

For the use of Cardiologist and Internal Medicine Specialties only

## Abbreviated Prescribing Information

# Ticagrelor Tablets

## Brilinta<sup>®</sup> 90 mg and 60mg

### 1. QUALITATIVE AND QUANTITATIVE COMPOSITION

#### 1.1 General description

Ticagrelor film-coated tablets contain ticagrelor as active substance which is a new chemical class of antiplatelet agents called cyclopentyltriazolepyrimidines.

#### 1.2 Qualitative and quantitative composition

Film-coated tablets 90 mg: each tablet contains 90 mg of ticagrelor.

Film-coated tablets 60 mg: each tablet contains 60 mg of ticagrelor.

### 2. PHARMACEUTICAL FORM

Film-coated tablets

90 mg - Round, biconvex, yellow, film-coated tablets. The tablets are marked with “90” above “T” on one side and plain on the other.

60 mg - Round, biconvex, pink, film coated tablets. The tablets are marked with “60” above “T” on one side and plain on the other.

### 3. CLINICAL PARTICULARS

#### 3.1 Therapeutic indications

##### Ticagrelor 90 mg

Ticagrelor 90 mg is indicated for the prevention of thrombotic events (cardiovascular death, myocardial infarction and stroke) in patients with Acute Coronary Syndromes ([ACS] 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 bypass grafting (CABG).

##### Ticagrelor 60 mg

Ticagrelor 60 mg is indicated for the prevention of thrombotic events (cardiovascular death, myocardial infarction and stroke) in patients with a history of myocardial infarction (MI occurred at least one year ago) and a high risk of developing a thrombotic event.

### **3.2 Posology and method of administration**

#### **Ticagrelor 90 mg**

In patients with Acute Coronary Syndromes, ticagrelor treatment should be initiated with a single 180 mg loading dose (two tablets of 90 mg) and then continued at 90 mg twice daily. Treatment is recommended for at least 12 months unless discontinuation of ticagrelor is clinically indicated. After one year, patients initiated on 90 mg twice daily may continue treatment with 60 mg twice daily without interruption.

Patients taking ticagrelor should also take a daily low maintenance dose of acetylsalicylic acid (ASA) of 75-150 mg, unless specifically contraindicated. An initial loading dose of ASA is recommended for patients with ACS.

#### **Ticagrelor 60 mg**

In patients with a history of Myocardial Infarction (MI occurred at least one year ago) no loading dose of ticagrelor is required and the recommended dose is 60 mg twice daily. Long-term treatment is recommended unless discontinuation of ticagrelor is clinically indicated.

Patients taking ticagrelor should also take a daily low maintenance dose of acetylsalicylic acid (ASA) of 75-150 mg, unless specifically contraindicated.

Patients may start treatment with ticagrelor 60 mg twice daily, regardless of their previous antiplatelet regimen, and irrespective if there has been a lapse in therapy or not.

Patients should discontinue their current antiplatelet therapy before initiating ticagrelor with low dose ASA at the next scheduled dose.

Patients initiated on ticagrelor 90 mg twice daily at the time of the acute event, after one year, may continue treatment with 60 mg twice daily without interruption.

#### **Ticagrelor 60 and 90 mg**

Lapses in therapy should be avoided. A patient who misses a dose of ticagrelor should take their next dose at its scheduled time.

Premature discontinuation with any antiplatelet therapy, including ticagrelor, could result in an increased risk of cardiovascular (CV) death or MI due to the patient's underlying disease. Physicians who desire to switch patients to ticagrelor should administer the first dose of ticagrelor 24 hours following the last dose of the other antiplatelet medication.

### **Special Populations**

#### **Paediatric patients:**

Safety and efficacy in children below the age of 18 have not been established.

**Elderly patients:**

No dose adjustment is required.

**Patients with renal impairment:**

No dose adjustment is necessary for patients with renal impairment. No information is available concerning treatment of patients on renal dialysis.

**Patients with hepatic impairment:**

No dose adjustment is necessary for patients with mild hepatic impairment. Ticagrelor has not been studied in patients with severe hepatic impairment and there is limited information on treatment of patients with moderate hepatic impairment.

**Administration**

For oral use. Ticagrelor can be taken with or without food.

**Ticagrelor film-coated tablets only:**

For patients who are unable to swallow the tablet(s) whole, ticagrelor tablets can be crushed to a fine powder and mixed in half a glass of water and drunk immediately. The glass should be rinsed with a further half glass of water and the contents drunk. The mixture can also be administered via a nasogastric tube (CH8 or greater). It is important to flush the nasogastric tube through with water after administration of the mixture.

**3.3 Contraindications**

Hypersensitivity to ticagrelor or any of the excipients. Listed in section 4.1

Active pathological bleeding

History of intracranial haemorrhage

Severe hepatic impairment

**3.4 Special warnings and special precautions for use****Bleeding risk**

As with other antiplatelet agents, the use of ticagrelor in patients at known increased risk for bleeding should be balanced against the benefit in terms of prevention of thrombotic events. If clinically indicated, ticagrelor should be used with caution in the following patient groups:

- Patients with a propensity to bleed (e.g. due to recent trauma, recent surgery, active or recent gastrointestinal bleeding, or moderate hepatic impairment). The use of ticagrelor is contraindicated in patients with active pathological bleeding and in those with history of intracranial haemorrhage, and severe hepatic impairment.
- Patients with concomitant administration of medicinal products that may increase the risk of bleeding (e.g. non-steroidal anti-inflammatory drugs (NSAIDs), oral anticoagulants and/or fibrinolytics within 24 hours of ticagrelor dosing).

