)
- asetasoolamied ('n medisyne om gloukoom te behandel)
- die varicella vaksien ('n medisyne wat waterpokkies of gordelroos voorkom, binne 6 weke nadat CLOPIDOGREL ASPIRIN 75/75 mg PD geneem is, of indien u 'n aktiewe waterpokkies of gordelroosinfeksie het
- levotiroksien ('n medisyne om lae skildklieraktiwiteit te behandel)
- valproïensuur, valproaat en karbamasepien (medisyne wat sommige vorme van epilepsie behandel)
- tenofovir ('n antiretrovirale medisyne wat gebruik word vir die behandeling van menslike immuniteitsgebreksvirus (MIV))
- rosuvastatien (gebruik om u cholesterolvlak te verlaag)
- opioïede: terwyl u met klopidogrel behandel word, moet u u dokter inlig, voordat enige opioïede voorgeskryf word (gebruik om erge pyn te behandel, bv. morfien).

Alkohol: Die gebruik van alkohol, mag die werking van CLOPIDOGREL ASPIRIN 75/75 mg PD beïnvloed; dit mag bloedverlies en maagirritasie veroorsaak. Vrae asseblief u dokter vir meer inligting. Alkohol moet versigtig gebruik word, indien u CLOPIDOGREL ASPIRIN 75/75 mg PD neem.

U moet ander klopidogrel behandelings staak en u dokter raadpleeg, voordat u enige ander aspirien-bevattende medisyne neem, terwyl u CLOPIDOGREL ASPIRIN 75/75 mg PD gebruik.

CLOPIDOGREL ASPIRIN 75/75 mg PD saam met kos en drinkgoed
CLOPIDOGREL ASPIRIN 75/75 mg PD kan saam met, of sonder kos geneem word.
Alkohol moet versigtig gebruik word, indien u CLOPIDOGREL ASPIRIN 75/75 mg PD neem (sien Ander medisyne saam met CLOPIDOGREL ASPIRIN 75/75 mg PD).

Swangerskap, borsvoeding en fertiliteit
Swangerskap en borsvoeding:
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 ASPIRIN 75/75 mg PD gebruik.

U moet nie CLOPIDOGREL ASPIRIN 75/75 mg PD neem, indien u swanger is, if u baba borsvoed nie (sien afdeling 2).

Fertiliteit:
Geen data is beskikbaar vir klopidogrel/asetielsalisielsuur en fertiltiteit nie.

Bestuur en hantering van masjiene
CLOPIDOGREL ASPIRIN 75/75 mg PD behoort nie u vermoë om te bestuur, of masjiene te hanteer beïnvloed nie.
Dit is nie altyd moontlik om te voorspel, tot watter mate CLOPIDOGREL ASPIRIN 75/75 mg PD met die daaglikse aktiwiteite van 'n pasiënt sal inmeng nie. Pasiënte moet verseker dat hulle nie by bogenoemde aktiwiteite betrokke raak, totdat hulle bewus is tot watter mate CLOPIDOGREL ASPIRIN 75/75 mg PD hulle aantas nie.

CLOPIDOGREL ASPIRIN 75/75 mg PD bevat laktose en kasterolie
CLOPIDOGREL ASPIRIN 75/75 mg PD bevat laktose. Indien u dokter aangedui het, dat u 'n onverdraagsaamheid teenoor sommige suikers toon, raadpleeg u dokter, voordat u CLOPIDOGREL ASPIRIN 75/75 mg PD neem.

CLOPIDOGREL ASPIRIN 75/75 mg PD bevat gehidrogeneerde kasterolie, wat maagongesteldheid en diarree mag veroorsaak.

3. Hoe om CLOPIDOGREL ASPIRIN 75/75 mg PD te neem

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

Volwassenes:
Die gewone dosis is 1 CLOPIDOGREL ASPIRIN 75/75 mg PD tablet per dag, mondeliks, met 'n glas water, saam met, of sonder kos.

U moet u medisyne op dieselfde tyd elke dag neem.
U moet CLOPIDOGREL ASPIRIN 75/75 mg PD neem vir solank as wat u dokter voortgaan om dit voor te skryf.

