# CENTER FOR DRUG EVALUATION AND RESEARCH

## Approval Package for:

## *APPLICATION NUMBER:*

## 022542Orig1s006

| | |
|---|---|
| ***Trade Name:*** | VIOKACE |
| ***Generic or Proper Name:*** | (pancrelipase) |
| ***Sponsor:*** | VIOKACE LLC. |
| ***Approval Date:*** | July 2, 2021 |
| ***Indication:*** | VIOKACE® is a combination of porcine-derived lipases, proteases, and amylases. VIOKACE, in combination with a proton pump inhibitor, is indicated in adults for the treatment of exocrine pancreatic insufficiency due to chronic pancreatitis or pancreatectomy. |

# CENTER FOR DRUG EVALUATION AND RESEARCH

## 022542Orig1s006

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# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# 022542Orig1s006

# APPROVAL LETTER

BLA 022542/S-006

**APPROVAL LETTER**

Viokace, LLC
c/o Aimmune Therapeutics, Inc.
Attention: Vandana Garikipati
Director, Regulatory Affairs
8000 Marina Boulevard, Ste 300
Suite 300
Brisbane, CA 94005

Dear Mr. Garikipati:

Please refer to your supplemental biologics license application (sBLA) dated and received March 12, 2021, and your amendment, submitted under section 351(a) of the Public Health Service Act for Viokace® (pancrelipase) tablets, for oral use.

This Prior Approval sBLA provides for a change in the high-performance liquid chromatography test method and subsequently the specifications for the Enzyme Chromatographic Profile test for the pancrelipase drug substance and Viokace® (pancrelipase) Tablets.

**APPROVAL**

We have completed our review of this supplemental application, as amended. This supplement is approved.

This information will be included in your biologics license application file.

If you have any questions, call Melinda Bauerlien, Regulatory Business Process Manager, at (301) 796 - 0906.

Sincerely,

*{See appended electronic signature page}*

Amy Rosenberg, M.D.
Director
Division of Biotechnology Review and Research III
Office of Biotechnology Products
Office of Pharmaceutical Quality
Center for Drug Evaluation and Research

Amy Rosenberg

Digitally signed by Amy Rosenberg
Date: 7/02/2021 09:30:34AM
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# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# 022542Orig1s006

# PRODUCT QUALITY REVIEW(S)

**Department of Health and Human Services**
**Food and Drug Administration**
**Center for Drug Evaluation and Research**

Office of Pharmaceutical Quality
Office of Biotechnology Products
10903 New Hampshire Avenue
Silver spring, MD 20993

**Memorandum of Review**

| | |
|---|---|
| **STN** | BLA022542/Supplement 0006 |
| **Subject** | **Prior Approval Supplement (PAS)**:<br>This PAS proposes the following:<br>• change the test method and specifications for the Enzyme Chromatographic Profile using high-performance liquid chromatography (HPLC) for the pancrelipase drug substance and Viokace (pancrelipase) Tablets |
| **Submission Date** | 03/12/2021 |
| **Review/Revision Date** | 05/03/2021, 06/14/2021, 06/29/2021 |
| **Primary Reviewer** | Zhong Zhao, Ph.D., DBRR III |
| **Secondary/Tertiary Review** | Susan Kirshner, Ph.D., DBRR III |
| **RPM** | Melinda Bauerlien |
| **Applicant** | Nestlé HealthCare Nutrition, Inc. |
| **Product** | Viokace (pancrelipase) Tablets |
| **Indication** | Treatment of adults with exocrine pancreatic insufficiency due to chronic pancreatitis or pancreatectomy |
| **Filing Action Date** | 05/12/2021 |
| **PDUFA Due Date** | 07/12/2021 |

## 1 SUMMARY OF RECOMMENDATION

### Recommendation

I recommend approval of this supplement.

**Justification**

In this PAS, the Sponsor proposes a change in the HPLC method and subsequently the specifications for the Enzyme Chromatographic Profile for the pancrelipase drug substance (DS) and Viokace (pancrelipase) drug product (DP).

- The Sponsor provided the information that Enzyme Chromatographic Profile is used as identity and content test for pancrelipase DS release and Viokace DP release and stability. The chromatographic column used in the current method is no longer available, resulting in the inability to release batches to the market. The Sponsor provides the validation results to demonstrate adequate specificity, accuracy, precision, linearity, sensitivity, and robustness for the proposed Enzyme Chromatographic Profile.

