Hitica™

(Ticagrelor)

Highnoon

COMPOSITION
Hitica 60mg Tablet:
Each film-coated tablet contains:
Ticagrelor 60mg
Hitica 90mg Tablet:
Each film-coated tablet contains:
Ticagrelor 90mg

DESCRIPTION
Hitica contains ticagrelor, a cyclopentyl triazolopyrimidine, inhibitor of platelet activation and aggregation mediated by the P2Y12 ADP-receptor.

MECHANISM OF ACTION
Ticagrelor and its major metabolite reversibly interact with the platelet P2Y12 ADP-receptor to prevent signal transduction and platelet activation. Ticagrelor and its active metabolite are approximately equipotent.

PHARMACOKINETICS
Ticagrelor is rapidly absorbed from gastrointestinal tract with a mean absolute bioavailability of about 36%. Both Ticagrelor and its active metabolite are extensively bound to plasma proteins (>99.7%) the systemic exposure to the active metabolite is about 30 to 40% of the exposure to the ticagrelor. The steady state volume of distribution for Ticagrelor is about 88 liters and mean half-life is about 7 hours for ticagrelor and 8.5 to 9 hours for the active metabolite. Ticagrelor is mainly metabolized in the liver by cytochrome p450 isoenzymes CYP3A4 and to a lesser extent CYP3A5. The primary route of elimination of major metabolite of ticagrelor is likely to be biliary secretion. Recovery of ticagrelor and its major metabolite in the urine was less than 1% of the dose.

INDICATIONS AND USAGE
It is indicated in the following conditions:
- to reduce the risk of instead of rate of cardiovascular death, myocardial infarction, and stroke in patients with acute coronary syndrome (ACS) or a history of myocardial infarction (MI). For at least the first 12 months following ACS, it is superior to clopidogrel.
- to reduce the risk of instead of rate of stent thrombosis in patients who have been stented for treatment of ACS.
- to reduce the risk of a first MI or stroke in patients with coronary artery disease (CAD) at high risk for such events. Ticagrelor use is not limited to this only, its efficacy extends to population with type 2 diabetes mellitus as well.
- to reduce the risk of stroke in patients with acute ischemic stroke (NIH Stroke Scale score ≤5) or high-risk transient ischemic attack (TIA).

DOSAGE AND ADMINISTRATION
- In the management of ACS or history of MI, initiate treatment with a 180mg loading dose. Administer 90mg twice daily during the first year after an ACS event. After one year administer 60mg twice daily.
- In the management of CAD, administer 60mg twice daily.
- Use Ticagrelor with a daily maintenance dose of aspirin of 75-100 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 for up to 30 days. The treatment effect accrued early in the course of therapy.
  - o Use Ticagrelor with a loading dose of aspirin (300 to 325 mg) and a daily maintenance dose of aspirin of 75 to 100mg.
- In coronary artery disease but no prior stroke or MI; Administer 60mg of Ticagrelor twice daily. For all patients with ACS, initiate treatment with 180mg loading dose. Administer 90mg twice daily during the first year after an ACS event. After one year administer 60mg twice daily.
- Use Ticagrelor with a daily maintenance dose of Aspirin 75 to100mg.
- Do not administer it (Ticagrelor) with another oral P2Y12 platelet inhibitor. A patient who misses a dose of (Ticagrelor) should take one tablet (their next dose) at its scheduled time. For Patients who can not swallow tablet, its tablet can be crushed, mixed with water and drunk. The mixture can also be administered via a nasogastric tube.

CONTRAINDICATIONS
- It is contraindicated in patients with a history of intracranial hemorrhage (ICH) because of a high risk of recurrent ICH in this population.
- It is contraindicated in patients with active pathological bleeding such as peptic ulcer or intracranial hemorrhage.
- It is also contraindicated in patients with hypersensitivity (e.g., angioedema) to ticagrelor or any component of the product.
- Severe hepatic impairment.
- Co-administration of ticagrelor with strong CYP3A4 inhibitors (e.g. ketoconazole, clarithromycin, nefazodone, ritonavir and atazanavir), as co-administration may lead to a substantial increase in exposure to ticagrelor.

ADVERSE REACTIONS
The reported adverse events are bleeding, dyspnea, dizziness, headache, syncope, nausea, diarrhea, constipation, vertigo, intracranial hemorrhage, intrapericardial with cardiac tamponade, hypotension, hypovolemic shock, intraocular with permanent vision loss, decrease in haemoglobin, fall in hematocrit, serum uric acid levels increased, gout, increase in serum creatinine levels, thrombotic cytopenic purpura, hypersensitivity reactions including angioedema, pruritus, rash, increase risk of bradycardia, central sleep apnea and Cheyne-Stokes respiration.

DRUG INTERACTIONS
- Strong CYP3A inhibitors substantially increase ticagrelor exposure and so increase the risk of dyspnea, bleeding, and other adverse events. Avoid the use of strong inhibitors of CYP3A (e.g., ketoconazole, itraconazole, voriconazole, clarithromycin, nefazodone, ritonavir, saquinavir, nelfinavir, indinavir, atazanavir, and telithromycin).
- Strong CYP3A inducers substantially reduce ticagrelor exposure and so decrease the efficacy of ticagrelor. Avoid use with strong inducers of CYP3A (e.g., rifampin, phenytoin, carbamazepine, phenobarbital).
- Use of Ticagrelor with aspirin maintenance doses above 100mg reduced the effectiveness of Ticagrelor.
- As with other oral P2Y12 inhibitors, co-administration of opioid agonists delays and reduces the absorption of ticagrelor and its active metabolite, presumably, because of slowed gastric emptying. Consider the use of a parenteral anti-platelet agent in acute coronary syndrome patients requiring co-administration of morphine or other opioid agonists.
- Ticagrelor increases serum concentrations of simvastatin and lovastatin because these drugs are metabolized by CYP3A4. Avoid simvastatin and lovastatin doses greater than 40mg.
- Ticagrelor inhibits the P-glycoprotein transporter; monitor digoxin levels with initiation of or change in ticagrelor therapy.

