

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
022433Orig1s000

REMS

Initial REMS Approval: 07/2011

BRILINTA REMS DOCUMENT

NDA 22-433

BRILINTA™ (ticagrelor) tablets

Class of Product: cyclopentyltriazolopyrimidines (CPTPs)

AstraZeneca LP
1800 Concord Pike
P.O.Box 8355
Wilmington, DE 19850

Contact: The Information Center at AstraZeneca

1-800-236-9933

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOALS:

The goals of the BRILINTA REMS are:

1. To inform healthcare professionals and patients of the serious risks associated with BRILINTA, particularly the increased risk of bleeding.
2. To inform healthcare professionals and patients that the daily maintenance dose of aspirin, co-administered with BRILINTA, should not exceed 100 mg.

II. REMS ELEMENTS:

A. Medication Guide

A Medication Guide will be dispensed with each BRILINTA prescription in accordance with 21 CFR 208.24.

The Medication Guide is part of the REMS and is appended.

B. Communication Plan

AstraZeneca will implement a communication plan targeted to healthcare professionals who are likely to prescribe and dispense BRILINTA to inform them of the serious risks associated with BRILINTA, particularly the increased risk of bleeding and that the daily maintenance dose of aspirin, co-administered with BRILINTA, should not exceed 100 mg. This element of the REMS is not intended to continue over the lifetime of the product; it will function for a period of 2 years after the approval of the REMS. The communication plan will include the following:

1. Dear Healthcare Professional Letter

A Dear Healthcare Professional Letter (DHCPL) will be distributed to: interventional cardiologists; clinical cardiologists; emergency medicine physicians; internal medicine physicians; primary care physicians; nurse practitioners; physician assistants; pharmacists; critical care nurses, and cardiac nurse specialists. The letter will be distributed within 60 days of the REMS approval date, again at 6 months, 12 months and 24 months after the approval of the REMS, via electronic distribution or by mail.

In addition, for 2 years after the approval of the REMS new prescribers will be sent the DHCPL and the sales force will provide a copy of the letter upon initial contact with all potential BRILINTA prescribers.

The DHCPL will be distributed to the target audience using the PDR Network as well as other 3rd party lists. The DHCPL will be delivered electronically via email or fax. If DHCPL cannot be delivered electronically to the target professional for any reason or, in the case of email, remains unopened for 72 hours, a hardcopy will be sent via mail.

Product labeling and the Medication Guide will be provided in conjunction with the letter.

The Dear Healthcare Professional Letter is part of the REMS and is appended.

2. BRILINTA REMS Website

Within 30 days of REMS approval, AstraZeneca will post information for healthcare professionals and patients on the BRILINTA REMS website (www.Brilintarems.com). This information will remain on the website for a period of 2 years.

The content of the web-based material will include the following:

- Goals of the REMS
- Information about the risk
- Prescribing information for BRILINTA
- Medication Guide for BRILINTA
- DHCP letter (for a period of 2 years)

The web-based material is part of the REMS and is appended.

3. Letters to Professional Organizations

A Professional Organization Letter will be distributed within 60 days of the REMS approval date. This communication to professional organizations will include the same information as that contained in the Dear Healthcare Professional Letter. AstraZeneca will request that these organizations disseminate this information to their members. AstraZeneca will communicate via letter to the leadership of the following professional organizations:

- The American Heart Association (AHA)
- The American College of Cardiologists (ACC)
- The Society for Cardiovascular Angiography and Interventions (SCIA)
- Association of Emergency Physicians (AEP)
- The American College of Chest Physicians (ACCP)
- Association of Black Cardiologists (ABC)
- The American Academy of Family Physicians (AAFP)
- The American College of Physicians (ACP)
- The National Medical Association (NMA)
- The American Academy of Nurse Practitioners (AANP)
- The American Academy of Physician Assistants (AAPA)
- American College of Clinical Pharmacy (ACCP)
- American Society of Health-System Pharmacists (ASHP)
- American Pharmacists Association (APhA)
- American Association of Critical-Care Nurses (AACCN)
- National Association of Clinical Nurse Specialists (NACNS)

Product labeling and the Medication Guide will be provided in conjunction with the letter.

The Professional Organization Letter is part of the REMS and is appended.

C. Timetable for Submission of Assessments

AstraZeneca will submit REMS Assessments to FDA at 18 months, 3 years and 7 years from the date of the approval of the REMS. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. AstraZeneca will submit each assessment so that it will be received by the FDA on or before the due date.

