BILINTA

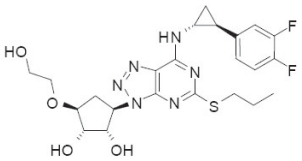
(T i c a g r e l o r)

بلنٹا

Tablets 90mg

DESCRIPTION

BILINTA contains ticagrelor, a cyclopentyltriazolopyrimidine, inhibitor of platelet activation and aggregation mediated by the P2Y12 ADP-receptor. Chemically it is (1S,2S,3R,5S)-3-[7-[[(1R,2S)-2-(3,4-difluorophenyl)cyclopropyl]amino}-5¬(propylthio)-3H-[1,2,3]-triazolo[4,5-d]pyrimi-din-3-yl]-5-(2-hydroxyethoxy)cyclopentane-1,2-diol. The empirical formula of ticagrelor is $C_{23}H_{28}F_2N_6O_4S$ and its molecular weight is 522.57. The chemical structure of ticagrelor is:



QUALITATIVE & QUANTITATIVE COMPOSITION

BILINTA (Ticagrelor) is available for oral administration as:
1. **BILINTA** TABLETS 90MG
Each film coated tablet contains
Ticagrelor……..90mg

CLINICAL PHARMACOLOGY

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.

Pharmacodynamics

Onset of action

In patients with stable coronary artery disease (CAD) on ASA, ticagrelor demonstrates a rapid onset of pharmacological effect as demonstrated by a mean inhibition of platelet aggregation (IPA) for ticagrelor at 0.5 hours after 180 mg loading dose of about 41%, with the maximum IPA effect of 89% by 2-4 hours post dose, and maintained between 2-8 hours. 90% of patients had final extent IPA >70% by 2 hours post dose.

Offset of action

If a CABG procedure is planned, ticagrelor bleeding risk is increased compared to clopidogrel when discontinued within less than 96 hours prior to procedure.

Switching data

Switching from clopidogrel 75 mg to ticagrelor 90 mg twice daily results in an absolute IPA increase of 26.4% and switching from ticagrelor to clopidogrel results in an absolute IPA decrease of 24.5%. Patients can be switched from clopidogrel to ticagrelor without any interruption of antiplatelet effect

Pharmacokinetics

Absorption

BILINTA can be taken with or without food. Absorption of ticagrelor occurs with a median tmax 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 tmax 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 Cmax, but resulted in a 21% increase in AUC. The Cmax of its major metabolite was decreased by 22% with no change in AUC.

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). Recoveries of ticagrelor and the active metabolite in urine were both less than 1% of the dose. The primary route of elimination for the major metabolite of ticagrelor is most likely to be biliary secretion. The mean t1/2 is approximately 7 hours for ticagrelor and 9 hours for the active metabolite.

SPECIAL POPULATION

Age

Higher exposures to ticagrelor (approximately 25% for both Cmax and AUC) and the active metabolite were observed in elderly (≥75years) ACS patients compared to younger patients by the population pharmacokinetic analysis. These differences are not considered clinically significant.

Paediatric

Ticagrelor has not been evaluated in a paediatric population.

Gender

Higher exposures to ticagrelor and the active metabolite were observed in women compared to men. These differences are not considered clinically significant.

Renal Impairment

Exposure to ticagrelor was approximately 20% lower and exposure to the active metabolite was approximately 17% higher in patients with severe renal impairment (creatinine clearance <30 ml/min) compared to subjects with normal renal function.

Hepatic Impairment

Cmax and AUC for ticagrelor were 12% and 23% higher in patients with mild hepatic impairment compared to matched healthy subjects, respectively, however, the IPA effect of ticagrelor was similar between the two groups. No dose adjustment is needed for patients with mild hepatic impairment. Ticagrelor has not been studied in patients with severe hepatic impairment and there is no pharmacokinetic information in patients with moderate hepatic impairment.

