

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

215413Orig1s000

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

IND 114820

**MEETING REQUEST-
WRITTEN RESPONSES**

ViiV Healthcare Company
c/o GlaxoSmithKline
Attention: Stephen Hyatt
Manager, Global Regulatory Affairs
Five Moore Drive
P.O. Box 13398
Research Triangle Park, NC 27709

Dear Mr. Hyatt:¹

Please refer to your investigational new drug application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for Triumeq (abacavir, dolutegravir, and lamivudine) tablets for oral suspension.

We also refer to your submission dated March 9, 2021, containing a meeting request. The purpose of the requested meeting was to discuss your proposal to satisfy food effect requirements for your planned original NDA submission, preassigned NDA 215413, for Triumeq (abacavir, dolutegravir, and lamivudine) tablets for oral suspension.

Further reference is made to our Meeting Granted letter dated March 18, 2021, wherein we agreed that written responses to your questions would be provided in lieu of a meeting.

The enclosed document constitutes our written responses to the questions contained in your April 2, 2021 background package.

¹ 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>.

If you have any questions, call me at 301-837-7467 or 301-796-1500.

Sincerely,

{See appended electronic signature page}

Kevin Allen, MS
Regulatory Project Manager
Antivirals Group
Division of Regulatory Operations for Infectious
Diseases
Office of Regulatory Operations
Center for Drug Evaluation and Research

Enclosure:

- Written Responses



WRITTEN RESPONSES

Meeting Type: Type B

Meeting Category: Pre-NDA

Application Number: 114820

Product Name: Triumeq (abacavir, dolutegravir, and lamivudine) tablets for oral suspension

Indication: Treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults and in pediatric patients weighing at least 14 kg

Sponsor Name: ViiV Healthcare Company

Regulatory Pathway: 505(b)(1) of the Federal Food, Drug, and Cosmetic Act

1.0 BACKGROUND

Triumeq is a fixed dose combination tablet containing abacavir 600 mg, dolutegravir 50 mg, and, lamivudine 300 mg. Triumeq was approved August 22, 2014 for the treatment of HIV-1 infection in patients 12 years and older. Upon approval of Triumeq, the Agency issued PREA PMRs to study Triumeq in pediatric patients 2 to less than 18 years of age.

The Sponsor has proposed to submit an original NDA for Triumeq dispersible tablet formulation to support use in pediatric patients ≥ 14 to < 25 kg. For pediatric patients ≥ 25 to < 40 kg, the sponsor plans to submit a supplemental application to NDA 205551 Triumeq tablets.

The purpose of the requested meeting is to discuss the Sponsor's proposal to satisfy food effect requirements for the planned original NDA submission, preassigned NDA 215413, for Triumeq (abacavir, dolutegravir, and lamivudine) tablets for oral suspension.

2.0 QUESTIONS AND RESPONSES

2.1. Clinical Pharmacology

Question 1: Does the Agency agree that the proposed data package outlined in Appendix 1 provides a reasonable approach to supporting an initial NDA with dosing administration of Triumeq dispersible tablet without regard to food?

FDA Response to Question 1: While it is a review issue, the existing data would unlikely support the administration of Triumeq dispersible tablet without regard to food as we previously communicated to you (FDA Information Request, sent on October 22, 2020, NDA 205551). This would likely result in recommending the administration of Triumeq dispersible tablets under fasting conditions only.

We recognize that labeling the drug for administration only under fasting conditions is not ideal, especially for pediatric patients. Therefore, the agency recommends submitting the application with the results of the food effect study if the results are expected to be available in the next several months.

3.0 PREA REQUIREMENTS

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.

Please be advised that under the Food and Drug Administration Safety and Innovation Act (FDASIA), you must submit an Initial Pediatric Study Plan (iPSP) within 60 days of an End-of-Phase-2 (EOP2) meeting. In the absence of an EOP2 meeting, refer to the draft guidance below. The iPSP must contain an outline of the pediatric study or studies that you plan to conduct (including, to the extent practicable study objectives and design, age groups, relevant endpoints, and statistical approach); any request for a deferral, partial waiver, or waiver, if applicable, along with any supporting documentation, and any previously negotiated pediatric plans with other regulatory authorities. The iPSP should be submitted in PDF and Word format. Failure to include an Agreed iPSP with a marketing application could result in a refuse to file action.

For additional guidance on the timing, content, and submission of the iPSP, including an iPSP Template, please refer to the draft guidance for industry *Pediatric Study Plans: Content of and Process for Submitting Initial Pediatric Study Plans and Amended*

*Pediatric Study Plans.*² In addition, you may contact the Division of Pediatric and Maternal Health at 301-796-2200 or email Pedsdrugs@fda.hhs.gov. For further guidance on pediatric product development, please refer to FDA.gov.³

5.0 DATA STANDARDS FOR STUDIES

Under section 745A(a) of the FD&C Act, electronic submissions “shall be submitted in such electronic format as specified by [FDA].” FDA has determined that study data contained in electronic submissions (i.e., NDAs, BLAs, ANDAs and INDs) must be in a format that the Agency can process, review, and archive. Currently, the Agency can process, review, and archive electronic submissions of clinical and nonclinical study data that use the standards specified in the Data Standards Catalog.⁴

