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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

Hyman, Phelps & McNamara, P.C. submits this Citizen Petition to the Food and Drug Administration ("FDA") on behalf of InvaGen Pharmaceuticals, Inc. ("InvaGen"), and 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, InvaGen respectfully requests that FDA assign a Therapeutic Equivalence Evaluation Code ("TE Code") for the company's Lanreotide Injection, 60 mg/0.2 mL, 90 mg/0.3 mL, and 120 mg/0.5 mL, drug products, which FDA approved on December 17, 2021, under New Drug Application ("NDA") 215395, and that was submitted to the Agency pursuant to FDC Act § 505(b)(2).

I. ACTION REQUESTED

InvaGen requests that FDA assign in the Agency's Orange Book a TE Code of "AP" to the 60 mg/0.2 mL, 90 mg/0.3 mL, and 120 mg/0.5 mL, drug products approved under NDA 215395 for InvaGen's Lanreotide Injection. A TE Code is necessary so that InvaGen will, among other things, be exempt from, or can otherwise obtain a refund of, any Prescription Drug User Fee Act annual "program fee" FDA may assess with respect to NDA 215395 for Fiscal Year 2023 and thereafter.[2]

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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 (42nd ed., 2022), at xxiv.

[2] Under the FDC Act, a prescription drug product is not assessed a program fee under FDC Act § 736(a)(2)(B)(ii) if such product qualifies for an exception under FDC Act

(continued . . .)

As demonstrated below, InvaGen's Lanreotide Injection, 60 mg/0.2 mL, 90 mg/0.3 mL, and 120 mg/0.5 mL, drug products meet the requirements for a TE Code with respect to Ipsen Pharma Biotech SAS's ("Ipsen's") Somatuline Depot (lanreotide) Injection, 60 mg/0.2 mL, 90 mg/0.3 mL and 120 mg/0.5 mL, drug products that FDA approved under NDA 022074 on August 30, 2007, insofar as the drug products are pharmaceutical equivalents that have been demonstrated to be bioequivalent.

II. STATEMENT OF GROUNDS

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 (42nd ed., 2022), at xiii (emphasis in original).

An FDA regulation defines the term "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).[3] FDA further explains in the Orange Book Preface that:

> FDA classifies as therapeutically equivalent those drug products that meet the following general criteria:

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§ 736(a)(2)(B) (*i.e.*, if such product is "the same product as another product " approved under an NDA or Abbreviated NDA and that is listed in the Prescription Drug Product List section of the Orange Book).

[3] Another FDA regulation defines the term "pharmaceutical equivalents" to mean:

> drug products in identical dosage forms and route(s) of administration that contain identical amounts of the identical active drug ingredient, 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 or 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.

21 C.F.R. § 314.3(b).

> (1) they are approved as safe and effective;
>
> (2) they are pharmaceutical equivalents in that they (a) contain identical amounts of the identical active drug ingredient in the identical dosage form and route of administration, and (b) meet compendial or other applicable standards of strength, quality, purity, and identity;
>
> (3) they are bioequivalent in that (a) they do not present a known or potential bioequivalence problem, and they meet an acceptable in vitro standard, or (b) if they do present such a known or potential problem, they are shown to meet an appropriate bioequivalence standard;
>
> (4) they are adequately labeled; and
>
> (5) they are manufactured in compliance with Current Good Manufacturing Practice regulations.

Orange Book Preface (42nd ed., 2022), at vii (reformatted).

> 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 at xiii-xiv. The Orange Book Preface also defines and explains FDA's policies for various "A" sub-codes. In particular, the TE Code "AP" is defined as "Injectable aqueous solutions and, in certain instances, intravenous non-aqueous solutions." Orange Book Preface at xvi.

FDA has approved two NDAs for pharmaceutically equivalent versions of Lanreotide Injection: (1) InvaGen's Lanreotide Injection, 60 mg/0.2 mL, 90 mg/0.3 mL, and 120 mg/0.5 mL, which was approved on December 17, 2021, under NDA 215395; and (2) Ipsen's Somatuline Depot Injection, 60 mg/0.2 mL, 90 mg/0.3 mL, and 120 mg/0.5 mL, which FDA approved under NDA 022074 on August 30, 2007. Both NDAs appear as follows in the electronic version of the Orange Book:

