



DBSQC/OCBQ ANALYTICAL METHOD REVIEW MEMO

To: The file: STN 125722/0

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Applicant: PTC Therapeutics, Inc. (PTC)

Subject: Review of Bioburden, Sterility, Endotoxin (b) (4) Analytical
Methods used for KEBILIDI (eladocagene exuparovec)

Recommendation: Approval

Executive Summary:

The bioburden, sterility, endotoxin, (b) (4) analytical methods used for testing and release of KEBILIDI (eladocagene exuparovec) and the associated analytic method qualifications, were reviewed. The assays were adequately described and shown to be suitable for their intended purpose.

Conclusion:

The analytical methods and their qualifications reviewed for KEBILIDI (eladocagene exuparovec) (b) (4) drug product were found to be adequate for their intended use.

Documents Reviewed

Information in sections of the original submission that describe control of (b) (4) Drug Product (DP) (3.2.S.4 and 3.2.P.5, respectively), including descriptions of (b) (4) DP specifications, analytical procedures of (b) (4) DP and qualifications of these analytical procedures were reviewed. In addition, the responses to CBER's Information Requests (IR) received on June 14, 2024 (Amendment 8), October 11, 2024 (Amendment 52), and October 18, 2024 (Amendment 55) were also reviewed.

Background:

PTC Therapeutics (PTC) submitted BLA 125722/0 on March 15, 2024, KEBILIDI (eladocagene exuparvovec), a gene replacement therapy for use in the treatment of aromatic L-amino acid decarboxylase (AADC) deficiency. PTC initial proposed proprietary name was UPSTAZA, which was not approved and later changed to KEBILIDI, which was approved by the Advertising and Promotional Labeling Branch (APLB) within CBER on September 25, 2024.

AADC deficiency is a rare genetic disorder that typically causes severe physical, mental, and behavioral disability and suffering from the first months of life. People with AADC deficiency may also experience episodes of distressing seizure-like oculogyric crises causing the eyes to roll up in the head, frequent vomiting, behavioral problems, and difficulty sleeping. KEBILIDI is a recombinant adeno-associated virus serotype 2 (AAV2)-based gene therapy containing the human dopa decarboxylase (DDC) gene. It is designed to correct the underlying genetic defect by delivering a functioning DDC gene directly into the putamen, increasing the AADC enzyme and restoring dopamine production.

KEBILIDI will be available as a solution for bilateral infusion into the putamen. The product strength is 1.8×10^{11} vg of rAAV2-hAADC (320 μ l). The dosing schedule will be a single administration in an inpatient setting.

KEBILIDI single dose vials contain a volume of 500 μ L at a concentration of 2.8×10^{11} vg/ 0.5 mL. Vials are packaged (b) (4) shipped via commercial shipping. Upon receipt, the product vials should be removed immediately from the shipping container and stored at (b) (4) until required for patient administration.

This review focuses on the qualification of the bioburden, sterility, endotoxin, and (b) (4) tests as performed on the (b) (4) final DP, to indicate the methods are suitable their intended use.

1. Bioburden Method (b) (4)

Introduction

Bioburden testing for eladocagene exuparvovec (b) (4)

[Redacted text block]

Review of Method

The bioburden test is performed (b) (4)

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(b) (4)

Review of Method Qualification

(b) (4)

(b) (4)

(b) (4)

Conclusion

The method suitability test was performed and compliant with (b) (4) and the test results indicate there is no product inhibition of microorganism growth, thus indicating the (b) (4) method suitable for determining bioburden under the actual conditions of use.

2. Sterility Method (DP)

Introduction

Sterility testing for DP is performed at (b) (4)
Specification of 'No growth' must be met for release of eladocagene exuparovec DP.

Methods

(b) (4)

The method is described in more detail below together with the tests that were performed to determine suitability of the test method.

Information Request and Review:

The original qualification report for sterility lacked sufficient information to complete the review; therefore, an IR was sent to PTC, requesting environmental isolates to be included in their method qualification or provide justification for not performing these studies if the known environmental isolates from (b) (4) (b) (4) facility/facilities are similar to the (b) (4) microorganisms. Response was received on October 11, 2024 (Amendment 52), stating that while the drug product formulation provides a low inherent risk for inhibition of human commensal organism growth, PTC agrees to evaluate suitability with (b) (4) post-BLA approval.

A follow-up IR was sent to PTC, requesting PTC to confirm their commitment to evaluate suitability with (b) (4) as environmental isolates post-BLA approval/PMC and to provide the date PTC will submit the report in their Annual Report (AR). Response was received on October 18, 2024 (Amendment 55), PTC confirmed their commitment to evaluate suitability with (b) (4) as environmental isolates in addition to the indicated (b) (4) microorganisms. The qualification suitability report will be submitted to CBER in AR on January 31, 2026, which CBER found it acceptable.

Sterility Qualification for DP

(b) (4)

(b) (4)

(b) (4)

(b) (4)

Conclusion

The method suitability tests were performed and compliant with (b) (4) and the test results indicate there is no product interference from DP test samples, thus indicating the (b) (4) sterility test method is appropriate under the actual conditions of use. PTC confirmed their commitment to evaluate suitability with (b) (4) as environmental isolates in addition to the indicated (b) (4) microorganisms and will submit the qualification suitability results to CBER in AR on January 31, 2026, which CBER found it acceptable.

3. Endotoxin Method (b) (4) DP)

Introduction

Endotoxin testing for eladocagene exuparovec (b) (4) . Specifications of (b) (4) DP must be met for release of KEBILIDI.

Review of Method

(b) (4)

The method is described in more detail below together with the tests performed to determine suitability of the test method for its intended use.

Information Request and Review:

The original qualification reports for endotoxin lacked sufficient information to complete the review; therefore, two IRs were sent to PTC, requesting complete

qualification reports of endotoxin test for (b) (4) drug product. CBER requested the report to include lot numbers of product tested, maximum valid (b) (4)

Responses were received on October 11, 2024 (Amendment 52), and October 18, 2024 (Amendment 55), which were found acceptable and reviewed as part of the (b) (4) DP endotoxin testing below.

Method Qualification for (b) (4)

(b) (4)

(b) (4)

Method Qualification for DP

(b) (4)

(b) (4)

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