Belinta

Ticagrelor INN

Composition
Belinta 90 Tablet: Each film coated tablet contains Ticagrelor INN 90 mg.
Belinta 60 Tablet : Each film coated tablet contains Ticagrelor INN 60 mg.

Pharmacology
Ticagrelor reversibly blocks ADP-receptors which are the subtype P2Y12 and thus prevents the signal transduction and platelet aggregation. Eventually thrombus formation is inhibited and thus thrombotic cardiovascular events are prevented.

Indications and usage
Ticagrelor is indicated

- to reduce the risk of Cardiovascular (CV) death, Myocardial Infarction (MI), and stroke in patients with Acute Coronary Syndrome (ACS) or a history of MI. For at least the first 12 months following ACS, it is superior to clopidogrel. Ticagrelor also reduces the risk of stent thrombosis in patients who have been stented for treatment of ACS.
- to reduce the risk of first MI or stroke in patients with Coronary Artery Disease (CAD) at high risk for such events. While use is not limited to this setting, the efficacy of Ticagrelor was established in a population with Type-2 Diabetes Mellitus (T2DM).
- to reduce then risk of stroke in patients with acute ischemic stroke (NIH Stroke Scale Score ≤ 5) or high-risk transient attack (TIA).

Dosage & Administration
Acute Coronary Syndrome or a History of Myocardial Infarction:
Initiate treatment with a 180 mg loading dose of Ticagrelor. Administer 90 mg of Ticagrelor twice daily during the first year after an ACS event. After one year, administer 60 mg of Ticagrelor twice daily. Use Ticagrelor with a daily maintenance dose of Aspirin of 75 mg to 100 mg.

Coronary Artery Disease but No Prior Stroke or Myocardial Infarction
Administer 60 mg of Ticagrelor twice daily. Use Ticagrelor with a daily maintenance dose of Aspirin of 75 mg to 100 mg.

Acute Ischemic Stroke or Transient Ischemic Attack (TIA)
Initiate treatment with a 180 mg loading dose of Ticagrelor and then continue with 90 mg twice daily up to 30 days. The treatment effect accrued early in the course of therapy. Use Ticagrelor with loading dose of Aspirin (300 to 325 mg) and daily maintenance dose of Aspirin of 75 to 100 mg.

Patient with Renal Impairment : No dosage adjustment is needed for the patient with renal impairment .
Patient with Hepatic Impairment : Ticagrelor has not been studied in patient with moderate hepatic impairment. Risks and benefits should be considered for the treatment with Ticagrelor. In patients with severe hepatic impairment, Ticagrelor is contraindicated.
Pediatric Patient : No such data has been established yet on the safety and effectiveness of Ticagrelor on pediatric patient.

Side Effects
The most common side effects are shortness of breath (dyspnea), various types of bleeding such as; hematoma, nose bleed, gastrointestinal, subcutaneous or dermal bleeding. Ticagrelor should be administered with caution or avoided in patients with advanced sinoauricular disease. Allergic skin reactions such as rash and itching have been observed in less than 1% of patients.

Contraindication
History of Intracranial Hemorrhage : Ticagrelor is contraindicated in patients with history of intracranial hemorrhage (ICH) because of a high risk of recurrent ICH in this population.
Active Bleeding : Ticagrelor is contraindicated in patients with active pathological bleeding such as peptic ulcer or intracranial hemorrhage.
Hypersensitivity : Ticagrelor is contraindicated in patient with hypersensitivity to Ticagrelor or any component of the product.

Warnings and Precautions
General Risk of Bleeding : Drugs that inhibit platelet function including Ticagrelor increase the risk of bleeding. If possible, manage bleeding without discontinuing Ticagrelor . Stopping Ticagrelor increases the risk of subsequent cardiovascular events.
Dyspnea : Dyspnea was reported more frequently with Ticagrelor than with control agents in clinical trials. Dyspnea resulting from Ticagrelor is self-limiting.
Severe Hepatic Impairment : Ticagrelor is contraindicated in patients with severe hepatic impairment because it may reduce synthesis of coagulation proteins. Severe hepatic impairment is likely to increase serum concentration of Ticagrelor.

Specific Population
Pregnancy: Ticagrelor is pregnancy category C drug. There is no adequate and well-controlled clinical data available on the exposure of Ticagrelor. But animal study showed that it caused structural abnormalities. Pregnant women should therefore use Ticagrelor with caution, unless the potential benefit outweighs the potential risk of the fetus.

Lactation : It is not known whether Ticagrelor or its active metabolites are excreted in human milk.

Smoking : Habitual smoking, increases population mean clearance of Ticagrelor by approximately 22% when compared to non-smokers. No dose adjustment is necessary for Ticagrelor, based on smoking status.

Drug Interaction
Inhibitors of the liver enzyme CYP3A4, such as Ketoconazole, Itraconazole, Voriconazole, Clarithromycin, Nefazodone, Ritonavir, Saquinavir, Nelfinavir, Atazanavir and Telithromycin increase blood plasma levels and consequently can lead to bleeding and other adverse effects. Simvastatin and Lovastatin drugs (over 40 mg) that are metabolized by CYP3A4, increase plasma levels and side effects if combined with Ticagrelor.
CYP3A4 inductors, for example Rifampicin, Dexamethasone, Phenytoin, Carbamazepine, Phenobarbital and possibly St. John's wort, can reduce the effectiveness of Ticagrelor .The drug also inhibits P-glycoprotein (P-gp), leading to increases plasma levels of Digoxin, Cyclosporin and other P-gp substrates. Ticagrelor and AR-C124910XX levels are not significantly influenced by P-gp inhibitors.
Other anti-platelet drug such as Aspirin may reduce the effectiveness of Ticagrelor when Ticagrelor is used with maintenance dose of Aspirin above 100 mg.
Digoxin inhibits the P-glycoprotein transporter, so level of Digoxin should be monitored during the initiation of or any change in Ticagrelor.

Overdosage
Bleeding is the expected pharmacological effect of overdosing, which can be corrected with appropriate measures. Other effects of overdose may include nausea, vomiting, diarrhea, ventricular pause etc. which can be corrected accordingly.

Storage
Do not store above 30^0 C. Protect from light. Keep out of the reach of children.

Packaging
Belinta 90 Tablet : Each box contains 2 X 10's tablets in blister pack.
Belinta 60 Tablet : Each box contains 2 X 10's tablets in blister pack.

Manufactured by
ZISKA PHARMA
Ziska Pharmaceuticals Ltd.
Kaliakoir, Gazipur, Bangladesh
Version: 01