PRODUCT MONOGRAPH

PrVIOKACE™

Pancrelipase tablets

10,440 USP and 20,880 USP units of lipase

USP

Pancreatic enzymes

A09AA02

Aptalis Pharma Canada Inc.
597 Sir-Wilfrid-Laurier Blvd.
Mont-Saint-Hilaire, Québec
Canada J3H 6C4

Date of Approval: June 5, 2015

Date of Revision: June 22, 2015

Submission Control No: 172743

Table of Contents

VIOKACE™

Pancreatic enzymes

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Non-medicinal Ingredients
Oral	Tablet (10,440 USP units lipase) Lipase : 10,440 USP units Amylase : 56,400 USP units Protease : 57,100 USP units	Lactose monohydrate *For a complete listing see Dosage Forms, Composition and Packaging section.*
Oral	Tablet (20,880 USP units lipase) Lipase : 20,880 USP units Amylase : 113,400 USP units Protease : 112,500 USP units	Lactose monohydrate *For a complete listing see Dosage Forms, Composition and Packaging section.*

INDICATIONS AND CLINICAL USE

VIOKACE (pancrelipase, USP) is indicated in adult patients for:

- treatment of exocrine pancreatic insufficiency (EPI) attributed to cystic fibrosis, chronic pancreatitis, or any other medically defined pancreatic disease that might require pancreatic enzyme therapy.

VIOKACE tablets are used in conjunction with a proton pump inhibitor.

PATIENT SUBSETS

Geriatrics (> 65 years of age):
Clinical studies conducted with VIOKACE tablets 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.

Pediatrics (< 18 years of age):
The safety and efficacy 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. 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). 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.

CONTRAINDICATIONS

VIOKACE (pancrelipase, USP) should not be used in patients who are hypersensitive to porcine protein, pancreatic enzymes or any excipient.

VIOKACE should not be used during acute pancreatitis or the acute exacerbation of chronic pancreatitis.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

Pancreatic enzymes products, including VIOKACE (Pancrelipase, USP) have been associated with fibrosing colonopathy (strictures of the ileo-caecum and large intestine) if given at high doses chronically to patients with cystic fibrosis. It is not clear whether this complication is caused by high dosages of pancreatic enzymes, or whether the underlying disease is responsible. Unusual abdominal symptoms should be reviewed to exclude the possibility of colonic damage, especially if the patient is taking in excess of 2,500 lipase units/kg of body weight per meal (or greater than 10,000 lipase units/kg of body weight per day) or greater than 4,000 lipase units/g fat ingested per day.

VIOKACE cannot be substituted (unit for unit) with other pancreatic enzyme products because they are biological products, and therefore, differ in their manufacturing processes, formulations, exact composition, enzymatic activities, stability and bioactivity in the small intestine, the response of the patient to the estimated dose must be monitored and adjusted as necessary. Special attention to the response of the patient is required during any change in treatment from one pancreatic enzyme to another.

General

Should hypersensitivity develop, discontinue medication and treat the patient symptomatically.
It is important to ensure adequate hydration in patients at all times during therapy with pancreatic enzymes.
VIOKACE should always be taken with food. Tablets should be swallowed whole with adequate amounts of liquid at mealtimes. VIOKACE should not be crushed or chewed. Since VIOKACE is not enteric-coated, it should not be mixed with food. Patients who cannot swallow VIOKACE

tablets whole should not use VIOKACE. 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 (See DOSAGE AND ADMINISTRATION).

Endocrine and Metabolism

Pancreatic enzyme replacement therapy, in patients in whom both the exocrine and endocrine pancreas are not functioning, may interact with insulin therapy of diabetes. High-dose pancreatin may improve, but not fully normalize fat absorption, possibly because of the residual influence of diabetes and malnutrition on absorptive function. Since control of blood glucose may be brittle in malnourished, insulin-dependent patients, enzyme adjustment should be carefully supervised in-hospital to avoid exacerbation of pancreatic dysfunction.

Potential Viral Exposure from 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, 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.

