

**PANCREASE®**  
 brand of  
**PANCRELIPASE**  
 ENTERIC COATED  
 MICROSPHERES  
 Capsules

**Prescribing Information**

**DESCRIPTION**

PANCREASE® (pancrelipase) Capsules are a pancreatic enzyme supplement for oral administration. Pancrelipase, the active ingredient in PANCREASE Capsules, is a natural product harvested by extraction from the pancreas of the hog. Pancrelipase powder is a slightly brown amorphous powder with a faint characteristic odor. It is partly soluble in water and practically insoluble in alcohol or ether.

PANCREASE Capsules contain enteric coated microspheres of porcine pancreatic enzyme concentrate in the following theoretical quantities:

Lipase	4,500 U.S.P. Units
Amylase	20,000 U.S.P. Units
Protease	25,000 U.S.P. Units

Inactive ingredients are povidone, sodium starch glycolate, sugar (sucrose) spheres, cellulose acetate phthalate, diethyl phthalate, talc, corn starch, titanium dioxide, gelatin, and other trace ingredients.

**PRECLINICAL**

Studies in a small number of rats administered indomethacin or ibuprofen and pancrelipase enzymes concomitantly revealed intestinal and liver lesions. The clinical significance of these findings is not known.

**CLINICAL PHARMACOLOGY**

The enteric-coated microspheres contained in PANCREASE Capsules resist gastric inactivation and deliver enzymes into the duodenum. The enzymes in PANCREASE act locally in the gastrointestinal tract. The enzymes are present in the form of pH-sensitive enteric-coated microspheres of less than 3 mm in diameter which are filled into gelatin capsules. The microspheres, which are released from the capsule into the stomach, are enteric coated to resist inactivation at low pH. Once released the microspheres are distributed into the stomach and pass into the duodenum where, when the pH reaches approximately 5.5, the enteric coating begins to dissolve and the release of the enzymes is initiated. The enzymes catalyze the hydrolysis of fats into glycerol and fatty acids, protein into proteoses and derived substances, and starch into dextrins and sugars. Duodenal availability studies in adults indicate that following oral administration of PANCREASE to adults, measurable levels of enzymes are present in the duodenum. Once they have accomplished their digestive function the enzymes may be digested in the intestine. The constituents may be partially absorbed and subsequently excreted in the urine. Any undigested enzymes are excreted in the feces.

**INDICATIONS AND USAGE**

PANCREASE is indicated for the treatment of steatorrhea secondary to pancreatic insufficiency such as cystic fibrosis or chronic alcoholic pancreatitis.

**CONTRAINDICATIONS**

PANCREASE Capsules are contraindicated in patients known to be hypersensitive to pork protein or any other component of this product.

**WARNINGS**

Cases of fibrotic strictures in the colon have been reported primarily in cystic fibrosis patients with the use of enzyme supplements, generally at dosages above the recommended range. Some cases required surgery including resection of the bowel. If symptoms suggestive of gastrointestinal obstruction occur, the possibility of bowel strictures should be considered.

Any change in pancreatic enzyme replacement therapy (e.g., dose or brand of medication) should be made cautiously and only under medical supervision. It is recommended that therapy be initiated at a low dose, followed by titration to an effective dose. The titration schedule should be guided by measured changes in 3-day fecal fat excretion. (See **DOSAGE AND ADMINISTRATION**.)

**PRECAUTIONS**

**General**

TO PROTECT THE ENTERIC COATING, MICROSPHERES SHOULD NOT BE CRUSHED OR CHEWED. Intact capsules should be swallowed with liquids at mealtime. If an intact capsule can not be swallowed, it may be opened and the contents taken with small amounts of food that do not require chewing. (See **DOSAGE AND ADMINISTRATION**.)

**Information for Patients**

Patients should be advised that:

- PANCREASE Capsules must not be crushed or chewed;
- intact capsules should be swallowed with liquid at mealtimes;
- the microspheres from opened capsules should be swallowed immediately and not be retained in the mouth;
- doses should only be taken with meals or snacks;
- fluids should be consumed liberally while dosing with PANCREASE;
- any change in pancreatic enzyme replacement therapy (e.g., dose or brand of medication) should be made only under medical supervision.

