James Mahanna
Teva Pharmaceuticals USA, Inc.
200 Elmora Avenue
Elizabeth, NJ 07202
Telephone: 908.659.2510
jim.mahanna@actavis.com

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VIA ELECTRONIC SUBMISSION

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

CITIZEN PETITION

Teva Pharmaceuticals USA, Inc. ("Teva") submits this Petition to the Food and Drug Administration ("FDA") in accordance with 21 C.F.R § 10.25(a) and § 10.30[1] and pursuant to Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act ("FDC Act"). For the reasons discussed below, Teva respectfully requests that FDA assign a Therapeutic Equivalence Evaluation Code ("TE Code") for the company's Fosaprepitant Dimeglumine for Injection, Eq. 150 mg base/vial, which FDA approved on September 5, 2019 under New Drug Application ("NDA") 210064. NDA 210064 was submitted by Teva to FDA pursuant to FDC Act § 505(b)(2). Teva's Fosaprepitant Dimeglumine for Injection, Eq. 150 mg base/vial is approved for the use in combination with other antiemetic agents for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC).

I. FDA ACTION REQUESTED

Teva requests that FDA assign in the Agency's Orange Book a TE code of "AP" to Teva's Fosaprepitant Dimeglumine for Injection, Eq. 150 mg base/vial. As demonstrated below, Teva's Fosaprepitant Dimeglumine for Injection, Eq. 150 mg base/vial meets all applicable requirements for a TE Code with respect to Merck and Co., Inc.'s ("Merck") EMEND® (fosaprepitant dimeglumine), Eq. 150 mg base/vial which FDA approved under NDA 022023 on November 12, 2010. There is no basis for FDA to deny this request. Accordingly, the assignment of a TE code is warranted.

II. STATEMENT OF GROUNDS

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[1] In the Preface to FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations* ("Orange Book"), the Agency states that "[a] person seeking to have a therapeutic equivalence rating for a drug product approved in a 505(b)(2) application may petition the Agency through the citizen petition procedure (*see* 21 CFR 10.25(a) and 21 CFR 10.30.)" Orange Book Preface (39th ed., 2019), at xxiv.

A. Factual and Regulatory Background

The Orange Book Preface explains that there are "two basic categories into which multisource drugs have been placed: (1) "A-rated drug products (i.e., "Drug products that FDA considers to be therapeutically equivalent to other pharmaceutically equivalent products": and (2) "B-rated" drug products (i.e., "Drug products that FDA at this time, considers not to be therapeutically equivalent to other pharmaceutically equivalent products"). Orange Book Preface (39th ed., 2019), at xiii (emphasis in original).

FDA defines "therapeutic equivalents" to mean "approved drug products that are pharmaceutical equivalents for which bioequivalence has been demonstrated, and that can be expected to have the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling." 21 C.F.R. § 314.3(b). FDA defines "pharmaceutical equivalents" to mean:

> drug products in identical dosage forms and route(s) of administration that contain identical amounts of the identical active drug product, i.e., the same salt or ester of the same therapeutic moiety, or, in the case of modified-release dosage forms that require a reservoir of overage or such forms as prefilled syringes where residual volume may vary, that deliver identical amounts of the active drug ingredient over the identical dosing period; do not necessarily contain the same inactive ingredients; and meet the identical compendial or other applicable standard of identity, strength, quality and purity, including potency and, where applicable, content uniformity, disintegration times and/or dissolution rates.

Id. Drug products designated with an "A" TE Code fall under one of two main policies:

(1) for those active ingredients or dosage forms for which no in vivo bioequivalence issue is known or suspected, the information necessary to show bioequivalence between pharmaceutically equivalent products is presumed and considered self-evident based on other data in the application for some dosage forms (e.g., solutions) or satisfied by a showing that an acceptable in vitro dissolution standard is met. A therapeutically equivalent rating is assigned such products so long as they are manufactured in accordance with Current Good Manufacturing Practice regulations and meet the other requirements of their approved applications (these are designated AA, AN, AO, AP or AT, depending on the dosage form, as described below); or

(2) for those Drug Efficacy Study Implementation (DESI) drug products containing active ingredients or dosage forms that have been identified by FDA as having actual or potential bioequivalence problems, and for post-1962 drug products in a dosage form presenting a potential bioequivalence problem, an evaluation of therapeutic equivalence is assigned to pharmaceutical equivalents only if the approved application contains adequate scientific evidence establishing through in vivo and/or in vitro studies, the bioequivalence of the product to a selected reference product (these products are designated as AB).

