

Available through both



Pancrelipase capsules are contraindicated in patients known to be hypersensitive to pork protein. Pancrelipase capsules are contraindicated in patients with acute pancreatitis or with acute exacerbations of chronic pancreatic diseases.

This product and any claims have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.



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**References:** 1. Yasoo Health, Inc. Receives Nearly \$1 Million to Develop Novel Nutritional Formulation [press release]. PRNewswire; Feb. 7, 2006. Available at: <http://www.yasoo.com/press.htm>. 2. Cystic Fibrosis Foundation. Living with Cystic Fibrosis: staying healthy. Available at: <http://www.cff.org/LivingWithCF/StayingHealthy/>. Accessed November 12, 2006. 3. AquADEKs™ Pediatric Liquid Product Insert, AquADEKs™ Softgel Product Insert. 4. Papas, K et al. Treatment of Cystic Fibrosis patients with an antioxidant solution: a pilot study. The Nineteenth Annual North American Cystic Fibrosis Conference. S 28, 2005. 5. ULTRASE®/ULTRASE® MT (pancrelipase) Capsules Prescribing Information. 6. Feranchak, A.P. et al. Prospective, long-term study of fat-soluble vitamin status in children with cystic fibrosis identified by newborn screen. *J Pediatr*, 1999. 135(5): p. 601-10. 7. Renner S. et al. Effects of beta-carotene supplementation for six months on clinical and laboratory parameters in patients with cystic fibrosis. *Thorax*, 2001. 56(1): p. 48-52. 8. ADEKs® Tablets Product Information, ADEKs® Liquid Product Information. 9. Borowitz D, Baker RD, Stallings V. Consensus report on nutrition for pediatric patients with cystic fibrosis. *J Pediatr Gastroenterol*. 2002;35:246-259. 10. [http://www.sourcecf.com/pdf/vitamin\\_comparison\\_pocket\\_guide.pdf](http://www.sourcecf.com/pdf/vitamin_comparison_pocket_guide.pdf) 11. Halliwell B, Cross CE. Oxygen-derived species: their relation to human disease and environmental stress. *Environmental Health Perspectives*, 1994. 102 (suppl. 10): p. 5-12. Available at: <http://www.pubmed-central.nih.gov/pagerender.fcgi?artid=1566996&pageindex=2#page>. Accessed November 13, 2006. 12. Wood, L.G. et al. Improved antioxidant and fatty acid status of patients with cystic fibrosis after antioxidant supplementation is linked to improved lung function. *Am J Clin Nutr*, 2003. 77(1): p. 150-9.

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AQ001-1106

# Overcoming Malabsorption

## A Guide to Improving Nutritional Status with Vitamin Supplements



*A guide for Cystic Fibrosis (CF) patients and their families brought to you by Axcan Pharma®, provider of AquADEKs™ nutritional supplements*



# Introduction

We are pleased to provide important patient information, which is designed to educate patients about nutrition, malabsorption, and the importance of proper vitamin supplementation.

According to the Cystic Fibrosis Foundation, optimal nutrition remains one of the best options CF patients have to slow down the progression of their disease, and vitamins that are better absorbed could be more effective.<sup>1,2</sup>

AquADEKs™ aims to advance the nutritional standard of care for CF patients by providing optimum absorption of fat-soluble vitamins and nutrients.<sup>3,4</sup> Axcan Pharma® is committed to the continued effort to meet the therapeutic needs of the CF community, and we hope this brochure can help you to better understand the importance of nutritional therapy.

**AQUADEKs™**

# Malabsorption and Cystic Fibrosis

In patients with Cystic Fibrosis, many of the pancreatic enzymes needed to break down and absorb fats in the intestine are absent, causing a condition known in the medical community as “malabsorption.”

Malabsorption is the inadequate absorption of nutrients from the intestinal tract. It is the result of an underlying problem that causes the digestive process to stall. Partially digested particles pass through the gastrointestinal system without supplying important nutrients to the bloodstream.



