PIDOGREL® 75 mg

Clopidogrel

1. WHAT IS PIDOGREL 75 mg?

Pharmaceutical form

Pidogrel 75mg is presented in round pink coated tablet; Box of 30 – 60 – 90 tablets.

Pharmacological class

Pharmacotherapeutic group: platelet aggregation inhibitors excl. heparin, ATC Code: B01AC04.

Composition

Each tablet contains:

Clopidogrel (as hydrogenosulfate) ..... 75 mg Excipients: Methylcellulose, lactose, crospovidone, sodium stearyl fumarate, anhydrous colloidal silica, OPADRY II white, POADRY II pink ..... s.q.f. one tablet

2. IN WHICH CASE CAN PIDOGREL 75 mg BE USED?

Pidogrel 75mg is indicated in the prevention of ischemic attacks due to atherothrombosis:

➢ Patients suffering from myocardial infarction (from a few days until less than 35 days), ischemic stroke (from 7 days until less than 6 months) or established peripheral arterial disease.

➢ Patients suffering from acute coronary syndrome :

• Non-ST segment elevation acute coronary syndrome (unstable angina or non-Q-wave myocardial infarction), including patients undergoing a stent placement following percutaneous coronary intervention, in combination with acetylsalicylic acid (ASA).

• ST segment elevation acute myocardial infarction, in combination with ASA in medically treated patients eligible for thrombolytic therapy.

3. WHAT IS NECESSARY TO BE KNOWN BEFORE TAKING PIDOGREL 75 mg?

Contraindications

- Hypersensitivity to any component of the drug;
- Severe hepatic insufficiency.
- Current hemorrhagic lesions like gastrointestinal ulcer or intra-cranial hemorrhage.

Warnings and precautions of use

• Because of hemorrhagic and hematologic risks, a blood count and/or any other appropriate investigation must be rapidly done when we suspect a hemorrhagic accident in Pidogrel 75mg treated patients. Like all the antiplatelet aggregation agents, Pidogrel 75mg must be used with caution in tight hemorragic risk patients due to trauma, surgery or any other reason and in patients simultaneously treated by salicylates, non steroidal anti-inflammatory drugs, heparin, anti-GPIIb/IIIa or with thrombolytic drugs. Concomitant administration of Clopidogrel and Warfarin is not recommended because of the high risk of haemorrhage.

• Unless emergency, we must stop Pidogrel 75mg 7 days before surgery.

• The patient must be informed about the negative effect of Clopidogrel on the hemostasis. Than they must consult the doctor in the case of abnormal bleeding (by its localization or by its duration). The patient must inform the doctor or the dentist about his Clopidogrel treatment before any surgical procedure or any new drug prescription.

• Very rare cases of thrombotic thrombocytopenic purpura (TTP) have been attributed to Clopidogrel use, even after short exposition. TTP impose an emergency treatment including plasmapheresis.

• Because of lack of data about its use in the early days (less than 7 days) after ischemic cerebral attack, Clopidogrel should not be used in this indication.

• We have a limited data about the safety of Clopidogrel in patients with renal or hepatic insufficiency. It should be administered with caution in these patients.

• Experience is limited in patients with moderate hepatic disease who may have bleeding diatheses. Clopidogrel should therefore be used with caution in this population.

• Pidogrel contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Use during pregnancy and breastfeeding

• Pregnancy

As no clinical data on exposure to clopidogrel during pregnancy are available, it is preferable not to use clopidogrel during pregnancy as a precautionary measure.

• Breastfeeding

As a precautionary measure, breast-feeding should not be continued during treatment with clopidogrel.

Effects on the ability to drive or operate on machines

Pidogrel 75mg has no effect on the psychomotor performance and on the ability to drive or to operate on machines.

Drug interactions

- Non steroidal Anti-inflammatory (NSAI): caution is recommended in case of combination with Clopidogrel-NSAI.
- Warfarin, Anti-GPIIb/IIIa, acetylsalicylic Acid (AAS) and Heparin: A pharmacodynamic interaction between Clopidogrel and these drugs is possible, with an increase in the risk of bleeding. Consequently, caution is recommended in case concomitant administration of clopidogrel and one of these products.
- The tolerance of the concomitant administration of Clopidogrel and thrombolytic drugs was not evaluated. This combination is to be effected with caution.
- The pharmacodynamic activity of Clopidogrel did not present significant modification in the event of simultaneous administration of phenobarbital, cimetidine or estrogens.
- The concomitant administration of Clopidogrel did not modify the pharmacokinetic parameters of digoxine and theophylline. The antacids did not have an influence on the absorption of Clopidogrel.
- patients entered into clinical trials with clopidogrel received a variety of concomitant medicinal products including diuretics, beta blockers, ACEI, calcium antagonists, cholesterol lowering agents, coronary vasodilators, antidiabetic agents (including insulin), antiepileptic agents and GPIIb/IIIa antagonists without evidence of clinically significant adverse interactions.

4. HOW TO USE PIDOGREL 75 mg?

Dosage and mode of administration

Adult and old patients:

1 tablet of PIDOGREL 75 mg, once a day, takes in or without meals.

