PRODUCT MONOGRAPH

PrULTRESA®

(Pancrelipase USP)

Capsule (Delayed- Release)

13,800, 20,700 and 23,000 USP units of lipase

USP

Pancreatic enzymes
A09AA02

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ULTRESA®

Pancreatic enzymes

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Non-Medicinal Ingredients
Oral	Capsule (Delayed-Release):13,800 USP units of lipase Lipase: 13,800 USP units Amylase: 58,800 USP units Protease: 53,400 USP units	*For a complete listing see Dosage Forms, Composition and Packaging section.*
Oral	Capsule (Delayed-Release):20,700 USP units of lipase Lipase: 20,700 USP units Amylase: 88,200 USP units Protease: 80,000 USP units	*For a complete listing see Dosage Forms, Composition and Packaging section.*
Oral	Capsule (Delayed-Release):23,000 USP units of lipase Lipase: 23,000 USP units Amylase: 98,000 USP units Protease: 88,900 USP units	*For a complete listing see Dosage Forms, Composition and Packaging section.*

INDICATIONS AND CLINICAL USE

ULTRESA (pancrelipase) is indicated in pediatric and adult patients for the treatment of exocrine pancreatic insufficiency (EPI) due to cystic fibrosis (CF) or any other medically defined pancreatic disease that might require pancreatic enzyme therapy, including but not limited to:

- Cystic fibrosis
- Chronic pancreatitis
- Post-pancreatectomy
- Post-gastrointestinal bypass surgery (e.g. Billroth II gastroenterostomy)
- Ductal obstruction from neoplasm (e.g. of the pancreas or common bile duct)
- Pancreatic Cancer
- Gastrectomy
- Swachman-Diamond Syndrome

Geriatrics (> 65 years of age):
Clinical studies with ULTRESA capsules 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 (< 16 years of age):
The short-term safety and efficacy of ULTRESA were assessed in two clinical studies in pediatric patients with EPI due to CF (see WARNINGS AND PRECAUTIONS, Special populations).

CONTRAINDICATIONS

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

ULTRESA 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 ULTRESA (pancrelipase) 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.

ULTRESA 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.

The capsules should not be chewed or crushed because the coating (that is formulated to deliver the enzymes to the correct place in the intestines) will be destroyed. If the capsules are opened and the contents shaken onto soft food, it should not have an alkaline pH (e.g., milk, custard, ice cream, other dairy products) because the enteric coating will dissolve prematurely and limit absorption (see DOSAGE AND ADMINISTRATION).

To avoid irritation of the mouth, lips and tongue, opened capsules should be swallowed immediately before meals or snacks to minimize the probability of retaining some of the drug in the mouth. Proteolytic enzymes present in ULTRESA, when retained in the mouth, may begin to digest the mucous membranes and cause ulcerations.

Any change in pancreatic enzyme replacement therapy (e.g., dose or brand of medication) should be made cautiously and only under medical supervision. Pancreatic extracts can form insoluble complexes with folic acid, resulting in folic acid deficiency.

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

Hepatic/Biliary/Pancreatic

ULTRESA may cause hyperuricosuria and hyperuricemia with very high doses.

Potential Viral Exposure from Product Source

As with all currently marketed porcine pancreatin products, ULTRESA is sourced from pancreatic tissue from pigs used for food consumption. Although the risk that ULTRESA 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.

Special Populations

Pregnant Women:

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

Pediatrics (≤ 18 years of age):
There are no special warnings or precautions for use in pediatrics.

Geriatrics (> 65 years of age):
There are no special warnings or precautions for use in elderly patients

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 CF patients (see WARNINGS AND PRECAUTIONS).

Allergic or hypersensitivity reactions 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.*

The short-term safety of ULTRESA (pancrelipase) was assessed in two clinical trials conducted in patients with EPI due to CF. Study 1 (UMT20CF05-01) was conducted in 30 patients, ages 8 years to 37 years and Study 2 (UMT20CF07-01) conducted in 9 patients, ages 7 years to 11 years.