# Symptoms

It is important to talk with your healthcare team if you have any combination of the symptoms below. They could be a sign of malabsorption, which if left untreated can seriously compromise your nutritional status.

- Diarrhea and/or steatorrhea (pale, fatty/oily, soft, bulky stools)
- Abdominal cramps
- Fluid retention
- Weakness
- Weight loss or the inability to gain weight

**AQUADEKs™**

*For optimum absorption*

# Diagnosis & Treatment

To confirm malabsorption, your doctor may order a test called a stool fat analysis. This noninvasive, reliable test is used to detect large amounts of fat in the stool, which may indicate malabsorption. Your doctor may also order blood tests to identify vitamin and mineral deficiencies.

When pancreatic insufficiency is thought to be a contributing factor in malabsorption, pancreatic enzymes like ULTRASE® and ULTRASE® MT (pancrelipase) may be prescribed to deliver bioactive enzymes to the site of digestion and provide relief from symptoms.<sup>5</sup>

There are also steps you can take to enhance your body's absorption of essential vitamins and nutrients, like taking the right vitamin supplement. Studies showed that many CF patients have lower than normal blood levels of important "fat-soluble" vitamins and antioxidants.<sup>6,7</sup> One vitamin supplement designed especially for patients with CF is AquADEKs™.

# AquADEKs™ Supplements: Meeting the Unique Needs of CF Patients<sup>3,4</sup>

AquADEKs™ is a new innovative vitamin formulation that addresses the problem of nutrient absorption in CF patients. It is a product provided by Axcan Pharma® that builds on the popular ADEKs® supplements, long used by CF patients to improve nutritional status. AquADEKs™ was developed by Yasoo Health Inc., in partnership with the Cystic Fibrosis Foundation.

## **What Makes AquADEKs™ Unique?**

AquADEKs™ is a highly absorbable, antioxidant-rich nutritional supplement that is specially formulated to overcome the malabsorption of fat-soluble vitamins. Compared with ADEKs® and Source CF®, AquADEKs™ contains higher amounts of Vitamins D\* and K in water-soluble form to meet current recommendations for supplementation in CF patients.<sup>3,8-10</sup> It also contains important antioxidants such as coenzyme Q<sub>10</sub>, beta-carotene, and gamma-tocopherol.<sup>3,4</sup>

Research suggests that improved nutritional and antioxidant status may decrease

\* AquADEKs™ Softgels only

oxidative stress and improve clinical outcomes in Cystic Fibrosis.<sup>7</sup>

Oxidative stress is a term that refers to cell damage caused by free radicals (highly reactive chemicals that contain oxygen and are often produced through normal chemical reactions in the body). Antioxidants destroy free radicals.<sup>11</sup> CF patients with malnutrition have decreased antioxidant status, which means they have a decreased ability to fight free radicals and therefore more oxidative stress. Oxidative stress has been associated with decreased lung function in CF patients.<sup>7,12</sup>

## **What Dosage Forms are Available?**

Available without a prescription in liquid or softgels, the AquADEKs™ all-in-one formulation provides the vitamins and nutrients a CF patient needs, in a unique water-soluble form.<sup>3</sup>

***Ask your CF team if AquADEKs™ is right for you.***

**AquADEKs™ Softgels**  
(aque-dex)  
Antioxidant Enriched Multivitamin  
and Mineral Supplement

**KEY FACTS**

- Formulated to meet Cystic Fibrosis nutritional guidelines and the latest scientific evidence
- Safely and effectively increases plasma levels of fat-soluble nutrients and antioxidants
- Contains important antioxidants which reduce oxidative stress in the body
- Enhanced vitamin D and K content for improved bone health

**BRIEF SUMMARY OF PRODUCT INFORMATION**

AquADEKs™ Softgels are a complete nutritional supplement specifically designed to meet the needs of cystic fibrosis patients and those who have difficulty absorbing fat-soluble vitamins and nutrients.\* AquADEKs™ uses microsphere technology to enhance the absorption of this antioxidant rich multivitamin and mineral supplement.