In patients suffering from acute coronary syndrome

• Non-ST segment elevation acute coronary syndrome (unstable angina or non-Q-wave myocardial infarction), clopidogrel treatment should be initiated with a single 300 mg loading dose and then continued at 75 mg once a day (with acetylsalicylic acid (ASA) 75 mg-325 mg daily). Since higher doses of ASA were associated with higher bleeding risk it is recommended that the dose of ASA should not be higher than 100 mg. The optimal duration of treatment has not been formally established. Clinical trial data support use up to 12 months, and the maximum benefit was seen at 3 months.

• ST segment elevation acute myocardial infarction: clopidogrel should be given as a single daily dose of 75 mg initiated with a 300mg loading dose in combination with ASA and with or without thrombolytics. For patients over 75 years of age, clopidogrel should be initiated without a loading dose. Combined therapy should be started as early as possible after symptoms start and continued for at least four weeks. The benefit of the combination of clopidogrel with ASA beyond four weeks has not been studied in this setting.

After the loading dose, Clopidogrel should be given as a single daily dose of 75 mg with or without food.

Children and adolescents:

Tolerance and effectiveness of clopidogrel 75 mg are not proved in less than 18 years old patients.

Renal impairment

Therapeutic experience is limited in patients with renal impairment.

Hepatic impairment

Therapeutic experience is limited in patients with moderate hepatic disease who may have bleeding diatheses.

Overdosage

Overdose following clopidogrel administration may lead to prolonged bleeding time and subsequent bleeding complications. 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.

5. WHAT ARE THE UNDESIRABLE EFFECTS?

Adverse reactions that occurred either during clinical studies or that were spontaneously reported are presented in the table below. Their frequency is defined using the following conventions: common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000). Within each system organ class, adverse drug reactions are presented in order of decreasing seriousness.

- Blood and the lymphatic system disorders:
• Uncommon: Thrombocytopenia, leucopenia, eosinophilia.
• Rare: Neutropenia, including severe Neutropenia.
• Very rare: Thrombotic thrombocytopenic purpura (TTP), aplastic anaemia, pancytopenia, agranulocytosis, severe thrombocytopenia, granulocytopenia, anaemia
- Immune system disorders: Very rare: Serum sickness, anaphylactoid reactions.
- Psychiatric disorders: Very rare: Hallucinations, confusion.
- Nervous system disorders:
• Uncommon: Intracranial bleeding (some cases were reported with fatal outcome), headache, paraesthesia, dizziness.
• Very rare: Taste disturbances.
- Eye disorders: Uncommon: Eye bleeding (conjunctival, ocular, retinal).
- Ear and labyrinth disorders: Rare: Vertigo
- Vascular disorders:
• Common: Haematoma.
• Very rare: Serious haemorrhage, haemorrhage of operative wound, vasculitis, and hypotension.
- Respiratory, thoracic and mediastinal disorders:
• Common: Epistaxis.
• Very rare: Respiratory tract bleeding (haemoptysis, pulmonary haemorrhage), bronchospasm, interstitial pneumonitis
- Gastrointestinal disorders:
• Common: Gastrointestinal haemorrhage, diarrhoea, abdominal pain, dyspepsia.
• Uncommon: Gastric ulcer and duodenal ulcer, gastritis, vomiting, nausea, constipation, flatulence
• Rare: Retroperitoneal haemorrhage.
• Very rare: Gastrointestinal and retroperitoneal haemorrhage with fatal outcome, pancreatitis, colitis (including ulcerative or lymphocytic colitis), stomatitis.
- Hepato-biliary disorders: Very rare: Acute liver failure, hepatitis, abnormal liver function test.
- Skin and subcutaneous tissue disorders:
• Common: Bruising.
• Uncommon: Rash, pruritus, skin bleeding (purpura).
• Very rare: Bullous dermatitis (toxic epidermal necrolysis, Stevens Johnson Syndrome, erythema multiforme), angioedema, rash erythematous, urticaria, eczema, lichen planus.
- Musculoskeletal, connective tissue and bone disorders: Very rare: Musculo-skeletal bleeding (haemarthrosis), arthritis, arthralgia, and myalgia.
- Renal and urinary disorders:
• Uncommon: Haematuria.
• Very rare: Glomerulonephritis, blood creatinine increased.
- General disorders and administration site conditions:
• Common : Bleeding at puncture site
• Very rare: Fever.
- Investigations: Uncommon: Bleeding time prolonged, neutrophil count decreased, platelet count decreased.

6. HOW TO STORE PIDOGREL 75 mg?

Pidogrel 75mg tablet must be stored in the external original packaging.

7. WHAT ARE THE DELIVERY CONDITIONS OF PIDOGREL 75 mg?

List I, under medical prescription.

8. PRESENTATION AND M.A NUMBER

Speciality	Presentation	M.A number
PIDOGREL 75 mg	Box of 30 tablets	923 347 1
PIDOGREL 75 mg	Box of 60 tablets	923 347 2
PIDOGREL 75 mg	Box of 90 tablets	923 347 3

9. DATE OF THE LAST REVISION OF THE LEAFLET : 03/2011

This is a drug

- A drug is a specific product agent.
- A drug is a product acting on your health and its use, contrary to prescriptions may be dangerous for you.
- Strictly respect the doctor's prescription and the instructions of use he has prescribed.
- Follow your pharmacist's kmow this drug ; its indiations and contra-indications.
- Do not discontinue the drug intake by yourself during the prescription period.
- Do not repeat the prescription or increase the dosage without consulting your doctor.

KEEP ANY DRUG OUT OF THE REACH OF CHILDREN.

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