Ticalog™ 90

Ticagrelor INN 90 mg

Composition
Each film coated tablet contains Ticagrelor INN 90 mg.

Pharmacology
Ticagrelor is a selective adenosine diphosphate (ADP) receptor antagonist acting on the P2Y12 ADP-receptor that can prevent ADP-mediated platelet activation and aggregation. Ticagrelor reversibly interacts with the platelet P2Y12 ADP-receptor. Ticagrelor does not interact with the ADP binding site itself, but interacts with platelet P2Y12 ADP-receptor to prevent signal transduction. Thus it prevents platelet activation & aggregation.

Pharmacokinetics
Absorption: Absorption of Ticagrelor occurs with a median t_{max} of 1.5 hour (range 1.0-4.0). The formation of major circulating metabolite of Ticagrelor occurs with a median t_{max} of 2.5 hours (range 1.5-5.0).
Distribution: Ticagrelor and the active metabolite are extensively bound to human plasma proteins (> 99%).
Metabolism: CYP3A4 is the major enzyme responsible for Ticagrelor metabolism & the formation of its major active metabolite. Ticagrelor & its major active metabolite are weak P-glycoprotein substrates & inhibitors.
Excretion: The primary route of ticagrelor elimination is hepatic metabolism. When radiolabeled Ticagrelor is administered, the mean recovery of radioactivity is approximately 84% (58% in feces & 26% in urine).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 & 9 hours for the active metabolite.

Indication
Ticalog™ is indicated for the prevention of atherothrombotic events in adult patients with Acute Coronary Syndromes (unstable angina, non ST elevation Myocardial Infarction [NSTEMI] or ST elevation Myocardial Infarction [STEMI]); including patients managed medically, and those who are managed with percutaneous coronary intervention (PCI) or coronary artery by-pass grafting (CABG).

Dosage & Administration
Ticalog™ treatment should be initiated with a single 180 mg loading dose (two tablets of 90 mg) and then continued at 90 mg twice daily. Patients taking **Ticalog**™ should also take aspirin daily, unless specifically contraindicated. Following an initial dose of aspirin (usually 325 mg), **Ticalog**™ should be used with a maintenance dose of aspirin of 75-100 mg. Maintenance dose of Aspirin above 100 mg decreased the efficacy of **Ticalog**™. So, maintenance dose of aspirin above 100 mg should be avoided.
A patient who misses a dose of **Ticalog**™ should take only one 90 mg tablet (the next dose) at its scheduled time. Patients treated with Clopidogrel can be directly switched to **Ticalog**™ if needed. Switching from prasugrel to ticagrelor has not been investigated.
Treatment is recommended for up to 12 months unless discontinuation of **Ticalog**™ is clinically indicated. **Ticalog**™ can be administered with or without food.

Contraindication
Ticagrelor is contraindicated in case of –
- hypersensitivity to Ticagrelor or to any of the excipients
- active pathological bleeding (peptic ulcer)
- history of intracranial haemorrhage
- moderate to severe hepatic impairment
- co-administration of Ticagrelor with strong CYP3A4 inhibitors (e.g., ketoconazole, clarithromycin, nefazodone, ritonavir, and atazanavir)

Side effects
Dyspnea, bleeding, headache, cough, dizziness, nausea, atrial fibrillation, hypertension, non-cardiac chest pain, diarrhea, back pain, hypotension, fatigue, chest pain.

Drug Interaction
CYP3A inhibitors: Avoid use of strong inhibitors of CYP3A (e.g., ketoconazole, itraconazole, voriconazole, clarithromycin, nefazodone, ritonavir, saquinavir, nelfinavir, indinavir, atazanavir and telithromycin).
CYP3A inducers: Avoid use with potent inducers of CYP3A (e.g., rifampin, dexamethasone, phenytoin, carbamazepine and phenobarbital).
Aspirin: Use of Ticagrelor with aspirin maintenance doses above 100 mg reduced the effectiveness of Ticagrelor.
Simvastatin, Lovastatin: Ticagrelor will result in higher serum concentrations of simvastatin and lovastatin because these drugs are metabolized by CYP3A4. Avoid simvastatin and lovastatin doses greater than 40 mg.
Digoxin: Because of inhibition of the P-glycoprotein transporter, monitor digoxin levels with initiation of or any change in ticagrelor therapy.
Other Concomitant Therapy: Ticagrelor can be administered with unfractionated or low-molecular-weight heparin, GPIIb/IIIa inhibitors, proton pump inhibitors, beta-blockers, angiotensin converting enzyme inhibitors, and angiotensin receptor blockers.

Overdose
There is currently no known antidote to reverse the effects of Ticagrelor and it is not expected to be dialysable. Treatment of overdose should follow local standard medical practice. The expected effect of excessive ticagrelor dosing is prolonged duration of bleeding risk associated with platelet inhibition. If bleeding occurs appropriate supportive measures should be taken.

Use in Pregnancy and Lactation
Pregnancy: Pregnancy category C. There are no or limited amount of data from the use of Ticagrelor in pregnant women. Ticagrelor is not recommended during pregnancy.
Nursing mothers: Available pharmacodynamic/toxicological data in animals have shown excretion of Ticagrelor and its active metabolites in milk. A risk to newborns/infants cannot be excluded. A decision must be made whether to discontinue breastfeeding or to discontinue/abstain from ticagrelor therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the women.

Paediatric Use: The safety and efficacy of ticagrelor in children below the age of 18 in the approved adult indication has not been established.

Storage
Protect from light & moisture. Store below 25^0 C. Keep out of reach of children.

How Supplied
Each box contains 10's tablets in Alu-PVDC blister pack.

Manufactured by
SQUARE
PHARMACEUTICALS LTD.
BANGLADESH