Platelet transfusion did not reverse the antiplatelet effect of ticagrelor in healthy volunteers and is unlikely to be of clinical benefit in patients with bleeding. Since co-administration of ticagrelor with desmopressin did not decrease template bleeding time, desmopressin is unlikely to be effective in managing clinical bleeding events.

Antifibrinolytic therapy (aminocaproic acid or tranexamic acid) and/or recombinant factor VIIa therapy may augment haemostasis. Ticagrelor may be resumed after the cause of bleeding has been identified and controlled.

## **Surgery**

- If a patient requires surgery, physicians should consider each patient's clinical profile as well as the benefits and risks of continued antiplatelet therapy when determining when discontinuation of ticagrelor treatment should occur.
- Because of the reversible binding of ticagrelor, restoration of platelet aggregation occurs faster with ticagrelor compared to clopidogrel. In the OFFSET study, mean Inhibition of Platelet Aggregation (IPA) for ticagrelor at 72 hours post-dose was comparable to mean IPA for clopidogrel at 120 hours post-dose. The more rapid offset of effect may predict a reduced risk of bleeding complications, eg, in settings where antiplatelet therapy must be temporarily discontinued due to surgery or trauma.
- In PLATO patients undergoing CABG, ticagrelor had a similar rate of major bleeds compared to clopidogrel at all days after stopping therapy except Day 1 where ticagrelor had a higher rate of major bleeding.
- If a patient is to undergo elective surgery and antiplatelet effect is not desired, ticagrelor should be discontinued 5 days prior to surgery.

## **Patients with prior ischaemic stroke**

ACS patients with prior ischaemic stroke can be treated with ticagrelor for up to 12 months (PLATO study).

In PEGASUS, patients with history of MI with prior ischaemic stroke were not included. Therefore, in the absence of data, caution is advised for treatment beyond one year

## **Patients with moderate hepatic impairment**

There is limited experience with ticagrelor in patients with moderate hepatic impairment, therefore, caution is advised in these patients. Use of ticagrelor is contraindicated in patients with severe hepatic impairment.

## **Patients at risk for bradycardic events**

Due to observations of mostly asymptomatic ventricular pauses in an earlier clinical study, patients with an increased risk of bradycardic events (e.g. patients without a pacemaker who have sick sinus syndrome, 2<sup>nd</sup> or 3<sup>rd</sup> degree AV block or bradycardic-related syncope) were excluded from the main studies evaluating the safety and efficacy of ticagrelor. Therefore, due to the limited clinical experience in

these patients, caution is advised.

### **Dyspnoea**

Dyspnoea, usually mild to moderate in intensity and often resolving without need for treatment discontinuation, is reported in patients treated with ticagrelor. The mechanism has not yet been elucidated. If a patient reports new, prolonged or worsened dyspnoea this should be investigated fully and if not tolerated, treatment with ticagrelor should be stopped.

### **Other**

Based on a relationship observed in PLATO between maintenance ASA dose and relative efficacy of ticagrelor compared to clopidogrel, co-administration of ticagrelor and high maintenance dose ASA (>300 mg) is not recommended.

Co-administration of ticagrelor with strong CYP3A4 inhibitors (eg, ketoconazole, clarithromycin, nefazodone, ritonavir, and atazanavir) should be avoided as co- administration may lead to a substantial increase in exposure to ticagrelor.

### **Discontinuations**

Patients who require discontinuation of ticagrelor are at increased risk for cardiac events. Premature discontinuation of treatment should be avoided. If ticagrelor must be temporarily stopped due to an adverse event(s), it should be re-initiated as soon as possible when the benefits outweigh the risks of the adverse event or when the adverse event has come to resolution.

The most commonly reported adverse drug reactions in patients treated with ticagrelor were bleeding and dyspnoea.

## **4. PHARMACEUTICAL PARTICULARS**

### **4.1 List of excipients**

#### **90 mg film-coated tablet**

##### **Core:**

Mannitol (E421), Dibasic calcium phosphate, Magnesium stearate, Sodium starch glycolate Hydroxypropyl cellulose.

##### **Coating**

Talc, Titanium dioxide (E171), Ferric oxide yellow (E172), Polyethylene glycol 400, Hypromellose

#### **60 mg film -coated- tablet**

##### **Core**

Mannitol (E421), Dibasic calcium phosphate, Magnesium stearate, Sodium starch glycolate Hydroxypropyl cellulose.

##### **Coating**

Titanium dioxide (E171), Ferric oxide black (E172), Ferric oxide red (E172), Polyethylene glycol 400, Hypromellose

**4.2 Incompatibilities** : Not applicable

**4.3 Shelf-life**: Outer carton

**4.4 Special precautions for storage**

Do not store above 30°C

**4.5 Pack size** : Please refer to outer carton for pack size.

Brilinta is registered trademark in India

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**For more information refer full prescribing information V7 dated May 2016**