BLA 761208/S-007

SUPPLEMENT APPROVAL/
FULFILLMENT OF POSTMARKETING REQUIREMENT

Seagen Inc.
Attention: Sharmi Patel, PharmD, MBA
Senior Manager, Regulatory Affairs
21823 30th Drive SE
Bothell, WA 98021

Dear Dr. Patel:

Please refer to your supplemental biologics license application (sBLA), dated November 9, 2023, received November 9, 2024, submitted under section 351(a) of the Public Health Service Act for TIVDAK (tisotumab vedotin-tftv), for injection.

This Prior Approval supplemental biologics license application provides for regular approval of TIVDAK for the treatment of adult patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy.

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 Prescribing Information, and Medication Guide 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]

[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.

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 the 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).

SUBPART E FULFILLED

We approved this BLA under the regulations at 21 CFR 601 Subpart E for Accelerated Approval of Biological Products for Serious or Life-Threatening Illnesses. Approval of this supplement fulfills your commitments made under 21 CFR 601.41.

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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

FULFILLMENT OF POSTMARKETING REQUIREMENT

We have received your submission dated November 9, 2023, containing the final report for the following postmarketing requirement listed in the September 20, 2021, approval letter for BLA 761208.

4131-1 Conduct the clinical trial innovaTV 301 titled, "Tisotumab Vedotin versus Chemotherapy in Recurrent or Metastatic Cervical Cancer" and provide the final overall survival (OS) and progression-free survival (PFS) analyses to describe and verify the clinical benefit of tisotumab vedotin in patients with recurrent or metastatic cervical cancer.

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

We remind you that there are postmarketing requirements and postmarketing commitments listed in the September 20, 2021, letter that are still open.

POSTMARKETING REQUIREMENTS UNDER 505(o)

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

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 a known serious risk of severe ocular toxicity.

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.

Finally, we have determined that only a clinical trial (rather than a nonclinical or observational study) will be sufficient to assess this known serious risk.

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

4632-1 Conduct a study of tisotumab vedotin, to include prospectively specified, scheduled ophthalmologic assessments in approximately 100 enrolled patients to further characterize the incidence and severity of tisotumab vedotin-related ocular toxicity. The study will include scheduled comprehensive ophthalmologic exams and a mechanism to collect, classify, and analyze data on ocular toxicity and exam findings. The scheduled ophthalmologic exams must be conducted prior to each cycle for the first 9 cycles of treatment, monthly for 90 days (+/- 7) following last treatment, and as clinically indicated, in order to assess and further characterize ocular adverse events and evaluate risk mitigation strategies. The ophthalmologic exam must include, at a minimum, slit lamp exam of the anterior segment of the eye, visual acuity, intraocular pressure, and elicitation for visual symptoms.

The timetable you submitted on April 12, 2024, states that you will conduct this trial according to the following schedule:

Draft Protocol Submission:	09/2024
Final Protocol Submission:	01/2025
Interim Report Submission:	07/2026
Study Completion:	08/2027
Final Report Submission:	02/2028

The 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]

Submit clinical protocol(s) to your IND 135476 with a cross-reference letter to this BLA. Submit nonclinical and chemistry, manufacturing, and controls protocols and all 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).**

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 the FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B(a)(1) 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.

The FDA will consider the submission of your annual report under section 506B(a)(1) 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.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

4632-2 Conduct an integrated analysis of data from clinical trials and other data sources such as post-marketing reports, real-world evidence, and other sources, to further characterize the safety and efficacy of tisotumab vedotin in racial and ethnic minority patients with recurrent or metastatic cervical cancer (r/mCC). The population should be representative of the US population of patients with r/mCC, including racial and ethnic minorities, and allow for characterization of the results in these populations.

The timetable you submitted on April 12, 2024, states that you will conduct this study according to the following schedule:

[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.

Draft Protocol Submission (Analysis Plan):	03/2025
Final Protocol Submission (Analysis Plan):	09/2025
Study Completion:	09/2026
Final Report Submission:	03/2027

A final submitted protocol is one that the FDA has reviewed and commented upon, and you have revised as needed to meet the goal of the study or clinical trial.

Submit clinical protocols to your IND 135476 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this BLA. In addition, under 21 CFR 601.70 you should include a status summary of each commitment in your annual progress report of postmarketing studies to this BLA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients/subjects entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

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]
You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. 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 that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety- related information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety-related 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 314.70(a)(4).

[4] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[6] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

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, call Zohal Hamidi, Regulatory Project Manager, at 301-796-6383 or zohal.hamidi@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Laleh Amiri-Kordestani, MD
Director
Division of Oncology 1
Office of Oncologic Diseases
Center for Drug Evaluation and Research
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Medication Guide

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/

LALEH AMIRI KORDESTANI
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