Efigrel™

Prasugrel Hydrochloride

Antiplatelet agent

Composition

Efigrel™ 5: Each film coated tablet contains 5.49 mg Prasugrel Hydrochloride INN equivalent to 5 mg prasugrel.

Efigrel™ 10: Each film coated tablet contains 10.98 mg Prasugrel Hydrochloride INN equivalent to 10 mg prasugrel.

Pharmacology

Prasugrel is a thienopyridine derivative which is formulated as a hydrochloride salt. Prasugrel is an inhibitor of platelet activation and aggregation through the irreversible binding of its active metabolite to the $P2Y_{12}$ class of ADP receptors on platelets. Since platelets participate in the initiation and/or evolution of thrombotic complications of atherosclerotic disease, inhibition of platelet function can result in the reduction of the rate of cardiovascular events such as death, myocardial infarction or stroke.

Pharmacokinetics

Prasugrel is a prodrug and is rapidly metabolized to a pharmacologically active metabolite and inactive metabolites. The active metabolite has an elimination half-life of about 7 hours (range 2-15 hours). Healthy subjects, patients with stable atherosclerosis, and patients undergoing PCI show similar pharmacokinetics.

Absorption/Distribution:

Following oral administration, ≥ 79% of the dose is absorbed. The absorption and metabolism are rapid, with peak plasma concentrations (Cmax) of the active metabolite occurring approximately 30 minutes after dosing. The active metabolite is bound about 98% to human serum albumin.

Metabolism/Elimination:

Prasugrel is not detected in plasma following oral administration. It is rapidly hydrolyzed in the intestine to a thiolactone, which is then converted to the active metabolite by a single step, primarily by CYP3A4 and CYP2B6 and to a lesser extent by CYP2C9 and CYP2C19. The active metabolite is further metabolized to two inactive compounds by S-methylation or conjugation with cysteine. Approximately 68% of the prasugrel dose is excreted in the urine and 27% in the feces as inactive metabolites.

Indication & uses

Efigrel™ is indicated to reduce the rate of thrombotic cardiovascular (CV) events (including stent thrombosis) in patients with acute coronary syndrome (ACS) who are to be managed with percutaneous coronary intervention (PCI) as follows:

- Patients with unstable angina (UA) or non-ST-elevation myocardial infarction (NSTEMI).
- Patients with ST-elevation myocardial infarction (STEMI) when managed with primary or delayed PCI.

Dosage & Administration

Prasugrel should be initiated with a single 60 mg loading dose and then continued at 10 mg once a day. Patients taking Prasugrel should also take aspirin (75 mg to 325 mg) daily. Prasugrel may be administered with or without food.

In patients with acute coronary syndrome (ACS) who are managed with PCI, premature discontinuation of any antiplatelet agent, including Prasugrel, could result in an increased risk of thrombosis, myocardial infarction or death due to the patient's underlying disease. A treatment of up to 12 months is recommended, unless the discontinuation of Prasugrel is clinically indicated.

In case of patients weighing ≤ 60 kg or patient's ≥ 75 years old, Prasugrel should be given as a single 60 mg loading dose and then continued at a 5 mg once-daily dose.

Contraindication

Prasugrel should be avoided in case of hypersensitivity to the active substance or to any of the excipients, active pathological bleeding, and history of stroke or transient ischaemic attack (TIA), severe hepatic impairment.

Special warning & precaution

General Risk of Bleeding: Thienopyridines, including Prasugrel, increase the risk of bleeding. Prasugrel should not be used in patients with active bleeding, prior TIA or stroke

Age ≥ 75 years: Because of the risk of bleeding (including fatal bleeding) and uncertain effectiveness in patients ≥ 75 years of age, use of Prasugrel is generally not recommended in these patients, except in high-risk situations (patients with diabetes or history of myocardial infarction) where its effect appears to be greater and its use may be considered.

Propensity to bleed (e.g., recent trauma, recent surgery, recent or recurrent gastrointestinal (GI) bleeding, active peptic ulcer disease, or severe hepatic impairment): Prasugrel should be used with caution.

Coronary Artery Bypass Graft surgery related bleeding: The risk of bleeding is increased in patients receiving Prasugrel who undergo CABG. If possible, Prasugrel should be discontinued at least 7 days prior to CABG. Do not start Prasugrel in patients likely to undergo urgent CABG.

Discontinuation of Prasugrel: Discontinue thienopyridines, including Prasugrel, for active bleeding, elective surgery, stroke, or TIA.

Adverse effect

Bleeding (non-CABG related & CABG related) and Thrombotic thrombocytopenic purpura. Besides this hypertension, headache, back pain, dizziness, cough, bradycardia, rash & peripheral edema etc. may happen.

Drug interaction

Coadministration of prasugrel and warfarin increases the risk of bleeding. Coadministration of Prasugrel and NSAIDs (used chronically) may increase the risk of bleeding.

Prasugrel can be administered with drugs that are inducers or inhibitors of cytochrome P450 enzymes. Prasugrel can be administered with aspirin (75 mg to 325 mg per day), heparin, GPIIb/IIIa inhibitors, statins, digoxin, and drugs that elevate gastric pH, including proton pump inhibitors and H_2 blockers.

Overdosage

Overdose of Prasugrel may lead to prolonged bleeding time and subsequent bleeding complications. No data are available on the reversal of the pharmacological effect of prasugrel; however, if prompt correction of prolonged bleeding time is required, platelet transfusion and/or other blood products may be considered.

Use in pregnancy & lactation

Pregnancy Category B. There are no adequate and well-controlled studies of Prasugrel use in pregnant women. Prasugrel should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus.
It is not known whether Prasugrel is excreted in human milk. Because many drugs are excreted in human milk, prasugrel should be used during nursing only if the potential benefit to the mother justifies the potential risk to the nursing infant.

Pediatric use

Safety and effectiveness in pediatric patients have not been established.

Geriatric Use

The use of Prasugrel in patients ≥75 years of age is generally not recommended because these patients are at greater risk of bleeding, including fatal bleeding, compared to patients <75 years of age. If prescribed, a lower maintenance dose of 5 mg should be used.

Storage

Store in a dry & cool place. Protect from light & moisture. Keep out of the reach of children.

How supplied

Efigrel™ 5: Each box contains 20 tablets in blister pack.
Efigrel™ 10: Each box contains 20 tablets in blister pack.

Manufactured by:

SQUARE
PHARMACEUTICALS LTD.
BANGLADESH

TM - Trade Mark