MEDICATION GUIDE

BRILINTA™ (brih-LIN-tah)
(ticagrelor)
Tablets

Read this Medication Guide before you start taking BRILINTA and each time you get a refill. There may be new information. This information does not take the place of talking with your doctor about your medical condition or your treatment.

What is the most important information I should know about BRILINTA?

BRILINTA is used to lower your chance of having a heart attack or dying from a heart attack or stroke **but BRILINTA (and similar drugs) can cause bleeding that can be serious and sometimes lead to death.** In cases of serious bleeding, such as internal bleeding, the bleeding may result in the need for blood transfusions or surgery. While you take BRILINTA:

- you may bruise and bleed more easily
- you are more likely to have nose bleeds
- it will take longer than usual for any bleeding to stop

Call your doctor right away, if you have any of these signs or symptoms of bleeding while taking BRILINTA:

- bleeding that is severe or that you cannot control
- pink, red or brown urine
- vomiting blood or your vomit looks like “coffee grounds”
- red or black stools (looks like tar)
- coughing up blood or blood clots

Do not stop taking BRILINTA without talking to the doctor who prescribes it for you. People who are treated with a stent, and stop taking BRILINTA too soon, have a higher risk of getting a blood clot in the stent, having a heart attack, or dying. If you stop BRILINTA because of bleeding, or for other reasons, your risk of a heart attack or stroke may increase.

When instructed by your doctor, you should stop taking BRILINTA 5 days before you have elective surgery. This will help to decrease your risk of bleeding with your surgery or procedure. Your doctor should tell you when to start taking BRILINTA again, as soon as possible after surgery.

Taking BRILINTA with aspirin

BRILINTA is taken with aspirin. Talk to your doctor about the dose of aspirin that you should take with BRILINTA. You should not take a dose of aspirin higher than 100 mg daily because it can affect how well BRILINTA works. Do not take doses of aspirin higher than what your doctor tells you to take. Tell your doctor if you take other medicines that contain aspirin, and do not take new over-the-counter medicines with aspirin in them.

What is BRILINTA?

BRILINTA is a prescription medicine used to treat people who:

- have had a recent heart attack or severe chest pain that happened because their heart was not getting enough oxygen.
- have had a heart attack or chest pain and are being treated with medicines or with a procedure to open blocked arteries in the heart.

BRILINTA is used with aspirin to lower your chance of having another serious problem with your heart or blood vessels, such as heart attack, stroke, or blood clots in your stent. These can be fatal.

Platelets are blood cells that help with normal blood clotting. BRILINTA helps prevent platelets from sticking together and forming a clot that can block an artery.

It is not known if BRILINTA is safe and works in children.

Who should not take BRILINTA?

Do not take BRILINTA if you:

- are bleeding now
- have a history of bleeding in the brain
- have bleeding from your stomach or intestine now (an ulcer)
- have severe liver problems

When instructed by your doctor, you should stop taking BRILINTA 5 days before you have elective surgery. This will help to decrease your risk of bleeding with your surgery or procedure. Your doctor should tell you when to start taking BRILINTA again, as soon as possible after surgery.

What should I tell my doctor before taking BRILINTA?

Before you take BRILINTA, tell your doctor if you:

- have had bleeding problems in the past
- have had any recent serious injury or surgery
- plan to have surgery or a dental procedure
- have a history of stomach ulcers or colon polyps
- have lung problems, such as COPD or asthma
- have liver problems
- have a history of stroke
- are pregnant, or are plan to become pregnant. It is not known if BRILINTA will harm your unborn baby. You and your doctor should decide if you will take BRILINTA.
- are breastfeeding. It is not known if BRILINTA passes into your breast-milk. You and your doctor should decide if you will take BRILINTA or breastfeed. You should not do both without talking with your doctor.

Tell all of your doctors and dentists that you are taking BRILINTA. They should talk to the doctor who prescribed BRILINTA for you before you have any surgery or invasive procedure.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. **BRILINTA may affect the way other** medicines work, and other medicines may affect how BRILINTA works.

Especially tell your doctor if you take:

- an HIV-AIDS medicine
- medicine for heart conditions or high blood pressure
- medicine for high blood cholesterol levels
- an anti-fungal medicine by mouth
- an anti-seizure medicine
- a blood thinner medicine
- rifampin (Rifater, Rifamate, Rimactane, Rifadin)

Ask your doctor or pharmacist if you are not sure if your medicine is listed above.

Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

How should I take BRILINTA?