Respiratory

The fine powder of pancreatic enzyme tablets such as VIOKACE may be irritating to the nasal mucosa and the respiratory tract.

Hepatic/Biliary/Pancreatic

VIOKACE may cause hyperuricosuria and hyperuricemia with very high doses.

Special Populations

Pregnant Women:

There is insufficient data from the use of VIOKACE in pregnant women. Although some animal studies have been conducted, no adequate, well-controlled studies have been conducted in pregnant women. VIOKACE should only be used during pregnancy if, in the opinion of the physician, the benefits outweigh the potential risks.

Nursing Women:

There is insufficient data to assess the risks. Pancreatic enzymes act locally in the gastrointestinal tract, and cannot be absorbed in their intact state systemically. Some of the constituent amino acids and nucleic acids are probably absorbed with dietary protein. However, the possibility of protein constituents being secreted into breast milk cannot be excluded. VIOKACE should be used only if, in the opinion of the physician, the potential benefits outweigh the potential risks.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

The most common adverse reactions are abdominal discomfort and pain. Other gastrointestinal reactions are less common and include abnormal stool and diarrhea. Nausea and vomiting have been reported, but these are not common.

At extremely high doses, hyperuricosuria and hyperuricaemia have been reported. Fibrosing colonopathy have been reported in cystic fibrosis patients (See WARNINGS AND PRECAUTIONS, Renal).

Allergy or hypersensitivity reactions of the skin have been reported.

Clinical Trial Adverse Drug Reactions

Because clinical trials are conducted under very specific conditions the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

The short-term safety and efficacy of VIOKACE (pancrelipase, USP) 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). 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%).

Table 1 presents adverse reactions that occurred in at least 1 patient (≥ 3%) treated with VIOKACE at a higher rate than with placebo. As such, all the adverse reactions mentioned in Table 1 were to be considered as common (frequent) adverse reactions (>1%).

TABLE 1: Adverse Drug Reactions Occurring in at Least 1 Patient (greater than or equal to 3%) in Chronic Pancreatitis or Pancreatectomy

MedDRA Primary System Organ Class/ Adverse Reactions	VIOKACE n= 30 (%)	Placebo n= 20 (%)
Gastrointestinal Disorders		
Abdominal pain	1 (3)	0
Anal pruritus	2 (7)	0
Skin and Subcutaneous Tissue Disorders		
Rash	1 (3)	0

Post-Market Adverse Drug Reactions

Post-marketing data for VIOKACE have been available since 2000. 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.

The Adverse Drug Reactions seen with VIOKACE are:

Gastrointestinal disorders: Abdominal discomfort, Abdominal distension, Abdominal pain, Abdominal pain upper, Constipation, Diarrhoea, Dyspepsia, Flatulence, Frequent bowel movements, Nausea.
Immune system disorders: Hypersensitivity.
Respiratory, thoracic and mediastinal disorders: Oropharyngeal pain, Rhinorrhoea.
Skin and subcutaneous tissue disorders: Rash, Urticaria.

DRUG INTERACTIONS

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

DOSAGE AND ADMINISTRATION

Dosing Considerations

Patients with pancreatic insufficiency should consume a high-calorie, unrestricted fat diet appropriate for their age and clinical status. A nutritional assessment should be performed regularly as a component of routine care, and additionally when the dosage of pancreatic enzyme replacement is made.

Dosage should be adjusted according to the severity of the exocrine pancreatic enzyme deficiency. The number of tablets, or dosage strength given with meals and/or snacks should be determined by assessing at which dose steatorrhea is minimized and good nutritional status is maintained.

It is important to ensure adequate hydration at all times, especially during periods of increased loss of fluids. Inadequate hydration may aggravate constipation.

Take the medication immediately. Do not store it to be taken later.

Recommended Dose and Dosage Adjustment

Dosage recommendations for pancreatic enzyme replacement therapy were published following the Cystic Fibrosis Foundation Consensus Conferences. VIOKACE (pancrelipase, USP) 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. 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. 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. 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 unit/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). 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.

Missed Dose

If a dose of VIOKACE is missed, the next dose should be taken with the next meal or snack as directed. Doses should not be doubled.

