CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

022542Orig1s007

Trade Name:	VIOKACE
Generic or Proper Name:	(pancrelipase)
Sponsor:	VIOKACE LLC.
Approval Date:	September 28, 2022
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

022542Orig1s007

CONTENTS

Reviews / Information Included in this NDA Review.

Approval Letter	**X**
Other Action Letters	
Labeling	**X**
REMS	
Summary Review	
Officer/Employee List	
Office Director Memo	
Cross Discipline Team Leader Review	
Clinical Review(s)	
Product Quality Review(s)	**X**
Non-Clinical Review(s)	
Statistical Review(s)	
Clinical Microbiology / Virology Review(s)	
Clinical Pharmacology Review(s)	
Other Reviews	
Risk Assessment and Risk Mitigation Review(s)	
Proprietary Name Review(s)	
Administrative/Correspondence Document(s)	**X**

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022542Orig1s007

APPROVAL LETTER

BLA 022542/S-007 **CORRECTED SUPPLEMENT APPROVAL**

Viokace, LLC
Attention: Vandana Garikipati, PhD
Vice President, Regulatory Affairs
8000 Marina Boulevard, Suite 300
Brisbane, CA 94005

Dear Dr. Garikipati:

Please refer to your supplemental biologics license application (sBLA), dated and received March 23, 2022, and your amendments, submitted under section 351(a) of the Public Health Service Act for Viokace (pancrelipase) tablets. We also refer to the approval letter dated September 28, 2022, which contained the following errors:

- Incorrect applicant name on the approval letter
- Incorrect "manufactured by" name, address, and license number in the Prescribing Information, Medication Guide and carton and container labeling.

This corrected action letter incorporates the correction of the error. The effective action date will remain September 28, 2022, the date of the original letter.

This Prior Approval supplemental biologics application provides for revisions to the Viokace labeling to conform to the labeling requirements for biological products regulated under section 351 of the PHS act.

APPROVAL & LABELING

We acknowledge your November 15, 2022, submission containing corrected Prescribing Information and Medication Guide.

We have completed our review of this application. It is approved, effective September 28, 2022, 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,

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

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]

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).

CARTON AND CONTAINER LABELING

We acknowledge your September 6, 2022, submission containing printed carton and container labeling. We also acknowledge your November 15, 2022, submission containing corrected printed carton and container labeling.

For information on FDA's compliance policy for requirements related to BLA-specific labeling revisions, see guidance for industry, *The "Deemed to be a License" Provision of the BPCI Act: Questions and Answers*.[3]

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.

[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.

[3] Available at: https://www.fda.gov/media/119274/download. For the most recent version of a guidance, check the FDA Guidance Documents Database at https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

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]

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 Anum Shami, PharmD, Regulatory Project Manager, at 301-837-7103 or anum.shami@fda.hhs.gov

Sincerely,

{See appended electronic signature page}

Juli Tomaino, MD, MS
Deputy Director
Division of Gastroenterology
Office of Immunology and Inflammation
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide
- Carton and Container Labeling

[4] For the most recent version of a guidance, check the FDA guidance web page athttps://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

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022542Orig1s007

LABELING

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use VIOKACE safely and effectively. See full prescribing information for VIOKACE

VIOKACE®(pancrelipase) tablets, for oral use
Initial U.S. Approval: 2012

----------INDICATIONS AND USAGE ----------
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. (1)

----------DOSAGE AND ADMINISTRATION ----------
VIOKACE is not interchangeable with any other pancrelipase product. VIOKACE tablets should be swallowed whole. Do not crush or chew tablets. (2.1) Dosing should not exceed the recommended maximum dosage set forth by the Cystic Fibrosis Foundation Consensus Conferences Guidelines. (2.2)

- Begin with 500 lipase units/kg of body weight per meal to a maximum of 2,500 lipase units/kg of body weight per meal (or less than or equal to 10,000 lipase units/kg of body weight per day), or less than 4,000 lipase units/g fat ingested per day. (2.2)
- Individualize dosage based on clinical symptoms, the degree of steatorrhea present and the fat content of the diet. (2.2)

----------DOSAGE FORMS AND STRENGTHS ----------
- Tablets: 10,440 USP units of lipase; 39,150 USP units of protease; 39,150 USP units of amylase (3)
- Tablets: 20,880 USP units of lipase; 78,300 USP units of protease; 78,300 USP units of amylase (3)

----------CONTRAINDICATIONS----------
- None. (4)

----------WARNINGS AND PRECAUTIONS----------
- Fibrosing colonopathy is associated with high-dose use of pancreatic enzyme replacement. Exercise caution when doses of VIOKACE exceed 2,500 lipase units/kg of body weight per meal (or greater than 10,000 lipase units/kg of body weight per day). (5.1)
- To avoid irritation of oral mucosa, do not chew VIOKACE or retain in the mouth. (5.2)
- Exercise caution when prescribing VIOKACE to patients with gout, renal impairment, or hyperuricemia. (5.3)
- There is theoretical risk of viral transmission with all pancreatic enzyme products including VIOKACE. (5.4)
- Exercise caution when administering pancrelipase to a patient with a known allergy to proteins of porcine origin. (5.5)

----------ADVERSE REACTIONS ----------
- Adverse reactions occurring in at least 2 chronic pancreatitis or pancreatectomy patients (greater than or equal to 7%) receiving VIOKACE are biliary tract stones and anal pruritus. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Nestlé HealthScience at 1-833-920-2178 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch.*

----------USE IN SPECIFIC POPULATIONS----------
- The safety and effectiveness of VIOKACE in pediatric patients have not been established. (8.4)
- VIOKACE use in pediatric patients may result in suboptimal growth due to tablet degradation in the gastric environment. In general, delayed-release (enteric-coated) capsules should be used for pediatric patients. (8.4)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 09/2022

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

VIOKACE tablets, in combination with a proton pump inhibitor, is indicated in adults for the treatment of exocrine pancreatic insufficiency due to chronic pancreatitis or pancreatectomy.

2 DOSAGE AND ADMINISTRATION

VIOKACE is not interchangeable with any other pancrelipase product.

VIOKACE is orally administered. Therapy should be initiated at the lowest recommended dose and gradually increased. The dosage of VIOKACE should be individualized based on clinical symptoms, the degree of steatorrhea present, and the fat content of the diet as described in the Limitations on Dosing below [*see Dosage and Administration (2.2) and Warnings and Precautions (5.1)*].

2.1 Administration

Since VIOKACE is not enteric-coated, it should be taken in combination with a proton pump inhibitor [*see Indications and Usage (1)*].

VIOKACE should be taken during meals or snacks, with sufficient fluid. Tablets should be swallowed whole. Do not crush or chew tablets. Care should be taken to ensure that no drug is retained in the mouth to avoid mucosal irritation.

2.2 Dosage

VIOKACE is a mixture of enzymes including lipases, proteases, and amylases and dosing is based on lipase units. Dosage recommendations for pancreatic enzyme replacement therapy were published following the Cystic Fibrosis Foundation Consensus Conferences.[1,2,3] VIOKACE should be administered in a manner consistent with the recommendations of the Conferences provided in the following paragraph. Only the adult dosing guidelines are shown below. Patients may be dosed on a fat ingestion-based or actual body weight-based dosing scheme.

Additional recommendations for pancreatic enzyme therapy in patients with exocrine pancreatic insufficiency due to chronic pancreatitis or pancreatectomy are based on a clinical trial conducted in these populations.

Enzyme dosing should begin with 500 lipase units/kg of body weight per meal to a maximum of 2,500 lipase units/kg of body weight per meal (or less than or equal to 10,000 lipase units/kg of body weight per day), or less than 4,000 lipase units/g fat ingested per day.

Usually, half of the prescribed VIOKACE dose for an individualized full meal should be given with each snack. The total daily dosage should reflect approximately three meals plus two or three snacks per day.

In one clinical trial, patients received VIOKACE at a dose of 125,280 lipase units per meal while consuming 100 g of fat per day *[see Clinical Studies (14)]*. Lower starting doses recommended in the literature are consistent with the 500 lipase units/kg of body weight per meal lowest starting dose recommended for adults in the Cystic Fibrosis Foundation Consensus Conferences Guidelines.[1, 2, 3, 4] The initial starting dose and increases in the dose per meal should be individualized based on clinical symptoms, the degree of steatorrhea present, and the fat content of the diet.

Limitations on Dosing

Dosing should not exceed the recommended maximum dosage set forth by the Cystic Fibrosis Foundation Consensus Conferences Guidelines.[1,2,3] If symptoms and signs of steatorrhea persist, the dosage may be increased by the healthcare professional. Patients should be instructed not to increase the dosage on their own. There is great inter-individual variation in response to enzymes; thus, a range of doses is recommended. Changes in dosage may require an adjustment period of several days. If doses are to exceed 2,500 lipase units/kg of body weight per meal, further investigation is warranted. Doses greater than 2,500 lipase units/kg of body weight per meal (or greater than 10,000 lipase units/kg of body weight per day) should be used with caution and only if they are documented to be effective by 3-day fecal fat measures that indicate a significantly improved coefficient of fat absorption. Doses greater than 6,000 lipase units/kg of body weight per meal have been associated with colonic stricture, indicative of fibrosing colonopathy, in children less than 12 years of age *[see Warnings and Precautions (5.1)]*. Patients currently receiving higher doses than 6,000 lipase units/kg of body weight per meal should be examined and the dosage either immediately decreased or titrated downward to a lower range.

3 DOSAGE FORMS AND STRENGTHS

Tablets are available in the following strengths:

- 10,440 USP units of lipase; 39,150 USP units of protease; 39,150 USP units of amylase tablets are tan, round, biconvex and have VIO9111 engraved on one side and 9111 on the other side.

- 20,880 USP units of lipase; 78,300 USP units of protease; 78,300 USP units of amylase tablets are tan, oval, biconvex with V^{16} engraved on one side and 9116 on the other side.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Fibrosing Colonopathy

Fibrosing colonopathy has been reported following treatment with different pancreatic enzyme products.[5,6] Fibrosing colonopathy is a rare, serious adverse reaction initially described in association with high-dose pancreatic enzyme use, usually over a prolonged period of time and most commonly reported in pediatric patients with cystic fibrosis. The underlying mechanism of fibrosing colonopathy remains unknown. Doses of pancreatic enzyme products exceeding 6,000 lipase units/kg of body weight per meal

have been associated with colonic stricture in children less than 12 years of age.[1] Patients with fibrosing colonopathy should be closely monitored because some patients may be at risk of progressing to stricture formation. It is uncertain whether regression of fibrosing colonopathy occurs.[1] It is generally recommended, unless clinically indicated, that enzyme doses should be less than 2,500 lipase units/kg of body weight per meal (or less than 10,000 lipase units/kg of body weight per day) or less than 4,000 lipase units/g fat ingested per day *[see Dosage and Administration (2.2)]*.

Doses greater than 2,500 lipase units/kg of body weight per meal (or greater than 10,000 lipase units/kg of body weight per day) should be used with caution and only if they are documented to be effective by 3-day fecal fat measures that indicate a significantly improved coefficient of fat absorption. Patients receiving higher doses than 6,000 lipase units/kg of body weight per meal should be examined and the dosage either immediately decreased or titrated downward to a lower range.

5.2 Potential for Irritation to Oral Mucosa

Care should be taken to ensure that no drug is retained in the mouth to avoid irritation of oral mucosa, and/or loss of enzyme activity. VIOKACE should not be crushed or chewed *[see Dosage and Administration (2.1) and Patient Counseling Information (17.1)]*.

5.3 Potential for Risk of Hyperuricemia

Caution should be exercised when prescribing VIOKACE to patients with gout, renal impairment, or hyperuricemia. Porcine-derived pancreatic enzyme products contain purines that may increase blood uric acid levels.

5.4 Potential for Viral Exposure from the Product Source

VIOKACE is sourced from pancreatic tissue from pigs used for food consumption. Although the risk that VIOKACE will transmit an infectious agent to humans has been reduced by testing for certain viruses during manufacturing and by inactivating certain viruses during manufacturing, there is a theoretical risk for transmission of viral disease, including diseases caused by novel or unidentified viruses. Thus, the presence of porcine viruses that might infect humans cannot be definitely excluded. However, no cases of transmission of an infectious illness associated with the use of porcine pancreatic extracts have been reported.

5.5 Allergic Reactions

Caution should be exercised when administering pancrelipase to a patient with a known allergy to proteins of porcine origin. Rarely, severe allergic reactions including anaphylaxis, asthma, hives, and pruritus, have been reported with other pancreatic enzyme products with different formulations of the same active ingredient (pancrelipase). The risks and benefits of continued VIOKACE treatment in patients with severe allergy should be taken into consideration with the overall clinical needs of the patient.

5.6 Potential for Exacerbation of Symptoms of Lactose Intolerance

VIOKACE tablets contain lactose monohydrate. Patients who have lactose intolerance may not be able to tolerate VIOKACE.

6 ADVERSE REACTIONS

The most serious adverse reactions reported with different pancreatic enzyme products of the same active ingredient (pancrelipase) that are described elsewhere in the label include fibrosing colonopathy, hyperuricemia and allergic reactions *[see Warnings and Precautions (5.1, 5.3 and 5.5)]*.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to the rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The short-term safety of VIOKACE was assessed in a single, multicenter, randomized, parallel, placebo-controlled, double-blind study of 50 patients, ages 24-70 years, with exocrine pancreatic insufficiency (EPI) due to chronic pancreatitis or pancreatectomy. VIOKACE Tablets (20,880 USP units of lipase per tablet) or placebo were administered as 22 tablets per day (6 tablets with 3 meals and 2 tablets with 2 of 3 snacks). Duration of exposure ranged from 6 to 7 days. The majority of the subjects were Caucasian (96%) and male (82%).

The most common adverse reactions (greater than or equal to 7%) were biliary tract stones and anal pruritus. Table 1 enumerates adverse reactions that occurred in at least 1 patient (greater than or equal to 3%) treated with VIOKACE at a higher rate than with placebo. Two adverse reactions reported in greater than one patient were biliary tract stones and anal pruritus.

TABLE 1 Adverse Reactions Occurring in at Least 1 Patient (greater than or equal to 3%) in Chronic Pancreatitis or Pancreatectomy		
	Treatment Group	
MedDRA Primary System Organ Class/ Adverse Reactions	**VIOKACE (N=30)**	**Placebo (N=20)**
Blood And Lymphatic System Disorders		
Anemia	1 (3%)	0
Gastrointestinal Disorders		
Anal pruritus	2 (7%)	0
Abdominal pain	1 (3%)	0
Ascites	1 (3%)	0
Flatulence	1 (3%)	0
General Disorders and Administration Site Conditions		
Edema peripheral	1 (3%)	0
Hepatobiliary Disorders		
Biliary tract stones	2 (7%)	0
Hydrocholecystis	1 (3%)	0
Infections and Infestations		
Viral infection	1 (3%)	0
Nervous System Disorders		
Headache	1 (3%)	0
Renal and Urinary Disorders		
Renal cyst	1 (3%)	0
Skin and Subcutaneous Tissue Disorders		
Rash	1 (3%)	0

6.2 Postmarketing Experience

Post-marketing data for VIOKACE have been available since 2003. The safety data are similar to that described below. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Pancreatic enzyme products (delayed and immediate-release) with different formulations of the same active ingredient (pancrelipase) have been used for the treatment of patients with exocrine pancreatic insufficiency due to cystic fibrosis and other conditions, such as chronic pancreatitis. The long-term safety profile of these products has been described in the medical literature. The most serious adverse events included fibrosing colonopathy, distal intestinal obstruction syndrome (DIOS), recurrence of pre-existing carcinoma, and severe allergic reactions including anaphylaxis, asthma, hives, and pruritus. The most commonly reported adverse events were gastrointestinal disorders, including abdominal pain, diarrhea, flatulence, constipation and nausea, and skin disorders including pruritus, urticaria and rash.

