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Virata™
(Ticagrelor)

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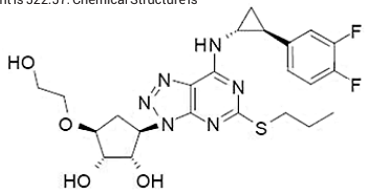
COMPOSITION:
Virata Tablet 60 mg:
Each film coated tablet contains:
Ticagrelor ..... 60 mg.

Product Specs.: Innovator

Virata Tablet 90 mg:
Each film coated tablet contains:
Ticagrelor ..... 90 mg.

Product Specs.: Innovator

DESCRIPTION:
VIRATA contains ticagrelor, a cyclopentyltriazolopyrimidine, inhibitor of platelet activation and aggregation mediated by the $P2Y_{12}$ ADP-receptor. The empirical formula of ticagrelor is $C_{23}H_{28}F_2N_6O_4S$ and its molecular weight is 522.57. Chemical Structure is



CLINICAL PHARMACOLOGY:
Mechanism of Action: Ticagrelor and its major metabolite reversibly interact with the platelet $P2Y_{12}$ ADP-receptor to prevent signal transduction and platelet activation. Ticagrelor and its active metabolite are approximately equipotent.
Pharmacokinetics:
Absorption: VIRATA can be taken with or without food. Absorption of ticagrelor occurs with a median t_{max} of 1.5 h (range 1.0–4.0). The formation of the major circulating metabolite AR-C124910XX (active) from ticagrelor occurs with a median t_{max} of 2.5 h (range 1.5-5.0). The mean absolute bioavailability of ticagrelor is about 36% (range 30%-42%). Ingestion of a high-fat meal had no effect on ticagrelor C_{max}, but result in a 21% increase in AUC. The C_{max} of its major metabolite is decreased by 22% with no change in AUC. VIRATA as crushed tablets mixed in water, given orally or administered through a nasogastric tube into the stomach, is bioequivalent to whole tablets.
Distribution: The steady state volume of distribution of ticagrelor is 88 L. Ticagrelor and the active metabolite are extensively bound to human plasma proteins (>99%).
Metabolism: CYP3A4 is the major enzyme responsible for ticagrelor metabolism and the formation of its major active metabolite. Ticagrelor and its major active metabolite are weak P-glycoprotein substrates and inhibitors. The systemic exposure to the active metabolite is approximately 30-40% of the exposure of ticagrelor.
Elimination: 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 and 9 hours for the active metabolite.
Pharmacokinetics in Special Populations: The effects of age, gender, ethnicity, renal impairment and mild hepatic impairment on the pharmacokinetics of ticagrelor are modest and do not require dose adjustment.
Effects of Other Drugs on Ticagrelor: CYP3A4 is the major enzyme responsible for ticagrelor metabolism and the formation of its major active metabolite. Strong CYP3A inhibitors (e.g., ketoconazole, itraconazole, and clarithromycin) substantially increase ticagrelor exposure. Moderate CYP3A inhibitors have lesser effects (e.g., diltiazem). CYP3A inducers (e.g., rifampin) substantially reduce ticagrelor blood levels. P-gp inhibitors (e.g., cyclosporine) increase ticagrelor exposure.
Effects of Ticagrelor on Other Drugs: Ticagrelor and AR-C124910XX were shown to have no inhibitory effect on human CYP1A2, CYP2C19, and CYP2E1 activity. For specific in vivo effects on the pharmacokinetics of simvastatin, atorvastatin, ethinyl estradiol, levonorgesterol, tolbutamide, digoxin and cyclosporine.

INDICATIONS AND USAGE:
VIRATA is indicated to reduce the 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. VIRATA also reduces the rate of stent thrombosis in patients who have been stented for treatment of ACS.

DOSAGE AND ADMINISTRATION:
In the management of ACS, initiate VIRATA treatment with a 180 mg loading dose. Administer 90 mg twice daily during the first year after an ACS event. After one year administer 60 mg twice daily.
- Do not administer VIRATA with another oral $P2Y_{12}$ platelet inhibitor.
- Use VIRATA with a daily maintenance dose of aspirin of 75-100 mg.
- A patient who misses a dose of VIRATA should take one tablet (their next dose) at its scheduled time.

Administration: For patients who are unable to swallow tablets whole, VIRATA tablets can be crushed, mixed with water and drunk.
Dose Modification Recommendations: No dose adjustment required for age, gender, ethnicity, renal impairment and mild hepatic impairment.