**Pregnancy: Teratogenic Effects**

**Pregnancy Category B**

Reproduction studies have been conducted in rats and rabbits at doses 0.44 times and 0.35 times the maximum daily human dose, respectively, and have revealed no evidence of impaired fertility or harm to the fetus due to PANCREASE. No fertility or peri-/postnatal studies have been performed in animals. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

**Nursing Mothers**

Pancreatic enzymes act locally in the gastrointestinal tract and are not likely to be systemically absorbed. Some of the constituent amino and nucleic acids are likely to be absorbed along with dietary proteins. The possibility of the protein constituents appearing in the breast milk can not be excluded.

**Pediatric Use**

Colonic strictures, particularly in children with cystic fibrosis, have been associated with doses generally above the recommended dosing range. (See **WARNINGS**.) Patients currently receiving doses >2,500 lipase units/kg/meal or 4,000 lipase units/gm fat/day 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.

**Geriatric Use**

Studies on the relationship of age to the effects of pancrelipase have not been conducted. However, geriatric-specific problems that would limit the usefulness of this medication in the elderly are not expected.

**ADVERSE REACTIONS**

Clinical evidence indicates that PANCREASE Capsules are well-tolerated.

The most frequently reported adverse events resulting from the post-marketing experience with PANCREASE were gastrointestinal and include diarrhea, abdominal pain, intestinal obstruction, vomiting, flatulence, nausea, constipation, melena, and perianal irritation. Frequently reported adverse events in other body systems included weight decrease and pain. Hyperuricemia and hyperuricosuria have been reported with the use of pancrelipase products, primarily with non-enteric coated formulations. Cases of fibrosing colonopathy have been reported primarily in cystic fibrosis patients. (See **WARNINGS**.)

**OVERDOSAGE**

There have been no reports of acute overdosage.

**DOSAGE AND ADMINISTRATION**

**General**

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

Dosage should be individualized and determined by the degree of steatorrhea and the fat content of the diet. Therapy should be initiated at the lowest possible dose and gradually increased until the desired control of steatorrhea is obtained. Dosage should be adjusted based on 3-day fecal fat studies.

PANCREASE Capsules should only be taken with meals or snacks.

It is important to ensure that patients ingest a liberal amount of liquids to maintain adequate hydration while dosing with PANCREASE.

Whenever possible, PANCREASE Capsules should be swallowed intact with generous amounts of liquid. However, if swallowing of capsules is difficult, they may be opened and the microspheres sprinkled onto a small quantity of soft food on a teaspoon or tablespoon and ingested immediately. Foods which do not require chewing and have a pH lower than 7.3 are recommended. Examples of such foods are apricot, banana and sweet potato baby foods, applesauce, instant pudding and gelatin snacks. Contact of the microspheres 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 and destroy enzyme activity.

To avoid irritation of the mouth, lips, and tongue, opened PANCREASE Capsules should be swallowed immediately before regular feedings or meals to minimize the likelihood that the microspheres are retained in the mouth. Proteolytic enzymes present in pancrelipase, when retained in the mouth, may begin to digest the mucous membranes and cause ulcerations.

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

**Infants: (up to 12 months)**

**Fat-consumption scheme**

2,000-4,000 U.S.P. 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 infant 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.

**Children and Older**

**Weight-based scheme**

- < 4 yrs: Begin with 1,000 U.S.P. lipase units/kg/meal to a maximum of 2,500 lipase units/kg/meal.
- > 4 yrs: Begin with 400 U.S.P. lipase units/kg/meal to a maximum of 2,500 lipase units/kg/meal.

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

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

Colonic strictures, particularly in children with cystic fibrosis, have been associated with doses generally above the recommended dosing range. (See **WARNINGS**.) Patients currently receiving doses >2,500 lipase units/kg/meal or 4,000 lipase units/gm fat/day 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.

**HOW SUPPLIED**

PANCREASE (pancrelipase) Capsules are supplied as white body, clear cap, dye-free capsules. PANCREASE Capsules are imprinted with "McNEIL" and "Pancrease" and are packaged in bottles of:

- 100-(NDC 0045-0095-60)
- 250-(NDC 0045-0095-69)

**Storage**

PANCREASE Capsules should be stored in a dry place below 25° C (77° F) in well-closed containers. Do not refrigerate.

Keep out of reach of children.

Rx only.

Manufactured by:  
 Shire US Manufacturing, Inc.  
 Owings Mills, Maryland 21117

Distributed by:

ORTHO-McNEIL PHARMACEUTICAL, INC.

Raritan, New Jersey 08869

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