Mkt. Status	Active Ingredient	Proprietary Name	Appl No	Dosage Form	Route	Strength	TE Code	RLD	RS	Applicant Holder
RX	LANREOTIDE ACETATE	LANREOTIDE ACETATE	N215395	SOLUTION	SUBCUTANEOUS	EQ 60MG BASE/0.2ML (EQ 60MG BASE/0.2ML)		RLD	RS	INVAGEN PHARMACEUTICALS INC
RX	LANREOTIDE ACETATE	LANREOTIDE ACETATE	N215395	SOLUTION	SUBCUTANEOUS	EQ 90MG BASE/0.3ML (EQ 90MG BASE/0.3ML)		RLD	RS	INVAGEN PHARMACEUTICALS INC
RX	LANREOTIDE ACETATE	LANREOTIDE ACETATE	N215395	SOLUTION	SUBCUTANEOUS	EQ 120MG BASE/0.5ML (EQ 120MG BASE/0.5ML)		RLD	RS	INVAGEN PHARMACEUTICALS INC
RX	LANREOTIDE ACETATE	SOMATULINE DEPOT	N022074	SOLUTION	SUBCUTANEOUS	EQ 60MG BASE/0.2ML (EQ 60MG BASE/0.2ML)		RLD	RS	IPSEN PHARMA BIOTECH SAS
RX	LANREOTIDE ACETATE	SOMATULINE DEPOT	N022074	SOLUTION	SUBCUTANEOUS	EQ 90MG BASE/0.3ML (EQ 90MG BASE/0.3ML)		RLD	RS	IPSEN PHARMA BIOTECH SAS
RX	LANREOTIDE ACETATE	SOMATULINE DEPOT	N022074	SOLUTION	SUBCUTANEOUS	EQ 120MG BASE/0.5ML (EQ 120MG BASE/0.5ML)		RLD	RS	IPSEN PHARMA BIOTECH SAS

Although InvaGen's Lanreotide Injection drug products appear, based on their Prescribing Information, to slightly differ in device vis-à-vis Somatuline Depot, in fact, both drug products are in identical dosage forms. Indeed, the Prescribing Information for each drug product describes each as a "injection":

> Injection
> 60 mg/0.2 mL, 90 mg/0.3 mL, and 120 mg/0.5 mL sterile, single-dose, prefilled syringes fitted with an automatic needle guard. The prefilled syringes contain a white to pale yellow, semi-solid formulation.

Somatuline Depot (NDA 022074), Prescribing Information, Section 3, Dosage Forms and Strengths (June 2019), *available at* https://dailymed.nlm.nih.gov/dailymed/getFile.cfm?setid=6e4a41fd-a753-4362-87ee-8cc56ed3660d&type=pdf.

> Injection
> 60 mg/0.2 mL, 90 mg/0.3 mL, and 120 mg/0.5 mL of lanreotide provided as lanreotide acetate, in single-dose, prefilled syringes packaged with a safety needle. The prefilled syringes contain a white to pale yellow, semi-solid formulation.

Lanreotide Injection (NDA 215395), Prescribing Information, Section 3, Dosage Forms and Strengths (Dec. 2021), *available at* https://dailymed.nlm.nih.gov/dailymed/getFile.cfm?setid=11da176a-99bc-4ada-8b3f-6bd2b37a6313&type=pdf.

InvaGen's Lanreotide Injection, which FDA determined to be bioequivalent to, and that is otherwise the same as Somatuline Depot Injection, was submitted to FDA pursuant FDC Act § 505(b)(2). The differences in devices between InvaGen's Lanreotide Injection and Somatuline Depot Injection are minor in nature and should not preclude the assignment of an "AP" TE Code.

B. Request for TE Code Assignment for InvaGen's Lanreotide Injection Drug Products

InvaGen's Lanreotide Injection, 60 mg/0.2 mL, 90 mg/0.3 mL and 120 mg/0.5 mL, drug products meet all applicable requirements for a TE Code with respect to Ipsen's Somatuline Depot Injection, 60 mg/0.2 mL, 90 mg/0.3 mL and 120 mg/0.5 mL, which FDA approved under NDA 022074 on August 30, 2007.

First, both InvaGen's Lanreotide Injection and Ipsen's Somatuline Depot Injection are pharmaceutical equivalents in that both drug products contain identical amounts of the identical active drug ingredient and are in identical dosage forms for the same route of administration.

Second, both InvaGen's Lanreotide Injection and Ipsen's Somatuline Depot Injection are equivalent to one another and are "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).

In addition, InvaGen's Lanreotide Injection drug products are manufactured in compliance with Current Good Manufacturing Practice regulations, and the drug products are adequately labeled. As such, InvaGen's Lanreotide Injection and Ipsen's Somatuline Depot Injection 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.

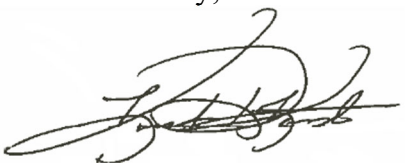
IV. ECONOMIC IMPACT STATEMENT

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.

Sincerely,



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