



ANDA 208906

**ANDA TENTATIVE APPROVAL**

Teva Pharmaceuticals USA, Inc.  
2945 West Corporate Lakes Blvd., Suite B  
Weston, FL 33331  
Attention: Alberto Rivalta  
Senior Director of Regulatory Affairs

Dear Alberto Rivalta:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on December 24, 2015, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Treprostinil Extended-Release Tablets, 0.125 mg, 0.25 mg, 1 mg, 2.5 mg, and 5 mg.

Reference is also made to the complete response letter issued by this office on August 20, 2021, and to any amendments thereafter.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug meets the requirements for approval under the FD&C Act. We have determined your Treprostinil Extended-Release Tablets, 0.125 mg, 0.25 mg, 1 mg, 2.5 mg, and 5 mg, to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Orenitram Extended-Release Tablets, 0.125 mg, 0.25 mg, 1 mg, 2.5 mg, and 5 mg, of United Therapeutics Corp. (United).

However, we are unable to grant final approval to your ANDA at this time because of the exclusivity issue noted below. Therefore, the ANDA is **tentatively approved**. This determination is based upon information available to the Agency at this time (e.g., information in your ANDA and the status of current good manufacturing practices (cGMPs) of the facilities used in the manufacturing and testing of the drug product). This determination is subject to change on the basis of new information that may come to our attention. This letter does not address issues related to the 180-day exclusivity provisions under section 505(j)(5)(B)(iv) of the FD&C Act.

The RLD upon which you have based your ANDA, United's Orenitram Extended-Release Tablets, 0.125 mg, 0.25 mg, 1 mg, 2.5 mg, and 5 mg, is subject to periods of patent protection. The following patents and expiration dates are currently listed in the Agency's publication titled *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book"):

<u>U.S. Patent Number</u>	<u>Expiration Date</u>
8,252,839 (the '839 patent)	May 24, 2024
9,050,311 (the '311 patent)	May 24, 2024
9,278,901 (the '901 patent)	May 24, 2024
9,422,223 (the '223 patent)	May 24, 2024
7,544,713 (the '713 patent)	July 14, 2024
9,393,203 (the '203 patent)	April 27, 2026
7,417,070 (the '070 patent)	July 30, 2026
9,593,066 (the '066 patent)	December 15, 2028
9,604,901 (the '901 patent)	December 15, 2028
8,410,169 (the '169 patent)	February 13, 2030
8,349,892 (the '892 patent)	January 22, 2031
8,747,897 (the '897 patent)	August 11, 2031
8,497,393 (the '393 patent)	December 15, 2028*

\*0.25 mg, 1 mg, and 2.5 mg strengths only

Your ANDA contains paragraph IV certifications to each of the patents<sup>1</sup> under section 505(j)(2)(A)(vii)(IV) of the FD&C Act stating that the patents are invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Treprostinil Extended-Release Tablets, 0.125 mg, 0.25 mg, 1 mg, 2.5 mg, and 5 mg, under this ANDA. You have notified the Agency that Teva Pharmaceuticals USA, Inc. (Teva) complied with the requirements of section 505(j)(2)(B) of the FD&C Act. With respect to the 0.125 mg and 5 mg strength, you have notified the Agency that no action for infringement was brought against Teva within the statutory 45-day period. With respect to the 2.5 mg strength, litigation was initiated within the statutory 45-day period against Teva for infringement of the '070, '713, '839, '892, '169, '393, '311, and '897 patents in the United States District Court for the District of New Jersey [United Therapeutics Corporation and Supernus Pharmaceuticals, Inc. v. Actavis Laboratories FL, Inc., Civil Action No. 16-01816]. With respect to the 0.25 mg and 1 mg, strengths, litigation was initiated within the statutory 45-day period against Teva for infringement of the '070, '713, '839, '892, '169, '393, '311, '897, and '901 patents in the United States District Court for the

District of New Jersey [United Therapeutics Corporation and Supernus Pharmaceuticals, Inc. v. Actavis Laboratories FL, Inc., Civil Action No. 16-03642]. You have also notified the Agency that these cases were dismissed.