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.

Since VIOKACE is not enteric-coated, it should be taken in combination with a proton pump inhibitor.

VIOKACE should be taken during meals or snacks, with sufficient fluid. Tablets should be swallowed whole. Patients should only take VIOKACE if they can swallow the tablets whole as VIOKACE should not be crushed or chewed. Care should be taken to ensure that no drug is retained in the mouth to avoid mucosal irritation

OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre.

Extremely high dosages of pancreatic enzymes have been reported to cause hyperuricosuria and hyperuricaemia. Most cases responded to supportive measures, including discontinuation of the enzyme therapy and ensuring adequate hydration.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

VIOKACE (pancrelipase, USP) tablets are not enteric-coated. 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 (e.g., maltose, maltriose) in the duodenum and proximal small intestine, thereby acting like digestive enzymes physiologically secreted by the normally functioning pancreas.

Pharmacokinetics

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

STORAGE AND STABILITY

Store at room temperature (20°C - 25°C). Protect from heat and moisture.

VIOKACE (pancrelipase, USP) tablets should be stored in a dry place in the original container. 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.

SPECIAL HANDLING INSTRUCTIONS

Dispense VIOKACE (pancrelipase, USP) tablets in tight container, preferably with a desiccant.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Each VIOKACE (pancrelipase, USP) tablet strength contains the specific amount of lipase, protease and amylase

- VIOKACE tablets (10,440 USP lipase units / tablet) : 10,440 USP units of lipase; 57,100 USP units of protease; 56,400 USP units of amylase
- VIOKACE tablets (20,880 USP lipase units / tablet) : 20,880 USP units of lipase; 112,500 USP units of protease; 113,400 USP units of amylase

VIOKACE (10,440 USP lipase units) is supplied in bottles of 100 tablets each (DIN 02230019). Tablets are tan, round, compressed and have the inscription VIO9111 on one side and 9111 on the other side. Tablets contain the following non-medicinal ingredients: colloidal silicone dioxide, croscarmellose sodium, lactose monohydrate, microcrystalline cellulose, stearic acid and talc.

VIOKACE (20,880 USP lipase units) is supplied in bottles of 100 tablets each (DIN 02241933). Tablets are tan, oval, biconvex and have the inscription V^{16} engraved on one side and 9116 on the other side. Tablets contain the following non-medicinal ingredients (in alphabetical order): colloidal silicone dioxide, croscarmellose sodium, lactose monohydrate, microcrystalline cellulose, stearic acid and talc.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Proper name:	Pancrelipase
Chemical name:	Not applicable
Molecular formula and molecular mass:	Not applicable
Structural formula:	Not applicable
Physicochemical properties:	The active pharmaceutical ingredient of VIOKACE™ is pancrelipase, an extract from porcine pancreas glands containing enzymes with lipolytic, amyolytic and proteolytic activity. Pancrelipase is a beige-white amorphous powder. It is miscible in water and practically insoluble in alcohol.

CLINICAL TRIALS

Exocrine Pancreatic Insufficiency:

A single Phase III study VIO16EPI07-01 investigating the efficacy of VIOKACE (pancrelipase, USP) tablets in patients with exocrine pancreatic insufficiency (EPI) was conducted. Study VIO16EPI07-01was a multicenter, randomized, double-blind, parallel, placebo-controlled study performed in chronic pancreatitis (CP) patients with EPI.

In this placebo-controlled study, the primary objective was to show superiority of VIOKACE compared to placebo on the primary efficacy endpoint, the coefficient of fat absorption (CFA).

The CFA determines the percentage of fat that is absorbed into the body taking into account fat intake and fecal excretion.

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 270 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 $p < 0.0001$.

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.

TOXICOLOGY

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

REFERENCES

1. 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 retrospective study of the same patients at two different ages. J Pediatr Gastroenterol Nutr. 1099;7 Suppl 1:S40-5.

2. 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.

3. Borowitz DS, Baker RD, Stallings V. Consensus report on nutrition for pediatric patients with cystic fibrosis. J Pediatr Gastroenterol Nutr. 2002 Sep;35:246-259.