Formulated to meet or exceed the consensus nutritional guidelines for Cystic Fibrosis and incorporating the latest scientific evidence, AquADEKs™ Softgels contain important antioxidants, such as coenzyme Q<sub>10</sub>, beta-carotene, and gamma-tocopherol. Emerging research indicates that CF patients have lower than normal levels of these antioxidants which can lead to increased oxidative damage. This product also contains increased vitamin D and K levels to support improved bone health. In addition, AquADEKs™ Softgels contain selenium, which is an essential cofactor for the body's own antioxidant system, and zinc, which has been shown to be deficient in CF patients.



AquADEKs™ forms micellar-like spheres that provide fat-soluble vitamins in a form that can be readily absorbed even when there is impaired digestion or impaired liver function.

**Usage Information**

AquADEKs™ Softgels may be used to supplement levels of the fat-soluble vitamins A, D, E, and K and other essential antioxidants and nutrients in children and adults who do not absorb sufficient amounts from their diets\*.

*\*This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.*

**Pharmacology**

Deficiencies of one or more fat-soluble vitamins may occur in individuals whose diets are deficient in these vitamins or who for any number of reasons have difficulty in absorbing fats from their diets. Any condition that diminishes the function of the pancreas, the liver, or the digestive system, can cause malabsorption. Fat-soluble vitamins can only be absorbed after they are incorporated into micelles through the actions of the body's bile and pancreatic secretions. These micelles are spherical particles that have lipophilic (fat-loving) interiors encapsulated by hydrophilic (water-loving) exteriors that facilitate absorption of fat-soluble vitamins in the body.

**SAFETY**

**Safely sealed for your protection. Do not use if seal is broken or missing. Keep this and all medications out of reach of children.**

Caregivers should use caution when administering to children or adults who may have difficulty swallowing softgels.

**CONTRAINDICATIONS**

**Do not take this product if you have a known sensitivity or allergy to any of the components.**

**Vitamin K interferes with the actions of anticoagulant therapy; persons taking anticoagulant medications should consult their physician before taking AquADEKs™.**

**DOSAGE AND ADMINISTRATION**

Recommended dosage:  
Age 4 – 10 years ..... 1 softgel daily  
Over age 10 ..... 2 softgels daily  
or as directed by a physician.

Supplement Facts	Amount per softgel	% DV
Serving size: 1 softgel		
Servings/container: 60		
Calories	5	
Total Vitamin A (as 92 % beta-carotene and 8 % palmitate)	18,167 IU	606
Vitamin C (sodium ascorbate)	75 mg	83
Vitamin D3 (cholecalciferol)	800 IU	400
Vitamin E (d-alpha-tocopherol)	150 IU	670
Vitamin E (mixed tocopherols)	80 mg	*
Vitamin K1 (phytonadione)	700 mcg	583
Vitamin B1 (thiamin mononitrate)	1.5 mg	125
Vitamin B2 (riboflavin)	1.7 mg	131
Niacin (niacinamide)	20 mg	125
Vitamin B6 (pyridoxine HCl)	1.9 mg	146
Folic Acid	200 mcg	50
Vitamin B12 (cyanocobalamin)	12 mcg	500
Biotin	100 mcg	333
Pantothenic acid (calcium d-pantothenate)	12 mg	240
Zinc (sulfate)	10 mg	91
Selenium (selenomethionine)	75 mcg	136
Beta-carotene	10 mg	*
Coenzyme Q <sub>10</sub>	10 mg	*

**\*Daily Value not established for these nutrients**

% Daily Values are based on the recommended Dietary Reference Intakes (DRIs) determined by the Food and Nutrition Board, Institute of Medicine, National Academies in 2004.

Other ingredients: medium chain triglycerides, d-alpha-tocopheryl polyethylene glycol-1000 succinate (TPGS), gelatin, glycerin, caramel color.

AquADEKs™ softgels are free of artificial colors and flavors.

**HOW SUPPLIED**

60 count bottles containing dark-brown, oblong softgels.

**STORAGE INSTRUCTIONS**

Store in a cool, dry place away from direct light.