7 DRUG INTERACTIONS

No drug interactions have been identified. No formal interaction studies have been conducted.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Published data from case reports with pancrelipase use in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes. Pancrelipase is minimally absorbed systematically; therefore, maternal use is not expected to result in fetal exposure to the drug. Animal reproduction studies have not been conducted with pancrelipase.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

8.2 Lactation

Risk Summary

There are no data on the presence of pancrelipase in either human or animal milk, the effects on the breastfed infant, or the effects on milk production. Pancrelipase is minimally absorbed systemically following oral administration, therefore maternal use is not expected to result in clinically relevant exposure of breastfed infants to the drug. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for VIOKACE and any potential adverse effects on the breastfed child from VIOKACE or from the underlying maternal conditions.

8.4 Pediatric Use

The safety and effectiveness of VIOKACE in pediatric patients have not been established. In general, delayed-release (enteric-coated) capsules should be used for pediatric patients. Due to greater degradation in the gastric environment, VIOKACE, a non-enteric-coated, pancreatic enzyme replacement product, may have decreased bioavailability and therefore may be less efficacious than enteric-coated formulations.[7, 8] Thus, use of VIOKACE in pediatric patients may increase the risk of inadequate treatment of pancreatic insufficiency and result in suboptimal weight gain, malnutrition and/or need for larger doses of pancreatic enzyme replacement *[See Warnings and Precautions (5.1)]* The efficacy of VIOKACE was established in adult patients with concomitant proton pump inhibitor (PPI) therapy. The long-term safety of PPI use in pediatric patients has not been established.

8.5 Geriatric Use

Clinical studies of VIOKACE did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection

for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

10 OVERDOSAGE

There have been no reports of overdose in clinical trials or post-marketing surveillance with VIOKACE. Chronic high doses of pancreatic enzyme products have been associated with fibrosing colonopathy and colonic strictures *[see Dosage and Administration (2) and Warnings and Precautions (5.1)]*. High doses of pancreatic enzyme products have been associated with hyperuricosuria and hyperuricemia, and should be used with caution in patients with a history of hyperuricemia, gout, or renal impairment *[see Warnings and Precautions (5.3)]*.

11 DESCRIPTION

Pancrelipase is a pancreatic enzyme product consisting of a mixture of enzymes including lipases, proteases, and amylases, and is an extract derived from porcine pancreatic glands.

VIOKACE (pancrelipase) tablets are for oral administration and available as follows:

10,440 USP units of lipase; 39,150 USP units of protease; 39,150 USP units of amylase tablets are tan, round biconvex and have VIO9111 engraved on one side and 9111 on the other side.

20,880 USP units of lipase; 78,300 USP units of protease; 78,300 USP units of amylase tablets are tan, oval, biconvex with V^{16} engraved on one side and 9116 on the other side.

Inactive ingredients in VIOKACE include colloidal silicon dioxide, crosscarmellose sodium, lactose monohydrate, microcrystalline cellulose, stearic acid and talc.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The pancreatic enzymes in VIOKACE catalyze the hydrolysis of fats to monoglycerides, glycerol and free fatty acids, proteins into peptides and amino acids, and starches into dextrins and short chain sugars such as maltose and maltriose in the duodenum and proximal small intestine, thereby acting like digestive enzymes physiologically secreted by the pancreas.

12.3 Pharmacokinetics

Pancreatic enzymes are not absorbed from the gastrointestinal tract in appreciable amounts.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity, genetic toxicology, and animal fertility studies have not been performed with pancrelipase.

14 CLINICAL STUDIES

The short-term safety and efficacy of VIOKACE were evaluated in a randomized, double-blind, placebo-controlled, parallel group study comparing VIOKACE Tablets (20,880 USP units of lipase per tablet) to placebo in 50 patients, ages 24 to 70, with exocrine pancreatic insufficiency (EPI) due to chronic pancreatitis (CP) or pancreatectomy. Eighteen patients had a history of pancreatectomy (11 were treated with VIOKACE). All patients were maintained on a controlled high fat diet of 100 grams of fat per day. After a wash-out period (6 to 7 days), patients were randomized to a fixed dose of VIOKACE (22 tablets per day; 6 tablets per meal and 2 tablets with 2 of 3 snacks) or placebo, in combination with a proton pump inhibitor. Forty-nine patients completed the double-blind treatment period (6 to 7 days); 29 patients received VIOKACE, and 20 patients received placebo.

The coefficient of fat absorption (CFA) was determined by a 72-hour stool collection during both treatments, when both fat excretion and fat ingestion were measured.

The wash-out period mean CFA was 48% in the VIOKACE treatment group and was 57% in the placebo group. At the end of the double-blind treatment period, the mean CFA was 86% with VIOKACE treatment compared to 58% with placebo. The mean difference in CFA at the end of the double-blind treatment period was 28 percentage points in favor of VIOKACE treatment with 95% Confidence Interval of (21, 37) and $p \leq 0.0001$.

Subgroup analyses of the CFA results showed that mean change in CFA with VIOKACE treatment (from the washout period to the end of the double-blind period) was greater in patients with lower wash-out period CFA values than in patients with higher wash-out period CFA values.

Only 2 of the patients with a history of total pancreatectomy were treated with VIOKACE. One of these patients had a CFA of 12% during the wash-out period and a CFA of 90% at the end of the double-blind period; the other patient had a CFA of 38% during the wash-out period and a CFA of 77% at the end of the double-blind period. The remaining 9 patients with a history of partial pancreatectomy treated with VIOKACE had a mean CFA of 56% during the wash-out period and a mean CFA of 86% at the end of the double-blind period.

15 REFERENCES

[1]Borowitz DS, Grand RJ, Durie PR, et al. Use of pancreatic enzyme supplements for patients with cystic fibrosis in the context of fibrosing colonopathy. *Journal of Pediatrics.* 1995; 127: 681-684.

[2]Borowitz DS, Baker RD, Stallings V. Consensus report on nutrition for pediatric patients with cystic fibrosis. *Journal of Pediatric Gastroenterology Nutrition.* 2002 Sep; 35: 246-259.

[3]Stallings VA, Start LJ, Robinson KA, et al. Evidence-based practice recommendations for nutrition-related management of children and adults with cystic fibrosis and pancreatic insufficiency: results of a systematic review. *Journal of the American Dietetic Association*. 2008; 108: 832-839.

[4]Dominguez-Munoz JE, Pancreatic enzyme therapy for pancreatic exocrine insufficiency. Current Gastroenterology Reports. 2007; 9: 116-122.

[5]Smyth RL, Ashby D, O'Hea U, et al. Fibrosing colonopathy in cystic fibrosis: results of a case-control study. *Lancet.* 1995; 346: 1247-1251.

[6]FitzSimmons SC, Burkhart GA, Borowitz DS, et al. High-dose pancreatic-enzyme supplements and fibrosing colonopathy in children with cystic fibrosis. *New England Journal of Medicine.* 1997; 336: 1283-1289.

[7]Gow R, Francis P, Bradbear R, et al. Comparative study of varying regimens to improve steatorrhoea and creatorrhoea in cystic fibrosis: effectiveness of an enteric-coated preparation with and without antacids and cimetidine. *Lancet.* November 14*,* 1981: 1071-1074.

[8] Ansaldi-Balocco N, Santini B, Sarchi C. Efficacy of pancreatic enzyme supplementation in children with cystic fibrosis: comparison of two preparations by random crossover study and a retrospective study of the same patients at two different ages. J Pediatr Gastroenterol Nutr. 1988;7 Suppl 1:S40-5.

16 HOW SUPPLIED/STORAGE AND HANDLING

VIOKACE tablets

10,440 USP units of lipase; 39,150 USP units of protease; 39,150 USP units of amylase
Each VIOKACE tablet is available as a tan, round, biconvex tablet with VIO9111 engraved on one side and 9111 on the other side supplied in bottles of 100 tablets (NDC 71881-310-10).

VIOKACE tablets

20,880 USP units of lipase; 78,300 USP units of protease; 78,300 USP units of amylase
Each VIOKACE tablet is available as a tan, oval, biconvex tablet with V^{16} engraved on one side and 9116 on the other side supplied in bottles of 100 tablets (NDC 71881-320-10).

Storage and Handling

Avoid heat. VIOKACE tablets should be stored in a dry place in the original container. Store at room temperature 20°C to 25°C (68°F to 77°F), and brief excursion permitted up to 40°C (104°F) for 24 hours. After opening, keep the container tightly closed between uses to protect from moisture.

VIOKACE is dispensed in bottles containing a desiccant. The desiccant packet should not be eaten. The desiccant packet will protect the product from moisture.

17 PATIENT COUNSELING INFORMATION

"See FDA-approved patient labeling (Medication Guide)"

17.1 Dosing and Administration

- Instruct patients and caregivers that VIOKACE should only be taken as directed by their doctor. Patients should be advised that the total daily dose should not exceed 10,000 lipase units/kg body weight/day unless clinically indicated. This needs to be especially emphasized for patients eating multiple snacks and meals per day. Patients should be informed that if a dose is missed, the next dose should be taken with the next meal or snack as directed. Doses should not be doubled *[see Dosage and Administration (2)]*.

- Instruct patients and caregivers that VIOKACE should always be taken with food. Patients should swallow the intact tablets with adequate amounts of liquid at mealtimes *[see Dosage and Administration (2)]*.

17.2 Fibrosing Colonopathy

Advise patients and caregivers to follow dosing instructions carefully, as doses of pancreatic enzyme products exceeding 6,000 lipase units/kg of body weight per meal have been associated with colonic strictures in children below the age of 12 years *[see Dosage and Administration (2) and Warnings and Precautions (5.1)]*.

17.3 Allergic Reactions

Advise patients and caregivers to contact their healthcare professional immediately if allergic reactions to VIOKACE develop *[see Warnings and Precautions (5.5)]*.

Manufactured by:
Viokace, LLC
1007 US Highway 202/206,
Bridgewater, NJ 08807, USA
US License No. 2196

Manufactured for:
Aimmune Therapeutics, Inc.
Brisbane, CA 94005, USA

All trademarks are owned by Société des Produits Nestlé S.A., Vevey, Switzerland or used with permission. ©2020 Nestlé.

v1.0USPI0112

73314NT10 300881-03

MEDICATION GUIDE

VIOKACE ® (vye-oh-kase)

(pancrelipase)

tablets

Read this Medication Guide before you start taking VIOKACE and each time you get a refill. There may be new information. This information does not take the place of talking with your doctor about your medical condition or treatment.

What is the most important information I should know about VIOKACE?

VIOKACE may increase your chance of having a rare bowel disorder called fibrosing colonopathy. This condition is serious and may require surgery. The risk of having this condition may be reduced by following the dosing instructions that your doctor gave you.

Call your doctor right away if you have any unusual or severe:

- stomach area (abdominal) pain
- bloating
- trouble passing stool (having bowel movements)
- nausea, vomiting, or diarrhea

Take VIOKACE exactly as prescribed by your doctor. Do not take more or less VIOKACE than directed by your doctor.

What is VIOKACE?

- VIOKACE is a prescription medicine used with a proton pump inhibitor medicine (PPI) to treat adults who cannot digest food normally. Adults with swelling of the pancreas that lasts a long time (chronic pancreatitis), or who have had some or all of their pancreas removed (pancreatectomy) may not digest food normally because they do not make enough enzymes or because their enzymes are not released into the bowel (intestine).
- VIOKACE contains a mixture of digestive enzymes (including lipases, proteases, and amylases) from pig pancreas.
- **It is not known if VIOKACE is safe and effective in children. Use of VIOKACE in children may result in poor nutrition and slowing of growth.**

What should I tell my doctor before taking VIOKACE?

Before taking VIOKACE, tell your doctor about all your medical conditions, including if you:

- are allergic to pork (pig) products
- have a history of blockage of your intestines, or scarring or thickening of your bowel wall (fibrosing colonopathy)
- have gout, kidney disease, or a condition called high blood uric acid (hyperuricemia)
- have trouble swallowing tablets
- are lactose intolerant
- have any other medical condition
- are pregnant or plan to become pregnant.
- are breastfeeding or plan to breastfeed. It is not known if VIOKACE passes into your breast milk. Talk to your doctor about the best way to feed your baby if you take VIOKACE.

Tell your doctor about all the medicines you take, including prescription and nonprescription medicines, vitamins, or herbal supplements.

Know the medicines you take. Keep a list of them and show it to your doctor and pharmacist when you get a new medicine.

How should I take VIOKACE?

- **Take VIOKACE tablets exactly as your doctor tells you.**
- You should not switch VIOKACE with any other pancreatic enzyme product without first talking to your doctor.
- Do not take more tablets in a day than the number your doctor tells you to take (total daily dose).
- Always take VIOKACE with a meal or a snack and enough liquid to swallow VIOKACE completely. If you eat a lot of meals or snacks in a day, be careful not to go over your total daily dose.
- Your doctor may change your dose based on the amount of fatty foods you eat or based on your weight.

- Your doctor should also prescribe a medicine for you called a proton pump inhibitor (PPI) to decrease stomach acid. VIOKACE should be taken with a PPI to help prevent VIOKACE from breaking down in your stomach.
- Swallow VIOKACE tablets whole. Do not crush or chew the tablets. Be careful to make sure that no VIOKACE is left in your mouth. Crushing, chewing or holding the VIOKACE tablets in your mouth may cause irritation in your mouth, or change the way VIOKACE works in your body.
- If you forget to take VIOKACE, wait until your next meal and take your usual number of tablets. Take your next dose at your usual time. **Do not take two doses at one time.**

What are the possible side effects of VIOKACE?
VIOKACE may cause serious side effects, including:

- See **"What is the most important information I should know about VIOKACE?"**
- **Irritation of the inside of your mouth.** This can happen if VIOKACE is not swallowed completely.
- **Increase in blood uric acid levels.** This may cause worsening of swollen, painful joints (gout) caused by an increase in your blood uric levels.
- **Allergic reactions,** including trouble with breathing, skin rashes, or swollen lips.

Call your doctor right away if you have any of these symptoms.

The most common side effects of VIOKACE include:
- you can develop stones that form in your gallbladder and the tubes that carry bile to your small intestines.
- anal itching

Other possible side effects:
VIOKACE and other pancreatic enzyme products are made from the pancreas of pigs, the same pigs people eat as pork. These pigs may carry viruses. Although it has never been reported, it may be possible for a person to get a viral infection from taking pancreatic enzyme products that come from pigs.

Tell your doctor if you have any side effect that bothers you or that does not go away.
These are not all the side effects of VIOKACE. For more information ask your doctor or pharmacist.
Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.
You may also report side effects to Nestlé HealthScience at 1-833-920-2178.

How should I store VIOKACE?

- Store VIOKACE at room temperature, 68°F to 77°F (20°C to 25°C). Avoid heat.
- Keep VIOKACE in a dry place and in its original container.
- After opening the bottle, keep it closed tightly between uses to protect from moisture.
- The VIOKACE bottle contains a desiccant packet to help keep your medicine dry (protect it from moisture). **Do not eat or throw away the desiccant packet.**

Keep VIOKACE and all medicines out of reach of children.

General information about the safe and effective use of VIOKACE
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use VIOKACE for a condition for which it was not prescribed. Do not give VIOKACE to other people to take, even if they have the same symptoms you have. It may harm them.
This Medication Guide summarizes the most important information about VIOKACE. If you would like more information, talk to your doctor. You can ask your pharmacist or doctor for information about VIOKACE that is written for healthcare providers.
For more information, go to www.viokace.com or call toll-free 1-833-920-2178.