4. Clinical Study Report Protocol No. VIO16EPI07-01: A Multicenter, Randomized, Double-Blind, parallel, Placebo-Controlled, Phase III Study to assess the Safety and Efficacy of VIOKACE for the Correction of Steatorrhea in Patients with Exocrine Pancreatic Insufficiency (2009).

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

6. FitzSimmons SC, Burkhart GA, Borowitz DS, et al. High-dose pancreatic-enzyme supplements and fibrosing colonopathy in children with cystic fibrosis. N Engl J Med.1997;336:1283-1289.

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

8. NCT00559364 : Safety and Efficacy Study of VIOKASE 16 for the Correction of Steatorrhea (2010).

9. 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.

10. Smyth RL, Ashby D, O'Hea U. Fibrosing colonopathy in cystic fibrosis: results of a case-control study. Lancet. 1995;345:1247-1251.

PART III: CONSUMER INFORMATION

PrVIOKACE™
(Pancrelipase)

This leaflet is Part III of the Prescribing Health Professional Information (Part I) and Scientific Information (Part II) for VIOKACE. Parts I and II are designed for health professionals while Part III is designed specifically for patients / consumers. This leaflet is a summary and will not tell you everything about VIOKACE. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
VIOKACE is used for the treatment of pancreatic insufficiency attributed to cystic fibrosis, chronic pancreatitis, or any other medically defined pancreatic disease that might require pancreatic enzyme therapy, as determined by the doctor.
VIOKACE is a prescription medicine used with a proton pump inhibitor medicine (PPI).

What it does:
VIOKACE is intended as a replacement therapy when your pancreas, which produces enzymes necessary to digest fat, protein and sugars, has stopped functioning or is not functioning as it should be. The medical term for this condition is pancreatic exocrine insufficiency. Symptoms of pancreatic exocrine insufficiency include steatorrhea (excess of fat in stools).

VIOKACE contains an enzyme mixture that helps you digest food. The enzymes are taken from pig pancreas glands.

The enzymes in VIOKACE work by digesting food as it passes through the gut. You should take VIOKACE before or with a meal or snack. This will allow the enzymes to mix thoroughly with the food.

When it should not be used:
VIOKACE should not be used if:

- You have known hypersensitivity to porcine protein, pancreatic enzymes or any excipients; and / or during acute pancreatitis or the acute exacerbation of chronic pancreatitis.

What the medicinal ingredient is:
The medicinal ingredient in VIOKACE is pancrelipase. VIOKACE is a mixture of pancreatic enzymes (lipase, amylase and protease).

What the important nonmedicinal ingredients are:
Colloidal silicon dioxide, croscarmellose sodium, lactose monohydrate, microcrystalline cellulose, stearic acid and talc

What dosage forms it comes in:
VIOKACE (10,440 USP units lipase): tablets with 10,440 USP units of lipase, 56,400 USP units of amylase and 57,100 USP units of protease.

VIOKACE (20,880 USP units lipase): Tablets with 20,880 USP units of lipase, 113,400 USP units of amylase and 112,500 USP units of protease.

WARNINGS AND PRECAUTIONS

Serious Warning and Precautions
A rare bowel condition called ″fibrosing colonopathy″, where your gut is narrowed, has been reported in patients with cystic fibrosis taking high doses of pancreatic enzymes. As a precaution, consult your doctor if you experience any unusual abdominal symptoms or any change in abdominal symptoms, especially if you are taking more than 10,000 units of lipase/kg body weight/day or more than 4,000 units of lipase/gram fat intake.

Talk to your doctor about all the drugs you are taking before taking VIOKACE.

Talk to your doctor before taking this medicine if you are pregnant, might become pregnant, or are breast-feeding. Your doctor will decide if you should take VIOKACE and at which dose.

Potential Viral Exposure from the Product Source: The pancreas glands used to make VIOKACE and other pancreatic enzyme products come from pigs used for food. These pigs may carry viruses. When VIOKACE is made several steps are taken to reduce the risk of viruses being spread, including their destruction and testing for specific viruses. The risk of infections caused by these or other unknown or novel viruses cannot be totally ruled out. However, there have not been any cases reported where infection of patients has occurred.