All the adverse reactions mentioned in Table 1 and Table 2 below occurred in at least 1 of the total 39 patients studied during these studies with frequencies from 3.3% to 11.1%. As such, they are to be considered as common (>1% and <10%) to very common (>10%) adverse reactions.

Table 1 **Adverse Reactions Occurring in at Least 1 Patient in UMT20CF05-01 a Multicenter, Randomized, Double-Blind, Crossover Study**

MedDRA SOC	Preferred Term	ULTRASE Capsules N=30 n (%)	Placebo N=31 n (%)
Gastrointestinal disorders	Abdominal pain	2 (6.7)	12 (38.7%)
	Abdominal pain upper	1 (3.3)	4 (12.9%)
	Constipation	2 (6.7)	1 (3.2%)
Investigations	Alanine aminotransferase increased	1 (3.3)	0 (0)

Table 2 **Adverse Reactions Occurring in at Least 1 Patient in UMT20CF07-01 a Multicenter, Phase III, Open-Label Study**

MedDRA SOC	Preferred Term	ULTRASE Capsules N=9 n (%)
Gastrointestinal disorders	Abdominal discomfort	1 (11.1)
	Abdominal pain	1 (11.1)
	Nausea	1 (11.1)
Investigations	Weight decreased	1 (11.1)

Post-Market Adverse Drug Reactions

The following adverse reactions have been identified during marketed use of ULTRESA. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or to establish a causal relationship to drug exposure.

Post-marketing data for ULTRESA has been available since 1992. The safety data is similar to that described below.

The adverse drug reactions seen with ULTRESA are:
Gastrointestinal disorders: Abdominal discomfort, Abdominal distension, Abdominal pain, Abdominal pain upper, Abnormal faeces (LLT: Feces abnormal smell of), Diarrhea, Flatulence, Frequent bowel movements, Nausea, Vomiting.

Immune system disorders: Hypersensitivity.
Investigations: Blood glucose increased.
Nervous system disorders: Headache.
Skin and subcutaneous tissue disorders: Blister, Pruritus generalised, Rash, Skin irritation, 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 capsules, or dosage strength given with meals and/or snacks should be estimated 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. Any mixture of the medication with food or liquid should be used immediately and not be stored.

Recommended Dose and Dosage Adjustment

Dosage recommendations for pancreatic enzyme replacement therapy were published following the Cystic Fibrosis Foundation Consensus Conferences. ULTRESA (pancrelipase) should be administered in a manner consistent with the recommendations of the Conferences provided in the following paragraph. Patients may be dosed on a fat ingestion-based or actual body weight-based dosing scheme.

Children Older than 12 months and Younger than 4 Years and Weight 14 kg or Greater
Children older than 12 months and younger than 4 years, weighing under 14 kg should not be dosed with this product because capsule dosage strengths cannot adequately provide dosing for these children.

Enzyme dosing should begin with 1,000 lipase units/kg of body weight per meal for children less than age 4 years 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 Weight 28 kg or Greater and Adults

Children 4 years and older, weighing under 28 kg should not be administered this product because capsule dosage strengths cannot be adequately titrated for children in this weight range.

Enzyme dosing should begin with 500 lipase units/kg of body weight per meal for those older than age 4 years 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 ULTRESA 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.

Enzyme doses expressed as lipase units/kg of body weight per meal should be decreased in older patients because they weigh more but tend to ingest less fat per kilogram of body weight.

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 a physician. 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). 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.

Use of ULTRESA in children is limited by the available capsule dosage strengths and their ability to provide the recommended dose based on age and weight. Attempting to divide the capsule contents in small fractions to deliver small doses of lipase is not recommended.

Missed Dose

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

Administration

ULTRESA is not interchangeable with any other pancrelipase product.

ULTRESA is orally administered. Therapy should be initiated at the lowest recommended dose and gradually increased. The dosage of ULTRESA should be individualized based on clinical symptoms, the degree of steatorrhea present, and the fat content of the diet.

