PRODUCT MONOGRAPH

PrPANCREASE® MT 2

2,600 USP Units Lipase/10,850 USP Units Amylase/6,200 USP Units Protease /Capsule

PrPANCREASE® MT 4

4,200 USP Units Lipase/17,500 USP Units Amylase/10,000 USP Units Protease/Capsule

PrPANCREASE® MT 10

10,500 USP Units Lipase/43,750 USP Units Amylase/25,000 USP Units Protease /Capsule

PrPANCREASE® MT 16

16,800 USP Units Lipase/70,000 USP Units Amylase/40,000 USP Units Protease /Capsule

PrPANCREASE® MT 20

21,000 USP Units Lipase/61,000 USP Units Amylase/37,000 USP Units Protease /Capsule

Pancrelipase

Delayed-Release Capsules

Digestant

VIVUS, Inc.
900 East Hamilton Avenue, Suite #550,
Campbell, California, USA 95008

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Pancrelipase Delayed-Release Capsules

Digestant

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Nonmedicinal Ingredients
oral	Capsules/ PANCREASE® MT 2	colloidal anhydrous silica, crospovidone, magnesium stearate, methacrylic acid ethyl acrylate copolymer, microcrystalline cellulose, montan glycol wax, simethicone emulsion, talc and triethyl citrate. The capsule shell contains hypromellose, titanium dioxide and iron oxide.
	Capsules/ PANCREASE® MT 4	colloidal anhydrous silica, crospovidone, magnesium stearate, methacrylic acid ethyl acrylate copolymer, microcrystalline cellulose, montan glycol wax, simethicone emulsion, talc and triethyl citrate. The capsule shell contains hypromellose, titanium dioxide and iron oxide.
	Capsules/ PANCREASE® MT 10	colloidal anhydrous silica, crospovidone, magnesium stearate, methacrylic acid ethyl acrylate copolymer, microcrystalline cellulose, montan glycol wax, simethicone emulsion, talc and triethyl citrate. The capsule shell contains hypromellose, titanium dioxide and iron oxide.
	Capsules/ PANCREASE® MT 16	colloidal anhydrous silica, crospovidone, magnesium stearate, methacrylic acid ethyl acrylate copolymer, microcrystalline cellulose, montan glycol wax, simethicone emulsion, talc, and triethyl citrate. The capsule shell contains hypromellose, titanium dioxide and iron oxide.

	Capsules/ PANCREASE® MT 20	colloidal anhydrous silica, crospovidone, magnesium stearate, methacrylic acid ethyl acrylate copolymer, microcrystalline cellulose, montan glycol wax, simethicone emulsion, talc, and triethyl citrate. The capsule shell contains hypromellose, and titanium dioxide.

PANCREASE® MT capsules contain enteric-coated microtablets of pure porcine pancreatic enzyme concentrate — predominantly steapsin (pancreatic lipase), amylase, and protease — isolated by a proprietary process that ensures high enzyme purity and activity.

INDICATIONS AND CLINICAL USE

PANCREASE® MT (pancrelipase) capsules are indicated 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.

Geriatrics (≥ 65 years of age):
It is recommended that enzyme doses, expressed as lipase units/kg/meal, be decreased in older patients since they weigh more but tend to ingest less fat per kilogram (see **DOSAGE AND ADMINISTRATION**).

Pediatrics (< 18 years of age):
PANCREASE® MT is approved for use in pediatrics 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 (see **DOSAGE AND ADMINISTRATION**).

CONTRAINDICATIONS

- Patients who have known hypersensitivity to porcine protein, pancreatic enzymes or any excipients; and
- During acute pancreatitis or the acute exacerbation of chronic pancreatitis.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

Pancreatic enzyme products, including PANCREASE® MT (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 6,000 lipase units/kg/meal.

PANCREASE® MT 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, so 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 product to another.

General

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). Should hypersensitivity occur, 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 PANCREASE® MT capsules should be swallowed immediately before regular feedings or meals to minimize the likelihood that the microtablets are retained in the mouth. Proteolytic enzymes present in PANCREASE® MT, 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.