Ethnicity

Patients of Asian descent have a 39% higher mean bioavailability compared to Caucasian patients. Patients self-identified as black had an 18% lower bioavailability of ticagrelor compared to Caucasian patients.

THERAPEUTIC INDICATIONS

BILINTA 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.

BILINTA also reduces the rate of stent thrombosis in patients who have been stented for treatment of ACS.

DOSAGE & ADMINISTRATION

- In the management of ACS, initiate **BILINTA** 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 **BILINTA** with another oral P2Y12 platelet inhibitor.
- Use **BILINTA** with a daily maintenance dose of aspirin of 75-100 mg.
- A patient who misses a dose of **BILINTA** should take one tablet (their next dose) at its scheduled time.
- For patients who are unable to swallow tablets whole, **BILINTA** tablets can be crushed, mixed with water and drunk. The mixture can also be administered via a nasogastric tube.

ADVERSE EFFECTS

The following adverse reactions are observed:
- Bleeding
- Dyspnea

CONTRAINDICATIONS

History of Intracranial Hemorrhage

BILINTA is contraindicated in patients with a history of intracranial hemorrhage (ICH) because of a high risk of recurrent ICH in this population.

Active Bleeding

BILINTA is contraindicated in patients with active pathological bleeding such as peptic ulcer or intracranial hemorrhage.

Hypersensitivity

BILINTA is contraindicated in patients with hypersensitivity (e.g., angioedema) to ticagrelor or any component of the product.

OVERDOSAGE

There is currently no known treatment to reverse the effects of **BILINTA**, 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.

WARNINGS AND PRECAUTIONS

General Risk of Bleeding

Drugs that inhibit platelet function including **BILINTA** increase the risk of bleeding. If possible, manage bleeding without discontinuing **BILINTA**. Stopping **BILINTA** increases the risk of subsequent cardiovascular events.

Concomitant Aspirin Maintenance Dose

Study show that with the use of **BILINTA** with maintenance doses of aspirin above 100 mg decreased the effectiveness of **BILINTA**. Therefore, after the initial loading dose of aspirin, use **BILINTA** with a maintenance dose of aspirin of 75 - 100 mg.

Dyspnea

If a patient develops new, prolonged, or worsened dyspnea that is determined to be related to **BILINTA**, no specific treatment is required; continue **BILINTA** without interruption if possible. In the case of intolerable dyspnea requiring discontinuation of **BILINTA**, consider prescribing another antiplatelet agent.

Discontinuation of BILINTA
Discontinuation of **BILINTA** will increase the risk of myocardial infarction, stroke, and death. If **BILINTA** must be temporarily discontinued (e.g., to treat bleeding or for significant surgery), restart it as soon as possible. When possible, interrupt therapy with **BILINTA** for five days prior to surgery that has a major risk of bleeding. Resume **BILINTA** as soon as hemostasis is achieved.

Severe Hepatic Impairment
Avoid use of **BILINTA** in patients with severe hepatic impairment. Severe hepatic impairment is likely to increase serum concentration of ticagrelor. There are no studies of **BILINTA** patients with severe hepatic impairment.

DRUG INTERACTIONS
• Avoid use with strong CYP3A inhibitors or CYP3A inducers.
• Patients receiving more than 40 mg per day of simvastatin or lovastatin may be at increased risk of statin-related adverse effects.
• Monitor digoxin levels with initiation of or any change in **BILINTA**.

STORAGE
Store at 25°C (excursions permitted to 15° to 30°C). Protect from sunlight and moisture.
The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED
BILINTA (Ticagrelor) 90mg tablets are available in blister pack of 20's.

Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

Please read the contents carefully before use.
This package insert is continually updated from time to time.

ہدایات:
دوا کو ۲۵ ڈگری سینٹی گریڈ درجہ حرارت پر رکھیں۔
(درجہ حرارت کی حد ۱۵ سے ۳۰ ڈگری سینٹی گریڈ ہے)
دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔

SCILIFE

Manufactured by:
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