



ANDA 216836

ANDA TENTATIVE APPROVAL

Syneos Health, LLC
U.S. Agent for Gland Pharma Limited
1030 Sync Street
Morrisville, NC 27560
Attention: Theresa Broomall
Publishing Consultant

Dear Theresa Broomall:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on November 17, 2021, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Methylsalsalate Injection, 12 mg/0.6 mL, Single-Dose Vial.

Reference is also made to the tentative approval letter issued by this office on May 5, 2023, 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 Methylsalsalate Injection, 12 mg/0.6 mL, Single-Dose Vial to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Relistor Injection, 12 mg/0.6 mL, of Salix Pharmaceuticals, Inc. (Salix) NDA - 021964.

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.

The reference listed drug (RLD) upon which you have based your ANDA, Salix's Relistor Injection, 12 mg/0.6 mL, 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>
8,247,425 (the '425 patent)	December 31, 2030
8,420,663 (the '663 patent)	September 30, 2029
8,822,490 (the '490 patent)	September 30, 2029
9,180,125 (the '125 patent)	September 30, 2029
9,492,445 (the '445 patent)	September 30, 2029

Your ANDA contains paragraph IV certifications to each of the patents 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 Methylaltraxone Bromide Injection, 12 mg/0.6 mL, Single-Dose Vial, under this ANDA. You have notified the Agency that Gland Pharma Limited (Gland) complied with the requirements of section 505(j)(2)(B) of the FD&C Act. Litigation was initiated within the statutory 45-day period against Gland for infringement of the '425, '663, '490, '125, and '445 patents in the United States District Court for the District of New Jersey [Bausch Health Companies Inc., Salix Pharmaceuticals, Inc., Progenics Pharmaceuticals, Inc., and Wyeth LLC, v. Gland Pharma Limited, Civil Action No. 22-00939]. You have also notified the Agency that this case was dismissed.

However, we are unable to grant final approval to your ANDA at this time. Prior to the submission of your ANDA, another applicant or applicants submitted a substantially complete ANDA providing for Methylaltraxone Bromide Injection, 12 mg/0.6 mL, Single-Dose Vial, and containing a paragraph IV certification. Your ANDA will be eligible for final approval on the date that is 180 days after the commercial marketing date identified in section 505(j)(5)(B)(iv) of the FD&C Act.

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.

For further information on the status of this ANDA or upon submitting an amendment to the ANDA, please contact Kim Brown, Regulatory Project Manager, at (301) 796 - 4292.

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



Paul
Levine

Digitally signed by Paul Levine
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