Kinders:
CLOPIDOGREL ASPIRIN 75/75 mg PD word nie vir kinders voorgeskryf nie.

U dokter sal u vertel vir hoe lank u behandeling met CLOPIDOGREL ASPIRIN 75/75 mg PD sal duur. Moet nie behandeling vroegtydig staak nie.
Indien u onder die indruk is dat die effek van CLOPIDOGREL ASPIRIN 75/75 mg PD té sterk, of té swak is, vertel u dokter of apteker.

Indien u meer CLOPIDOGREL ASPIRIN 75/75 mg PD neem as wat u moes
In die geval van oordosering, raadpleeg u dokter of apteker. Indien beide nie beskikbaar is nie, kontak die naaste hospitaal, of gifbeheersentrum.

Indien u vergeet om CLOPIDOGREL ASPIRIN 75/75 mg PD te neem
Indien u vergeet om CLOPIDOGREL ASPIRIN 75/75 mg PD te neem, maar binne 12 uur van u geskeduleerde tyd onthou, neem die tablet dadelik en gaan dan voort om die volgende tablet op die gewone tydstip te neem. Indien u vir meer as 12 uur vergeet, neem eenvoudig die volgende dosis op die gewone tyd. Moet nie 'n dubbeldosis neem, om op te maak vir die vergete, individuele doserings nie.

Indien u die gebruik van CLOPIDOGREL ASPIRIN 75/75 mg PD staak
Moet nie behandeling staak, tensy u dokter so aanbeveel nie. Kontak u dokter voordat u behandeling staak, of weer hervat.
Indien u enige verdere vrae het omtrent hierdie medisyne, vra u dokter of apteker.

4. Moontlike newe-effekte

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

Die mees algemene newe-effek wat opgemerk word met CLOPIDOGREL ASPIRIN 75/75 mg PD, is bloeding. Bloeding mag voorkom as bloeding in die maag, of derms, kneusing, hematoom (ongewone bloeding of kneusing onder die vel), neusbloeding, bloed in die urine. In 'n klein hoeveelheid gevalle, is bloeding in die oog, binne-in die kop, die long of die gewrigte ook aangemeld.

Indien u langdurige bloeding met CLOPIDOGREL ASPIRIN 75/75 mg PD gebruik ervaar:
Indien u uself sny of beseer, mag dit effens langer as gewoonlik neem vir bloeding om op te klaar. Dit word gekoppel aan die manier hoe CLOPIDOGREL ASPIRIN 75/75 mg PD werk, aangesien dit die vermoë vir bloedklonte om te vorm, verhoed. Daar is gewoonlik geen rede vir kommer met minder ernstige snye en beserings, bv. waar u uself sny of skeer nie. Indien u egter bekommerd is oor u bloeding, kontak u dokter dadelik (sien afdeling 2).

Indien enige van die volgende gebeur, staak die gebruik van CLOPIDOGREL ASPIRIN 75/75 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 en asemhaling mag bemoeilik
- uitslag of gejeuk
- floute
- indien u enige mediese toestand bekend as trombotiese trombositopeniese purpura (ook bekend as TTP) ontwikkel – die simptome mag koors, kneusing onder die vel, wat verskyn as rooi, speldpunt kolletjies, saam met, of sonder onverklaarbare uiterste moegheid, verwarring, vergeling van die vel of oë (geelsug), insluit – sien afdeling 2
- borspyn wat mag uitstraal na die nek of linkerarm, bleekheid, sweterigheid, naarheid, asemnood, lae bloeddruk. Hierdie simptome mag tekens van 'n hartprobleem, weens 'n allergie teenoor klopidogrel of aspirien, wees (Kounis sindroom)
- skielike, erge hoofpyne, aanvalle met geen vorige geskiedenis daarvan nie, swakheid in u arm of been, naarheid of braking (erg en aanhoudend), skielike moegheid, moeilike spraak, of begrip van spraak, balansverlies, handtremors, of bewussynsverlies. Hierdie simptome mag tekens van 'n lewensgevaarlike bloeding in u skedel wees
- stywe gevoel in die bors, hyging, hoes, of moeilike asemhaling, uitputting
- blaasvorming, afskilfering of bloeding op enige gedeelte van u vel (insluitend lippe, oë, mond, neus, geslagsdele, hande of voete), met, of sonder 'n uitslag. U mag ook griep-soortige simptome, soos koors, koue rillings, of seer spiere, uitslag, gesigswelling, vergrote limfnode en nier- of lewerbeskadiging, terselfdertyd ervaar. Hierdie mag tekens van ernstige velversteurings, soos Stevens-Johnson-sindroom, toksiese epidermale nekrolise (TEN) en geneesmiddelreaksie met eosinofilie en sistemiese simptome (GRESS), wees.