What are the ingredients in VIOKACE?
Active ingredient: lipase, protease and amylase
Inactive ingredients: colloidal silicon dioxide, crosscarmellose sodium, lactose monohydrate, microcrystalline cellulose, stearic acid and talc.

Manufactured by:
Viokace, LLC
1007 US Highway 202/206,
Bridgewater, NJ 08807, USA
US License No. 2196

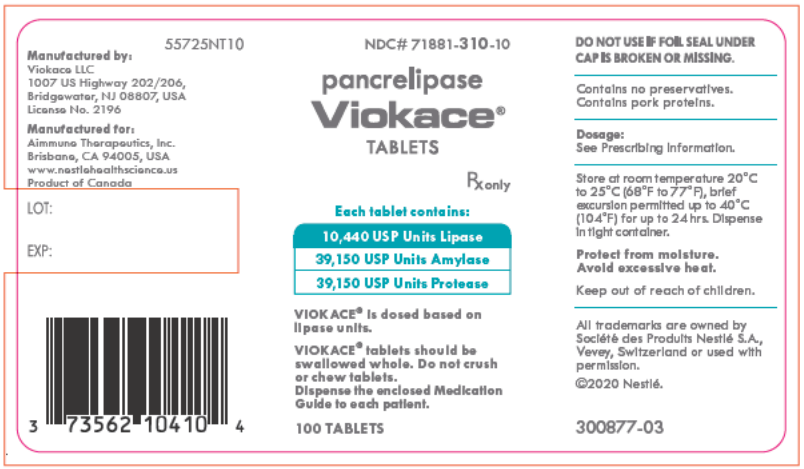
Manufactured for:
Aimmune Therapeutics, Inc.
Brisbane, CA 94005, USA

All trademarks are owned by Société des Produits Nestlé S.A., Vevey, Switzerland or used with permission.
©2020 Nestlé.
v1.0MG0112
73314NT10
300881-03

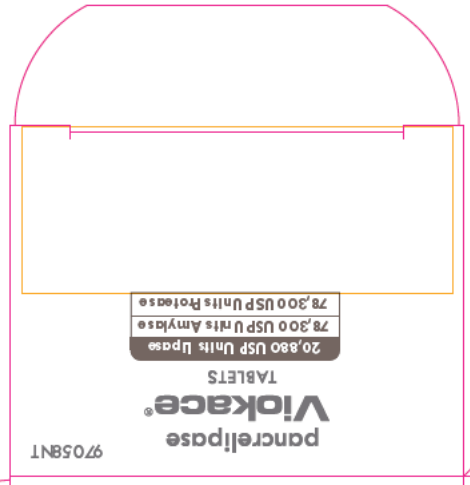
This Medication Guide has been approved by the U.S. Food and Drug Administration. Revised: 09/2022

(b) (4)

Reference ID: 5077996


55725NT10
Manufactured by:
Viokace LLC
1007 US Highway 202/206,
Bridgewater, NJ 08807, USA
License No. 2196
Manufactured for:
Aimmune Therapeutics, Inc.
Brisbane, CA 94005, USA
www.nestlehealthscience.us
Product of Canada
LOT:
EXP:
3 73562 10410 4
NDC# 71881-310-10
pancrelipase
Viokace®
TABLETS
℞only
Each tablet contains:
10,440 USP Units Lipase
39,150 USP Units Amylase
39,150 USP Units Protease
VIOKACE® is dosed based on lipase units.
VIOKACE® tablets should be swallowed whole. Do not crush or chew tablets.
Dispense the enclosed Medication Guide to each patient.
100 TABLETS
DO NOT USE IF FOIL SEAL UNDER CAP IS BROKEN OR MISSING.
Contains no preservatives.
Contains pork proteins.
Dosage:
See Prescribing Information.
Store at room temperature 20°C to 25°C (68°F to 77°F), brief excursion permitted up to 40°C (104°F) for up to 24 hrs. Dispense in tight container.
Protect from moisture.
Avoid excessive heat.
Keep out of reach of children.
All trademarks are owned by Société des Produits Nestlé S.A., Vevey, Switzerland or used with permission.
©2020 Nestlé.
300877-03

(b) (4)



Manufactured by:
Viokace LLC
1007 US Highway 202/206,
Bridgewater, NJ 08807, USA
License No. 2196

Manufactured for:
Aimmune Therapeutics, Inc.
Brisbane, CA 94005, USA
www.nestlehealthscience.us

Product of Canada
For product information please call
1-833-920-2178

66190NT10 300880-04

All trademarks are owned by Société des Produits Nestlé S.A., Vevey, Switzerland or used with permission.

©2020 Nestlé.

DO NOT USE IF FOIL SEAL UNDER CAP IS BROKEN OR MISSING.

NDC# 71881-320-10

pancrelipase Viokace®
TABLETS

℞ only

Each tablet contains:

20,880 USP Units Lipase
78,300 USP Units Amylase
78,300 USP Units Protease

VIOKACE® is dosed based on lipase units.
Contains no preservatives.
Contains pork proteins.

VIOKACE® tablets should be swallowed whole. Do not crush or chew tablets.

Dispense the enclosed Medication Guide to each patient.

100 TABLETS

Dosage:
See Prescribing Information.

Store at room temperature 20°C to 25°C (68°F to 77°F), brief excursion permitted up to 40°C (104°F) for up to 24 hrs. Dispense in tight container.

Protect from moisture.
Avoid excessive heat.

Keep out of reach of children.

3 73562 20810 9

Dieline G2 #971
60 x 47 x 123mm

(b) (4)

55730NT10

Manufactured by:
Viokace LLC
1007 US Highway 202/206,
Bridgewater, NJ 08807, USA
License No. 2196

Manufactured for:
Aimmune Therapeutics, Inc.
Brisbane, CA 94005, USA
www.nestlehealthscience.us
Product of Canada

LOT:

EXP:

3 73562 20810 9

NDC# 71881-320-10

pancrelipase
Viokace®
TABLETS

℞ only

Each tablet contains:

20,880 USP Units Lipase
78,300 USP Units Amylase
78,300 USP Units Protease

VIOKACE® is dosed based on lipase units.

VIOKACE® tablets should be swallowed whole. Do not crush or chew tablets.
Dispense the enclosed Medication Guide to each patient.

100 TABLETS

DO NOT USE IF FOIL SEAL UNDER CAP IS BROKEN OR MISSING.

Contains no preservatives.
Contains pork proteins.

Dosage:
See Prescribing Information.

Store at room temperature 20°C to 25°C (68°F to 77°F), brief excursion permitted up to 40°C (104°F) for up to 24 hrs. Dispense in tight container.

Protect from moisture.
Avoid excessive heat.

Keep out of reach of children.

All trademarks are owned by Société des Produits Nestlé S.A., Vevey, Switzerland or used with permission.
©2020 Nestlé.

300878-03

(b) (4)

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/

JULI A TOMAINO
12/07/2022 08:40:34 AM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022542Orig1s007

CLINICAL REVIEW(S)

DIVISION OF GASTROENTEROLOGY
Clinical Labeling Review

Trade Name (Established Name):

BLA 022210/S-024	Zenpep (pancrelipase) delayed-release capsules
BLA 022542/S-07	Viokace (pancrelipase) tablets
BLA 022175/S-08	Pertzye (pancrelipase) delayed-release capsules

Submission Dates:

Zenpep:	March 23, 2022; May 9, 2022; August 17, 2022; September 9, 2022; and September 21, 2022
Viokace:	March 23, 2022; May 4, 2022; August 17, 2022; September 6, 2022; and September 21, 2022
Pertzye:	April 15, 2022; August 17, 2022; and September 6, 2022

Sponsor: Zenpep and Viokace: Aimmune LLC
Pertzye: Digestive Care, Inc.

Reviewer: Joette M. Meyer, Pharm.D.
Associate Director for Labeling
Division of Gastroenterology

This submission is to comply with the transition provision of the Biologic Price Competition and Innovation (BPCI) Act of 2009 under which an application for a biological product approved under section 505 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355) as of March 23, 2020, will be deemed to be a license for the biological product under section 351 of the Public Health Service Act (PHS Act) (42 U.S.C. 262) on March 23, 2020 (the transition date). The transition provision is also known as the "deemed to be license" provision and FDA recommends that BLA holders submit a prior approval labeling supplement before March 23, 2022, to facilitate the implementation of the BLA-specific labeling changes by March 2025.

The applicants submitted labeling (Prescribing information, Medication Guide, Instructions for Use (Pertyze only); and carton and container) to conform to the labeling requirements for biological products regulated under section 351 of the Public Health Service Act, as described in the *Guidance for Industry: The "Deemed to be a License" Provision of the BPCI act: Questions and Answers*, Question 14.[1]

These supplements and corresponding labeling documents were reviewed by:

- Office of Biotechnology Products, Labeling Team
  - Zenpep: by Jennifer Kim dated September 23, 2022, in Panorama
  - Viokace: by Jennifer Kim dated September 23, 2022, in Panorama
  - Pertzye: by Jennifer Kim dated September 23, 2022, in Panorama

[1] https://www.fda.gov/media/119274/download

- Office of Biotechnology Products, Product Quality Team – memo to address the applicant's proposal for storage and handling excursion time, which was requested during the supplement review by OBP labeling team in Section 16 of the Prescribing Information
    - Zenpep: by Ian McWilliams dated September 9, 2022 in Panorama
    - Viokace: no memo needed
    - Pertzye: by Ian McWilliams dated September 9, 2022 in Panorama

- Division of Medication Error Prevention and Analysis:
    - Zenpep/Viokace/Pertzye reviews by Sherly Abraham dated August 19, 2022, and September 12, 2022

The review team found the Prescribing Information, Medication Guide, Instructions for Use (Pertyze only); and carton and container labeling acceptable, for submissions noted below, and the supplement is recommended for approval.

- Zenpep
  Prescribing Information and Medication Guide: September 9, 2022
  Carton/container: September 21, 2022

- Viokace
  Prescribing Information and Medication Guide: September 6, 2022
  Carton/container: September 21, 2022

- Pertzye
  Prescribing Information, Medication Guide, and Instructions for Use: September 6, 2022
  Carton/container: September 6, 2022

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/

JOETTE M MEYER
09/26/2022 05:29:38 PM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022542Orig1s007

OTHER REVIEW(S)

Center for Drug Evaluation and Research
Office of Pharmaceutical Quality
Office of Biotechnology Products

LABELS AND LABELING ASSESSMENT

Date of Assessment:	September 21, 2022
Assessor:	Jennifer Kim, PharmD Labeling Assessor Office of Biotechnology Products (OBP)
Through:	Tracy Denison, PhD, Product Quality Assessor OBP/Division of Biotechnology Review and Research 3
Application:	BLA 022542 / S-7
Applicant:	Aimmune LLC
Submission Date:	March 23, 2022
Product:	Viokace (pancrelipase)
Dosage form(s):	Tablet
Strength and Container-Closure:	10,440 USP units of lipase; 39,150 USP units of protease; 39,150 USP units of amylase in bottles of 100 tablets 20,880 USP units of lipase; 78,300 USP units of protease; 78,300 USP units of amylase in bottles of 100 tablets
Purpose of assessment:	The Applicant submitted a labeling supplement to be assessed for compliance with applicable requirements in the Code of Federal Regulations to update to BLA regulations.
Recommendations:	The prescribing information, medication guide, container labels, and carton labeling are **acceptable** from an OBP labeling perspective.

Materials Considered for this Label and Labeling Assessment	
Materials Assessed	**Appendix Section**
Proposed Labels and Labeling	A
Evaluation Tables	B
Acceptable Labels and Labeling	C

n/a = not applicable for this assessment

DISCUSSION

We assessed the proposed labels and labeling for compliance with applicable requirements in the Code of Federal Regulations. Also, we assessed the proposed labels and labeling for consistency with recommended labeling practices. (See Appendix B)

CONCLUSION

The prescribing information and medication guide submitted on September 6, 2022, container labels and carton labeling submitted on September 21, 2022, were assessed, and found to be acceptable (see Appendix C) from an OBP labeling perspective.

APPENDICES

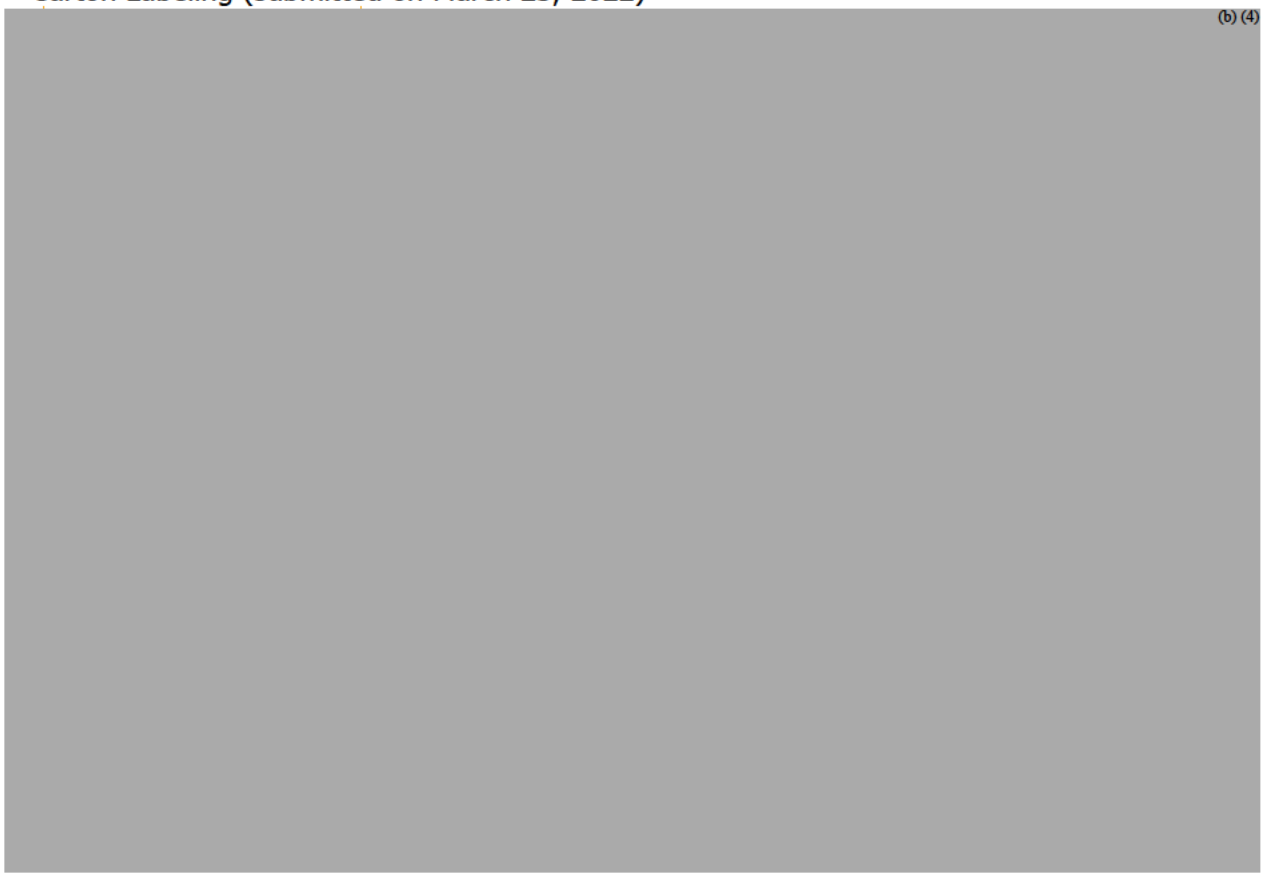
Appendix A: Proposed Labeling

- Prescribing Information (submitted on March 23, 2022)
  \\CDSESUB1\evsprod\bla022542\0103\m1\us\draft-package-insert-clean.doc