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 mini-microspheres improve but do 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.

Gastrointestinal

Fibrosing colonopathy has been reported following treatment with different pancreatic enzyme products. Fibrosing colonopathy is a rare serious adverse reaction initially described in association with high-dose pancreatic enzyme use, usually with use 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/meal have been associated with colonic strictures in children less than 12 years of age. Close monitoring of patients with fibrosing colonopathy is recommended because some patients may be at risk of progressing to stricture formation. It is uncertain whether regression of fibrosing colonopathy occurs. It is generally recommended, unless clinically indicated, that enzyme doses be less than 2,500 lipase units/kg/meal (corresponding to less than 10,000 lipase units/kg/day or 4,000 lipase units/g fat ingested/day).

Doses greater than 2,500 lipase units/kg/meal must 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. It is recommended that patients receiving higher doses than

6,000 lipase units/kg/meal be examined and the dosage either immediately decreased or titrated downward to a lower range, if possible.

Hepatic/Biliary/Pancreatic

PANCREASE® MT or other pancreatic enzyme products may cause hyperuricosuria and hyperuricemia with very high doses. Also at very high doses, perianal irritation and inflammation may occur.

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

Potential Viral Exposure from the Product Source

PANCREASE® MT is sourced from pancreatic tissue from swine used for food consumption. Although the risk that PANCREASE® MT 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.

Special Populations

Pregnant Women:

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

ADVERSE REACTIONS

Adverse Drug Reaction Overview

The most common adverse reactions are abdominal discomfort, constipation and dermatitis. Other gastrointestinal reactions are less common and include abnormal stool and diarrhea. Nausea and vomiting have been reported, but these are not common. With high doses, perianal irritation and inflammation have been reported (see **WARNINGS AND PRECAUTIONS**).

At extremely high doses, hyperuricosuria and hyperuricemia have been reported.

Allergic or hypersensitivity reactions of the skin have been reported (see **WARNINGS AND PRECAUTIONS, General**).

Post-Market Adverse Drug Reactions

The following adverse reactions have been reported during post-marketing experience (Table 1.1). The frequencies are provided according to the following convention:

Very common	≥ 1/10
Common	≥ 1/100 and < 1/10
Uncommon	≥ 1/1,000 and < 1/100
Rare	≥ 1/10,000 and < 1/1000
Very rare	< 1/10,000

Table 1.1: Adverse Drug Reactions Identified During Post-Marketing Experience with PANCREASE® MT by Frequency Category Estimated from Spontaneous Reporting Rates

Gastrointestinal Disorders	
Very rare	Abdominal distention, abdominal pain, diarrhea, intestinal obstruction*, nausea, vomiting
Skin and Subcutaneous Tissue Disorders	
Very rare	Rash

* Mainly cases of fibrosing colonopathy in pediatric subjects with cystic fibrosis (see **WARNINGS AND PRECAUTIONS**).

DRUG INTERACTIONS

No drug interactions have been identified.

DOSAGE AND ADMINISTRATION

General Guidelines

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 capsule strength given with meals and/or snacks should be estimated by assessing at which dose steatorrhea is minimized and good nutritional status is maintained. In some patients with pancreatic enzyme deficiency, satisfactory responses have been achieved with dosages (expressed in USP units of lipase) similar to the ones stated below. However, dosages should be adjusted according to the response of the patients. Dosage should be adjusted based on 3-day fecal fat studies.

Dose increases, if required, should be made slowly, with careful monitoring of response and symptomatology. It is important to ensure adequate hydration of patients at all times while administering PANCREASE® MT capsules.

There is considerable variation among individuals in response to enzymes with respect to control of steatorrhea; therefore, a range of doses is suggested.

If the patient cannot swallow whole capsules, they may be opened and the contents shaken onto a small quantity of soft food that does not require chewing e.g., applesauce, dessert gelatin, etc., but not milk, ice cream, other dairy products or custard because the pH is too high (see **WARNINGS AND PRECAUTIONS**).