- The Sponsor proposed the specification for the proposed Enzyme Chromatographic Profile for both pancrelipase DS and Viokace DP based on the statistical analysis on the results from 22 pancrelipase DS release batches, 13 Viokace DP release batches, and 4 Viokace DP stability batches using the proposed Enzyme Chromatographic Profile method. The proposed specifications are acceptable because the specifications were based on sufficient data collected with the validated method and analyzed by suitable statistical method.

- The Sponsor demonstrated that the proposed Enzyme Chromatographic Profile using the new chromatographic column results in more resolved peaks and more stable baseline. Although the new chromatographic method is not comparable to the current method, the new chromatographic method is analytically superior because it is capable of providing a better peak integration and ensuring repeatability and reproducibility in the analysis of pancrelipase DS at release and Viokace DP at release and during stability studies.

Based on the above assessment, I recommend approval of this supplement.

## 2 DRAFT COMMENTS TO SPONSOR

Please refer to your supplemental biologics license application (sBLA) dated March 12, 2021, received March 12, 2021, and your amendments, submitted under section 351(a) of the Public Health Service Act for Viokace® (pancrelipase) Tablets, for oral use.

This Prior Approval sBLA provides for a change in the high-performance liquid chromatography test method and subsequently the specifications for the Enzyme Chromatographic Profile test for the pancrelipase drug substance and Viokace® (pancrelipase) Tablets

**APPROVAL**

We have completed our review of this sBLA, as amended. This supplement is approved.

## 3 BACKGROUND

VIOKACE tablets, for oral use, was approved by the FDA in 2012. VIOKACE is a combination of porcine-derived lipases, proteases, and amylases. VIOKACE, in combination with a proton pump inhibitor, is indicated in adults for the treatment of exocrine pancreatic insufficiency due to chronic pancreatitis or pancreatectomy.

Pancrelipase, which is the drug substance used in Viokace Tablets, is a complex mixture of proteins obtained from porcine pancreas. The Enzyme Chromatographic Profile is an identification (ID) test comparing the area percent of the major peaks from the sample chromatograms to the corresponding peaks from the external pancrelipase active pharmaceutical ingredient (API) standard.

## 4 REVIEW OF CURRENT SUBMISSION

### Analytical procedures of Enzyme Chromatographic Profile

The Sponsor described that the Enzyme Chromatographic Profile is an ID test using Reversed Phase HPLC (RP-HPLC). The Sponsor proposed a new RP-HPLC method which utilizes a different column, (b) (4), and different chromatographic conditions, therefore, the chromatographic profile obtained with the new method differs from that obtained with the current method. The detailed information for Enzyme Chromatographic Profile using RP-HPLC is available in section 3.2.P.5.2.

The Sponsor provided the representative chromatogram for Enzyme Chromatographic Profile as the figure below.

(b) (4)

The Sponsor performed identity test for each peak and summarized the ID results in the Table below.

**Table 1 Comparison of Identified Peaks in Current and Proposed Enzyme Chromatographic Profile Method**

| Identified Peaks in Proposed Method | Identified Peaks in Current Method |
|---|---|
| (b) (4) | |

The Sponsor also provide the system suitability criteria for Enzyme Chromatographic Profile as the Table 2 below.

**Table 2 System Suitability Criteria**

| System Suitability Parameter | Acceptance Criteria |
|---|---|
| Compare the chromatographic profile of the injection of the SST solution with chromatogram (see Figure 1) | (b) (4) |
| Compare the chromatographic profile of the injections of the sample with the chromatogram of the reference | |
| Coefficient of variation of peak (b) (4) in three replicate injections of the SST solution | NMT (b) (4) |

(b) (4)


*Sponsor stated above, the proposed Enzyme Chromatographic Profile is analytically superior comparing to the current Enzyme Chromatographic Profile. So, it is impossible to compare these two-analysis methods side-by-side or perform bridging study.*

*In conclusion, the Sponsor adequately demonstrated suitability for the proposed Enzyme Chromatographic Profile used as ID and content test and the proposed specifications for Enzyme Chromatographic Profile are acceptable. So, this PAS is approvable.*

## 5 CONCLUSIONS:

I. **Recommendation:** Approval

II. **Sections Deferred to other reviewers:** None

III. **Post-marketing commitments:** None

IV. **Future Inspection Items:** None

Zhong Zhao

Digitally signed by Zhong Zhao
Date: 6/30/2021 11:21:11PM
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Susan Kirshner

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# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# 022542Orig1s006

# ADMINISTRATIVE AND CORRESPONDENCE DOCUMENTS

BLA 022542/S-006

**INFORMATION REQUEST**

Viokace, LLC
Attention: Vandana Garikipati, Ph.D.
Regulatory Affairs, Aimmune Therapeutics, Inc.
8000 Marina Boulevard, Suite 300
Brisbane, CA 94005

Dear Dr. Garikipati:

Please refer to your supplemental Biologics License Application (sBLA) dated March 12, 2021, received March 12, 2021, submitted under section 351(a) of the Public Health Service Act for Viokace (Pancrelipase) Tablet.