- Medication Guide (submitted on March 23, 2022)
  \\CDSESUB1\evsprod\bla022542\0103\m1\us\draft-medication-guide-clean.doc

- Container Labels (submitted on March 23, 2022)

- Carton Labeling (submitted on March 23, 2022)




(b) (4)

Appendix B: Evaluation Tables
Evaluation Tables: Label[1,2] and Labeling[3] Standards

Container[4] Label Evaluation

Proper Name (container label)	**Acceptable**
Regulations: 21 CFR 610.60(a)(1), 21 CFR 201.10(g)(2), 21 CFR 610.62(a), 21 CFR 610.62(b), 21 CFR 610.62(c), 21 CFR 610.60(c), 21 CFR 201.50(b), 21 CFR 201.10(a), 21 CFR 201.10(h)(2)(i)(1)(i)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices (placement of dosage form outside of parenthesis and/or below the proper name)	✓ Yes ☐ No ☐ N/A
Comment/Recommendation: Revise the first letter of the proper name to lowercase as follows: "pancrelipase" *The applicant revised as requested.*	

Manufacturer name, address, and license number (container label)	**Acceptable**
Regulations: 21 CFR 610.60(a)(2), 21 CFR 201.1(a), 21 CFR 610.60(c), 21 CFR 201.10(h)(2)(i)(1)(iv), 21 CFR 201.100(e)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices (using the qualifying phrase "Manufactured by:")	✓ Yes ☐ No ☐ N/A
Recommended labeling practices (U.S license number for container bearing a partial label[5])	✓ Yes ☐ No ☐ N/A
Comment/Recommendation: Revise to the appropriate qualifying phrase "Manufactured by" for the manufacturer information and "Manufactured for" for the distributor information as follows: Manufactured by: (b) (4)	

[1] Per 21 CFR 1.3(b) *Label* means any display of written, printed, or graphic matter on the immediate container of any article, or any such matter affixed to any consumer commodity or affixed to or appearing upon a package containing any consumer commodity.
[2] Per CFR 600.3(dd) *Label* means any written, printed, or graphic matter on the container or package or any such matter clearly visible through the immediate carton, receptacle, or wrapper.
[3] Per 21 CFR 1.3(a) *Labeling* includes all written, printed, or graphic matter accompanying an article at any time while such article is in interstate commerce or held for sale after shipment or delivery in interstate commerce.
[4] Per 21 CFR 600.3(bb) *Container* (referred to also as "final container") is the immediate unit, bottle, vial, ampule, tube, or other receptacle containing the product as distributed for sale, barter, or exchange.
[5] Per 21 CFR 610.60(c) *Partial Label.* If the container is capable of bearing only a partial label, the container shall show as a minimum the name (expressed either as the proper or common name), the lot number or other lot identification and the name of the manufacturer; in addition, for multiple dose containers, the recommended individual dose. Containers bearing partial labels shall be placed in a package which bears all the items required for a package label."

(b) (4)

Manufactured for:
Aimmune Therapeutics, Inc.
Brisbane, CA 94005, USA
The applicant revised as requested.

Revise the country-of-origin statement to read "Product of Canada" which is the preferred format.
The applicant revised as requested.

Lot number or other lot identification (container label)	**Acceptable**
Regulations: 21 CFR 610.60(a)(3), 21 CFR 610.60(c), 21 CFR 201.18, 21 CFR 201.100(b)(6), 21 CFR 201.10(h)(2)(i)(1)(iii)	✓ Yes ☐ No ☐ N/A

Expiration date (container label)	**Acceptable**
Regulations: 21 CFR 610.60(a)(4), 21 CFR 201.17	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: USP General Chapters <7> Labeling, Draft Guidance Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013 lines 178-184, which, when finalized, will represent FDA's current thinking on topic	✓ Yes ☐ No ☐ N/A

Beyond Use Date (Multiple-dose containers) (container label)	**Acceptable**
Recommended labeling practices: USP General Chapters: <659> Packaging and Storage Requirements and <7> Labeling	☐ Yes ☐ No ☒ N/A

Product Strength (container label)	**Acceptable**
Regulations: 21 CFR 201.10(d)(1), 21 CFR 201.100(b)(4)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices (expression of strength for injectable drugs) references: Draft Guidance Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013 line 176, which, when finalized, will represent FDA's current thinking on topic *USP General Chapters: <7> Labeling*	☐ Yes ☐ No ☒ N/A

Multiple-dose containers (container label)	**Acceptable**
Regulations: 21 CFR 610.60(a)(5), 21 CFR 201.55 *(recommended individual dose)*	☐ Yes ☐ No ☒ N/A

Statement: "Rx only" (container label)	**Acceptable**
Regulations: 21 CFR 610.60(a)(6), 21 CFR 201.100(b)(1)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices (prominence of Rx Only statement) reference: Draft Guidance Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013 line 147, which, when finalized, will represent FDA's current thinking on topic	✓ Yes ☐ No ☐ N/A

Medication Guide (container label)	**Acceptable**
Regulations: 21 CFR 610.60(a)(7), 21 CFR 208.24(d)	✓ Yes ☐ No ☐ N/A

No Package for container (container label)	**Acceptable**
Regulation: 21 CFR 610.60(b)	☐ Yes ☐ No ☒ N/A

No container label (container label)	**Acceptable**
Regulation: 21 CFR 610.60(d)	☐ Yes ☐ No ☒ N/A

Ferrule and cap overseal *(for vials only)*	**Acceptable**
Recommended labeling practices references: United States Pharmacopeia (USP) General Chapters: <7> Labeling (Ferrules and Cap Overseals)	☐ Yes ☐ No ☒ N/A

Visual inspection	**Acceptable**
Regulation: 21 CFR 610.60(e)	☐ Yes ☐ No ☒ N/A

Route of administration (container label)	**Acceptable**
Regulations: 21 CFR 201.5(f), 21 CFR 201.100(b)(3), 21 CFR 201.100(d)(1)	☐ Yes ☐ No ☒ N/A
Recommended labeling practices (route of administration statement to appear after the strength statement on the principal display panel)	☐ Yes ☐ No ☒ N/A

NDC numbers **(container label)**	**Acceptable**
Regulations: 21 CFR 201.2, 21 CFR 207.35	✓ Yes ☐ No ☐ N/A

Preparation instructions (container label)	**Acceptable**
Regulation: 21 CFR 201.5(g)	☐ Yes ☐ No ☒ N/A
Recommended labeling practices: Draft Guidance Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013 (lines 426-430), which, when finalized, will represent FDA's current thinking on topic	☐ Yes ☐ No ☒ N/A

Package type term (container label)	**Acceptable**
Recommended labeling practices: Guidance for Industry: Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use (October 2018) *USP chapter <659> Packaging and Storage Requirements*	☐ Yes ☐ No ☒ N/A

Misleading statements (container label)	**Acceptable**
Regulation: 21 CFR 201.6	☐ Yes ☐ No ☒ N/A

Prominence of required label statements (container label)	**Acceptable**
Regulation: 21 CFR 201.15	✓ Yes ☐ No ☐ N/A

Spanish-language (Drugs) (container label)	**Acceptable**
Regulation: 21 CFR 201.16	☐ Yes ☐ No ☒ N/A

FD&C Yellow No. 5 and/or FD&C Yellow No. 6 (container label)	**Acceptable**
Regulation: 21 CFR 201.20	☐ Yes ☐ No ☒ N/A

Bar code label requirements (container label)	**Acceptable**
Regulations: 21 CFR 201.25, 21 CFR 610.67	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: Guidance for Industry: Bar Code Label Requirements Questions and Answers, August 2011 *Draft Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013 (lines 511-512), lines 780-786), which, when finalized, will represent FDA's current thinking on topic*	✓ Yes ☐ No ☐ N/A

Strategic National Stockpile (exceptions or alternatives to labeling requirements for human drug products) (container label)	**Acceptable**
Regulations: 21 CFR 610.68, 21 CFR 201.26	☐ Yes ☐ No ☒ N/A

Net quantity (container label)	**Acceptable**
Regulation: 21 CFR 201.51	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: Draft Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors (line 461- 463) which, when finalized, will represent FDA's current thinking on topic *Allowable Excess Volume and Labeled Vial Fill Size in Injectable Drug and Biological Products Guidance for Industry, June 2015 (line 68, 93-99)* *USP General Chapters <1151> Pharmaceutical Dosage Forms (Excess volume in injections).*	☐ Yes ☐ No ☒ N/A

Statement of Dosage (container label)	**Acceptable**
Regulations: 21 CFR 610.60(a)(5), 21 CFR 610.60(c), 21 CFR 201.55, 21 CFR 201.100(b)(2)	✓ Yes ☐ No ☐ N/A
Comment/Recommendation: Revise the statement of dosage on the side panel from [redacted] (b) (4) [redacted] (b) (4) [redacted] to read "Dosage: See Prescribing Information." to be in alignment with PLR labeling format and to avoid clutter. *The applicant revised as requested.*	

Inactive ingredients (container label)	**Acceptable**
Regulation: 21 CFR 201.100	✓ Yes ☐ No ☐ N/A
Recommended labeling practices reference: USP General Chapters <1091> Labeling of Inactive Ingredients and USP General Chapters <7> Labeling	✓ Yes ☐ No ☐ N/A

Storage requirements (container label)	**Acceptable**
Recommended labeling practices references: USP General Chapters <7> Labeling, USP General Chapters <659> Packaging and Storage Requirements	✓ Yes ☐ No ☐ N/A
Comment/Recommendation: Revise the storage statement to read "Store at room temperature 20 to 25°C (68 to 77°F), brief excursion permitted up to 40°C (104°F) for up to 24 hrs." *The applicant revised as requested.*	

Dispensing container (container label)	**Acceptable**
Regulation: 21 CFR 201.100(b)(7)	☐ Yes ☐ No ☒ N/A

Other (container label)	**Acceptable**
	✓ Yes ☐ No ☐ N/A
Comment/Recommendation: Remove the statement [redacted] (b) (4) from the container label because our view is that 21 CFR 610.61(r) is not applicable. *The applicant revised as requested.*	

Based on CDER's current interpretation of 21 CFR 610.61(r) and after consultation with OBP Product Quality assessors, this regulation does not apply to this product because 1) no U.S. standard of potency has been prescribed for pancrelipase products (i.e., there is no specific test method described in regulation for pancrelipase products that establishes an official standard of potency) and 2) Product Quality assessors have determined that potency is not a factor within the meaning of § 610.61(r) for Viokace because lot variability is not a concern as the manufacturing process is appropriately controlled to ensure the consistency and quality of the final product. Accordingly, the phrase [redacted] (b) (4) *is not required to appear on the carton labeling.*

Package[6] Labeling Evaluation

Proper name (package labeling)	**Acceptable**
Regulations: 21 CFR 610.61(a), 21 CFR 201.50(b), 21 CFR 201.10(g)(2)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices (placement of dosage form outside of parenthesis and/or below the proper name)	✓ Yes ☐ No ☐ N/A
Comment/Recommendation: Revise the first letter of the proper name to lowercase as follows: "pancrelipase" *The applicant revised as requested.*	

Manufacturer name, address, and license number (package labeling)	**Acceptable**
Regulations: 21 CFR 610.61(b), 21 CFR 201.1(a), 21 CFR 201.1(i), 21 CFR 201.100(e)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices (using the qualifying phrase "Manufactured by:")	✓ Yes ☐ No ☐ N/A
Comment/Recommendation: Revise to the appropriate qualifying phrase "Manufactured by" for the manufacturer information and "Manufactured for" for the distributor information as follows: Manufactured by: [redacted] (b) (4) Manufactured for:	

[6] Per 21 CFR 600.3(cc) *Package* means the immediate carton, receptacle, or wrapper, including all labeling matter therein and thereon, and the contents of the one or more enclosed containers. If no package, as defined in the preceding sentence, is used, the container shall be deemed to be the package. Thus, this includes the carton, prescribing information, and patient labeling.

Aimmune Therapeutics, Inc.
Brisbane, CA 94005, USA
The applicant revised as requested.

Revise the country-of-origin statement to read "Product of Canada" which is the preferred format.
The applicant revised as requested.

Lot number or other lot identification (package labeling)	**Acceptable**
Regulation: 21 CFR 610.61(c), 21 CFR 201.18	✓ Yes ☐ No ☐ N/A
Comment/Recommendation: Ensure the lot number appears on the carton labeling. *The applicant confirms that the lot number appears on the carton labeling.*	

Expiration date (package labeling)	**Acceptable**
Regulations: 21 CFR 610.61(d), 21 CFR 201.17	✓ Yes ☐ No ☐ N/A
Comment/Recommendation: Ensure the expiration date appears on the carton labeling. *The applicant confirms that the expiration date appears on carton labeling.*	

Beyond Use Date (Multiple-dose containers) (package labeling)	**Acceptable**
Recommended labeling practices: USP General Chapters: <659> Packaging and Storage Requirements and <7> Labeling	☐ Yes ☐ No ☒ N/A

Preservative (package labeling)	**Acceptable**
Regulation: 21 CFR 610.61(e)	✓ Yes ☐ No ☐ N/A

Number of containers (package labeling)	**Acceptable**
Regulation: 21 CFR 610.61(f)	✓ Yes ☐ No ☐ N/A

Product Strength (package labeling)	**Acceptable**
Regulations: 21 CFR 610.61(g), 21 CFR 201.10(d)(1), 21 CFR 201.100(b)(4)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: Draft Guidance Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013 (line 176), which, when finalized, will represent FDA's current thinking on topic *USP General Chapters: <7> Labeling*	☐ Yes ☐ No ☒ N/A

Storage temperature/requirements (package labeling)	**Acceptable**
Regulation: 21 CFR 610.61(h)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices reference: USP General Chapters: <7> Labeling, USP General Chapters <659> Packaging and Storage Requirements	✓ Yes ☐ No ☐ N/A
Comment/Recommendation: Revise the storage statement to read "Store at room temperature 20 to 25°C (68 to 77°F), brief excursion permitted up to 40°C (104°F) for up to 24 hrs." *The applicant revised as requested.*	

Handling: "Do Not Shake", "Do not Freeze" or equivalent (package labeling)	**Acceptable**
Regulation: 21 CFR 610.61(i)	✓ Yes ☐ No ☐ N/A

Multiple dose containers (recommended individual dose) (package labeling)	**Acceptable**
Regulation: 21 CFR 610.61(j)	☐ Yes ☐ No ☒ N/A

Route of administration (package labeling)	**Acceptable**
Regulations: 21 CFR 610.61(k), 21 CFR 201.5(f), 21 CFR 201.100(d)(1)	☐ Yes ☐ No ☒ N/A
Recommended labeling practices (route of administration statement to appear after the strength statement on the principal display panel)	☐ Yes ☐ No ☒ N/A

Known sensitizing substances (package labeling)	**Acceptable**
Regulations: 21 CFR 610.61(l), 21 CFR 801.437 (User labeling for devices that contain natural rubber)	☐ Yes ☐ No ☒ N/A

Inactive ingredients (package labeling)	**Acceptable**
Regulations: 21 CFR 610.61, 21 CFR 201.100	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: USP General Chapters <1091> Labeling of Inactive Ingredients, USP General Chapters <7> Labeling	✓ Yes ☐ No ☐ N/A

Source of the product (package labeling)	**Acceptable**
Regulation: 21 CFR 610.61(p)	✓ Yes ☐ No ☐ N/A

