ANDA 214008

ANDA APPROVAL

Syneos Health, LLC
U.S. Agent for Natco Pharma Limited
1030 Sync Street
Morrisville, NC 27560
Attention: Glenda Bryant
Senior Regulatory Consultant, Global Regulatory Affairs Solutions

Dear Glenda Bryant:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on September 23, 2019, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Trifluridine and Tipiracil Tablets, 15 mg/6.14 mg and 20 mg/8.19 mg.

Reference is also made to the complete response letter issued by this office on February 21, 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. Accordingly the ANDA is **approved**, effective on the date of this letter. We have determined your Trifluridine and Tipiracil Tablets, 15 mg/6.14 mg and 20 mg/8.19 mg, to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Lonsurf Tablets, 15 mg/6.14 mg and 20 mg/8.19 mg, of Taiho Oncology Inc. (Taiho).

The RLD upon which you have based your ANDA, Taiho's Lonsurf Tablets, 15 mg/6.14 mg and 20 mg/8.19 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.S. Patent Number	Expiration Date
9,527,833 (the '833 patent)	June 17, 2034
10,456,399 (the '399 patent)	February 3, 2037
10,457,666 (the '666 patent)	June 17, 2034

10,960,004 (the '004 patent)	February 3, 2037
RE46,284 (the '284 patent)	September 22, 2029

Your ANDA contains paragraph IV certifications to each of the patents[1] 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 Trifluridine and Tipiracil Tablets, 15 mg/6.14 mg and 20 mg/8.19 mg, under this ANDA. You have notified the Agency that (Natco) 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 Natco for infringement of the '833 and '284 patents in the United States District Court for the District of Delaware [Taiho Pharmaceutical Co., Ltd., and Taiho Oncology, Inc. v. Natco Pharma Ltd. and Natco Pharma, Inc., Civil Action No. 19-02368]. Although this litigation remains ongoing, the 7.5 year period identified in section 505(j)(5)(B)(iii) of the FD&C Act, during which FDA was precluded from approving your ANDA, has expired.

With respect to 180-day generic drug exclusivity, we note that Natco was one of the first ANDA applicants for Trifluridine and Tipiracil Tablets, 15 mg/6.14 mg and 20 mg/8.19 mg, to submit a substantially complete ANDA with a paragraph IV certification. Therefore, with this approval, Natco may be eligible for 180 days of shared generic drug exclusivity for Trifluridine and Tipiracil Tablets, 15 mg/6.14 mg and 20 mg/8.19 mg. This exclusivity, which is provided for under 505(j)(5)(B)(iv) of the FD&C Act, would begin to run from the date of the commercial marketing identified in section 505(j)(5)(B)(iv). The Agency notes that Natco failed to obtain tentative approval of this ANDA within 30 months after the date of which the ANDA was filed. See section 505(j)(5)(D)(i)(IV) of the FD&C Act (forfeiture of exclusivity for failure to obtain tentative approval). The Agency is not, however, making a formal determination at this time of Natco's eligibility for 180-day generic drug exclusivity. We will do so only if a subsequent paragraph IV applicant becomes eligible for full approval (a) within 180 days after Natco begins commercial marketing of Trifluridine and Tipiracil Tablets, 15 mg/6.14 mg and 20 mg/8.19 mg, or (b) at any time prior to the expiration of the '833 and '284 patents if Natco has not begun commercial marketing. Please submit correspondence to this ANDA notifying the Agency within 30 days of the date of the first commercial marketing of this drug product or the RLD. If you do not notify the Agency within 30 days, the date of first commercial marketing will be deemed to be the date of the drug product's approval. See 21 CFR 314.107(c)(2).

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.

COMPENDIAL STANDARDS

A drug with a name recognized in the official United States Pharmacopeia or official National Formulary (USP-NF) generally must comply with the compendial standard for strength, quality, and purity, unless the difference in strength, quality, or purity is plainly stated on its label (see FD&C Act § 501(b), 21 USC 351(b)). FDA typically cannot share application-specific information contained in submitted regulatory filings with third parties, which includes USP-NF. To help ensure that a drug continues to comply with compendial standards, application holders may work directly with USP-NF to revise official USP monographs. More information on the USP-NF is available on USP's website as https://www.uspnf.com/.

REQUIREMENTS AND RECOMMENDATIONS POST APPROVAL

Under applicable statutes, regulations, and guidances, your ANDA 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.

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

[1] The Agency notes that the '399, '666 and '004 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.

Paul
Levine

Digitally signed by Paul Levine
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