We are reviewing the Drug Product section of your submission and have the following comments and information requests. We request a prompt written response by June 21, 2021 in order to continue our evaluation of your supplemental BLA.

Comments and information requests:

## A. Drug Product

- In your response to FDA Request for Information SN 0098, submitted and received on June 03, 2021, you provided the information that the Enzyme Chromatographic Profile test is used to test not only identity but also content and integrity of the protein components of Pancrelipase. We noted that the RP-HPLC chromatogram profile is significantly different between the current Enzyme Chromatographic Profile test and the proposed Enzyme Chromatographic Profile test. We also found that the current acceptance criteria for Enzyme Chromatographic Prolife test, as shown in Table 1, are different from the acceptance criteria for the proposed Enzyme Chromatographic Prolife test, as shown in Table 2 below.

**Table 1: Acceptance criteria for the Current Enzyme Chromatographic Profile Test**

| Chromatographic profile | Identification | DP Limits (%) |
|---|---|---|
| | | (b) (4) |

(b) (4)

**Table 2: Acceptance criteria for the Proposed Enzyme Chromatographic Profile Test**

| Chromatographic profile | Identification | DS Limits (%) | DP Limits (%) |
|---|---|---|---|

(b) (4)

Because the Enzyme Chromatographic Profile test is used as content test for pancrelipase drug substance (DS) and Viokace drug product (DP), please provide bridging data for the current and proposed Enzyme Chromatographic Profile tests to demonstrate that the proposed Enzyme Chromatographic Profile tests and acceptance criteria are able to ensure the consistency for the content of pancrelipase DS and Viokace DP after introduction of the proposed Enzyme Chromatographic Profile tests.

If you have any questions, please contact me at (301) 796 - 0906 or melinda.bauerlien@fda.hhs.gov.

Sincerely,

*{See appended electronic signature page}*

Melinda Bauerlien, MS
Senior Regulatory Business Process Manager
Office of Program and Regulatory Operations
Office of Pharmaceutical Quality
Center for Drug Evaluation and Research

Melinda Bauerlien

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BLA 022542/S-006

**INFORMATION REQUEST**

Viokace, LLC
Attention: Barry Ritz
Regulatory Affairs, Aimmune Therapeutics, Inc.
8000 Marina Boulevard, Suite 300
Brisbane, CA 94005

Dear Mr. Ritz:

Please refer to your supplemental Biologics License Application (sBLA) dated March 12, 2021, received March 12, 2021, submitted under section 351(a) of the Public Health Service Act for Viokace (Pancrelipase) Tablet.

We are reviewing the Drug Product section of your submission and have the following comments and information requests. We request a prompt written response by June 3, 2021 in order to continue our evaluation of your supplemental BLA.

Comments and information requests:

**A. Drug Product**

1. In Section 1.11.1 Quality Information Amendment [0094] and Section 3.2.P.5.2 Analytical Procedures [0094], you described that the Viokace Enzyme Chromatographic Profile using RP-HPLC is an identification (ID) test as a fingerprint/identification of the Pancrelipase drug substance (DS) and Viokace drug product (DP). However, in Section 3.2.P.5.1 Specification(s), the Viokace Enzyme Chromatographic Profile is also a stability test for Viokace DP. Confirm whether the Viokace Enzyme Chromatographic Profile is only used for ID test of Pancrelipase DS and Viokace DP or also used for purity/impurity or content tests of Pancrelipase DS and Viokace DP?

2. Specifications of the DS and DP are one part of a total control strategy designed to ensure product safety, quality, and consistency. The specifications should include assessments of product's physicochemical properties, biological activity, immunochemical properties, purity, impurities, contaminants, and quantity. If the Viokace Enzyme Chromatographic Profile is only used for ID test, provide the information what tests are used for purity/impurity for Pancrelipase DS and Viokace DP on release and stability? In addition, describe the control strategy to ensure the purity/impurity and quantity in Pancrelipase DS and Viokace DP.