- Take BRILINTA exactly as prescribed by your doctor.
- Your doctor will tell you how many BRILINTA tablets to take and when to take them.
- Take BRILINTA with a low dose (not more than 100 mg daily) of aspirin. You may take BRILINTA with or without food.
- Take your doses of BRILINTA around the same time every day.
- If you forget to take your scheduled dose of BRILINTA, take your next dose at its scheduled time. Do not take two doses at the same time unless your doctor tells you to.
- If you take too much BRILINTA or overdose, call your doctor or poison control center right away, or go to the nearest emergency room.

What are the possible side effects of BRILINTA?

BRILINTA can cause serious side effects, including:

- **See “What is the most important information I should know about BRILINTA?”**

- **Shortness of breath.** Call your doctor if you have new or unexpected shortness of breath when you are at rest, at night, or when you are doing any activity. Your doctor can decide what treatment is needed.

Tell your doctor if you have any side effect that bothers you or that does not go away.

These are not all of the possible side effects of BRILINTA. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store BRILINTA?

- Store BRILINTA at room temperature between 59°F to 86°F (15°C to 30°C).

Keep BRILINTA and all medicines out of the reach of children.

General information about BRILINTA

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use BRILINTA for a condition for which it was not prescribed. Do not give BRILINTA to other people, even if they have the same symptoms you have. It may harm them.

This Medication Guide summarizes the most important information about BRILINTA. If you would like more information about BRILINTA, talk with your doctor. You can ask your pharmacist or doctor for information about BRILINTA that is written for health professionals.

For more information call 1-800-236-9933 or go to www.Brilinta.com.

What are the ingredients in BRILINTA?

Active ingredient: ticagrelor

Inactive ingredients: mannitol, dibasic calcium phosphate, sodium starch glycolate, hydroxypropyl cellulose, magnesium stearate, hydroxypropyl methylcellulose, titanium dioxide, talc, polyethylene glycol 400, and ferric oxide yellow.

Issued: 07/2011

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Manufactured by: AstraZeneca, AB S-151 85 Södertälje Sweden
Marketed by: AstraZeneca LP, Wilmington, DE 19850

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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

Landing page of the BRILINTA REMS website

For US Audiences Only

Search

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BRILINTA
ticagrelor tablets

Prescribing BRILINTA

▶ Important Safety Information

▶ Full Prescribing Information for BRILINTA

▶ Medication Guide for BRILINTA

REMS Home

▶ Educational Materials

▶ Contact Us

Welcome to the BRILINTA REMS Web site

A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage known or potential serious risk(s) associated with a drug product, and is required by the Food and Drug Administration to ensure that the benefits of the drug outweigh its risks.

In order for AstraZeneca to communicate certain risks about BRILINTA, AstraZeneca has worked with the FDA to develop materials to communicate the risks that:

- BRILINTA, like other antiplatelet agents, can cause significant, sometimes fatal, bleeding
- Higher maintenance doses of aspirin (above 100 mg) decreased the efficacy of BRILINTA

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

The REMS is designed to communicate important information on the potential risk of bleeding and the appropriate maintenance dose of aspirin to use with BRILINTA. The BRILINTA REMS includes a Medication Guide (for patients) and a Communication Plan, including Dear Healthcare Professional Letter and Professional Organization Letter (for healthcare professionals).

To learn more about the serious risks see the [Full Prescribing Information for BRILINTA](#).

The goals of the BRILINTA REMS are:

- To inform healthcare professionals and patients of the serious risks associated with BRILINTA, particularly the increased risk of bleeding.
- To inform healthcare professionals and patients that the daily maintenance dose of aspirin, co-administered with BRILINTA, should not exceed 100 mg.

Important Prescribing Provisions Related to the Appropriate Aspirin Dose:

Dosage and Administration:

- Initiate BRILINTA treatment with a 180 mg (two 90 mg tablets) loading dose and continue treatment with 90 mg twice daily
- Limit concomitant aspirin maintenance dose to 75-100 mg/day
- BRILINTA can be administered with or without food
- A patient who misses a dose of BRILINTA should take one 90 mg tablet (the next dose) at its scheduled time

Warnings and Precautions:

- BRILINTA has been studied in combination with aspirin. Higher aspirin doses (above 100 mg) decreases the efficacy of BRILINTA.

▶ [Read the Dear Healthcare Professional Letter](#)

▶ [Read the Professional Society Letter](#)

Important Safety Information

PLACEHOLDER FOR ISI

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IMPORTANT DRUG WARNING

Disseminate this information to your members

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Sincerely,

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