TICAGRELOR **Brilinta®** **PLATELET AGGREGATION INHIBITOR**

Pharmacology
Ticagelor is an orally active, selective and reversibly bound inhibitor of platelet adenosine diphosphate, which prevents platelet activation and aggregation. Inhibition of platelet activity is directly related the amount of drug and active metabolite in the plasma. The onset of action is rapid – approximately 41% of the platelets are inhibited 30 minutes after dosing and the maximal effect is seen approximately 2 hours post dosing. Since Ticagrelor binds reversibly, as its concentration in the plasma declines, platelet function returns.

Pharmacokinetics
Ticagrelor demonstrates linear pharmacokinetics. Absorption is rapid following oral administration and is independent of the presence of ingested food. It is highly bound to plasma proteins. Ticagrelor is metabolized by the liver (CYP3A) and produces an active metabolite. Both Ticagrelor and its metabolite are finally excreted via the feces and urine in an inactive state.

Indications
Ticagrelor is indicated as secondary prevention of atherthrombotic events in acute myocardial infarctions (STEMI) through its anti-platelet activity.

Contraindications
Patients who are hypersensitive to this medication or any ingredient in its formulation (see non-medicinal ingredients under “Supplied”)
Patients with active pathologic bleeding such as peptic ulcer or intracranial hemorrhage.
Patients with a history of intracranial hemorrhage.
Patients with moderate to severe hepatic impairment
Patients who are taking strong CYP3A inhibitors ((e.g., ketoconazole, clarithromycin, nefazodone, ritonavir, and atazanavir).
Patients with concurrent use of NSAIDs (low dose ASA is not a contraindication), oral anti-coagulents or fibrinlolytics.
Current use of Ticagrelor, Clopidogrel, Prasugrel, Ticlopidine, Dipyridamole, or Cilostazol.

Patients with Sick Sinus Syndrome, 2nd or 3rd degree AV Blocks or bradycardic related syncope and are not protected by a pacemaker. LBBB or ventricular paced rhythms.
Female patients that are pregnant or nursing or of child bearing potential (< 1 year post menopause.

Additionally for the purpose of the **ATLANTIC trial**:
A time of ≥ 90 minutes from diagnostic ECG to arrival at the receiving Cath lab
SBP < 80 mmHg

Planned surgery in the next 30 days
Patient on dialysis
Thrombocytopenia
Anemia
Active Cancer
Study site staff or employee of AstraZeneca
Participation in another clinical trial in the last 30 days

Warnings
As with other anti-platelet agents, Ticagrelor should be used with caution in patients who may be at risk of increased bleeding from additional medications, surgery or other pathological condition(s).

Precautions
Respiratory – in the PLATO study 13.8% of the patients receiving Ticagrelor reported complaints of dyspnea (including, exertional, at rest, nocturnal and paroxysmal nocturnal dyspnea)

Renal – No dose adjustment is required for patients with renal impairment. A clinical study of Ticagrelor in renal dialysis has not been conducted (but is contraindicated for the ATLANTIC trial).

Geriatrics – Increasing age is not associated with an increased risk of bleeding.

Drug Interactions
Cytochrome P450 (CYP) 3A4/5 are the major enzymes responsible for the metabolism of Ticagrelor and the formation of the active metabolite. Current use of strong inhibitors of CYP3A is a contraindication to Ticagrelor administration. Co-administration with heparin, enoxaparin and ASA does not have any effect on Ticagrelor or its metabolite's plasma levels.
Results from the PLATO trial indicate better outcomes when combined low dose (<300mg a day) ASA.

Pregnancy and Lactation
The safety of Ticagrelor during pregnancy has not been established and therefore is not recommended in pregnancy, nursing or women of child bearing potential.

Pediatrics
The safety and efficacy has not been established in patients < 18 years of age and is therefore not recommended in this population.

Adverse Effects
The common adverse events reported by patients during the PLATO trial were:
Dyspnea, Headache and Epistaxis
The serious adverse events observed in the PLATO trial were:
Cardiac Failure, Non-cardiac chest pain, Dyspnea and Ventricular pauses.

Overdose and Treatment
The expected effect of excessive Ticagrelor ingestion is prolonged duration of the risk of bleeding from platelet inhibition. There is no antidote and supportive care should be provided.

Dosage
The recommended loading dose of Ticagrelor is 180 mg (2 x 90 mg tablets) followed by 90 mg twice a day (regardless of patient weight). It may be taken with or without food.

For the purpose of the **ATLANTIC trial**, a dose of 180 mg may be administered depending on the arm of the study the patient is randomized into.

Supplied
Store typically at room temperature (range 2-30°C). Blister packs or bottles. Each round, yellow, biconvex, film-coated tablet, engraved with a “90” over a “T” on one side

For the purpose of the **ATLANTIC trial**, the medication may be provided in a different physical format and packaging.

Non-Medicinal ingredients
Dibasic calcium phosphate, ferric oxide yellow, hydroxypropyl cellulose, hypromellose, magnesium stearate, mannitol, polyethylene glycol 400, sodium starch glycolate, talc and titanium dioxide.