Hierdie is alles baie ernstige newe-effekte. Indien u dit ondervind, kon u 'n ernstige allergiese reaksie teenoor CLOPIDOGREL ASPIRIN 75/75 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:

- koors, tekens van infeksie, of uiterste moegheid. Hierdie mag voorkom weens 'n skaars vermindering van sommige bloedselle (agranulositose, granulositopenie)
- tekens van lewerprobleme, soos vergeling van die vel en/of oë (geelsug, lewerversaking, hepatitis, lewerbeskadiging)
- hallusinasies (sien en hoor dinge wat nie teenwoordig is nie), verwarring
- asemnood, uitputting, geswelde bene en vinnige hartklop (simptome van hartversaking)
- vermindering van u hoeveelheid rooibloedselle (anemie) – simptome mag u moeg en swak laat voel, bleek laat voorkom en u mag meer geneig wees tot infeksies en ongekontroleerde bloeding (aplastiese anemie)
- bloeding (insluitend neusbloeding), of kneus makliker as gewoonlik. Tekens van bloeding mag ongewoon erge bloeding van snye en wonde, bloed wat opgehoes word, bloed in die urine, braking van bloed, of braaksel wat soos koffiekorrels lyk, bloederige, of swart stoelgang, ongewoon erge, of onverwagte menstruele bloeding, bloeding in die oë, insluit
- vermindering van u rooi- en witbloedselle en bloedplaatjies (aplastiese anemie) – simptome mag die volgende insluit: u voel swak en moeg en u is meer vatbaar vir infeksies en ongekontroleerde bloeding
- 'n ernstige velreaksie wat akute algemene ekseemagtige pustulose (AAEP) genoem word – simptome mag 'n rooi, skubberige, wydverspreide uitslag, met swelsels onder die vel (insluitend u velvoue, bolyf en boonste ledemate) en blase wat met wit/geel vloeistof gevul is, gepaardgaande met koors, insluit
- inflammasie van die pankreas, met simptome soos erge, boonste buikpyn (die buikpyn mag uitstraal na u rug), naarheid, braking, diarree, gevoeligheid wanneer u buik aangeraak word, koors
- longprobleme, wat nie-kardiogeniese pulmonêre edeem genoem word en 'n vloeistof-opgaring in die longe veroorsaak – simptome mag 'n droë hoes, koors, moeilike asemhaling, wanneer u lê, borspyn, asemnood, veroorsaak
- 'n toestand waar 'n sekere tipe witbloedsel (eosinofille genoem), in u longe opgaar (eosinofiliese pneumonie) – simptome mag koors, borspyn wat vererger met diep asemhaling, asemnood, hoes en 'n algemene gevoel van ongesteldheid, insluit
- lae bloedsuiker (hipoglisemie) – simptome mag bewerigheid, angstigheid of senuweeagtigheid, lighoofdigheid, duiseligheid, koue rillings, sweet of klammerige vel en vinnige hartklop, insluit
- insulien outo-immuun sindroom ('n toestand wat volgehoue lae bloedsuikervlakke mag veroorsaak)
- verhoging in bloeddruk (hipertensie)
- verlaging in bloeddruk (hipotensie)
- erge buikpyn, met of sonder rugpyn, verergering van koloninflammasie (kolitis), wat buikpyn en diarree veroorsaak
- ulkus perforasie (waar 'n ulkus deur die maag- en dermwand brand en 'n erge, skerp buikpyn veroorsaak)
- inflammasie van u bloedvate, met simptome soos koors, hoofpyn, moegheid, gewigsverlies, algemene pyne en skete, nagsweet, uitslag of senuweeprobleme, soos gevoelloosheid, of swakheid
- teenwoordigheid van bloed in urine, nierversaking of inflammasie van die niere – simptome mag swelling van die bene, enkels, voete of gesig, weens vloeistof retensie, afname in urinering, asemnood, uitputting en verwarring insluit
- koors.

