



BLA 761065/S-011

**SUPPLEMENT APPROVAL
NEW POSTMARKETING REQUIREMENT**

Theratechnologies, Inc.
c/o ICON Clinical Research LLC
Attention: Elizabeth Wishart, B.Sc., MBA
US Agent on behalf of Theratechnologies Inc.
2343 Alexandria Drive, Suite 100
Lexington, KY 40504

Dear Ms. Wishart:

Please refer to your supplemental biologics license application (sBLA), dated and received August 11, 2020, and your amendments, submitted under section 351(a) of the Public Health Service Act for Trogarzo (ibalizumab-uiyk) injection.

This Prior Approval supplemental biologics application provides for the following changes to the Trogarzo (ibalizumab-uiyk) Prescribing Information (PI):

- To update WARNINGS AND PRECAUTIONS with a new subsection, Embryo-Fetal Toxicity to provide information based on animal data regarding the potential risk of reversible immunosuppression in infants with *in utero* exposure to Trogarzo.
- To update USE IN SPECIFIC POPULATIONS, Pregnancy, with data from an enhanced pre- and post-natal development study in cynomolgus monkeys.
- To update Patient Counseling Information with embryo-fetal toxicity information.

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.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at

FDA.gov,¹ that is identical to the enclosed labeling (text for the Prescribing Information, Patient Package Insert) and include the labeling changes proposed in any pending “Changes Being Effected” (CBE) supplements.

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 via publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this BLA, including pending “Changes Being Effected” (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] 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).

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

Since Trogarzo was approved on March 6, 2018, we have become aware of the potential serious risk for reversible immunosuppression among infants with *in utero* exposure to Trogarzo. The signal for this serious risk was identified during FDA’s review of the findings in the enhanced pre- and post-natal development (ePPND) study in cynomolgus monkeys that was conducted to fulfill postmarketing requirement (PMR) 3283-2. The ePPND study demonstrated that infant monkeys exposed *in utero* to ibalizumab-uyk experienced significant changes in immune cell levels (CD4+ T cell and B cell lymphocytopenia) in the first weeks of life. We consider this information to be “new safety information” as defined in section 505-1(b)(3) of the FDCA.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess the signal of a serious risk of immunosuppression (CD4+ T cell and B cell lymphocytopenia) in infants born to mothers exposed to Trogarzo during pregnancy.

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>.

Furthermore, the active postmarket risk identification and analysis system as available under section 505(k)(3) of the FDCA will not be sufficient to assess this serious risk.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

- 3989-1 Conduct a study as a registry to collect prospective data in individuals exposed to Trogarzo (ibalizumab-uiyk) during pregnancy to monitor maternal and pregnancy outcomes, including adverse effects on the developing fetus, neonate, and infant. The study will assess infant outcomes, such as infections, hospitalizations, and death through the first year of life. The study will collect information for 10 years.

The timetable you submitted on March 26, 2021 states that you will conduct this study according to the following schedule:

Draft Submission Protocol: 07/2021
Final Protocol Submission: 10/2021
Study Completion: 01/2033
Final Report Submission: 04/2033

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.³

REQUIRED POSTMARKETING CORRESPONDENCE UNDER 505(o)

Submit the protocol(s) to your IND 139198, with a cross-reference letter to this BLA. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final report(s) to your BLA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: “**Required Postmarketing Protocol Under 505(o)**”, “**Required Postmarketing Final Report Under 505(o)**”, “**Required Postmarketing Correspondence Under 505(o)**”.

Submission of the protocol(s) for required postmarketing observational studies to your IND is for purposes of administrative tracking only. These studies do not constitute clinical investigations pursuant to 21 CFR 312.3(b) and therefore are not subject to the IND requirements under 21 CFR part 312 or FDA’s regulations under 21 CFR parts 50 (Protection of Human Subjects) and 56 (Institutional Review Boards).

³ See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019)*.
<https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 601.70 requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 601.70 to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 601.70. We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. 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*.⁴

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at FDA.gov.⁵ Information and Instructions for completing the form can be found at FDA.gov.⁶ All promotional materials for your drug product that include representations about your drug product must be promptly revised to make it consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 601.12(a)(4)]. The revisions to your promotional materials should include prominent disclosure of the important new safety information that appears in the revised labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 601.12(a)(4).

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

If you have any questions, contact Kevin Allen, Regulatory Project Manager, at 301-837-7467.

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

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/

POONAM MISHRA
04/22/2021 04:43:22 PM
on behalf of Division Director