WARNINGS AND PRECAUTIONS
- 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.
- The use of Ticagrelor with maintenance doses of aspirin above 100mg decreases the effectiveness of Ticagrelor. Therefore, after the initial loading dose of aspirin, use Ticagrelor with a maintenance dose of aspirin of 75-100 mg.
- If a patient develops new, prolonged, or worsened dyspnea that is determined to be related to Ticagrelor, no specific treatment is required; continue Ticagrelor without interruption if possible. In the case of intolerable dyspnea requiring discontinuation of Ticagrelor, consider prescribing another antiplatelet agent.
- Discontinuation of Ticagrelor will increase the risk of myocardial infarction, stroke, and death. If Ticagrelor must be temporarily discontinued (e.g., to treat bleeding or for significant surgery), restart it as soon as possible. When possible, interrupt therapy with Ticagrelor for five days prior to surgery that has a major risk of bleeding. Resume Ticagrelor as soon as haemostasis is achieved.
- Ticagrelor can cause ventricular pauses. Bradyarrhythmias including AV block have been reported. Patients with a history of sick sinus syndrome, 2nd or 3rd degree AV block or bradycardia-related syncope not protected by a pacemaker may be at increased risk of developing bradyarrhythmias with ticagrelor.
- Avoid the use of Ticagrelor in patients with severe hepatic impairment. Severe hepatic impairment is likely to increase the serum concentration of ticagrelor.
- Ticagrelor should not be given to patients with hematopoietic disorders such as neutropenia or thrombocytopenia, hemorrhagic diathesis, or other hemorrhagic disorders associated with prolong bleeding time, or condition with increased risk of bleeding such as peptic ulcer disease, intracranial hemorrhage, or moderate to severe liver dysfunction.
- It should be used with caution in patients with a history of asthma or chronic obstructive pulmonary disease.
- Central sleep apnea (CSA) including Cheyne-Stokes respiration (CSR) has been reported in patients taking ticagrelor, including recurrence or worsening of CSA/CSR following rechallenge. If central sleep apnea is suspected, consider further clinical assessment.
- Renal function should be monitored one month after starting treatment and thereafter at appropriate intervals.
- It should be used with caution in patients with a history of hyperuricemia or gouty arthritis.
- Ticagrelor has been reported to cause false negative results in platelet functional tests (to include, but may not be limited to, the heparin-induced platelet aggregation (HIPA) assay) for patients with Heparin Induced Thrombocytopenia (HIT). Based on the mechanism of Ticagrelor interference, Ticagrelor is not expected to impact PF4 antibody testing for HIT.

USE IN SPECIFIC POPULATIONS
Pregnancy
There are no adequate and well-controlled studies of Ticagrelor use in pregnant women.
Ticagrelor should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers
It is not known whether ticagrelor or its active metabolites are excreted in human milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from ticagrelor, a decision should be made whether to discontinue nursing or to discontinue ticagrelor.
Pediatric Use
The safety and effectiveness of ticagrelor in pediatric patients have not been established.
Geriatric Use
No overall differences in safety or effectiveness were observed between elderly and younger patients.
Hepatic Impairment
Ticagrelor is metabolized by the liver and impaired hepatic function can increase risks for bleeding and other adverse events. Avoid use of ticagrelor in patients with severe hepatic impairment. There is limited experience with ticagrelor in patients with moderate hepatic impairment; consider the risks and benefits of treatment, noting the probable increase in exposure to ticagrelor. No dosage adjustment is needed in patients with mild hepatic impairment.
Renal Impairment
No dosage adjustment is needed in patients with renal impairment. Patients receiving dialysis have not been studied.

OVER DOSAGE
There is currently no known treatment to reverse the effects of Ticagrelor, and ticagrelor is not expected to be dialyzable. Treatment of overdose should follow the local standard medical practice. Bleeding is the expected pharmacologic effect of overdosing. If bleeding occurs, appropriate supportive measures should be taken.

DOSAGE AND INSTRUCTIONS
To be sold and used on the prescription of a registered medical practitioner only. Keep out of reach of children. Do not store above 30°C. Keep in a dry place. Protect from light.

PRESENTATION
Hitica 60mg Tablets: Alu. Alu. Blister Pack of 1 x 10's.
Hitica 90mg Tablets: Alu. Alu. Blister Pack of 1 x 10's.

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(ٹیکاگریلور)

خوراک و ہدایات:

صرف مستند ڈاکٹر کے نسخہ کے مطابق ہی دوا فروخت اور استعمال کی جائے۔

بچوں کی پہنچ سے دور رکھیں۔ 30°C سے زیادہ درجہ حرارت پر نہ رکھیں۔

خشک جگہ پر رکھیں۔ روشنی سے بچائیں۔

Manufactured by
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