BEFORE you use VIOKACE talk to your doctor or pharmacist if:

- You are allergic to pork (pigs) products
- You have a history of intestinal blockage of your intestines or scarring or thickening of your bowel wall (fibrosing colonopathy)
- You have any other medical conditions
- You are pregnant or might become pregnant
- You are breast-feeding or plan to breast-feed

INTERACTIONS WITH THIS MEDICATION

There are no known drug interactions with VIOKACE.

Before taking VIOKACE tablets make sure you tell your doctor and pharmacist all the medications (including those without prescription) you are taking.

PROPER USE OF THIS MEDICATION

Take VIOKACE tablets exactly as your doctor tells you.

Do not switch VIOKACE with any other pancreatic enzyme product without first talking to your doctor.

Always take VIOKACE with a meal or a snack and enough liquid to swallow VIOKACE completely. This will allow the enzymes to mix thoroughly with the food and digest it as it passes through the gut. If you eat a lot of meals or snacks in a day, be careful not to go over your total daily dose.

Usual dose:

Your dose is measured in 'lipase units'. Lipase is one of the enzymes in VIOKACE. Different strengths of pancreatic enzymes may contain different amounts of lipase.

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.

Your doctor will adjust your dose to suit you. It will depend on:

- your illness
- your weight
- your diet
- how much fat is in your stools

Always take VIOKACE tablets with enough liquid to swallow the whole tablets. Do not take VIOKACE if you cannot swallow the tablets whole. Do not mix with food or 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 still have fatty stools or other stomach or gut problems (gastrointestinal symptoms), talk to your doctor as your dose may need to be adjusted.

The usual starting dose is 500 lipase units per kilogram body weight per meal. Usually, half the starting dose is given with snacks.

The maximum dose is 2,500 lipase units per kilogram body weight per meal (or less than or equal to 10,000 lipase units/kg body weight per day), or less than 4,000 lipase units/g fat ingested per day.

Overdose:

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

If you know or suspect that you have taken more of this product than you normally do, or notice any unusual symptoms, contact your doctor or nearest hospital emergency department immediately. Ensure that you are adequately hydrated during this time by drinking plenty of fluids.

Extremely high doses of pancreatic enzymes have sometimes caused too much uric acid in the urine (hyperuricosuria) and in the blood (hyperuricaemia).

Missed Dose:

If a dose of this medication has been missed, take your next dose at the usual time, with your next meal. Do not try to make up for the dose that you have missed.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, VIOKACE can cause side effects, although not everybody gets them. The following side effects were seen during studies in patients taking VIOKACE.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Common	Abdominal pain		√	
	Rash			√
Unknown	Hypersensitivity (allergic reaction)			√
	Urticaria			√

This is not a complete list of side effects. For any unexpected effects while taking VIOKACE, contact your doctor or pharmacist.

Tell your healthcare professional if you have any side effect that bothers you or that does not go away.

HOW TO STORE IT

Keep out of reach of children.

Keep VIOKACE in a dry place and in its original container.

Store VIOKACE in a dry place at room temperature (20°C to 25°C). Protect from heat and moisture.

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.**

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- **Report online at:**
  www.healthcanada.gc.ca/medeffect
- **Call toll-free at 1-866-234-2345**
- **Complete a Canada Vigilance Reporting Form and:**
  - Fax toll-free to 1-866-678-6789, or
  - Mail to: Canada Vigilance Program
  Health Canada
  Postal Locator 0701E
  Ottawa, Ontario
  K1A 0K9

  Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for healthcare professionals can be found at: www.actavis.com or by contacting the sponsor, Aptalis Pharma Canada Inc., at: 1855-892-8766

VIOKACE™ is a trademark of Actavis Specialty Pharmaceuticals Co. or its affiliates and is used under license.

This leaflet was prepared by Aptalis Pharma Canada Inc.

Last revised: June 22, 2015