Minimum potency of product (package labeling)	**Acceptable**
Regulation: 21 CFR 610.61(r)	☐ Yes ☐ No ☐ N/A
Comment/Recommendation: Remove the statement [redacted (b)(4)]" from the carton labeling because our view is that 21 CFR 610.61(r) is not applicable. *The applicant revised as requested.* *Based on CDER's current interpretation of 21 CFR 610.61(r) and after consultation with OBP Product Quality assessors, this regulation does not apply to this product because 1) no U.S. standard of potency has been prescribed for pancrelipase products (i.e., there is no specific test method described in regulation for pancrelipase products that establishes an official standard of potency) and 2) Product Quality assessors have determined that potency is not a factor within the meaning of § 610.61(r) for Viokace because lot variability is not a concern as the manufacturing process is appropriately controlled to ensure the consistency and quality of the final product. Accordingly, the phrase [redacted (b)(4)] is not required to appear on the carton labeling.*	

Rx only (package labeling)	**Acceptable**
Regulations: 21 CFR 610.61(s), 21 CFR 201.100(b)(1)	✓ Yes ☐ No ☐ N/A

Recommended labeling practices references: Draft Guidance Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013 (line 147-149), which, when finalized, will represent FDA's current thinking on topic	✓ Yes ☐ No ☐ N/A

Divided manufacturing (package labeling)	**Acceptable**
Regulation: 21 CFR 610.63 (Divided manufacturing responsibility to be shown)	☐ Yes ☐ No ☒ N/A

Distributor (package labeling)	**Acceptable**
Regulation: 21 CFR 610.64, 21 CFR 201.1(h)(5)	✓ Yes ☐ No ☐ N/A
Comment/Recommendation: Revise to the appropriate qualifying phrase "Manufactured by" for the manufacturer information and "Manufactured for" for the distributor information as follows: Manufactured by: (b) (4)  Manufactured for: Aimmune Therapeutics, Inc. Brisbane, CA 94005, USA *The applicant revised as requested.*	

Bar code (package labeling)	**Acceptable**
Regulations: 21 CFR 610.67, 21 CFR 201.25	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: *Guidance for Industry: Bar Code Label Requirements Questions and Answers, August 2011* *Draft Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013 (lines 511-512), lines 780-786)*	✓ Yes ☐ No ☐ N/A

Strategic National Stockpile (exceptions or alternatives to labeling requirements for human drug products) (package labeling)	**Acceptable**
Regulations: 21 CFR 610.68, 21 CFR 201.26	☐ Yes ☐ No

	☒ N/A

NDC numbers (package labeling)	**Acceptable**
Regulations: 21 CFR 201.2, 21 CFR 207.35	✓ Yes ☐ No ☐ N/A

Preparation instructions (package labeling)	**Acceptable**
Regulation: 21 CFR 201.5(g) and 21 CFR 610.61(i)	☐ Yes ☐ No ☒ N/A
Recommended labeling practices references: Draft Guidance Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013 (lines 426-430), which, when finalized, will represent FDA's current thinking on topic *USP General Chapters <7> Labeling*	☐ Yes ☐ No ☒ N/A

Package type term (package labeling)	**Acceptable**
Recommended labeling practices: Guidance for Industry: Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use (October 2018) *USP chapter <659> Packaging and Storage Requirements*	☐ Yes ☐ No ☒ N/A

Misleading statements (package labeling)	**Acceptable**
Regulation: 21 CFR 201.6	☐ Yes ☐ No ☒ N/A

Prominence of required label statements (package labeling)	**Acceptable**
Regulation: 21 CFR 201.15	✓ Yes ☐ No ☐ N/A

Spanish-language (Drugs) (package labeling)	**Acceptable**
Regulation: 21 CFR 201.16	☐ Yes ☐ No ☒ N/A

FD&C Yellow No. 5 and/or FD&C Yellow No. 6 (package labeling)	Acceptable
Regulation: 21 CFR 201.20	☐ Yes ☐ No ☒ N/A

Phenylalanine as a component of aspartame (package labeling)	Acceptable
Regulation: 21 CFR 201.21(c)	☐ Yes ☐ No ☒ N/A

Sulfites; required warning statements (package labeling)	Acceptable
Regulation: 21 CFR 201.22(b)	☐ Yes ☐ No ☒ N/A

Net quantity (package labeling)	Acceptable
Regulation: 21 CFR 201.51	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: Draft Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors (line 461- 463) which, when finalized, will represent FDA's current thinking on topic *Allowable Excess Volume and Labeled Vial Fill Size in Injectable Drug and Biological Products Guidance for Industry, June 2015 (line 68, 93-99)* *USP General Chapters <1151> Pharmaceutical Dosage Forms (Excess volume in injections).*	☐ Yes ☐ No ☒ N/A

Statement of Dosage (package labeling)	Acceptable
Regulations: 21 CFR 201.55, 21 CFR 201.100(b)(2)	✓ Yes ☐ No ☐ N/A
Comment/Recommendation: Revise the statement of dosage on the side panel from "(b) (4) (b) (4) (b) (4) to read "Dosage: See Prescribing Information." to be in alignment with PLR labeling format and to avoid clutter. *The applicant revised as requested.*	

Dispensing container (package labeling)	Acceptable
Regulation: 21 CFR 201.100(b)(7)	☐ Yes

	☐ No ☒ N/A

Medication Guide (package labeling)	**Acceptable**
Regulations: 21 CFR 610.60(a)(7), 21 CFR 208.24(d)	✓ Yes ☐ No ☐ N/A

Prescribing Information Evaluation

PRESCRIBING INFORMATION

Highlights of Prescribing Information	
PRODUCT TITLE	**Acceptable**
Regulation: 21 CFR 201.57(a)(2)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices reference: Draft Guidance for Industry on Product Title and Initial U.S. Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products - Content and Format (January 2018), which, when finalized, will represent FDA's current thinking on topic	✓ Yes ☐ No ☐ N/A

Highlights of Prescribing Information	
DOSAGE AND ADMINISTRATION	**Acceptable**
Recommended labeling practices reference: USP nomenclature for diluents and intravenous solutions	☐ Yes ☐ No ☒ N/A

Highlights of Prescribing Information	
DOSAGE FORMS AND STRENGTHS	**Acceptable**
Regulations: 21 CFR 201.57(a)(8), 21 CFR 201.10, 21 CFR 201.100	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: Guidance for Industry: Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use (October 2018) *USP chapter <659> Packaging and Storage Requirements* *USP General Chapters: <7> Labeling*	✓ Yes ☐ No ☐ N/A

Full Prescribing Information	
2 DOSAGE AND ADMINISTRATION	**Acceptable**
Regulation: 21 CFR 201.57(c)(3)(iv)] *Confirm appropriateness of specific direction on dilution, preparation, and administration of the dosage form and storage conditions for stability of the reconstituted or diluted drug; ensure verbatim statement for parenterals: "Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit."*	✓ Yes ☐ No ☐ N/A
Recommended labeling practices reference: USP nomenclature for diluents and intravenous solutions and storage instructions for reconstituted and diluted products; confirm the appropriateness of infusion bags, infusion sets (e.g., tubing, infusion aids, or filter membranes) incompatibilities with these components	☐ Yes ☐ No ☒ N/A
Comment/Recommendation: The statement "VIOKACE is a mixture of enzymes including lipases, proteases, and amylases and dosing is based on lipase units." added for clarity in dosing and to reflect recommended wording regarding the product that is also proposed for Section 11. *The applicant revised as requested.*	

Full Prescribing Information	
3 DOSAGE FORMS AND STRENGTHS	**Acceptable**
Regulation: 21 CFR 201.57(c)(4)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: Guidance for Industry: Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use (October 2018) *USP chapter <659> Packaging and Storage Requirements* *USP General Chapters: <7> Labeling*	☐ Yes ☐ No ☒ N/A
Comment/Recommendation: We relocated the dosing information to section 2. *The applicant revised as requested.* We deleted redundant information to improve readability of the information. *The applicant revised as requested.*	

Full Prescribing Information	
11 DESCRIPTION	**Acceptable**
Regulations: 21 CFR 201.57(c)(12), 21 CFR 610.61 (m), 21 CFR 610.61(o), 21 CFR 610.61 (p), 21 CFR 610.61 (q)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: USP General Chapters <1091>, USP General Chapters <7>	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
We deleted the proprietary name from the first paragraph, which describes the drug substance.
The applicant revised as requested.

The phrase [redacted] (b) (4) " revised to "pancreatic enzyme product."
The applicant revised as requested.

We relocated the route of administration information to the second paragraph, which discusses the drug product.
The applicant revised as requested.

We deleted the [redacted] (b) (4) and [redacted] (b) (4) information, which are not required in the Description section.
The applicant revised as requested.

We deleted [redacted] (b) (4) information and [redacted] (b) (4) information that are not required in the Description section.
The applicant revised as requested.

We relocated the inactive ingredient information to appear after the active ingredient information.
The applicant revised as requested.

Full Prescribing Information	
15 & 16 Hazardous Drug	**Acceptable**
Regulation: 21 CFR 201.57(c)(17)(iv) Section 15: References 1. OSHA Hazardous Drugs. OSHA. *http://www.osha.gov/SLTC/hazardousdrugs/index.html* Section 16: xxxx is a hazardous drug. Follow applicable special handling and disposal procedures.[1]	☐ Yes ☐ No ☒ N/A

Full Prescribing Information	
16 HOW SUPPLIED/ STORAGE AND HANDLING	**Acceptable**
Regulation: 21 CFR 201.57(c)(17)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices: to ensure placement of detailed storage conditions for reconstituted and diluted products	✓ Yes ☐ No ☐ N/A

Full Prescribing Information	
MANUFACTURER INFORMATION	**Acceptable**
Regulations: 21 CFR 201.100(e), 21 CFR 201.1	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: 21 CFR 610.61(b) (add the US license number for consistency with the carton labeling), and 21 CFR 610.64 (Name and address of distributor may appear and use a qualifying phrase for consistency with the carton labeling, when applicable)	✓ Yes ☐ No ☐ N/A
Comment/Recommendation: We revised to the appropriate qualifying phrase "Manufactured by" for the manufacturer information. *The applicant revised as requested.* We revised to the appropriate qualifying phrase "Manufactured for" for the distributor information. *The applicant revised as requested.*	

Medication Guide Evaluation

MEDICATION GUIDE	
TITLE (NAMES AND DOSAGE FORM)	**Acceptable**
Regulation for Medication Guide: 21 CFR 208.20(a)(7)	✓ Yes ☐ No ☐ N/A

MEDICATION GUIDE	
STORAGE AND HANDLING	**Acceptable**
Regulation for Medication Guide: 21 CFR 208.20(a)(2)	✓ Yes ☐ No ☐ N/A

MEDICATION GUIDE	
INGREDIENTS	**Acceptable**
Recommended labeling practice: To ensure labeling of inactive ingredients are in alphabetical order (see USP General Chapters <1091>)	✓ Yes ☐ No ☐ N/A

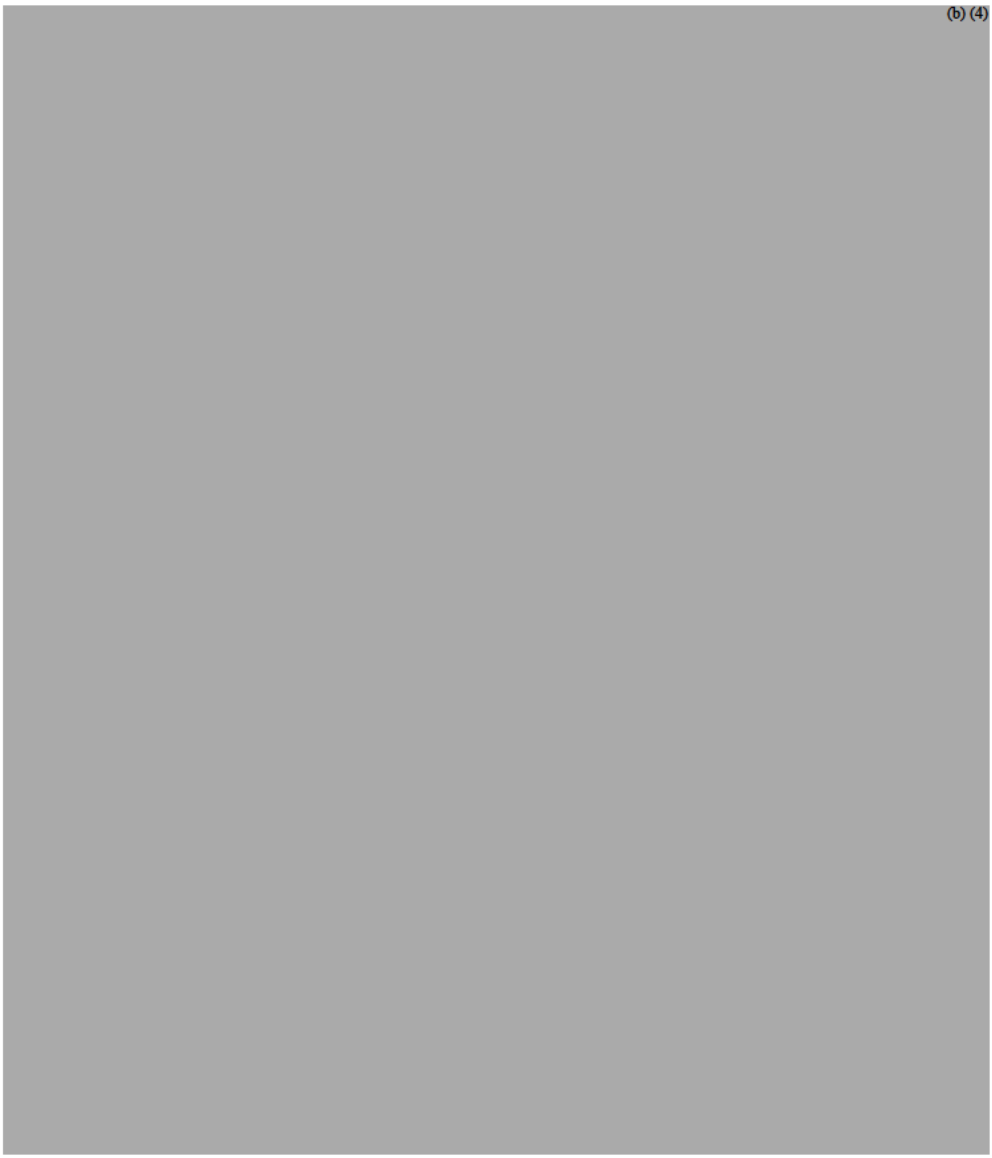
MEDICATION GUIDE	
MANUFACTURER INFORMATION	**Acceptable**
21 CFR 208.20(b)(8)(iii)	✓ Yes ☐ No ☐ N/A
21 CFR 610.61 (add the US license number for consistency with the carton labeling), 21 CFR 610.64 (Name and address of distributor may appear and use a qualifying phrase for consistency with the carton labeling, when applicable)	✓ Yes ☐ No ☐ N/A
Comment/Recommendation: We revised to the appropriate qualifying phrase "Manufactured by" for the manufacturer information. *The applicant revised as requested.* We revised to the appropriate qualifying phrase "Manufactured for" for the distributor information. *The applicant revised as requested.*	

APPENDIX C. Acceptable Labels and Labeling

- Prescribing Information (submitted on September 6, 2022)
  \\CDSESUB1\EVSPROD\bla022542\0108\m1\us\draft-package-insert-clean.pdf

- Medication Guide (submitted on September 6, 2022)
  \\CDSESUB1\EVSPROD\bla022542\0108\m1\us\draft-medication-guide-clean.pdf

- Container Labels (submitted on September 21, 2022)