UPC # 3 58914 01106 4

Manufactured in Canada for:



2109 West Market Street, Suite 122  
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www.yasoo.com

AquADEKs™, an ADEKs® brand product.  
Rev 08/06

**AquADEKs™ Pediatric Liquid**  
(aqua-dex)  
Antioxidant Enriched  
Multivitamin and Mineral Supplement

**KEY FACTS**

- Formulated to meet Cystic Fibrosis nutritional guidelines and the latest scientific evidence
- Safely and effectively increases plasma levels of fat-soluble nutrients and antioxidants
- Contains important antioxidants which reduce oxidative stress in the body
- Enhanced vitamin D and K content for improved bone health
- Great tasting black cherry flavor

**BRIEF SUMMARY OF PRODUCT INFORMATION**

AquADEKs™ Pediatric Liquid is a complete nutritional supplement specifically designed to meet the needs of cystic fibrosis patients and those who have difficulty absorbing fat-soluble vitamins and nutrients.\* AquADEKs™ uses microsphere technology to enhance the absorption of this antioxidant rich multivitamin and mineral supplement.

Formulated to meet or exceed the consensus nutritional guidelines for Cystic Fibrosis and incorporating the latest scientific evidence, AquADEKs™ Pediatric Liquid contains important antioxidants, such as coenzyme Q<sub>10</sub>, beta-carotene, and gamma-tocopherol. Emerging research indicates that CF patients have lower than normal levels of these antioxidants which can lead to increased oxidative damage. This product also contains increased vitamin D and K levels to support improved bone health. In addition, AquADEKs™ Pediatric Liquid contains selenium, which is an essential cofactor for the body's own antioxidant system, and zinc, which has been shown to be deficient in CF patients.



AquADEKs™ Pediatric Liquid has been clinically tested in CF patients with malabsorption.

AquADEKs™ forms micellar-like spheres that provide fat-soluble vitamins in a form that can be readily absorbed even when there is impaired digestion or impaired liver function.

*\*This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.*

**Usage Information**

AquADEKs™ Pediatric Liquid may be used to supplement levels of the fat-soluble vitamins A, D, E, and K and other essential antioxidants and nutrients in infants and children who do not absorb sufficient amounts from their diets.

**Pharmacology**

Deficiencies of one or more fat-soluble vitamins may occur in individuals whose diets are deficient in these vitamins or who for any number of reasons have difficulty in absorbing fats from their diets. Any condition that diminishes the function of the pancreas, the liver, or the digestive system, can cause malabsorption. Fat-soluble vitamins are absorbed after they are incorporated into micelles through the actions of the body's bile and pancreatic secretions. These micelles are spherical particles that have lipophilic (fat-loving) interiors encapsulated by hydrophilic (water-loving) exteriors that facilitate absorption of fat-soluble vitamins in the body.

**SAFETY**

**Safely sealed for your protection. Do not use if seal is broken or missing. Keep this and all medications out of reach of children.**

**CONTRAINDICATIONS**

**Do not take this product if you have a known sensitivity or allergy to any of the components.**

**Vitamin K interferes with the actions of anticoagulant therapy; persons taking anticoagulant medications should consult their physician before taking AquADEKs™ Pediatric Liquid.**

**DOSAGE AND ADMINISTRATION**

Recommended dosage:  
Age 0-12 months ..... 1 ml daily  
Age 1-3 years ..... 2 ml daily  
or as directed by a physician.  
**Shake well before each use.**