Orange Book Preface (39th ed., 2019) at xiii - xiv. The Orange Book also defines and explains FDA's policies for various "A" sub-codes. Specifically, the TE code "AP" is defined as "Injectable aqueous solutions and, in certain instances, intravenous non-aqueous solutions." Orange Book Preface (39th ed., 2019) at xvii. The electronic Orange Book entry for Merck's EMEND® (fosaprepitant dimeglumine), Eq. 150 mg base/vial is shown below:

RX	FOSAPREPITANT DIMEGLUMINE	EMEND	N022023	POWDER	INTRAVENOUS	EQ 150MG BASE/VIAL	AP	RLD	RS	MERCK AND CO INC
Mkt. Status	Active Ingredient	Proprietary Name	Appl No	Dosage Form	Route	Strength	TE Code	RLD	RS	Applicant Holder

The FDA has approved another ANDA for pharmaceutically equivalent versions of Merck's EMEND®. This ANDA appears as follows in the electronic version of the Orange Book:

RX	FOSAPREPITANT DIMEGLUMINE	FOSAPREPITANT DIMEGLUMINE	A206197	POWDER	INTRAVENOUS	EQ 150MG BASE/VIAL	AP			FRESENIUS KABI USA LLC
Mkt. Status	Active Ingredient	Proprietary Name	Appl No	Dosage Form	Route	Strength	TE Code	RLD	RS	Applicant Holder

B. <u>Request for TE Code Assignment for Teva's Fosaprepitant Dimeglumine for Injection, Eq. 150 mg base/vial</u>

According to FDA's website, FDA considers drug products to be pharmaceutical equivalents if they meet these three criteria:

- they contain the same active ingredient
- they are of the same dosage form and route of administration
- they are identical in strength or concentration

https://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm

As shown in Teva's Tentatively Approved NDA No. 210064, Teva's Fosaprepitant Dimeglumine for Injection, Eq. 150 mg base/vial product has exactly the same: active ingredient (fosaprepitant dimeglumine), strength (Eq. 150 mg base/vial), dosage form (powder) and route of

administration (intravenous) as the RLD (EMEND®). As such, Teva's Fosaprepitant Dimeglumine for Injection, Eq. 150 mg base/vial is a pharmaceutical equivalent.

Teva's Fosaprepitant Dimeglumine for Injection, Eq. 150 mg base/vial should be assigned a therapeutic equivalence code of "AP" because it has already been deemed bioequivalent to EMEND® by FDA as shown by the Tentative Approval of Teva's NDA No. 210064. Specifically Teva's Fosaprepitant Dimeglumine for Injection, Eq. 150 mg base/vial qualified for a bioequivalence waiver, pursuant to 21 C.F.R. § 320.22. Moreover, both Teva's Fosaprepitant Dimeglumine for Injection, Eq. 150 mg base/vial and Merck's EMEND® "can be expected to have the same clinical effect and safety profile when administered to patients under the conditions specified in the labelling." 21 C.F.R. § 314.3(b) (defining "therapeutic equivalents"). As such, Teva's § 320.22 and EMEND® are pharmaceutical and therapeutic equivalents and Teva's Fosaprepitant Dimeglumine for Injection, Eq. 150 mg base/vial should be identified in the Orange Book with an "AP" TE Code

III. ENVIRONMENTAL IMPACT

Petitioner claims a categorical exclusion under 21 C.F.R. § 25.31

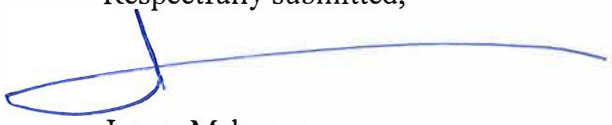
IV. ECONOMIC IMPACT STATEMENT

Petitioner will, upon request by the Commissioner, submit economic impact information, in accordance with 21 C.F.R. § 10.30(b)

V. 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 that are unfavorable to the Petition.

Respectfully submitted,



James Mahanna
Senior Director, Associate General Counsel,
NA Generics IP