3. (b) (4)

[redacted](b) (4). To demonstrate the specificity of the Viokace Enzyme Chromatographic Profile test for both DS and DP, provide the testing results of Viokace Enzyme Chromatographic Profile from no less than 3 DS batches and no less than 3 DP batches separately in the validation report. If you plan to demonstrate the specificity for Viokace Enzyme Chromatographic Profile using only DS batches or DP batches, you must adequately demonstrate that there is no matrix effect from the excipients in Viokace Enzyme Chromatographic Profile test.

If you have any questions, please contact me at (301) 796 - 0906 or melinda.bauerlien@fda.hhs.gov.

Sincerely,

*{See appended electronic signature page}*

Melinda Bauerlien, MS
Senior Regulatory Business Process Manager
Office of Program and Regulatory Operations
Office of Pharmaceutical Quality
Center for Drug Evaluation and Research

Melinda Bauerlien

Digitally signed by Melinda Bauerlien
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# PRODUCT QUALITY (Biotechnology)
## FILING REVIEW FOR BLA/NDA Supplements (OBP & DMPQ)

| BLA/NDA Number: | Applicant: | Stamp Date: |
|---|---|---|
| 22542/6 | Viokace LLC | 3/12/21 |
| **Established/Proper Name:** Viokace (pancrelipase) | **BLA/NDA Type:** PAS | |

| | |
|---|---|
| **Brief description of the change:** | provides for a change in the high-performance liquid chromatography (HPLC) test method and subsequently the specifications for the Enzyme Chromatographic Profile test for the pancrelipase drug substance and Viokace (pancrelipase) Tablets. |
| **Reviewer:** | Zhong Zhao |
| **Office/Division:** | OBP |

On **initial** overview of the BLA/NDA **supplement** for filing:

The following was submitted in support of the change (check all that apply):

| | |
|---|---|
| x | A detailed description of the proposed change |
| x | Identification of the product(s) involved |
| x | A description of the manufacturing site(s) or area(s) affected |
| x | A description of the methods used and studies performed to evaluate the effect of the change on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product |
| x | The data derived from such studies |
| x | Relevant validation protocols and data |
| x | A reference list of relevant standard operating procedures (SOP's) |

The following deficiencies were identified (identify those that are potential filing issues):

**IS THE PRODUCT QUALITY SECTION OF THE SUPPLEMENT FILEABLE? Yes**

If the supplement is not fileable from the product quality perspective, state the reasons and provide comments to be sent to the Applicant.

Please identify and list any potential review issues to be forwarded to the Applicant for the 74-day letter.

*{See appended electronic signature page}*

Product Quality Reviewer Date

*{See appended electronic signature page}*

Branch Chief/Team Leader/Supervisor Date

CC: Review Team, Review Team TLs, OBP Deputy Div Director

Susan Kirshner

Digitally signed by Susan Kirshner
Date: 5/05/2021 05:55:31PM
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Zhong Zhao

Digitally signed by Zhong Zhao
Date: 5/05/2021 01:13:53PM
GUID: 5a4d348b000a8c806ebfb44c8f02250a

BLA 22542/006

**ACKNOWLEDGEMENT --**
**PRIOR APPROVAL SUPPLEMENT**

Viokace, LLC
Attention: Carlos Alexandre Biella
Head of Regulatory Affairs, Nestle Healthcare Nutrition, Inc.
1007 US Highway 202/206 – JR2
Bridgewater, NJ 08807

Dear Mr. Biella:

We have received your Supplemental Biologics License Application (sBLA) submitted under section 351(a) of the Public Health Service Act for the following:

**BLA NUMBER:** 22542

**SUPPLEMENT NUMBER:** 006

**PRODUCT NAME:** Viokace (pancrelipase) Tablets

**DATE OF SUBMISSION:** March 12, 2021

**DATE OF RECEIPT:** March 12, 2021

This supplemental application proposes the following change: provides for a change in the high-performance liquid chromatography (HPLC) test method and subsequently the specifications for the Enzyme Chromatographic Profile test for the pancrelipase drug substance and Viokace (pancrelipase) Tablets.

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on May 11, 2021, in accordance with 21 CFR 601.2(a).

If the application is filed, the user fee goal date will be July 12, 2021.

If you have questions, call me, at (301) 796-0906.

Sincerely,

*{See appended electronic signature page}*

Melinda Bauerlien, M.S.
Senior Regulatory Business Process Manager
Office of Program and Regulatory Operations
Office of Pharmaceutical Quality
Center for Drug Evaluation and Research

Melinda Bauerlien

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