



IMPORTANT DRUG WARNING

SUBJECT:

- **Risk of Increased Bleeding**
- **Decreased Efficacy with BRILINTA (ticagrelor) in Combination with Aspirin Doses Exceeding 100 mg**

Dear Healthcare Professional:

The purpose of this letter is to inform you of important safety information for BRILINTA (ticagrelor), a P2Y₁₂ platelet inhibitor recently approved by the FDA. BRILINTA is indicated to reduce the rate of thrombotic cardiovascular events in patients with acute coronary syndrome (ACS) (unstable angina, non ST elevation myocardial infarction or ST elevation myocardial infarction). BRILINTA has been shown to reduce the rate of a combined endpoint of cardiovascular death, myocardial infarction or stroke compared to clopidogrel. The difference between treatments was driven by CV death and MI with no difference in stroke. In patients treated with PCI, it also reduces the rate of stent thrombosis.

BRILINTA has been studied in ACS in combination with aspirin. Maintenance doses of aspirin above 100 mg appear to decrease the efficacy of BRILINTA. Maintenance doses of aspirin should not exceed 100 mg daily.

The FDA has determined that a Risk Evaluation and Mitigation Strategy (REMS) is necessary to ensure that the benefits of BRILINTA outweigh the following potential risks:

- Increased risk of bleeding
- Decreased efficacy of BRILINTA with higher aspirin doses (above 100 mg)

Increased Risk of Bleeding

- BRILINTA, like other antiplatelet agents, can cause significant, sometimes fatal, bleeding.
- Do not use BRILINTA in patients with active bleeding or history of intracranial hemorrhage.

If possible, manage bleeding without discontinuing BRILINTA. Stopping BRILINTA increases the risk of subsequent cardiovascular events.

Importance of Appropriate Aspirin Dose

- BRILINTA has been studied in combination with aspirin. Use with aspirin maintenance dose of 75-100 mg once daily.
- Higher aspirin doses (above 100 mg) appear to decrease the efficacy of BRILINTA.

Talk to Your Patients:

Tell patients that they:

- Will bleed and bruise more easily
- Will take longer than usual to stop bleeding

Instruct patients to:

- Report any unanticipated, prolonged or excessive bleeding, or blood in their stool or urine
- Not take aspirin maintenance doses greater than 100 mg daily
- Not take any products containing aspirin for other conditions.
- List all prescription medications, over the counter medications or dietary supplements they are taking or plan to take so the physician knows about other treatment that may affect bleeding risk (e.g. warfarin, heparin).
- Inform physicians and dentists that they are taking BRILINTA before any surgery or dental procedure
- Tell the doctor performing any surgery or dental procedure to talk to the prescribing physician before stopping BRILINTA.

Medication Guide

The Medication Guide contains information to support patient counseling regarding the risks and benefits of treatment with BRILINTA. [The BRILINTA Medication Guide may be obtained from the website www.brilintarems.com or by calling Sponsor at 1-800-236-9933.]

Reporting Adverse Events

To report any adverse events with the use of BRILINTA contact:

- Sponsor at 1-800-236-9933 and/or
- FDA MedWatch program by phone at 1-800-FDA-1088 or online at www.fda.gov/medwatch/report.htm

This letter is not intended as a complete description of the benefits and risks associated with the use of BRILINTA. Please refer to the full Prescribing Information and Medication Guide (www.brilintarems.com).

For additional information, please call Sponsor at 1-800-236-9933 or visit www.brilintarems.com.

Sincerely,



James W. Blasetto, M.D., MPH
Vice President
US Strategic Development
AstraZeneca LP
1800 Concord Pike
P.O. Box 8355
Wilmington, DE 19803-8355

Enclosure: BRILINTA Full Prescribing Information and Medication Guide