Brirel®

Ticagrelor BP

Description
Ticagrelor, a cyclopentyltriazolopyrimidine which is a reversible platelet aggregation inhibitor.

Mode of action
Ticagrelor reversibly binds with the platelet $P2Y_{12}$ adenosine diphosphate (ADP) receptor and thereby inhibits signal transduction and platelet aggregation.

Pharmacokinetics
Absorption: Ticagrelor is absorbed quickly from the gut. Absorption of Ticagrelor occurs with a median tmax of 1.5 hour. The mean absolute bioavailability of Ticagrelor is about 36%.
Distribution: The steady state volume of distribution of Ticagrelor is 88 liter. Ticagrelor and the active metabolite are extensively bound to human plasma proteins (>99%).
Metabolism: CYP3A4 is the major enzyme responsible for Ticagrelor metabolism and the formation of its major active metabolite.
Excretion: The primary route of Ticagrelor elimination is hepatic metabolism. The primary route of elimination for the major metabolite of Ticagrelor is most likely to be biliary secretion. The mean $t_{1/2}$ is approximately 7 hours for Ticagrelor and 9 hours for the active metabolite.

Composition
Brirel® 60 mg Tablet: Each film-coated tablet contains Ticagrelor BP 60 mg.
Brirel® 90 mg Tablet: Each film-coated tablet contains Ticagrelor BP 90 mg.

Indications
Acute Coronary Syndrome. Ticagrelor is a $P2Y_{12}$ platelet inhibitor indicated to reduce the rate of thrombotic cardiovascular events in patients with Acute Coronary Syndrome (ACS) (unstable angina, non-ST elevation myocardial infarction, or ST elevated myocardial infarction). Ticagrelor has been shown to reduce the rate of cardiovascular death, myocardial infarction or stroke in ACS patients. In patients treated with PCI, it also reduces the rate of stent thrombosis.

Dosage & administration
Initiate treatment with 180 mg (two 90 mg tablets) oral loading dose. Continue treatment with 90 mg twice daily during the first year after an ACS event. After one year administer 60 mg twice daily.

Contraindications
History of intracranial hemorrhage, active pathological bleeding, severe hepatic impairment and hypersensitivity to the active ingredients.

Side effects
Most common side effects are bleeding & dyspnea. Other side effects are headache, back pain, nausea, dizziness, cough, hypertension, fatigue and atrial fibrillation etc.

Use in pregnancy & lactation
Pregnancy Category C. There are no adequate and well-controlled studies of Ticagrelor use in pregnant women.
Lactation: As it is not known whether Ticagrelor is excreted in human milk. Breastfeeding should be avoided by lactating patients who require therapy.

Precautions
Like other antiplatelet agents, Ticagrelor increases the risk of bleeding.

Drug interactions
Avoid use of strong inhibitors of CYP3A (e.g., ketoconazole, itraconazole, voriconazole, clarithromycin, nefazodone, ritonavir, saquinavir, nelfinavir, indinavir, atazanavir and telithromycin). Use of Ticagrelor with aspirin maintenance doses above 100 mg reduced the effectiveness of Ticagrelor. Ticagrelor will result in higher serum concentrations of simvastatin and lovastatin because these drugs are metabolized by CYP3A.

Over dosage
There is currently no known treatment to reverse the effects of Ticagrelor. Other effects of overdose may include gastrointestinal effects (nausea, vomiting, and diarrhea) or ventricular pauses. Monitor the ECG.

Storage
Keep out of reach of children. Store in a dry place, below 25°C temperature and protected from light.

Packaging
Brirel® 60 mg Tablet: Each carton contains 14X1 tablets in Alu-Alu blister pack.
Brirel® 90 mg Tablet: Each carton contains 10X1 tablets in Alu-PVC blister pack.