The RLD upon which you have based your ANDA, United's Orenitram Extended-Release Tablets, 0.125 mg, 0.25 mg, 1 mg, 2.5 mg, and 5 mg, is subject to a period of exclusivity. As noted in the Orange Book, the ODE-272 exclusivity is scheduled to expire on October 18, 2026. Your ANDA contains a statement that you do not seek to market Orenitram Extended-Release Tablets, 0.125 mg, 0.25 mg, 1 mg, 2.5 mg, and 5 mg, prior to the expiration of this exclusivity. Therefore, final approval cannot be granted until the ODE-272 exclusivity has expired, currently October 18, 2026.

Please note that if FDA requires a Risk Evaluation and Mitigation Strategy (REMS) for a listed drug, an ANDA referencing that listed drug also will be required to have a REMS. See section 505-1(i) of the FD&C Act.

### **REQUIREMENTS AND RECOMMENDATIONS POST APPROVAL**

Under applicable statutes, regulations, and guidances, if your ANDA receives final approval, it may be subject to certain requirements and recommendations post approval, including requirements regarding changes to approved ANDAs, postmarketing reporting, promotional materials, and annual facility fees, among others. For information on post-approval requirements and recommendations for ANDAs and a list of resources for ANDA holders, we refer you to: <https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/requirements-and-resources-approved-andas>.

### **RESUBMISSION**

To request final approval, please submit an amendment titled "FINAL APPROVAL REQUESTED" with enough time to permit FDA review prior to the date you believe that your ANDA will be eligible for final approval. A request for final approval that contains no new data, information, or other changes to the ANDA generally requires a period of 3 months for Agency review. Accordingly, such a request for final approval should be submitted no later than 3 months prior to the date on which you seek approval. A request for final approval that contains substantive changes to this ANDA or changes in the status of the manufacturing and testing facilities' compliance with cGMPs will be classified and reviewed according to OGD policy in effect at the time of receipt. Applicants should review available agency guidance for industry related to amendments under the generic drug user fee program to determine the duration of Agency review needed to review the changes submitted. As part of this consideration, applicants should monitor any changes to the RLD that occur after tentative approval, including changes in labeling, patent or exclusivity information, or marketing status. The submission of multiple amendments prior to final approval may also result in a delay in the issuance of the final approval letter.

The amendment requesting final approval should provide the legal/regulatory basis for your request for final approval and should include a copy of a court decision, settlement

or licensing agreement, or other information described in 21 CFR 314.107, as appropriate. It should also identify changes, if any, in the conditions under which the ANDA was tentatively approved, e.g., updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate. This amendment should be submitted even if none of these changes were made, and it should be designated clearly in your cover letter as a “FINAL APPROVAL REQUESTED.”

In addition to the amendment requested above, the Agency may request, at any time prior to the date of final approval, that you submit an additional amendment containing information as specified by the Agency. Failure to submit either or, if requested, both types of amendments described above may result in a delay in the issuance of the final approval letter.

This drug product may not be marketed without final Agency approval under section 505(j) of the FD&C Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under section 301 of the FD&C Act. Also, until the Agency issues the final approval letter, this drug product will not be deemed approved for marketing under section 505(j) of the FD&C Act, and will not be listed in the Orange Book. Should you believe that there are grounds for issuing the final approval letter prior to October 18, 2026, you should amend your ANDA accordingly.

For further information on the status of this ANDA or upon submitting an amendment to the ANDA, please contact Tom Ching, Regulatory Project Manager, at (301) 796 - 8445.

Sincerely yours,

*{See appended electronic signature page}*

For Edward M. Sherwood  
Director  
Office of Regulatory Operations  
Office of Generic Drugs  
Center for Drug Evaluation and Research

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<sup>1</sup> The agency notes that the 8'901, '203, '223, '066, and 4'901 patents were submitted to the Agency after submission of your ANDA. Litigation, if any, with respect to these patents would not create a statutory stay of approval.



Catherine  
Poole

Digitally signed by Catherine Poole

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