NDA 208627/S-006

sNDA APPROVAL – ANIMAL EFFICACY
FULFILLMENT OF POSTMARKETING
COMMITMENT

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 supplemental new drug application (sNDA) dated August 23, 2021, received August 23, 2021, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for TPOXX (tecovirimat) capsules, 200 mg.

This Prior Approval supplemental new drug application provides for new dosing recommendations for the treatment of human smallpox disease in adult and pediatric patients who weigh 120 kg or more.

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

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information.

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, Patient Package Insert, and Instructions for Use), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable 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.*[2]

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

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 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

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[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.

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.

   Reference is made to the postmarketing study requirement, PMR 3417-1 listed in the original NDA 208627 approval letter dated July 13, 2018 requiring you to conduct a field study. Reference is also made to the Agency's September 13, 2021, Release from Postmarketing Requirement and New Postmarketing Requirement letter, wherein PMR 3417-1 was released and reissued under PMR 3417-7.

   We note that this field study, PMR 3417-7, will be conducted in accordance with the protocol and current product labeling. This labeling has been revised to include a new dosing regimen for adult and pediatric patients weighing 120 kg or more.

   This requirement, along with any agreed upon completion dates, is listed below.

   3417-7 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.

   The timetable you submitted on August 11, 2021, states that you will submit the protocol according to the following schedule:

   Draft Protocol Submission: 02/2022
   Final Protocol Submission: 07/2022

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.

FULFILLMENT OF POSTMARKETING COMMITMENT

We have received your submission dated February 22, 2021, containing the final report for the following postmarketing commitment listed in our July 13, 2018 approval letter:

3417-4 Conduct a study to determine the pharmacokinetics of tecovirimat in subjects with body weight greater than 120 kilograms (>120 kg) and to further determine if a change in dosing regimen is needed in these subjects.

Draft Protocol Submission: 04/2019
Final Protocol Submission: 07/2019
Study/Trial Completion: 08/2020
Final Report Submission: 02/2021

We have reviewed your submission and conclude that the above commitment was fulfilled.

We remind you that there is a postmarketing requirement and a postmarketing commitment listed in the July 13, 2018 approval letter that are still open.

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).

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
  - Instructions for Use

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

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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