Usually, half the mealtime dose is given with a snack. The total daily dose should reflect approximately three meals and two snacks per day.

Instruct the patient to take the medication immediately and not store it to be taken later.

Dosing Considerations

If doses greater than 2,500 lipase units/kg/meal (4,000 lipase units/g fat/day) are required to control malabsorption, further investigation is warranted to rule out other causes of malabsorption. Doses greater than 2,500 units/kg/meal should be used with caution and only if they are documented to be effective by 3-day fecal fat studies.

Doses greater than 6,000 lipase units/kg/meal have been associated with colonic strictures, particularly in children with cystic fibrosis less than 12 years of age. Patients currently on higher doses than 6,000 lipase units/kg/meal should be re-evaluated and the dosage either immediately decreased or titrated downward to the lowest effective clinical dose as assessed by 3-day fecal fat excretion (see **WARNINGS AND PRECAUTIONS, Gastrointestinal**).

Recommended Dose and Dosage Adjustment

Infants (up to 12 months):

Fat Consumption Scheme

2,000-4,000 USP lipase units per 120 mL of formula or per breast-feeding. This provides approximately 450-900 lipase units per gram of fat ingested (based on 4.5 grams of fat per 120 mL standard cow's milk-based formula). Higher doses are used in infants because, on average, infants ingest 5 grams of fat per kilogram of body weight per day, whereas adults tend to ingest about 2 grams of fat per kilogram per day. Contents of the capsule **should not** be mixed directly into formula or breast milk as this may diminish efficacy.

Children (over 12 months) and Adults:

Weight-based Scheme

***Less than 4 years*:** Begin with 1,000 USP lipase units/kg/meal to a maximum of 2,500 lipase units/kg/meal.

***Over 4 years and Adults*:** Begin with 500 USP lipase units/kg/meal to a maximum of 2,500 lipase units/kg/meal.

Geriatrics (≥ 65 years of age):

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

Missed Dose

If the patient misses a dose, instruct him/her to wait until their next meal and take their usual number of capsules at their usual time. Inform patients not to make up for missed doses.

OVERDOSAGE

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

Chronic high doses of pancreatic enzyme products have been associated with fibrosing colonopathy and colonic strictures (see **WARNINGS AND PRECAUTIONS, Gastrointestinal**). Extremely high dosages of pancreatic enzymes have been reported to cause hyperuricosuria and hyperuricemia and should be used with caution in patients with a history of hyperuricemia, gout, or renal impairment (see **WARNINGS AND PRECAUTIONS, Hepatic/Biliary/Pancreatic**).

Most cases responded to supportive measures, including discontinuation of the enzyme therapy and ensuring adequate hydration.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

PANCREASE® MT microtablets resist gastric inactivation and deliver predictable, high levels of biologically active pancreatic enzymes (lipase, amylase, and protease) into the duodenum. The enzymes catalyze the hydrolysis of fats into glycerol and fatty acids, proteins into proteoses and derived substances, and starch into dextrins and sugars.

Pharmacokinetics

Absorption:

The intestinal bioavailability of PANCREASE® MT 16 capsules[I] was determined, *in vitro*, under simulated physiological conditions[1]. PANCREASE® MT capsules were placed into a test tube containing an incubation medium consisting of 2.0 g NaCl, 9.2 g NaH_2PO_4 and distilled water (total volume: 1 litre). Employing a disintegration tester, the contents of the test tube were shaken at a constant speed of 30 rpm at an incubation temperature of 37°C. The pH of the mixture was adjusted by adding 4N HCl or 4N NaOH.

To simulate the acidic conditions of the stomach during a meal, a pH of 4.0 was initially established and gradually reduced in increments of 0.5 at 30-minute intervals to a pH of 2.5. To simulate the relative alkalinity of the intestine, the preparation was then transferred to a buffer where a pH of 6.6 was maintained. While the preparation was exposed to the buffer, release of pancreatic lipase, the marker enzyme, was measured as a function of time. The lipase content of the incubation medium was determined every 15 minutes for 120 minutes. More than 90% of the enzyme activity of the PANCREASE® MT capsules was released at 15 minutes with peak levels (97%) occurring at 30 minutes. The results demonstrate that PANCREASE® MT capsules are nearly 100% bioavailable and rapidly release high levels of pancreatic enzymes.