- Carton Labeling (submitted on September 21, 2022)


(b) (4)

Jennifer Kim

Digitally signed by Jennifer Kim
Date: 9/23/2022 11:34:40AM
GUID: 5e5438d2008138bdbae1db8d4abc0580

Tracy Denison

Digitally signed by Tracy Denison
Date: 9/23/2022 12:28:11PM
GUID: 53725fbb0005b7b3ff10aa8a0ade1295

MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)

Office of Medication Error Prevention and Risk Management (OMEPRM)

Office of Surveillance and Epidemiology (OSE)

Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	September 12, 2022
Requesting Office or Division:	Division of Gastroenterology (DG)
Application Type and Number:	BLA 22210/S-024 (ZenPep) BLA 22542/S-007 (Viokace) BLA 22175/S-008 (Pertzye
Product Name and Strength:	ZenPep (pancrelipase) Delayed-release Capsules 3,000 USP units of lipase; 10,000 USP units of protease; 14,000 USP units of amylase 5,000 USP units of lipase; 17,000 USP units of protease; 24,000 USP units of amylase 10,000 USP units of lipase; 32,000 USP units of protease; 42,000 USP units of amylase 15,000 USP units of lipase; 47,000 USP units of protease; 63,000 USP units of amylase 20,000 USP units of lipase; 63,000 USP units of protease; 84,000 USP units of amylase 25,000 USP units of lipase; 79,000 USP units of protease; 105,000 USP units of amylase 40,000 USP units of lipase; 126,000 USP units of protease; 168,000 USP units of amylase) Viokace (pancrelipase) tablets 10,440 USP units of lipase; 39,150 USP units of protease; 39,150 USP units of amylase 20,880 USP units of lipase; 78,300 USP units of protease; 78,300 USP units of amylase Pertzye (pancrelipase) Delayed-release Capsules 4,000 USP units of lipase; 14,375 USP units of protease; 15,125 USP units of amylase 8,000 USP units of lipase; 28,750 USP units of protease; 30,250 USP units of amylase

Reference ID: 5044078

	16,000 USP units of lipase; 57,500 USP units of protease; 60,500 USP units of amylase) 24,000 USP units of lipase; 86,250 USP units of protease; 90,750 USP units of amylase
Applicant/Sponsor Name:	Aimimune LLC (Zenpep and Viokace) and Digestic Care, Inc (Pertzye)
OSE RCM #:	2022-765-1 2022-766-1 2022-767-1
DMEPA 1 Safety Evaluator:	Sherly Abraham, R.Ph.
DMEPA 1 Team Leader:	Idalia E. Rychlik, Pharm.D

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised container labels and carton labeling received on September 6, 2022 (Viokace and Pertzye) and September 9, 2022 (Zenpep). The Division of Gastroenterology (DG) requested that we review the revised container labels and carton labeling for Zenpep and Viokace, and Pertzye (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review.[a]

2 CONCLUSION

The Applicant implemented all of our recommendations and we have no additional recommendations at this time.

[a]Abraham, S. Label and Labeling Review for Zenpep, Viokace, and Pertzye (BLA 22210/S-024 (ZenPep) BLA 22542/S-007 (Viokace), and BLA 22175/S-008 (Pertzye). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2022 AUG 19. RCM No.: 2022-765, 2022-766, and 2022-767.

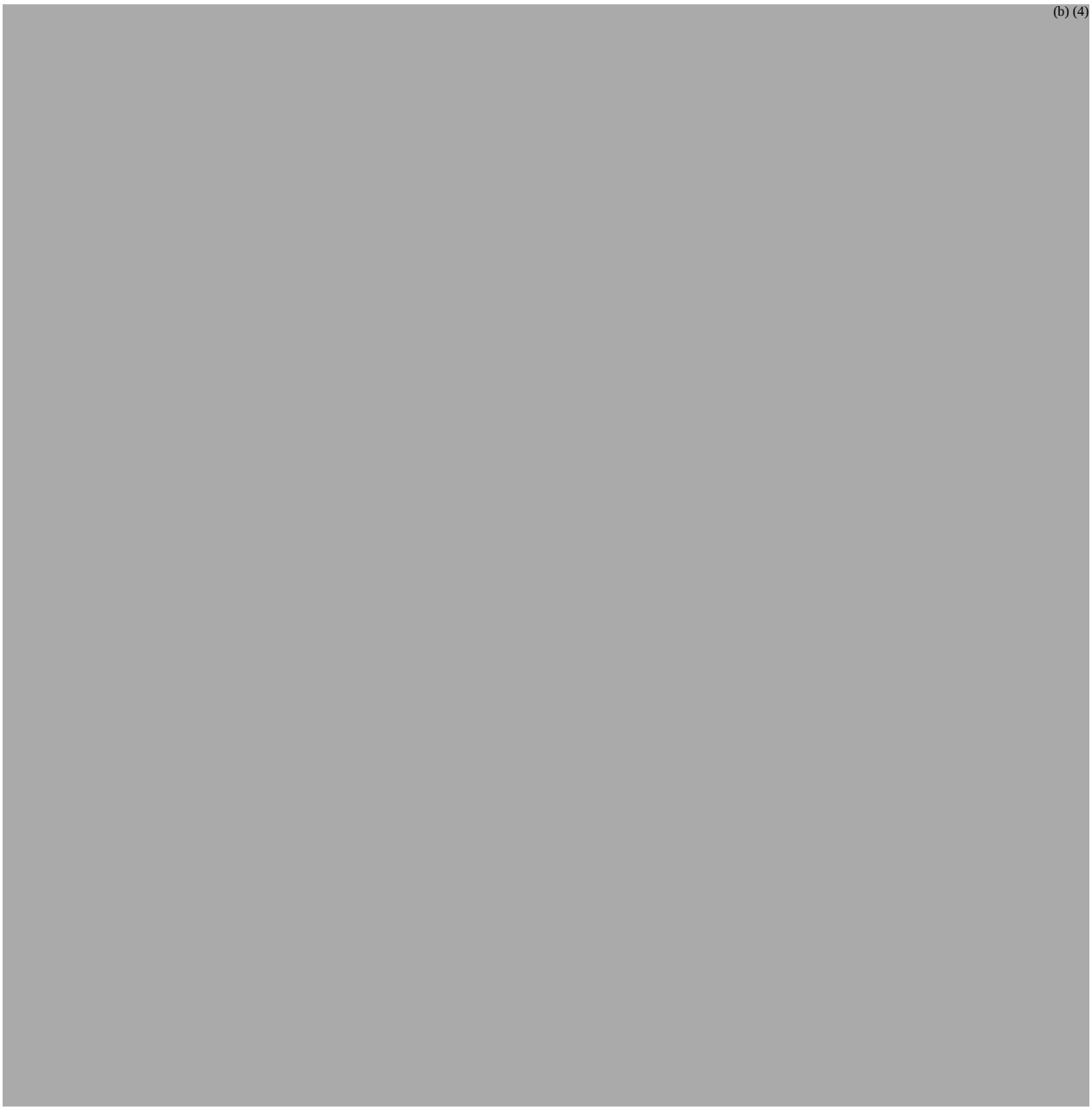
Reference ID: 5044078

APPENDIX A. IMAGES OF LABEL AND LABELING

Zenpep Container labels received on September 9, 2022

\\CDSESUB1\EVSPROD\bla022210\0068\m1\us\draft-container-label.pdf

(b) (4)



23 Pages of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page.

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/

SHERLY ABRAHAM
09/12/2022 01:03:49 PM

IDALIA E RYCHLIK
09/12/2022 03:27:38 PM

LABEL AND LABELING REVIEW
Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	August 19, 2022
Requesting Office or Division:	Division of Gastroenterology (DG)
Application Type and Number:	BLA 22210/S-024 (ZenPep) BLA 22542/S-007 (Viokace) BLA 22175/S-008 (Pertzye)
Product Name and Strength:	ZenPep (pancrelipase) Delayed-release Capsules 3,000 USP units of lipase; 10,000 USP units of protease; 14,000 USP units of amylase 5,000 USP units of lipase; 17,000 USP units of protease; 24,000 USP units of amylase 10,000 USP units of lipase; 32,000 USP units of protease; 42,000 USP units of amylase 15,000 USP units of lipase; 47,000 USP units of protease; 63,000 USP units of amylase 20,000 USP units of lipase; 63,000 USP units of protease; 84,000 USP units of amylase 25,000 USP units of lipase; 79,000 USP units of protease; 105,000 USP units of amylase 40,000 USP units of lipase; 126,000 USP units of protease; 168,000 USP units of amylase) Viokace (pancrelipase) tablets 10,440 USP units of lipase; 39,150 USP units of protease; 39,150 USP units of amylase 20,880 USP units of lipase; 78,300 USP units of protease; 78,300 USP units of amylase Pertzye (pancrelipase) Delayed-release Capsules 4,000 USP units of lipase; 14,375 USP units of protease; 15,125 USP units of amylase

Reference ID: 5033153

	8,000 USP units of lipase; 28,750 USP units of protease; 30,250 USP units of amylase 16,000 USP units of lipase; 57,500 USP units of protease; 60,500 USP units of amylase) 24,000 USP units of lipase; 86,250 USP units of protease; 90,750 USP units of amylase
Product Type:	Multi-ingredient product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Aimimune LLC (Zenpep and Viokace) Digestic Care, Inc (Viokace)
FDA Received Date:	March 23, 2022(Zenpep and Viokace) April 15, 2022(Pertzye)
OSE RCM #:	2022-765, 2022-766, and 2022-767
DMEPA 1 Safety Evaluator:	Sherly Abraham, R.Ph.
DMEPA 1 Team Leader:	Idalia E. Rychlik, Pharm.D.

1 REASON FOR REVIEW

On March 23, 2022, Aimimune LLC submitted prior approval supplements (PAS) for deemed BLA applications labeling revisions for Zenpep delayed-release capsules (BLA 22210/S-024) and Viokace tablets (BLA 22175/S-008). On April 15, 2022, Digestive Care Inc submitted a PAS for deemed BLA application labeling revisions for Pertzye delayed-release capsules (BLA 22175/S-008). These supplements align the product's labels and labeling to conform with the requirements established for biological products regulated under Section 351 of the PHS Act.

Subsequently, the Division of Gastroenterology (DG) requested that we review the proposed Zenpep, Viokace, and Pertzye Prescribing information (PI), medication guide (MG), Instructions for use (IFU), carton labeling, and container labels for areas of vulnerability that may lead to medication errors.

2 MATERIALS REVIEWED

Table 1. Materials Considered for this Label and Labeling Review

Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B
ISMP Newsletters*	C-N/A
FDA Adverse Event Reporting System (FAERS)*	D-N/A
Other	E-N/A
Labels and Labeling	F

N/A=not applicable for this review
*We do not typically search FAERS or ISMP Newsletters for our label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

3 CONCLUSION AND RECOMMENDATIONS

DMEPA evaluated the proposed Zenpep, Viokace, and Pertzye PI, MG, IFU, container labels, and carton labeling for areas of vulnerability in regard to medication error. We identified areas in the labels and labeling that can be improved to increase readability and prominence of important information. We provide the identified medication error issues, our rationale for concern, and our proposed recommendations to minimize the risk for medication error in Section 4 for DG, Section 5 for Aimmune LLC and in Section 6 for Digestive Care Inc.

Reference ID: 5033153

4 RECOMMEDATIONS FOR DIVISION OF GASTROENTEROLOGY (DG)

Table 2. Identified Issues and Recommendations for Division of Gastroenterology (DG)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Zenpep Prescribing Information – Section 16 How Supplied/Storage and Handling			
1.	The storage statements contain the symbols, "-" .	The usage of symbols may cause misinterpretation and confusion.[a]	Consider revising the sentence with their intended meaning.
Zenpep Medication Guide			
1.	The storage statement is not consistent with the container label and carton labeling.	Inconsistencies between PI and label and labeling may lead to misinterpretation in storage information.	Consider revising the sentence to read, "Store ZENPEP at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 40°C (59°F to 104°F)".
Viokace Prescribing Information-Section 16 How Supplied/Storage and Handling			
1.	The storage statement contains the symbol, "-" and the first temperature numerical for each range are missing degree symbols.	The usage of symbols may cause misinterpretation and confusion.[a]	Consider revising the sentence to read, "Store at room temperature 20°C to 25°C (68°F to 77°F), brief excursion permitted up to 40°C (104°F) for up to 24 hrs."
Viokace Medication Guide (MG)			
1.	As currently displayed, the storage statement beginning with "Store VIOKACE at room temperature...", storage temperature numbers in Fahrenheit (˚F) precede temperature numbers in Celsius (˚C), which is	Inconsistencies between MG and PI may lead to confusion of storage information of the product.	While DMEPA generally recommends consistency across all label and labeling , we are not aware of post-market storage medication errors related to the order of Celcisus (C) vs. Fahrenheit (F). Thus, we align to the order of

[a] ISMP's List of Error-Prone Abbreviations, Symbols, and Dose Designations [Internet]. Horsham (PA): Institute for Safe Medication Practices. 2015 [cited 2015 Sep 16]. Available from: http://www.ismp.org/tools/errorproneabbreviations.pdf.

Table 2. Identified Issues and Recommendations for Division of Gastroenterology (DG)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
	inconsistent with the proposed Prescribing Information (PI).		recommended by OPQ and DMPP/PLT.
Pertzye Prescribing Information- Section 16 How Supplied/Storage and Handling			
1.	The storage statement contains symbol, "-" and the first temperature numerical are missing degree symbols.	The usage of symbols may cause misinterpretation and confusion.[a]	Consider revising the sentence to read, "Store at room temperature 20°C to 25°C (68°F to 77°F), brief excursion permitted up to 40°C (104°F) for up to 24 hrs."
Pertzye Medication Guide (MG) and Instructions for Use (IFU)			
1.	As currently displayed, the storage statement beginning with "Store PERTYE at room temperature…", storage temperature numbers in Fahrenheit (˚F) precede temperature numbers in Celsius (˚C), which is inconsistent with the PI.	Inconsistencies between IFU and MG with PI may lead to confusion of storage information of the product.	While DMEPA generally recommends consistency across all label and labeling , we are not aware of post-market storage medication errors related to the order of Celcisus (C) vs. Fahrenheit (F). Thus, we align to the order of recommended by DMPP/PLT.

5 RECOMMENDATIONS FOR AIMMUNE LLC.

Table 3. Identified Issues and Recommendations for Genentech Roche (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Zenpep Container Label(s) and Carton Labeling			
1.	The format for expiration date is not defined.	Clearly define the expiration date will minimize confusion and risk	Identify the expiration date format you intend to use.

