Pedovex®

Clopidogrel Tablets

Composition:

Each tablet contains clopidogrel bisulphate equivalent to clopidogrel 75 mg.

Excipients: Microcrystalline cellulose, mannitol, hydroxypropyl cellulose, polyethylene glycol, croscarmellose sodium, sodium stearyl fumarate, opadry, ferric oxide (red), simethicone emulsion.

Properties:

Clopidogrel is an inhibitor of platelet aggregation, it selectively inhibits the binding of adenosine diphosphate (ADP) to its platelet receptor and the subsequent ADP-mediated activation of the glycoprotein GPIIb/IIIa complex, thereby inhibiting platelet aggregation.

Biotransformation of clopidogrel is necessary to produce inhibition of platelet aggregation, but an active metabolite responsible for the activity of the drug has not been isolated. Clopidogrel also inhibits platelet aggregation induced by agonists other than ADP by blocking the amplification of platelet activation by released ADP.

Clopidogrel acts by irreversibly modifying the platelet ADP receptor. Consequently, platelets exposed to clopidogrel are affected for the remainder of their lifespan, and recovery of normal platelet function occurs at a rate consistent with platelet turnover.

Clopidogrel does not inhibit phosphodiesterase activity.

Clopidogrel is extensively metabolized by the liver.

The elimination half-life of the main circulating metabolite was 8 hours after single and repeated administration.

Indications:

Pedovex is indicated for the prevention of atherothrombotic events in:

- 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 non-ST segment elevation, acute coronary syndrome (unstable angina or non-Q wave myocardial infarction) in combination with acetylsalicylic acid (ASA).

Contraindications:

Pedovex is contraindicated in patients with known hypersensitivity to any of its components, severe liver impairment, acute pathological bleeding such as peptic ulcer or intracranial hemorrhage, breast-feeding.

Precautions:

Clopidogrel should be used in pregnancy only if clearly needed.

It is not known whether this drug is excreted in human milk.

No impairment of driving or psychometric performance.

Interactions with other drugs:

Increased Effect/Toxicity: At high concentrations, clopidogrel may interfere with the metabolism of amlodarone, cisapride, cyclosporine, diltiazem, fluvastatin, irbesartan, losartan, oral hypoglycemics, paclitaxel, phenytoin, quinidine, sildenafil, tamoxifen, torsemide, verapamil, and some NSAID, which may result in toxicity. Clopidogrel and naproxen resulted in an increase of GI occult blood loss. Anticoagulants (warfarin, thrombolytics, Drotrecogin Alfa) or other anti-platelet agents may increase the risk of bleeding. Rifampin may increase the effects of clopidogrel.

Decreased Effect: Atorvastatin may attenuate the effects of clopidogrel. CYP3A4-inhibiting macrolide antibiotics may attenuate the effects of clopidogrel (including clarithromycin, erythromycin, and troleandomycin).

Two studies completed at the end of August 2009, looked into the effect of omeprazole on the blood levels of the active form of clopidogrel. The studies confirmed that omeprazole can reduce the levels of the active form of clopidogrel in the blood and reduce its anti-platelet effects, therefore supporting the conclusion that there is an interaction between clopidogrel and omeprazole and esomeprazole. Accordingly, the concomitant use of clopidogrel and omeprazole or esomeprazole should be discouraged.

Warnings:

Due to the risk of bleeding and haematological undesirable effect, blood cell count determination and/or other appropriate testing should be promptly considered whenever clinical symptoms suggestive of bleeding arise during the course of treatment. As with other anti-platelet agents, clopidogrel should be used with caution in patients who may be at risk of increased bleeding from trauma, surgery, or other pathological conditions and in patients receiving treatment with ASA, non-steroidal anti-inflammatory drugs, heparin, glycoprotein IIb/IIIa inhibitors or thrombolytics. Patients should be followed carefully for any signs of bleeding including occult bleeding especially during the first weeks of treatment and/or after invasive cardiac procedures or surgery.

The concomitant administration of clopidogrel with warfarin is not recommended since it may increase the intensity of bleedings. Thrombotic Thrombocytopenic purpura (TTP) has been reported very rarely following the use of clopidogrel, sometimes after a short exposure. Experience is limited in patients with severe renal impairment. Clopidogrel should be used with caution in these patients population.

- Warn about reduced effectiveness in patients who are poor metabolizers of clopidogrel. Poor metabolizers do not effectively convert clopidogrel to its active form in the body.
- Inform healthcare professionals that tests are available to identify genetic differences in CYT2C19 function.
- Advice healthcare professionals to consider use of other anti-platelet medications or alternative dosing strategies for clopidogrel in patients identified as poor metabolizers.

Dosage and Administration:

Adults and elderly:

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

In patients with non-ST segments 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 ASA 75 mg – 325 mg daily). It is recommended that the dose of ASA should not be higher than 100 mg. Clinical trial data support the use up to 12 months.

Children and adolescents:

Safety and efficacy in subjects below the age of 18 have not been established.

Overdosage:

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

Based on its pharmacology, platelet transfusion may be appropriate to reverse the effects of clopidogrel. After decontamination, treatment is symptomatic and supportive.

Side Effects:

As with all drugs which may affect hemostasis, bleeding is associated with clopidogrel.

Gastrointestinal: Abdominal pain, vomiting, dyspepsia, gastritis, constipation, diarrhea, and nausea.

Cardiovascular: Chest pain, edema, and hypertension.

Central nervous system: Headache, dizziness, depression, fatigue, and general pain.

Dermatologic: Rash, pruritus.

Endocrine and metabolic: Hypercholesterolemia.

Genitourinary: Urinary tract infection.

Hematological: Purpura, epistaxis.

Neuromuscular and skeletal: Arthralgia, back pain.

Respiratory: Dyspnea, rhinitis, bronchitis, cough, upper respiratory infection.

Miscellaneous: Flu-like syndrome.

Consult your Pharmacist or Physician if any side effect is observed.

Pharmaceutical Precautions:

Keep at room temperature (15-30°C).

Do not use beyond the imprinted expiry date or if the product shows any visible signs of deterioration.

Presentations:

Packs of 30 tablets each.

Hospital packs are available.

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THIS IS A MEDICAMENT

- Medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.
- Strictly follow the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.

Keep medicament out of reach of children.

Council of Arab Health Ministers & Union of Arab Pharmacists.

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