I This study, conducted in West Germany, used Panzytrat® 20000 (Nordmark Arzneimittel GmbH, Uetersen, West Germany) which contains microtablets that are the same formulation as those of PANCREASE® MT 16.

Excretion:
Unused enzymes in PANCREASE® MT capsules are excreted in the feces. Digested enzymes are absorbed and are subsequently excreted in the urine.

STORAGE AND STABILITY

Keep bottle tightly closed. Store between 10°C-25°C in a dry place. Dispense in a tight container. Do not refrigerate.

All PANCREASE® MT bottles contain a desiccant canister. DO NOT eat or throw away the canister (desiccant) in the bottle. The packet will protect the medicine from moisture.

DOSAGE FORMS, COMPOSITION AND PACKAGING

PANCREASE® MT 2 capsules, light orange opaque body and clear cap, imprinted "MT 2" on clear cap, and "VIVUS" on body, containing: lipase 2,600 USP units, amylase 10.850 USP units and protease 6,200 USP units. Capsules are filled with white-grey microtablets.

PANCREASE® MT 4 capsules, yellow opaque body and clear cap, imprinted "MT 4" on clear cap, and "VIVUS" on body, containing: lipase 4,200 USP units, amylase 17,500 USP units and protease 10,000 USP units. Capsules are filled with white-grey microtablets.

PANCREASE® MT 10 capsules, flesh opaque body and clear cap, imprinted "MT 10" on clear cap, and "VIVUS" on body, containing: lipase 10,500 USP units, amylase 43,750 USP units and protease 25,000 USP units. Capsules are filled with white-grey microtablets.

PANCREASE® MT 16 capsules, flesh opaque body and clear cap, imprinted "MT 16" on clear cap, and "VIVUS" on body, containing: lipase 16,800 USP units, amylase 70,000 USP units and protease 40,000 USP units. Capsules are filled with white-grey microtablets.

PANCREASE® MT 20 capsules, white opaque body and cap, imprinted "MT 20" on cap, and "VIVUS" on body, containing: lipase 21,000 USP units, amylase 61,000 USP units and protease 37,000 USP units. Capsules are filled with white-grey microtablets.

Composition
PANCREASE® MT capsules contain the following inactive ingredients: colloidal anhydrous silica, crospovidone, magnesium stearate, methacrylic acid ethyl acrylate copolymer, microcrystalline cellulose, montan glycol wax, simethicone emulsion, talc, and triethyl citrate. The capsule shell contains hypromellose, titanium dioxide and iron oxide.

Packaging
Bottles of 100 capsules are available for each strength.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: Pancrelipase

Chemical name: Pancrelipase drug substance is a complex biological non-recombinant material comprising various enzymes of lipolytic, amylolytic, and proteolytic activities (including trypsin, chymotrypsin, kallikrein, amylase, lipase, colipase and some isoforms).

Molecular formula and molecular mass: Not applicable

Structural formula: Not applicable

Physicochemical properties: Pancreatic enzymes, especially lipase, are acid-sensitive in that they are increasingly and irreversibly inactivated with further decreasing pH values below pH 4.

Product Characteristics

Macroscopic Appearance
Pancrelipase, the enzyme component of PANCREASE® MT capsules, is a white-grey granulate.

Similarity to Other Compounds
PANCREASE® MT capsules closely relate to other lipase-enriched pancrelipase preparations and to pancreatin. PANCREASE® MT capsules differ from conventional pancreatic enzyme preparations in that the pancreatic enzymes are prepared as small enteric-coated microtablets (2 mm diameter). The pH-sensitive coating reduces or prevents inactivation of the enzymes by the acidic environment of the stomach. The extremely small size of the microtablets promotes rapid and uniform dispersion with food in the stomach and emptying into the duodenum with the chyme. In addition, a proprietary pancrelipase extraction process ensures that the microtablets contain high-potency, biologically active pancreatic enzymes, including activated proteases.

