



NDA 22433/S-013

SUPPLEMENT APPROVAL

AstraZeneca LP
ATTENTION: Robert Griffin
Director, Regulatory Affairs
One MedImmune Way
Gaithersburg, MD, 20878

Dear Mr. Griffin:

Please refer to your Supplemental New Drug Application (sNDA) dated 22 May 2014, received 22 May 2014, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FDCA) for BRILINTA (ticagrelor) 90 mg Tablets.

We acknowledge receipt of your amendment dated 30 October 2014.

This Prior Approval supplemental new drug application provided for language regarding dosing recommendations for crushed tablets (b) (4)

The agreed upon changes are as follows:

- A new subsection, **2.1 Administration Options**, was added under Section 2 (**DOSAGE AND ADMINISTRATION**). This new subsection appears as follows:

“For patients who are unable to swallow the tablet(s) whole, BRILINTA tablets can be crushed, mixed with water and drunk immediately. The glass should be refilled with water, stirred and the contents drunk. The mixture can also be administered via a nasogastric tube (CH8 or greater). It is important to flush the nasogastric tube through with water after administration of the mixture [see *Clinical Pharmacology (12.3)*].”

The above change is also reflected in the Highlights.

- Under Section 12, **CLINICAL PHARMACOLOGY**, subsection 12.3 (**Pharmacokinetics**), the following was added under Absorption,

“BRILINTA as crushed tablets mixed in water, given orally or administered through a nasogastric tube into the stomach, is bioequivalent to whole tablets (AUC and C_{max} within 80-125% for ticagrelor and AR-C124910XX) with a median t_{max} of 1.0 hour (range 1.0 – 4.0) for ticagrelor and 2.0 hours (range 1.0 – 8.0) for AR-C124910XX.”

- The following language was added to the Medication Guide:

“**If you have trouble swallowing the tablet(s).**”

If you are unable to swallow the tablet(s) whole, BRILINTA tablets can be crushed, mixed with water and drunk immediately. The glass should be refilled with water, stirred and the contents drunk.”

- Other editorial changes were also made throughout the label.

We do not agree with proposed language regarding

(b) (4)

We do not believe that these data sufficiently support

(b) (4)

We recommend that you submit a more thorough integration of the available data and conduct further studies to elucidate

(b) (4)

All reports should contain a thorough description of the methodology used.

APPROVAL & LABELING

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling (text for the package insert and Medication Guide), with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled “SPL Standard for Content of Labeling Technical Qs and As at

<http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(1)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, please contact:

Alison Blaus, RAC
Regulatory Project Manager
(301) 796-1138

Sincerely,

{See appended electronic signature page}

Mary Ross Southworth, Pharm.D.
Deputy Director for Safety
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

MARY R SOUTHWORTH
03/26/2015