CONTRAINDICATIONS:
- VIRATA is contraindicated in patients with a history of intracranial hemorrhage (ICH) because of a high risk of recurrent ICH in this population
- VIRATA is contraindicated in patients with active pathological bleeding such as peptic ulcer or intracranial hemorrhage.
- VIRATA is contraindicated in patients with hypersensitivity (e.g., angioedema) to ticagrelor or any component of the product.

WARNINGS AND PRECAUTIONS:
- Drugs that inhibit platelet function including VIRATA increase the risk of bleeding. If possible, manage bleeding without discontinuing VIRATA. Stopping VIRATA increases the risk of subsequent cardiovascular events.
- After the initial loading dose of aspirin, use VIRATA with a maintenance dose of aspirin of 75-100 mg.
- Usually mild to moderate in intensity and often resolve during continued treatment. If a patient develops new, prolonged, or worsened dyspnea that is determined to be related to VIRATA, no specific treatment is required; continue VIRATA without interruption if possible. In the case of intolerable dyspnea requiring discontinuation of VIRATA, consider prescribing another antiplatelet agent.
- Discontinuation of VIRATA will increase the risk of myocardial infarction, stroke, and death. If VIRATA must be temporarily discontinued (e.g., to treat bleeding or for significant surgery), restart it as soon as possible. When possible, interrupt therapy with VIRATA for five days prior to surgery that has a major risk of bleeding. Resume VIRATA as soon as hemostasis is achieved.
- Avoid use of VIRATA in patients with severe hepatic impairment. Severe hepatic impairment is likely to increase serum concentration of ticagrelor.

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DRUG INTERACTIONS:
Strong CYP3A Inhibitors: Strong CYP3A inhibitors substantially increase ticagrelor exposure and so increase the risk of dyspnea, bleeding, and other adverse events. Avoid use of strong inhibitors of CYP3A (e.g., ketoconazole, itraconazole, voriconazole, clarithromycin, nefazodone, ritonavir, saquinavir, nelfinavir, indinavir, atazanavir and telithromycin).
Strong CYP3A Inducers: 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 and phenobarbital).
Aspirin: Use of VIRATA with aspirin maintenance doses above 100 mg reduced the effectiveness of VIRATA.
Simvastatin, Lovastatin: VIRATA increases serum concentrations of simvastatin and lovastatin because these drugs are metabolized by CYP3A4. Avoid simvastatin and lovastatin doses greater than 40 mg.
Digoxin: VIRATA inhibits the P-glycoprotein transporter; monitor digoxin levels with initiation of or change in VIRATA therapy.

USE IN SPECIFIC POPULATIONS:
Pregnancy.
Pregnancy Category C: VIRATA 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 VIRATA, a decision should be made whether to discontinue nursing or to discontinue VIRATA.
Pediatric Use: The safety and effectiveness of VIRATA in pediatric patients have not been established.
Geriatric Use: There is no overall differences in safety or effectiveness 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 VIRATA in patients with severe hepatic impairment. There is limited experience with VIRATA 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.

ADVERSE REACTIONS:
The most common adverse reactions associated with the use of ticagrelor bleeding and dyspnea. Use of ticagrelor may be associated with bradycardia, Syncope, pre-syncope and loss of consciousness.
Less commonly: Dizziness, Nausea, Diarrhea.
Lab abnormalities: Serum Uric Acid and Serum Creatinine may increase with the use of Virata.

OVERDOSAGE:
There is currently no known treatment to reverse the effects of VIRATA, and ticagrelor is not expected to be dialyzable. Treatment of overdose should follow local standard medical practice. Bleeding is the expected pharmacologic effect of overdosing. If bleeding occurs, appropriate supportive measures should be taken.
Other effects of overdose may include gastrointestinal effects (nausea, vomiting, and diarrhea) or ventricular pauses. Monitor the ECG.

INSTRUCTIONS:
- Store below 30°C.
- Protect from heat, sunlight & moisture.
- Keep out of the reach of children.
- To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:

Virata Tablet 60 mg	:	Pack of 1 x 10 tablets.
Virata Tablet 90 mg	:	Pack of 2 x 10 tablets.

ہدایات:
۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گرمی، دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف ڈاکٹر کے نسخہ پر فروخت کریں۔

FOR FURTHER INFORMATION PLEASE CONTACT:

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