Physical and Chemical Compatibilities
To protect the enteric coating, the microtablets should not be crushed or chewed. Diminished clinical effectiveness could result if the microtablets are crushed.[5] If patients have difficulty swallowing capsules, the PANCREASE® MT capsules may be opened and the microtablets may be shaken onto a small quantity of a soft food which does not require chewing (e.g., applesauce, dessert gelatin, etc.), and swallowed immediately. Contact of the microtablets with foods having a pH greater than 7.3 (e.g., milk, custard, ice cream, and many other dairy products) can dissolve the protective enteric coating.

The pancrelipase powder is partly soluble in water and practically insoluble in alcohol or ether.

General Stability

Temperature

The enteric coating and the potency of the pancreatic enzymes may be adversely affected by high temperature.

Moisture

The enteric coating and the potency of the pancreatic enzymes may be adversely affected by high humidity.

pH Stability

The enteric-coated microtablets are completely resistant to gastric acid, as indicated by testing for 2 hours in 0.1 N HCl (simulated gastric fluid). *In vitro*, the microtablets begin to dissolve above a pH of 5.5, with nearly 100% dissolution occurring within 30 minutes at a pH of 6.0. Exposing the microtablets to simulated intestinal fluid (pH 6.6) results in a 93% enzyme release within 15 minutes.[1]

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PART III: CONSUMER INFORMATION

PrPANCREASE® MT 2
PrPANCREASE® MT 4
PrPANCREASE® MT 10
PrPANCREASE® MT 16
PrPANCREASE® MT 20

Pancrelipase Delayed-Release Capsules

This leaflet is Part III of a three-part "Product Monograph" published when PANCREASE® MT was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about PANCREASE® MT. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
PANCREASE® MT is 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 your doctor.

What it does:
PANCREASE® MT is classified as a digestant. This means that PANCREASE® MT capsules contain enzymes that help in the digestion of food. These enzymes – called lipase, amylase and protease – break down the fats, proteins and starches in food and convert them into substances that can be easily used by the body. The tiny microtablets inside each capsule of PANCREASE® MT contain a certain amount of each of these enzymes. Because these microtablets are enteric coated, they are not digested by the stomach but work directly in the lower gastrointestinal tract. Once they have done their work, any undigested enzymes are simply passed out of the body in the feces (bowel movements).

When it should not be used:
PANCREASE® MT 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:
Each capsule of enteric-coated porcine pancreatic enzyme concentrate microtablets contains:

PANCREASE® MT 2	Lipase	2,600 USP Units
	Amylase	10,850 USP Units
	Protease	6,200 USP Units
PANCREASE® MT 4	Lipase	4,200 USP Units
	Amylase	17,500 USP Units
	Protease	10,000 USP Units
PANCREASE® MT 10	Lipase	10,500 USP Units
	Amylase	43,750 USP Units
	Protease	25,000 USP Units
PANCREASE® MT 16	Lipase	16,800 USP Units
	Amylase	70,000 USP Units
	Protease	40,000 USP Units
PANCREASE® MT 20	Lipase	21,000 USP Units
	Amylase	61,000 USP Units
	Protease	37,000 USP Units

What the nonmedicinal ingredients are:
colloidal anhydrous silica, crospovidone, magnesium stearate, methacrylic acid ethyl acrylate copolymer, microcrystalline cellulose, montan glycol wax, simethicone emulsion, talc, and triethyl citrate. The capsule shell contains hypromellose, titanium dioxide and iron oxide (except for PANCREASE MT 20).

What dosage forms it comes in:
PANCREASE® MT 2 Capsules
PANCREASE® MT 4 Capsules
PANCREASE® MT 10 Capsules
PANCREASE® MT 16 Capsules
PANCREASE® MT 20 Capsules

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

Pancreatic enzyme products, including PANCREASE® MT, have been associated with strictures of the ileo-caecum and large intestine if given at high doses chronically to patients with cystic fibrosis.