ULTRESA should be taken during meals or snacks, with sufficient fluid. ULTRESA capsules should be swallowed whole. ULTRESA capsules and capsule contents should not be crushed or chewed.

For patients who are unable to swallow intact capsules, the capsules may be carefully opened and the contents sprinkled on a small amount of applesauce, yogurt and other acidic soft food with a pH of 4.5 or less at room temperature.

The ULTRESA–soft food mixture should be swallowed immediately without crushing or chewing, and followed with water or juice to ensure complete ingestion. Care should be taken to ensure that no drug is retained in the mouth to avoid mucosal irritation.

Any unused portion of capsule contents should be discarded, and not used for subsequent dosing. The remaining exposed contents may lose potency and become less effective.

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

The pancreatic enzymes in ULTRESA (pancrelipase) 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 maltotriose in the duodenum and proximal small intestine, thereby acting like digestive enzymes physiologically secreted by the pancreas.

Pharmacokinetics

The pancreatic enzymes in ULTRESA are enteric-coated to minimize destruction or inactivation in gastric acid. ULTRESA is designed to release most of the enzymes *in vivo* at pH greater than 5.5. Pancreatic enzymes are not absorbed from the gastrointestinal tract in appreciable amounts.

STORAGE AND STABILITY

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

ULTRESA (pancrelipase) should be stored in a dry place in the original container. After opening, keep the container tightly closed between uses to protect from moisture. ULTRESA is dispensed in bottles containing a desiccant. The dessicant packet will protect the product from moisture.

Keep ULTRESA in a safe place out of the reach of children.

DOSAGE FORMS, COMPOSITION AND PACKAGING

ULTRESA (pancrelipase) is available as orally administered delayed-release capsules containing enteric-coated minitablets of porcine pancreatic enzyme concentrate, predominantly pancreatic lipase, amylase, and protease. ULTRESA is dosed by lipase units and is available in 3 color coded delayed-release capsule strengths.

ULTRESA 13,800 USP units lipase

Each white and yellow capsule printed "13800UL" and "AXCA" of enteric-coated minitablet contains 13,800 USP units of lipase, 58,800 USP units of amylase, and 53,400 USP units of protease.

Non-medicinal ingredients: colloidal silicon dioxide, croscarmellose sodium, gelatin, hydrogenated castor oil, hydroxypropyl methylcellulose phthalate (HP 55) (as dry substance), iron oxide (yellow), magnesium stearate, microcrystalline cellulose, talc, triethyl citrate and titanium dioxide. Bottles of 100.

ULTRESA 20,700 USP units of lipase

Each grey and white capsule printed "20700UL" and "AXCA" of enteric-coated minitablet contains 20,700 USP units of lipase, 88,200 USP units of amylase, and 80,000 USP units of protease.

Non-medicinal ingredients: colloidal silicon dioxide, croscarmellose sodium, gelatin, hydrogenated castor oil, hydroxypropyl methylcellulose phthalate (HP 55) (as dry substance), iron oxide (black), magnesium stearate, microcrystalline cellulose, talc, triethyl citrate and titanium dioxide. Bottles of 100.

ULTRESA 23,000 USP units of lipase

Each grey and yellow capsule printed "23000UL" and "AXCA" of enteric-coated minitablet contains 23,000 USP units of lipase, 98,000 USP units of amylase, and 88,900 USP units of protease.

Non-medicinal ingredients: colloidal silicon dioxide, croscarmellose sodium, gelatin, hydrogenated castor oil, hydroxypropy l methylcellulose phthalate (HP 55) (as dry substance),

iron oxides (black and yellow), magnesium stearate, microcrystalline cellulose, talc, triethyl citrate and titanium dioxide. Bottles of 100.

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 ULTRESA® 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 or insoluble in alcohol and ether.

CLINICAL TRIALS

Exocrine Pancreatic Insufficiency:

The short-term efficacy and safety of ULTRESA (pancrelipase) were evaluated in 2 studies conducted in 40 patients, ages 7 to 37 years, with EPI associated with CF.