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

Vertel u dokter indien u enige van die volgende opmerk:
Newe-effekte wat dikwels voorkom:

- abdominale pyn, indigestie, diarree
- bloeding in die spysverteringskanaal (mond tot anus)
- kneusing
- bloeding by die punksie plek
- braking, naarheid, hardlywigheid, uitermatige winderigheid in die maag of derms, gastritis ('n inflammasie van die maagwand).

Minder algemene newe-effekte:

- oogbloeding, gebroke bloedvate in die oog, bloeding in die retina
- vertigo (balansverlies, draaisensasie)
- uitslag, gejeuk, uitslag met pers kolletjies op die vel, veroorsaak deur interne bloeding vanuit klein bloedvate.

Die volgende newe-effekte is aangemeld, maar die frekwensie van voorkoms, is onbekend:

- smaaksteurnisse, smaakverlies
- urtikarie, ekseem, perserige, jeukerige, plat swelsels, of kantagtige, wit vlekke in die mond, somtyds met pynlike sere
- artritis, gewrigspyn, spierpyn
- abnormale urientoetsresultate
- vergrote borste by mans
- jig
- gehoorverlies, gelui in die ore
- edeem – swelling veroorsaak deur vloeistof wat vasgevang word in u liggaamsweefsels (hoofsaaklik die voete, bene en enkels).

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 by SAHPRA via die Med Safety toepassing (Medsafety X SAHPRA) en eReporting platform (who-umc.org), wat op SAHPRA se webtuiste gevind kan word, aanmeld.
'n E-pos kan direk aan die maatskappy gestuur word: pharmacovigilance@pharmadynamics.co.za om die veiligheid van die produk te verseker.
U kan help om meer inligting aangaande die veiligheid van CLOPIDOGREL ASPIRIN 75/75 mg PD in te win, deur newe-effekte aan te meld.

5. Hoe om CLOPIDOGREL ASPIRIN 75/75 mg PD te bewaar

Bewaar alle medisyne buite die bereik van kinders.
Bewaar teen of benede 25 °C, in 'n koel, droë, plek.
Hou stulpstroke in die kartonhouer, totdat dit benodig word vir gebruik.
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 rioolstelsels (bv. toilet), weggooi nie.

6. Verpakkingsinhoud en ander inligting

Wat CLOPIDOGREL ASPIRIN 75/75 mg PD bevat:
Die aktiewe bestandele is klopidogrel waterstofsulfaat ekwivalent aan klopidogrel 75 mg, en asetielsalisielsuur (ASA) (aspirien) 75 mg.

Die ander bestanddele is:
Tablet kern:
Geel ysteroksied, gehidrogeneerde kasterolie, gehidreerde kolloïdale silika, hidroksiepropielsellulose, mannitol, mikrokristallyne sellulose, poli-etileenglikool, steariensuur.

Filmbedekking (Opadry II geel):
Geel ysteroksied, hipromellose, laktosemonohidraat, titaandioksied, triasetien.

Hoe CLOPIDOGREL ASPIRIN 75/75 mg PD lyk en die verpakkingsinhoud
Geel-kleurige, ovaalvormige, filmbedekte tablette, gedebosseleer met "I" aan een kant en glad aan die teenoorgestelde kant.

CLOPIDOGREL ASPIRIN 75/75 mg PD tablette is beskikbaar in:
Alu-Alu stulpverpakkings, in 'n gedrukte buitenste kartonhouer.
Verpakkingshoeveelhede: 30

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
Registrasiedatum: 30 September 2025

Registrasienommer
A58/8.2/0137

D034583-00