PANCREASE® MT 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, so the response of the patient to the estimated dose must be monitored and adjusted as necessary.

BEFORE you use PANCREASE® MT 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 high blood uric acid (hyperuricemia)
- have trouble swallowing capsules
- have any other medical condition
- are pregnant or plan to become pregnant. It is not known if PANCREASE® MT will harm your unborn baby
- are breast-feeding or plan to breast-feed. It is not known if PANCREASE® MT passes into your breast milk. You and your doctor should decide if you will take PANCREASE® MT or breast-feed.

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

PROPER USE OF THIS MEDICATION

PANCREASE® MT capsules and capsule contents should not be **crushed or chewed**. Capsules should be swallowed whole. If there is a problem with taking capsules whole (younger children may sometimes have a problem swallowing the capsules) the capsules may be opened up and the microtablets mixed with soft food which does not require chewing e.g., applesauce, dessert gelatin, etc., but not milk, ice cream, other dairy products or custard because the pH is too high. If you sprinkle PANCREASE® MT on food, give the PANCREASE® MT and food mixture to your child right away. Do not store PANCREASE® MT that is mixed with food.

Your doctor will do special tests periodically and, if necessary, will adjust the number of capsules you or your child take. **Do not change the number of capsules unless your doctor tells you to. Taking too many capsules over a long period of time may lead to complications.**

You should always drink plenty of fluids to maintain your body's fluid balance.

Usual dose
Adults and Children:
Because PANCREASE® MT acts as a digestant, the capsules should be taken with, and only with, meals and snacks. Your doctor will tell you how many capsules to take with each meal and with snacks. The doctor may instruct you to start with a small number of capsules and gradually increase the number until the best effect is achieved. **Follow your doctor's instructions carefully.** The number of capsules you should take is calculated according to age, weight and the results of special tests. Usually, a certain number of capsules are taken with each meal and half that number are taken with each snack. The total number of capsules per day usually reflects 3 meals and 2 snacks per day.

Infants < 12 months:
Give PANCREASE® MT right before each feeding of formula or breast milk. Do not mix PANCREASE® MT capsule contents directly into formula or breast milk. Do not store PANCREASE® MT that is mixed with food. **Follow your doctor's instructions carefully.**

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.

Missed Dose:
If you forget to take PANCREASE® MT, call your healthcare provider or wait until your next meal and take your usual number of capsules. Take your next dose at your usual time. **Do not make up for missed doses.**

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

The most common adverse reactions are abdominal discomfort, constipation and dermatitis. Other gastrointestinal reactions are less common and include abnormal stool and diarrhea. Nausea and vomiting have been reported, but are not common. With high doses, perianal irritation and inflammation have been reported.

Allergic or hypersensitivity reactions of the skin have been reported.
Increase in blood uric acid levels. This may cause worsening of swollen, painful joints (gout) caused by an increase in your blood uric acid levels.

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

Symptom / effect		Talk with your doctor		Stop taking drug and call your doctor immediately
		Only if severe	In all cases	
Very rare	abdominal pain, bloating, nausea, vomiting, diarrhea and/or constipation	✓		✓
Rare	Allergic reactions : • trouble breathing • skin rash • swollen lips	✓		✓

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

HOW TO STORE IT

You should keep the capsules in the bottle with the lid tightly closed. Store the bottle in a dry place with a temperature of 10ºC-25ºC (room temperature). Do not refrigerate.

All PANCREASE® MT bottles contain a desiccant canister. DO NOT eat or throw away the canister (desiccant) in your medicine bottle. This packet will protect your medicine from moisture.

Keep out of the sight and reach of children.

If you have any questions that have not been answered in this leaflet, please consult your doctor, pharmacist or other health care professional.

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.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting**
- **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 1908C
    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.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting

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

For questions, concerns, or the full product monograph go to:
www.vivuspharma.ca
or contact the manufacturer, VIVUS, Inc., at:
1-888-998-4887.

This leaflet was prepared by
VIVUS, Inc.
Campbell, California, USA 95008

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