The primary endpoint was 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.

Study UMT20CF05-01

Study UMT20CF05-01 was a randomized, double-blind, placebo-controlled, crossover study of 31 patients, ages 8 to 37 years, with EPI due to CF. The final analysis population was limited to 24 patients, who completed both treatment periods and had stool results available for each treatment period.

Patients were randomized to receive ULTRESA (at a dose not to exceed 2,500 lipase units per kilogram per meal or snack) or matching placebo for 6 to 7 days of treatment followed by crossover to the alternate treatment for an additional 6 to 7 days. The mean dose during the

controlled treatment periods was 6,270 lipase units per kilogram per day. All patients consumed a high-fat diet (2 grams of fat per kilogram of body weight per day) during the treatment periods.

The CFA was determined by a 72-hour stool collection during both treatments, when both fat excretion and fat ingestion were measured. Each patient's CFA during placebo treatment was used as their no-treatment CFA value. Mean CFA was 89% with ULTRESA treatment compared to 56% with placebo treatment. The mean difference in CFA was 35 percentage points in favor of ULTRESA treatment with 95% CI: (25, 45) and $p<0.0001$.

Study UMT20CF07-01

Study UMT20CF07-01 was an open-label study of 9 patients, ages 7 years to 11 years (mean 10 years), with EPI due to CF. The final analysis population was limited to 7 patients who completed both the washout and treatment phases of the study.

After a 15 day screening period on individually-titrated doses of ULTRESA not to exceed 2,500 lipase units per kilogram per meal, patients entered a 7-day washout phase (no treatment) before returning to a 12-day treatment phase on the same individually-titrated dose of ULTRESA. The mean daily dose of ULTRESA during the treatment phase was 6,846 lipase units per kilogram body weight per day. All patients consumed a high-fat diet (2 grams of fat per kilogram of body weight per day) during both the washout phase and the treatment phase.

The mean CFA was determined during the washout phase (no treatment) and during the ULTRESA treatment phase. Mean CFA was 35% during the washout phase and was 83% during the ULTRESA treatment phase.

TOXICOLOGY

Non-clinical data show no relevant acute, subchronic or chronic toxicity. Carcinogenicity, genetic toxicology, and animal fertility studies have not been performed.

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PART III: CONSUMER INFORMATION

ULTRESA®
Pancrelipase

This leaflet is part III to complement the Prescribing Health Professional Information (Part I) and Scientific Information (Part II) for ULTRESA. 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 ULTRESA. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

ULTRESA is a medication used to treat people who cannot digest food normally because their pancreas does not produce enough enzymes due to various medical conditions such as:

- Cystic fibrosis (rare inherited disorder).
- Chronic pancreatitis (inflammation of the pancreas).
- Pancreatic surgery (pancreatectomy).
- Gastrointestinal bypass surgery (e.g., Billroth II gastroenterostomy) (surgical opening between the stomach wall and intestine).
- Ductal obstruction of the pancreas or the common bile duct (e.g., from tumor).

What it does:

ULTRESA 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 exocrine pancreatic insufficiency. Symptoms of exocrine pancreatic insufficiency include steatorrhea (excess of fat in stools).

ULTRESA contains an enzyme mixture (lipases, proteases, amylases) that helps you digest food. The enzymes are taken from pig pancreas glands.

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

When it should not be used:

ULTRESA should not be used:

- if you have a known hypersensitivity to porcine protein, pancreatic enzymes or any excipients.
- during acute pancreatitis or the acute exacerbation of chronic pancreatits.

What the medicinal ingredient is:

Pancrelipase (lipase, protease and amylase).

What the important nonmedicinal ingredients are:

Colloidal silicon dioxide, croscarmellose sodium, gelatin, hydrogenated castor oil, hydroxypropyl methylcellulose phthalate (HP 55) (as dry substance), iron oxides, magnesium stearate, microcrystalline cellulose, talc, triethyl citrate and titanium dioxide.