On December 17, 2014, FDA issued the guidance for industry *Providing Electronic Submissions in Electronic Format--- Standardized Study Data*. This guidance describes the submission types, the standardized study data requirements, and when standardized study data are required. Further, it describes the availability of implementation support in the form of a technical specifications document, Study Data Technical Conformance Guide,⁵ as well as email access to the eData Team (cdereadata@fda.hhs.gov) for specific questions related to study data standards. Standardized study data are required in marketing application submissions for clinical and nonclinical studies that started after December 17, 2016. Standardized study data are required in commercial IND application submissions for clinical and nonclinical studies that started after December 17, 2017. CDER has produced a Study Data Standards Resources web page⁶ that provides specifications for sponsors regarding implementation and submission of clinical and nonclinical study data in a standardized format. This web page will be updated regularly to reflect CDER's growing experience in order to meet the needs of its reviewers.

For commercial INDs and NDAs, Standard for Exchange of Nonclinical Data (SEND) datasets are required to be submitted along with nonclinical study reports for study types that are modeled in an FDA-supported SEND Implementation Guide version. The FDA Data Standards Catalog, which can be found on the Study Data Standards Resources web page noted above, lists the supported SEND Implementation Guide versions and associated implementation dates.

Although the submission of study data in conformance to the standards listed in the

² When final, this guidance will represent the FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at

<https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

³ <https://www.fda.gov/drugs/development-resources/pediatric-and-maternal-health-product-development>

⁴ <http://www.fda.gov/forindustry/datastandards/studydatastandards/default.htm>

⁵ <https://www.fda.gov/media/88173/download>

⁶ <http://www.fda.gov/ForIndustry/DataStandards/StudyDataStandards/default.htm>

FDA Data Standards Catalog will not be required in studies that started on or before December 17, 2016, CDER strongly encourages IND sponsors to use the FDA supported data standards for the submission of IND applications and marketing applications. The implementation of data standards should occur as early as possible in the product development lifecycle, so that data standards are accounted for in the design, conduct, and analysis of clinical and nonclinical studies. For clinical and nonclinical studies, IND sponsors should include a plan (e.g., in the IND) describing the submission of standardized study data to FDA. This study data standardization plan (see the FDA Study Data Technical Conformance Guide) will assist FDA in identifying potential data standardization issues early in the development program.

If you have not previously submitted an eCTD submission or standardized study data, we encourage you to send us samples for validation following the instructions at FDA.gov.⁷ For general toxicology, supporting nonclinical toxicokinetic, and carcinogenicity studies, submit data in the Standards for the Exchange of Nonclinical Data (SEND) format. The validation of sample submissions tests conformance to FDA supported electronic submission and data standards; there is no scientific review of content.

The Agency encourages submission of sample data for review before submission of the marketing application. These datasets will be reviewed only for conformance to standards, structure, and format. They will not be reviewed as a part of an application review. These datasets should represent datasets used for the phase 3 trials. The FDA Study Data Technical Conformance Guide⁸ (Section 7.2 eCTD Sample Submission pg. 30) includes the link to the instructions for submitting eCTD and sample data to the Agency. The Agency strongly encourages sponsors to submit standardized sample data using the standards listed in the Data Standards Catalog referenced on the FDA Study Data Standards Resources web site.⁹ When submitting sample data sets, clearly identify them as such with **SAMPLE STANDARDIZED DATASETS** on the cover letter of your submission.

Additional information can be found at FDA.gov.¹⁰

6.0 LABORATORY TEST UNITS FOR CLINICAL TRIALS

CDER strongly encourages IND sponsors to identify the laboratory test units that will be reported in clinical trials that support applications for investigational new drugs and product registration. Although Système International (SI) units may be the standard

⁷ <https://www.fda.gov/industry/study-data-standards-resources/study-data-submission-cder-and-cber>

⁸ <https://www.fda.gov/media/88173/download>

⁹ <https://www.fda.gov/ForIndustry/DataStandards/StudyDataStandards/default.htm>

¹⁰ <https://www.fda.gov/industry/study-data-standards-resources/study-data-submission-cder-and-cber>

reporting mechanism globally, dual reporting of a reasonable subset of laboratory tests in U.S. conventional units and SI units might be necessary to minimize conversion needs during review. Identification of units to be used for laboratory tests in clinical trials and solicitation of input from the review divisions should occur as early as possible in the development process. For more information, please see the FDA website entitled Study Data Standards Resources¹¹ and the CDER/CBER Position on Use of SI Units for Lab Tests website.¹²

7.0 SECURE EMAIL COMMUNICATIONS

Secure email is required for all email communications from FDA when confidential information (e.g., trade secrets, manufacturing, or patient information) is included in the message. To receive email communications from FDA that include confidential information (e.g., information requests, labeling revisions, courtesy copies of letters), you must establish secure email. To establish secure email with FDA, send an email request to SecureEmail@fda.hhs.gov. Please note that secure email may not be used for formal regulatory submissions to applications (except for 7-day safety reports for INDs not in eCTD format).

¹¹ <http://www.fda.gov/ForIndustry/DataStandards/StudyDataStandards/default.htm>

¹² <https://www.fda.gov/media/109533/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/

KEVIN L ALLEN
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