Table 3. Identified Issues and Recommendations for Genentech Roche (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
		for deteriorated drug medication errors.	FDA recommends that the human-readable expiration date on the drug package label include a year, month, and non-zero day. FDA recommends that the expiration date appear in YYYY-MM-DD format if only numerical characters are used or in YYYY-MMM-DD if alphabetical characters are used to represent the month. If there are space limitations on the drug package, the human-readable text may include only a year and month, to be expressed as: YYYY-MM if only numerical characters are used or YYYY-MMM if alphabetical characters are used to represent the month. FDA recommends that a hyphen or a space be used to separate the portions of the expiration date.
2.	Inconsistent terminology is used for recommended dosage statement.	Inconsistencies between PI and label and labeling may lead to misinterpretation in dosage information.	To ensure consistency with the Prescribing Information, revise the statement, (b) (4) (b) (4) (b) (4) , prescribing information. (b) (4) (b) (4)

Table 3. Identified Issues and Recommendations for Genentech Roche (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
3.	The storage statement contains the symbol, "-" and the first temperature numerical is missing the degree symbol.	The usage of symbols may cause misinterpretation and confusion.[b] Lack of clarity	Replace the dash symbol with its intended meaning and insert the missing degree symbol after the first temperature numerical of each temperature range. Revise the sentence to read "Storage Conditions: Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 40°C (59°F to 104°F)
4.	The lot number statement and the expiration date statement ("Lot/exp") are on the same line.	The lot number statement should be clearly differentiated from the expiration date statement.[c]	Ensure that the lot number statement and expiration date statement ("Lot/exp") are on separate lines.
5.	The net quantity statement is prominent and takes the reader's attention away from more important product information, such as the product strength.	Post-marketing experience shows that the risk of numerical confusion between the strength and net quantity increases when the net quantity statement is more prominent.	Decrease the prominence of net quantity statement.
6.	Most of the container labels and carton labeling have the following duplicative statements, (b) (4)	Duplicative statements may crowd the label and labeling and distract the reader from more important information such as the warning statement.	Delete the duplicative statements, (b) (4) underneath the

[b] ISMP's List of Error-Prone Abbreviations, Symbols, and Dose Designations [Internet]. Horsham (PA): Institute for Safe Medication Practices. 2015 [cited 2015 Sep 16]. Available from: http://www.ismp.org/tools/errorproneabbreviations.pdf.

[c] Institute for Safe Medication Practices. Safety briefs: Lot number, not expiration date. ISMP Med Safe Alert Acute Care. 2014;19(23):1-4.

Table 3. Identified Issues and Recommendations for Genentech Roche (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
	(b) (4) underneath the WARNINGS statement on the side panel.		WARNINGS statement on the side panel.
7.	The following statements, (b) (4) (b) (4)", and (b) (4) are found on the carton labeling, but they are absent in the PI.	Inconsistencies between PI and label and labeling may lead to misinterpretation in storage information.	Delete the statements, (b) (4) (b) (4)", and (b) (4) (b) (4)" from the side panel.
8.	The statement, "AFTER OPENING, KEEP BOTTLE TIGHTLY CLOSED between uses to PROTECT FROM MOISTURE." is found in the PI, but this statement is missing from the carton labeling and container labels.	As currently presented, (b) (4) and (b) (4) are found on the carton labeling and container labels. These statements are missing the importance of keeping the bottle tightly closed in between uses after opening the bottle. Incorrect storage of the product may after the quality of the product.	Add the statement, "AFTER OPENING, KEEP BOTTLE TIGHTLY CLOSED between uses to PROTECT FROM MOISTURE." to carton labeling and container labels. Delete the statements, (b) (4) and " (b) (4) from label and labeling.
Zenpep Container Label			
1.	The linear barcode is missing from container labels.	The drug barcode is often used as an additional verification before drug administration in the hospital setting; therefore, it is an important safety feature.	Add a linear barcode to container labels.
Zenpep Carton Labeling			

Table 3. Identified Issues and Recommendations for Genentech Roche (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
1.	It is unclear where the machine-readable product identifier is located on the label.	The Drug Supply Chain Security Act (DSCSA) requires, for certain prescription products, that the smallest saleable unit display a human-readable and machine-readable (2D data matrix barcode) product identifier.	The guidance also recommends the format of the human-readable portion be located near the 2D data matrix barcode as the following: NDC: [insert NDC] SERIAL: [insert serial number] LOT: [insert lot number] EXP: [insert expiration date]
Viokace Container Labels and Carton Labeling			
1.	Inconsistent terminology is used for recommended dosage statement.	Inconsistencies between PI and label and labeling may lead to misinterpretation in dosage information.	To ensure consistency with the Prescribing Information, revise the statement, (b) (4) to read "Dosage: See prescribing information. (b) (4) (b) (4)
2.	The statement, (b) (4) is on the side panel.	(b) (4) The statement referring to package insert (b) (4) may cause unnecessary confusion to the reader.	Remove the statement, (b) (4) from the side panel.
	The storage statement contains the symbol, "-" and is not consistent with the Prescribing Information (PI).	The usage of symbols may cause misinterpretation and confusion. Inconsistencies between PI and label and labeling may lead to misinterpretation in storage information.	Replace the dash symbol with its intended meaning and insert the missing degree symbol after the first temperature numerical of each temperature range. "Store at room temperature 20°C to 25°C (68°F to 77°F),

Table 3. Identified Issues and Recommendations for Genentech Roche (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			brief excursion permitted up to 40°C (104°F) for up to 24 hrs."
Viokace Container Labels			
1.	The format for expiration date is not defined.	Clearly define the expiration date will minimize confusion and risk for deteriorated drug medication errors.	Identify the expiration date format you intend to use. FDA recommends that the human-readable expiration date on the drug package label include a year, month, and non-zero day. FDA recommends that the expiration date appear in YYYY-MM-DD format if only numerical characters are used or in YYYY-MMM-DD if alphabetical characters are used to represent the month. If there are space limitations on the drug package, the human-readable text may include only a year and month, to be expressed as: YYYY-MM if only numerical characters are used or YYYY-MMM if alphabetical characters are used to represent the month. FDA recommends that a hyphen or a space be used to separate the portions of the expiration date.
Viokace Carton Labeling			
1.	The expiration date is missing.	The expiration date should be clearly defined to minimize confusion and risk for deteriorated drug medication errors.	Submit expiration date in the format that is stated below. FDA recommends that the human-readable expiration date on the drug package label include a year, month, and

Table 3. Identified Issues and Recommendations for Genentech Roche (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			non-zero day. FDA recommends that the expiration date appear in YYYY-MM-DD format if only numerical characters are used or in YYYY-MMM-DD if alphabetical characters are used to represent the month. If there are space limitations on the drug package, the human-readable text may include only a year and month, to be expressed as: YYYY-MM if only numerical characters are used or YYYY-MMM if alphabetical characters are used to represent the month. FDA recommends that a hyphen or a space be used to separate the portions of the expiration date.
2.	The lot number statement is missing.	The lot number statement is required as per 21 CFR 201.10(i)(1)	Display the intended placement of the lot number statement.
3.	It is unclear where the machine-readable product identifier is located on the label. Additionally, the format of the human-readable portion of the product identifier is not identified.	The Drug Supply Chain Security Act (DSCSA) requires, for certain prescription products, that the smallest saleable unit display a human-readable and machine-readable (2D data matrix barcode) product identifier.	The DSCSA guidance on product identifiers recommends a machine-readable (2D data matrix barcode) product identifier and a human-readable product identifier. Include the machine-readable data matrix barcode to the carton labeling. The guidance also recommends the format of the human-readable portion be located near the 2D data matrix barcode as the following: NDC: [insert NDC]

Table 3. Identified Issues and Recommendations for Genentech Roche (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			SERIAL: [insert serial number] LOT: [insert lot number] EXP: [insert expiration date] We recommend that you review the draft guidance to determine if the product identifier requirements apply to your product's labeling. The draft guidance is available from: https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm621044.pdf.

6 RECOMMENDATIONS FOR DIGESTIVE CARE INC.

Table 4. Identified Issues and Recommendations for Genentech Roche (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
All Container Labels			
1.	The proper name lacks prominence.	21 CFR 610.62 (b)	Revise the proper name to be at least as prominent as the point size and typeface used in designating the trade name.
2.	Inconsistent terminology is used for recommended dosage statement.	Inconsistencies between PI and label and labeling may lead to misinterpretation in dosage information.	To ensure consistency with the Prescribing Information, revise the statement, (b) (4) to read "Dosage:

Table 4. Identified Issues and Recommendations for Genentech Roche (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			See prescribing information. (b) (4)
3.	The storage statement contains the symbol, "-" and the first temperature numerical is missing the degree symbol.	The usage of symbols may cause misinterpretation and confusion.[d] Lack of clarity	Replace the dash symbol with its intended meaning and insert the missing degree symbol after the first temperature numerical of each temperature range. Revise the sentence to read "STORAGE: Store at room temperature 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 40°C (59°F to 104°F).
4.	The statement, "After opening, keep the container tightly closed between uses to protect from moisture." is found in the PI, but this statement is missing from the carton labeling and container labels.	As currently presented, (b) (4) " and (b) (4)" are found on the carton labeling and container labels. These statements are missing the importance of keeping the bottle tightly closed in between uses after opening the bottle. Incorrect storage of the product may after the quality of the product.	Add the statement, "After opening, keep the container tightly closed between uses to protect from moisture." to carton labeling and container labels. Delete the statements, (b) (4) and (b) (4) (b) (4) from label and labeling.
Professional Sample Container Labels			
1.	The format for expiration date is not defined.	Clearly define the expiration date will minimize confusion and risk	Identify the expiration date format you intend to use.

[d] ISMP's List of Error-Prone Abbreviations, Symbols, and Dose Designations [Internet]. Horsham (PA): Institute for Safe Medication Practices. 2015 [cited 2015 Sep 16]. Available from: http://www.ismp.org/tools/errorproneabbreviations.pdf.

Table 4. Identified Issues and Recommendations for Genentech Roche (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
		for deteriorated drug medication errors.	FDA recommends that the human-readable expiration date on the drug package label include a year, month, and non-zero day. FDA recommends that the expiration date appear in YYYY-MM-DD format if only numerical characters are used or in YYYY-MMM-DD if alphabetical characters are used to represent the month. If there are space limitations on the drug package, the human-readable text may include only a year and month, to be expressed as: YYYY-MM if only numerical characters are used or YYYY-MMM if alphabetical characters are used to represent the month. FDA recommends that a hyphen or a space be used to separate the portions of the expiration date.

APPENDICES: METHODS & RESULTS FOR EACH MATERIAL REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Zenpep, Viokace, and Pertzye that Aimimune LLC (Zenpep and Viokace) and Digestic Care, Inc (Viokace) submitted on March 23, 2022, and April 15, 2022.

Table 2. Relevant Product Information for Zenpep, Viokace, and Pertzye			
Product Name	Zenpep	Viokace	Pertzye
Application Number	BLA 22210	BLA 22542	BLA 22175
Initial Approval Date	August 27, 2009	March 1, 2012	May 17, 2012
Proper Name	pancrelipase		
Indication	treatment of exocrine pancreatic insufficiency due to cystic APPEARS THIS WAY ON ORIGINAL	treatment of exocrine pancreatic insufficiency due to chronic pancreatitis or pancreatectomy.	For the treatment of exocrine pancreatic insufficiency due to cystic fibrosis or other conditions.
Route of Administration	oral		
Dosage Form	delayed-release capsule	tablet	delayed-release capsule
Strengths	3,000 USP units of lipase; 10,000 USP units of protease; 14,000 USP units of amylase 5,000 USP units of lipase; 17,000 USP units of protease; 24,000 USP units of amylase 10,000 USP units of lipase;	10,440 USP units of lipase; 39,150 USP units of protease; 39,150 USP units of amylase 20,880 USP units of lipase; 78,300 USP units of	4,000 USP units of lipase; 14,375 USP units of protease; 15,125 USP units of amylase. 8,000 USP units of lipase; 28,750 USP units of protease; 30,250 USP units of amylase.

Table 2. Relevant Product Information for Zenpep, Viokace, and Pertzye			
Product Name	Zenpep	Viokace	Pertzye
	32,000 USP units of protease; 42,000 USP units of amylase 15,000 USP units of lipase; 47,000 USP units of protease; 63,000 USP units of amylase 20,000 USP units of lipase; 63,000 USP units of protease; 84,000 USP units of amylase 25,000 USP units of lipase; 79,000 USP units of protease; 105,000 USP units of amylase 40,000 USP units of lipase; 126,000 USP units of protease; 168,000 USP units of amylase	protease; 78,300 USP units of amylase	16,000 USP units of lipase; 57,500 USP units of protease; 60,500 USP units of amylase. 24,000 USP units of lipase; 86,250 USP units of protease; 90,750 USP units of amylase.
Dose and Frequency	*Infants (up to 12 months)* Infants may be given 3,000 lipase units (one capsule) per 120 mL of formula or per breast-feeding. Do not mix Zenpep capsule contents directly into formula or breast milk prior to administration. *Children Older than 12 Months and Younger than 4 Year*	Begin with 500 lipase units/kg of body weight per meal to a maximum of 2,500 lipase units/kg of body weight per meal (or less than or equal to 10,000 lipase units/kg of body weight per day), or less than 4,000	*Infants (up to 12 months)* Infants may be given 4,000 lipase units (one capsule) per 120 mL of formula or per breast feeding. Do not mix PERTZYE capsule contents directly into formula

Table 2. Relevant Product Information for Zenpep, Viokace, and Pertzye			
Product Name	Zenpep	Viokace	Pertzye
	Enzyme dosing should begin with 1,000 lipase units/kg of body weight per meal to a maximum of 2,500 lipase units/kg of body weight per meal (or less than or equal to 10,000 lipase units/kg of body weight per day), or less than 4,000 lipase units/g fat ingested per day. *Children 4 Years and Older and Adults* Enzyme dosing should begin with 500 lipase units/kg of body weight per meal to a maximum of 2,500 lipase units/kg of body weight per meal (or less than or equal to 10,000 lipase units/kg of body weight per day), or less than 4,000 lipase units/g fat ingested per day. Usually, half of the prescribed ZENPEP dose for an individualized full meal should be given with each snack. The total daily dose should reflect approximately three meals plus two or three snacks per day.	lipase units/g fat ingested per day. Individualize dosage based on clinical symptoms, the degree of steatorrhea present and the fat content of the diet.	or breast milk prior to administration. *Children Older than 12 Months and Younger than 4 Years* Enzyme dosing should begin with 1,000 lipase units/kg of body weight per meal to a maximum of 2,500 lipase units/kg of body weight per meal (or less than or equal to 10,000 lipase units/kg of body weight per day), or less than 4,000 lipase units/g fat ingested per day. *Children 4 Years and Older and Adults* Enzyme dosing should begin with 500 lipase units/kg of body weight per meal to a maximum of 2,500 lipase units/kg of body weight per meal (or less than or equal to 10,000 lipase units/kg of body weight per day), or less than 4,000 lipase units/g fat ingested per day.
How Supplied	Bottles of 100 capsules	Bottles of 100 tablets	Bottles of 80 and 100 capsules

Table 2. Relevant Product Information for Zenpep, Viokace, and Pertzye			
Product Name	Zenpep	Viokace	Pertzye
Storage	(b) (4) Avoid excessive heat. Store at room temperature (68-77°F; 20-25°C), brief excursions permitted to 15-40°C (59-104°F). Protect from moisture. AFTER OPENING, KEEP BOTTLE TIGHTLY CLOSED between uses to PROTECT FROM MOISTURE. Repackaged HDPE container: Avoid excessive heat. Store at up to 30°C (86°F) for up to 6 months. Brief excursions permitted to 15-40°C (59-104°F) for up to 30 days. Protect from moisture. AFTER OPENING, KEEP BOTTLE TIGHTLY CLOSED between uses to PROTECT FROM MOISTURE. Dispense in tight container (USP). Keep out of reach of children. DO NOT CRUSH ZENPEP delayed-release capsules	Avoid heat. VIOKACE tablets should be stored in a dry place in the original container. Store at room temperature (20-25°C, 68-77°F), brief excursion permitted up to 40°C (104°F) for up to 24 hrs. After opening, keep the container tightly closed between uses to protect from moisture. VIOKACE is dispensed in bottles containing a desiccant. The desiccant packet should not be eaten. The desiccant packet will protect the product from moisture.	Store at room temperature 20-25°C (68-77°F), (b) (4) excursions permitted to 15-40°C (59-104°F). PERTZYE hard gelatin capsules should be stored in a dry place in the original container or equivalent air tight container. After opening, keep the container tightly closed between uses to protect from moisture. PERTZYE is dispensed in bottles containing a desiccant. The desiccant packet should not be eaten or thrown away. The desiccant packet will protect the product from moisture.