What dosage forms it comes in:

Ultresa is available in 3 strengths as orally administered delayed-release capsules containing microtablets of the porcine pancreatic enzyme concentrate.

ULTRESA (13,800 USP units lipase): containing 13,800 USP units of lipase, 58,800 USP units of amylase, and 53,400 USP units of protease.

ULTRESA (20,700 USP units lipase): containing 20,700 USP units of lipase, 88,200 USP units of amylase, and 80,000 USP units of protease.

ULTRESA (23, 000 USP units lipase): containing 23,000 USP units of lipase, 98,000 USP units of amylase, and 88,900 USP units of protease.

WARNINGS AND PRECAUTIONS

Serious Warnings 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 before taking this medicine if you are pregnant, might become pregnant, or are breast-feeding. Your doctor will decide if you should take ULTRESA and at which dose.

Potential Viral Exposure from the Product Source:
The pancreas glands used to make ULTRESA and other pancreatic enzyme products come from pigs used for food.

These pigs may carry viruses. When ULTRESA is made, several steps are taken to reduce the risk of viruses being spread, including destruction of viruses 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 ULTRESA talk to your doctor or pharmacist 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 any other medical condition.
- are pregnant or plan to become pregnant.
- are breastfeeding or plan to breastfeed.
- have trouble swallowing capsules.

INTERACTIONS WITH THIS MEDICATION

There are no known drug interactions with ULTRESA.

Tell your doctor or pharmacist if you are taking or have recently taken any other prescription or over-the-counter medicines, vitamins or natural health products during your treatment with ULTRESA.

PROPER USE OF THIS MEDICATION

Take ULTRESA exactly as your doctor tells you.

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

Always take ULTRESA with a meal or snack and enough liquid to swallow.

Swallow ULTRESA capsules whole. Do not crush or chew the ULTRESA capsules or their contents, and do not hold the capsule or capsule contents in your mouth. Crushing, chewing or holding the ULTRESA capsules in your mouth may cause irritation in your mouth or change the way ULTRESA works in your body. Do not divide the capsule contents into small amounts to give small doses of ULTRESA.

If you have difficulty swallowing capsules, open the capsule and sprinkle the contents on a small amount of soft acidic food including applesauce or yogurt. Swallow it right after you mix it and drink plenty of water or juice to make sure the medicine is swallowed completely. Do not store ULTRESA that is mixed with food. Throw away any unused portion of capsule contents. Ask your doctor about other foods you can mix with ULTRESA.

Usual dose:

Your dose is measured in 'lipase units'. Lipase is one of the enzymes in ULTRESA.

Different strengths of pancreatic enzymes may contain different amounts of lipase.

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.

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 for children under 4 years of age is 1,000 lipase units per kilogram body weight per meal.
- The usual starting dose for children 4 years of age and over, adolescents and adults is 500 lipase units per kilogram body weight per meal.
- Usually, half the standard dose is given with snacks.
- The maximum dose is 2,500 lipase units per kilogram body weight per meal.

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 causes too much uric acid in the urine (hyperuricosuria) and in the blood (hyperuricaemia).

Missed Dose:

If a dose of ULTRESA 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

As with all medicines, patients taking ULTRESA may experience side effects, although not everybody gets them.

The most common side effects of ULTRESA include abdominal discomfort and abdominal pain.

Other reactions are less common such as abnormal stools and diarrhea. Cases of allergic reactions have also been reported.

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		√	
	Vomiting		√	
Unknown	Allergic reactions: skin rash, itching or hives.		√	√

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

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

HOW TO STORE IT

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

Store ULTRESA® capsules in a dry place and in the original container. After opening the bottle, keep it closed tightly between uses to protect from moisture. The ULTRESA 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 ULTRESA out of reach of children.

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 health professionals can be found at: www.actavis.com by contacting the sponsor, Aptalis Pharma Canada Inc., at: 1-855-892-8766

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