

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

214518Orig1s000

***Trade Name:* TPOXX, 200mg injection**

***Generic or Proper Name:* (tecovirimat)**

***Sponsor:* SIGA Technologies, Inc.**

***Approval Date:* May 18, 2022**

***Indication:* Provides for the use of TPOXX (tecovirimat) 200 mg injection for the treatment of human smallpox disease caused by variola virus in adults and pediatric patients weighing at least 3 kg.**

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APPROVAL LETTER



NDA 214518

NDA APPROVAL – ANIMAL EFFICACY

SIGA Technologies, Inc.
Attention: Paul Long, RPh, MBA
Senior Director, Regulatory Affairs
4575 SW Research Way
Suite 110
Corvallis, OR 97333

Dear Mr. Long:

Please refer to your new drug application (NDA) dated and received April 30, 2021, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for TPOXX (tecovirimat) 200 mg injection.

We acknowledge receipt of your major amendment dated December 10, 2021, which extended the goal date by three months.

This new drug application provides for the use of TPOXX (tecovirimat) 200 mg injection for the treatment of human smallpox disease caused by variola virus in adults and pediatric patients weighing at least 3 kg.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.¹ Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and Patient Package Insert) as well as annual reportable

¹ <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

changes not included in the enclosed labeling. Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*, available at FDA.gov.²

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (April 2018, Revision 5)*. For administrative purposes, designate this submission “**Final Printed Carton and Container Labeling for approved NDA 214518.**” Approval of this submission by FDA is not required before the labeling is used.

DATING PERIOD

Based on the stability data submitted to date, the expiry dating period for TPOXX (tecovirimat) 200 mg injection shall be 24 months from the date of manufacture when stored at 2°C to 8°C (36°F to 46°F).

SUBPART I APPROVAL REQUIREMENTS

Approvals under 21 CFR Part 314, Subpart I (Approval of New Drugs When Human Efficacy Studies Are Not Ethical or Feasible) are subject to three requirements:

- (1) *Approval with restrictions to ensure safe use.* This subsection permits the Agency to require postmarketing restrictions as are needed to ensure safe use of the drug product, commensurate with the specific safety concerns presented by the drug product. We have concluded that we have concluded that TPOXX® (tecovirimat) can be safely used without restrictions on distribution or use.
- (2) *Information to be provided to patient recipients.* This subsection requires applicants to prepare labeling to be provided to patient recipients for drug products approved under this subpart. We conclude that the FDA-Approved Patient Labeling and Instructions For Use for TPOXX (tecovirimat) meets the requirements of this subsection. We remind you that the patient labeling and

² We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database
<https://www.fda.gov/RegulatoryInformation/Guidances/default.htm><https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

instructions for use must be available with the product to be provided, when possible, prior to administration or dispensing of the drug product for the use approved under this subpart.

(3) *Postmarketing Studies*. This subsection requires you to conduct postmarketing studies, such as field studies, to verify and describe the drug's clinical benefit and to assess its safety when used as indicated when such studies are feasible and ethical. We remind you of your postmarketing requirement specified in your submission dated May 13, 2022. This requirement, along with any agreed upon completion dates, is listed below.

4278-1 Collaborate with US public health agencies to conduct a field study to evaluate the clinical response, drug concentrations, and safety profile of tecovirimat when used for the treatment of human smallpox disease due to variola virus infection. This trial should evaluate tecovirimat vs. brincidofovir vs. tecovirimat and brincidofovir combination therapy.

Final Protocol Submission: 07/2022

Submit clinical protocols to your IND 111390 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) include a status summary of each commitment in your annual report to this NDA. The status summary should include expected study/trial completion and final report submission dates, any changes in plans since the last annual report, and, for studies/trials, the number of patients entered into each study/trial. All submissions, including supplements, relating to this postmarketing commitment should be prominently labeled "**Postmarketing Protocol**," "**Postmarketing Final Report**," or "**Postmarketing Correspondence**."

Submit final reports to this NDA as a supplemental application. For administrative purposes, all submissions relating to this postmarketing requirement must be clearly designated "**Subpart I Postmarketing Requirements**."

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because the drug for this indication has orphan drug designation, you are exempt from this requirement.

PROMOTIONAL MATERIALS

Under 21 CFR 601.45, you are required to submit, during the application pre-approval review period, all promotional materials, including promotional labeling and advertisements, that you intend to use in the first 120 days following marketing approval (i.e., your launch campaign). If you have not already met this requirement, you must immediately contact the Office of Prescription Drug Promotion (OPDP) at (301) 796-1200. Please ask to speak to a regulatory project manager or the appropriate reviewer to discuss this issue.

As further required by 21 CFR 601.45, submit all promotional materials that you intend to use after the 120 days following marketing approval (i.e., your post-launch materials) at least 30 days before the intended time of initial dissemination of labeling or initial publication of the advertisement. We ask that each submission include a detailed cover letter together with three copies each of the promotional materials, annotated references, and approved Prescribing Information, Medication Guide, and Patient Package Insert (as applicable).

For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs*.³

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

³ For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

If you have any questions, call Andrew Gentles, PharmD, BCPS AQ-ID, Senior Regulatory Project Manager, at (240) 402-5708 or the mainline at (301) 796-1500.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, MD
Director
Division of Antivirals
Office of Infectious Diseases
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
 - Prescribing Information
 - Patient Package Insert
- Carton and Container Labeling

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

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