APPENDIX B. PREVIOUS DMEPA REVIEWS

On July 6, 2022, we searched for previous DMEPA reviews relevant to this current review using the terms, Zenpep, Viokace, and Pertzye. Our search identified 17 previous reviews[e,f,g,h,i,j,k,l,m,n,o,p,q,r, s,t,u] and we considered our previous recommendations to see if they are applicable for this current review.

APPENDIX F. LABELS AND LABELING

F.1 List of Labels and Labeling Reviewed

APPEARS THIS WAY ON ORIGINAL

[e]Wood-Cummings, T. Label and Labeling Review for Zenpep (BLA 22210). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2014 Jan 7. 2013-2788.

[f]Khoslov, L. Label and Labeling Review for Zenpep (BLA 22210). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2014 Aug 14. 2013-1972.

[g]Merchant, L. Label and Labeling Review for Zenpep (BLA 22210). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2011 July 11 DEC 17. 2011-2202

[h] Brennan, C. Label and Labeling Review for Zenpep (BLA 22210). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2011 June 1. 2011-56

[r]Brennan, C. Label and Labeling Review for Zenpep (BLA 22210). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2011 May 25. 2011-1400

Using the principles of human factors and Failure Mode and Effects Analysis,[v] along with postmarket medication error data, we reviewed the following Zenpep, Viokace, and Pertzye labels and labeling submitted by Aimmune and Digestive Care Inc.

- Zenpep Carton Labeling received on March 23, 2022
- Zenpep Container Label received on March 23, 2022
- Zenpep Prescribing Information (Image not shown) received on March 23, 2022 available from \\CDSESUB1\evsprod\bla022210\0065\m1\us\annotated-draft-pi.pdf
- Zenpep Medication Guide (Image not shown) received on March 23, 2022, available from \\CDSESUB1\evsprod\bla022210\0065\m1\us\draft-medguide.docx
- Viokace Carton Labeling received on March 23, 2022
- Viokace Container Label received on March 23, 2022

---

[j] Brennan, C. Label and Labeling Review for Zenpep (BLA 22210). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2010 Jan 10. 2010-2347

[k] Merchant, L. Label and Labeling Review for Zenpep (BLA 22210). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2010 Jan 6. 2010-2518

[l]Stokes-Hamilton, D. Label and Labeling Review for Zenpep (BLA 22210). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2009 May 5. 2008-1231

[m]Siapoushan, M. Label and Labeling Review for Viokace (BLA 22542). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2011 Oct 7. 11-2287

[n]Chan, I. Label and Labeling Review for Viokace (BLA 22542). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2010 Feb 5. 2009-2130

[o] Chan, I. Label and Labeling Review for Pertzye. NDA 22175. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2010 JUN 22 32 p. OSE RCM No.:2010-441

[p] Siahpoushan, M. Label and Labeling Review for Pertzye. NDA 22175. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2012 FEB 23 32 p. OSE RCM No.:2011-4358

[q]Abraham, S. Label and Labeling Review for Pertzye. NDA 22175. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2014 SEP 03 32 p. OSE RCM No.:2014-3026.

[r] Abraham, S. Label and Labeling Review for Pertzye. NDA 22175. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2014 SEP 03 32 p. OSE RCM No.:2014-3026

[s] Barlow, M. Label and Labeling Review for Pertzye. NDA 22175. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 Jun 16. OSE RCM No.: 2017-590

[t] Barlow, M. Label and Labeling Review for Pertzye. NDA 22175. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 Jun 21. OSE RCM No.: 2017-590-1

[u] Barlow, M. Label and Labeling Review for Pertzye. NDA 22175. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 Jul 12. OSE RCM No.: 2017-590-2

[v] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

- Viokace Prescribing Information (Image not shown) received on March 23, 2022 available from\\CDSESUB1\evsprod\bla022542\0103\m1\us\draft-package-insert-annotated.pdf
- Viokace Medication Guide (Image not shown) received on March 23, 2022, available from \\CDSESUB1\evsprod\bla022542\0103\m1\us\draft-medication-guide-annotated.pdf
- Pertzye Carton Labeling received on April 15, 2022
- Pertzye Container Label received on April 15, 2022
- Pertzye Prescribing Information (Image not shown) received on April 15, 2022 available from \\CDSESUB1\evsprod\bla022175\0095\m1\us\114-labeling\draft\labeling\draft-label-text-pi-tracked-04-2022.docx
- Pertzye Medication Guide and Instruction for Use (Image not shown) received on April 15, 2022, available from \\CDSESUB1\evsprod\bla022175\0095\m1\us\114-labeling\draft\labeling\draft-label-text-mg-ifu-tracked-04-2022.docx

Zenpep Container Labels:

\\CDSESUB1\evsprod\bla022210\0065\m1\us\draft-carton-and-container-labeling.pdf

\\CDSESUB1\evsprod\bla022210\0065\m1\us\draft-carton-and-container-labeling.pdf

19 Pages of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page.

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/

SHERLY ABRAHAM
08/19/2022 01:58:47 PM

IDALIA E RYCHLIK
08/19/2022 01:59:39 PM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022542Orig1s007

ADMINISTRATIVE AND CORRESPONDENCE DOCUMENTS

From: Shami, Anum
Sent: Tue, 8 Nov 2022 15:11:03 +0000
To: 'Vandana Garikipati'
Subject: REVISIONS REQUESTED: Corrections for Zenpep and Viokace Labeling
Attachments: copy BLA 022210 Zenpep_S24 Approval.pdf, copy BLA 022542 Viokace_S7 Approval.pdf
Importance: High

Dear Vandana:

It was a pleasure speaking with you regarding the corrections for the approval letters.

I am requesting that you send in the **corrected labeling** (All parts: PI, MedGuide, Carton and Containers, etc.) by **11/15/22 10AM EST** for both Viokace and Zenpep labels so we can issue the correction letters. Please let me know when the appropriate labeling has been shared via the ESG gateway.

Kindly note:

1. The Zenpep labeling (USPI, MG, IFU, carton/containers, etc.) should have had the following name, addresses and license #s:

   Zenpep, LLC
   (b) (4)
   US License No. 2198

2. All Viokace labeling should have this address and license # associated:

   Viokace, LLC
   (b) (4)
   US License No. 2196

Please let me know if you have any questions for me. Kindly acknowledge receipt of this email. I look forward to the corrected labeling for both Viokace and Zenpep so we can resolve this issue quickly.

Regards,
Anum Shami, PharmD
Regulatory Project Manager
Gastroenterology
Division of Regulatory Operations for Immunology and Inflammation
Office of Regulatory Operations
Center for Drug Evaluation and Research
Email: Anum.Shami@fda.hhs.gov
Phone: 301-837-7103
Fax: 301-837-6170
U.S. FOOD & DRUG ADMINISTRATION

From: Shami, Anum
Sent: Wednesday, September 28, 2022 1:00 PM
To: Vandana Garikipati <vgarikipati@aimmune.com>
Subject: Courtesy Copy: Deemed BLA supplement approvals
Importance: High

Dear Vandana:

Thank you for working so closely with me on these 2 Deemed BLA supplement approvals. Please see copies above for both Zenpep and Viokace.

A formal copy will be mailed to you in the coming weeks.

Thank you!

Anum Shami, PharmD
Regulatory Project Manager
Gastroenterology
Division of Regulatory Operations for Immunology and Inflammation
Office of Regulatory Operations
Center for Drug Evaluation and Research
Email: Anum.Shami@fda.hhs.gov
Phone: 301-837-7103
Fax: 301-837-6170

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/

ANUM A SHAMI
11/08/2022 10:34:12 AM

From:	Shami, Anum
To:	Vandana Garikipati
Subject:	REVISION REQUESTED: provide your response by 9/21/22 1pm EST VIOKACE
Date:	Wednesday, September 14, 2022 3:06:00 PM
Attachments:	image001.png
Importance:	High

Dear Dr. Garikipati:

Please acknowledge receipt of this request by reply email and provide your response by **9/21/22 1pm EST** for the following labeling supplement**:**

Regarding Viokace:

Please refer to your labeling supplement for Viokace (BLA 022542/S-007). We have the following request:

1. Regarding your proposed carton labeling submitted on September 6, 2022. Remove the statement "[redacted] (b) (4)" from the carton labeling because our view is that 21 CFR 610.61(r) is not applicable.

Thank you,

Anum Shami, PharmD
Regulatory Project Manager
Gastroenterology
Division of Regulatory Operations for Immunology and Inflammation
Office of Regulatory Operations
Center for Drug Evaluation and Research
Email: Anum.Shami@fda.hhs.gov
Phone: 301-837-7103
Fax: 301-837-6170

FDA U.S. FOOD & DRUG ADMINISTRATION

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/

ANUM A SHAMI
09/14/2022 04:22:01 PM

From: Shami, Anum
Sent: Tue, 30 Aug 2022 14:36:52 +0000
To: Vandana Garikipati
Cc: Shami, Anum
Subject: REVISIONS REQUESTED: BLA 022542 Viokace S-007: DUE Sept 6, 22 at 2pm EST
Attachments: Viokace BLA 022542.7 Carton and Container Comments.docx, 8.17.22 viokace-medication-guide-clean.docx, 8.17.22 viokace-package-insert-clean.docx
Importance: High

Dear Dr. Garikipati:

Please refer to your deemed BLA labeling for BLA 022542 Viokace S-007. We are reviewing you labeling documents and have the following requests for revisions:

- Please see the labeling attached above with Agency comments.

Please acknowledge receipt of this request by reply email and provide your response **by Tuesday 9/6/22 2pm EST**.

Please don't hesitate to contact me with any questions.

Please confirm receipt of this email.

Regards,
Anum Shami, PharmD
Regulatory Project Manager
Gastroenterology
Division of Regulatory Operations for Immunology and Inflammation
Office of Regulatory Operations
Center for Drug Evaluation and Research
Email: Anum.Shami@fda.hhs.gov
Phone: 301-837-7103
Fax: 301-837-6170
FDA U.S. FOOD & DRUG ADMINISTRATION

Anum Shami, PharmD
Regulatory Project Manager
Gastroenterology
Division of Regulatory Operations for Immunology and Inflammation
Office of Regulatory Operations
Center for Drug Evaluation and Research
Email: Anum.Shami@fda.hhs.gov
Phone: 301-837-7103
Fax: 301-837-6170
FDA U.S. FOOD & DRUG ADMINISTRATION

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/

ANUM A SHAMI
08/30/2022 11:29:40 AM

From: Shami, Anum
Sent: Wed, 10 Aug 2022 17:13:13 +0000
To: Vandana Garikipati
Subject: LABELING REVISIONS REQUESTED: REPONSE REQUIRED: BLA 022542 / S007: VIOKACE
Attachments: Viokace draft-medication-guide.docx, Viokace draft-package-insert-clean.docx
Importance: High

Dear Dr. Garikipati:

Please refer to your supplemental deemed **BLA 022542 / S007: VIOKACE** submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act (FDCA) for **Viokace**. We are reviewing you labeling documents and have the following requests for revisions:

- Please see the labeling attached above with Agency comments.

Please acknowledge receipt of this request by reply email and provide your response **by Wednesday 8/17/22 2pm EST**.

Please don't hesitate to contact me with any questions.

Please confirm receipt of this email.

Regards,
Anum Shami, PharmD
Regulatory Project Manager
Gastroenterology
Division of Regulatory Operations for Immunology and Inflammation
Office of Regulatory Operations
Center for Drug Evaluation and Research
Email: Anum.Shami@fda.hhs.gov
Phone: 301-837-7103
Fax: 301-837-6170
FDA U.S. FOOD & DRUG ADMINISTRATION

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/

ANUM A SHAMI
08/10/2022 02:56:30 PM

From:	Shami, Anum
To:	vgarikipati@aimmune.com
Cc:	Shami, Anum
Subject:	INFORMATION REQUEST: BLA 022542 Viokace and BLA 022210 Zenpep C/C labels: Respond by 5/4/22 by COB
Date:	Friday, April 29, 2022 12:24:37 PM
Attachments:	image001.png
Importance:	High

Dear Dr. Garikipati

Division of Gastroenterology is in the process reviewing the PAS supplement labeling for BLA 022542 Viokace and BLA 022210 Zenpep.

We request the **annotated version of the carton and container labels** for both BLA 022542 Viokace and BLA 022210 Zenpep.

Kindly submit them to the electronic gateway by 5/4/22 by COB.

Respond to this email to confirm receipt.

Thank you,

Anum Shami, PharmD
Regulatory Project Manager
Gastroenterology
Division of Regulatory Operations for Immunology and Inflammation
Office of Regulatory Operations
Center for Drug Evaluation and Research
Email: Anum.Shami@fda.hhs.gov
Phone: 301-837-7103
Fax: 301-837-6170

FDA U.S. FOOD & DRUG ADMINISTRATION

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/

ANUM A SHAMI
04/29/2022 12:35:35 PM

From:	Shami, Anum
To:	vgarikipati@aimmune.com
Cc:	Shami, Anum
Subject:	INFORMATION REQUEST: BLA 022542 Viokace and BLA 022210 Zenpep C/C labels: Respond by 5/4/22 by COB
Date:	Friday, April 29, 2022 12:24:37 PM
Attachments:	image001.png
Importance:	High

Dear Dr. Garikipati

Division of Gastroenterology is in the process reviewing the PAS supplement labeling for BLA 022542 Viokace and BLA 022210 Zenpep.

We request the **annotated version of the carton and container labels** for both BLA 022542 Viokace and BLA 022210 Zenpep.

Kindly submit them to the electronic gateway by 5/4/22 by COB.

Respond to this email to confirm receipt.

Thank you,

Anum Shami, PharmD
Regulatory Project Manager
Gastroenterology
Division of Regulatory Operations for Immunology and Inflammation
Office of Regulatory Operations
Center for Drug Evaluation and Research
Email: Anum.Shami@fda.hhs.gov
Phone: 301-837-7103
Fax: 301-837-6170

FDA U.S. FOOD & DRUG ADMINISTRATION

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/

ANUM A SHAMI
04/29/2022 12:35:35 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Division/Office)*:
Mail: OSE

FROM: Kristina Luong, PharmD, BCPS
Regulatory Project Manager, Gastroenterology
Division of Regulatory Operations for Immunology and Inflammation
Office of Regulatory Operations
Center for Drug Evaluation and Research

DATE	IND NO.	BLA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
4/19/2022		022542	PAS labeling supplement	3/23/2022

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Viokace (pancrelipase)	Standard	Digestive enzymes; pancreatic enzyme product	8/23/2022

NAME OF FIRM: Aimmune Therapeutics, Inc.

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE--NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☒ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☐ MEDICATION ERRORS
- ☐ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

DG kindly request a DMEPA reviewer. DG has received 3 PAS labeling supplements for BLA-specific labeling changes for deemed BLA pancrelipase products: ZenPep (BLA 022210), Viokace (BLA 022542), and Pertyze (BLA 022175). If possible, please assign the same DMEPA reviewer for all three labeling supplements. We plan to complete all 3 labeling supplements together at the same time with a **single midcycle meeting**, which will be sometime at the end of July. The goal date will be Friday, September 23, 2022, and are aiming for a consult deadline of 1 month before August 23, 2022.

Links for BLA 022542:
Lorenz: View submission in docuBridge

EDR Location: \\CDSESUB1\evsprod\BLA022542\0103

SIGNATURE OF REQUESTER Kristina Luong	METHOD OF DELIVERY (Check all that apply) ☐ MAIL ☒ DARRTS ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

06/18/2013

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/

KRISTINA N LUONG
04/19/2022 10:26:02 AM