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November 2, 2020

By Electronic Submission

Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061 (HFA-305)
Rockville, MD 20852

Re: ANDA Suitability Petition: Ticagrelor Tablets for Oral Use, 90 mg

Citizen Petition

The undersigned ("Petitioner") submits this Citizen Petition pursuant to the Federal Food, Drug and Cosmetic Act ("FDC Act") Section 505(j)(2)(C) and in accordance with 21 C.F.R. § 10.25 and 10.30 with regard to a modified route of administration for Ticagrelor Tablets for oral use, 60 mg and 90 mg. The current reference listed drug and the several generic versions approved under an ANDA, are for use as oral tablets that may be administered with or without food as whole tablets or as crushed tablets mixed in water, given orally or administered through a nasogastric tube into the stomach.

Action Requested

The petitioner requests that the Commissioner of the Food and Drug Administration declare that a drug product containing Ticagrelor 90 mg in an orally disintegrating tablet (ODT) form is suitable for submission as an Abbreviated New Drug Application.

Statement of Grounds

The Commissioner may allow an ANDA to be filed for a drug product which is not identical to a listed drug in route of administration, dosage form, and strength, if the person first obtains permission from FDA to submit such an ANDA.[1] The Commissioner can approve a Citizen's Petition properly submitted under sections §10.25 and §10.30 within 90 days unless investigations must be conducted to show

[1] 21 C.F.R § 314.93(b)

the safety and effectiveness of the drug product or its route of administration, which differs from the reference listed drug or any of the proposed changes from the listed drug would jeopardize the safe or effective use of the product so as to necessitate significant labeling changes to address the newly introduced safety or effectiveness problem.[2]

The Reference Listed Drug on which this petition is based is Brilinta® (NDA 022433, first approved 7/20/2011). Brilinta® contains Ticagrelor in an oral immediate release (IR) tablet dosage form of either 60 mg or 90 mg dosages and is indicated for treatment 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). There are no patents in the Orange Book for an orally disintegrating tablet containing Ticagrelor active ingredient.

The change of the 90 mg IR tablet already approved and in distribution in the United States, to an ODT dosage form would provide a dosage form that is more convenient to use and that could address potential issues of patient compliance for certain patient populations, It is anticipated that an ODT would not necessitate new investigations to confirm the safety and effectiveness of the drug product because it has already been established that either IR or ODT dosage forms containing Ticagrelor active ingredient provide equivalent bioavailability. In studies summarized for public review and supporting a request for marketing an ODT dosage form of Ticagrelor, the European Medicines Authority (EMA) disclosed that:

> *The results from this study demonstrated that when dispersed in saliva and swallowed without water, or suspended in water and administered through a nasogastric tube into the stomach, ticagrelor 90 mg OD tablets were bioequivalent in terms of Cmax, AUC and AUC(0-t) to ticagrelor 90 mg IR tablets.[3](Attachment 1)*

If this petition is approved, an ANDA application for the ODT dosage form would demonstrate USP disintegration of 30 second or less, as recommended in FDA's December 2008 *Guidance for Industry: Orally Disintegrating Tablets*. Also, the application would demonstrate equivalent *in vitro* dissolution curves compared to the IR Brilanta and the ODT currently approved for distribution in the European Union. Both *in vitro* studies would be supported by human bioequivalence studies that will demonstrate comparable bioavailability to the RLD

[2] 21 C.F.R. § 314.93(e)(1)(i) and (iv)
[3] EMA/274695/2017; Committee for Medicinal Products for Human Use (CHMP) Assessment Report on Extension of Marketing Authorisation: Brilique (ticagrelor)

Likewise, an ODT dosage form would not necessitate significant labeling changes. As the proposed drug product would contain the same active ingredient in the same strength as the RLD, and the indication, dosing regimen and patient population would be unchanged, the approved prescribing information labeling for Brilinta® would be almost entirely applicable to the proposed drug product with changes only to the inactive ingredient listing and references to the current tablet dosage form. Current labeling for Brilinta® appears as Attachment 2 to this petition with draft labeling text for the proposed drug product as Attachment 3.

Introduction of a 90 mg ODT would provide benefits for patients who have difficulty swallowing the approved film-coated tablets or for situations where water is not available (e.g. for urgent treatment). The product can be administered with or without food. The tablet should be placed on the tongue, where it will rapidly disperse in saliva. It can then be swallowed with or without water. The tablet can also be dispersed in water and administered via a nasogastric tube which should be flushed through with water after administration of the mixture.

Pediatric Assessment

The requirements of the Pediatric Research Equity Act under 21 U.S.C. § 355c(a)(4)(A)(ii) for all pediatric age groups was waived by the Food and Drug Administration (FDA) in their NDA approval letter for the RLD. Because it has been established with clinical evidence that ODT and IR dosage forms are bioequivalent, a pediatric assessment is not necessary for the reasons provided in FDA's waiver, namely:

> *We are waiving the pediatric study requirement for this application because necessary studies are impossible or highly impracticable. There are too few children with this disease/condition to study.*

Environmental Impact:

This petition hereby claims categorical exclusion under 21 C.F.R § 25.31(a) from the requirement to provide an environmental assessment. As the proposed drug substance already exists in the marketplace for the proposed indication and at the proposed strength, introduction of a new dosage form is unlikely to significantly increase usage of this active ingredient and moieties as sales volume is expected to come primarily from users of the existing tablet dosage form who switch to the ODT form based on prescriber's preference.

Economic Impact

In accordance with 21 C.F.R § I 0.30(b)(3), economic impact information will be submitted upon request by the Commissioner.

Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned , this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Sincerely,

[redacted]

Attachments:

1. EMA/274695/2017; Committee for Medicinal Products for Human Use (CHMP) *Assessment Report on Extension of Marketing Authorisation: Brilique (ticagrelor)*
2. Approved labeling for the RLD, Brilinta®
3. Draft labeling for the proposed product, Ticagrelor Orally Disintegrating Tablet 90 mg