Supplement Facts	% Daily Values for Children			
Serving Size: 1 ml	Amount Per ml	0-6 months	7-12 months	1-3 years
Servings per container: 60				
Calories	0			
Total Vitamin A (as 87% beta-carotene and 13% palmitate)	57515 IU	432	345	576
Vitamin C	45 mg	113	90	300
Vitamin D3 (cholecalciferol)	400 IU	200	200	200
Vitamin E (d-alpha-tocopherol)	50 IU	839	671	559
Vitamin E (mixed tocopherols)	15 mg	*	*	*
Vitamin K1 (phytonadione)	400 mcg	20,000	16,000	1,333
Vitamin B1 (thiamin HCl)	0.60 mg	300	200	120
Vitamin B2 (riboflavin 5'-phosphate)	0.6 mg	200	150	120
Niacin (niacinamide)	6 mg	300	150	100
Vitamin B6 (pyridoxine HCl)	0.60 mg	600	200	120
Biotin	15 mcg	300	250	188
Pantothenic acid (calcium d-pantothenate)	3 mg	176	167	150
Zinc (gluconate)	5 mg	250	167	167
Selenium (selenomethionine)	10 mcg	67	50	50
Beta-carotene	3 mg	*	*	*
Coenzyme Q <sub>10</sub>	2 mg	*	*	*

**\*Daily Value not established for these nutrients**

% Daily Values are based on the recommended Dietary Reference Intakes (DRIs) determined by the Food and Nutrition Board, Institute of Medicine, National Academies in 2004.

Other ingredients: purified water, d-alpha-tocopheryl polyethylene glycol-1000 succinate (TPGS), sucralose, natural flavors, potassium sorbate, sodium benzoate, EDTA, BHA, BHT, Vitamin B12 (cyanocobalamin).

Free of artificial colors and flavors

**HOW SUPPLIED**

60 ml bottle  
1 ml graduated dropper in cellophane wrap  
**STORAGE INSTRUCTIONS**  
Store in a cool place away from direct light.  
Shake well before each use.

UPC # 3 58914 21460 1

AquADEKs™, an ADEKs® brand product.

REV. 07/06

Manufactured for:



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www.yasoo.com

## ULTRASE®

(‘ul-trás)  
(pancrelipase) Capsules  
Enteric-Coated Microspheres

### Prescribing Information

#### DESCRIPTION:

ULTRASE® (pancrelipase) Capsules are orally administered and contain 250 mg of enteric-coated microspheres of porcine pancreatic enzyme concentrate, predominantly pancreatic lipase, amylase, and protease.

#### Each ULTRASE® Capsule contains:

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

Inactive ingredients: povidone, talc, sugar, methacrylic acid copolymer (Type C), triethyl citrate, simethicone emulsion.

#### CLINICAL PHARMACOLOGY:

ULTRASE® (pancrelipase) Capsules are designed to prevent inactivation by gastric acid thereby resulting in the delivery of high levels of biologically active enzymes into the duodenum. The enzymes catalyze the hydrolysis of fats into glycerol and fatty acids, starch into dextrins and sugars, and protein into proteoses and derived substances.

#### INDICATIONS AND USAGE:

ULTRASE® (pancrelipase) Capsules are indicated for patients with partial or complete exocrine pancreatic insufficiency caused by:

- Cystic fibrosis (CF)
- Chronic pancreatitis due to alcohol use or other causes
- Surgery (pancreatico-duodenectomy or Whipple’s procedure, with or without Wirsung duct injection, total pancreatectomy)
- Obstruction (pancreatic and biliary duct lithiasis, pancreatic and duodenal neoplasms, ductal stenosis)
- Other pancreatic disease (hereditary, post traumatic and allograft pancreatitis, hemochromatosis, Shwachman’s Syndrome, lipomatosis, hyperparathyroidism)
- Poor mixing (Billroth II gastrectomy, other types of gastric bypass surgery, gastrinoma)

Pancrelipase capsules are effective in controlling steatorrhea.<sup>1-9</sup>

#### CONTRAINDICATIONS:

Pancrelipase capsules are contraindicated in patients known to be hypersensitive to pork protein. Pancrelipase capsules are contraindicated in patients with acute pancreatitis or with acute exacerbations of chronic pancreatic diseases.

#### WARNINGS:

Should hypersensitivity occur, discontinue medication and treat symptomatically.

#### PRECAUTIONS:

*General*  
TO PROTECT ENTERIC COATING, MICROSPHERES MUST NOT BE CRUSHED OR CHEWED. Where swallowing of capsules is difficult, they may be opened and the microspheres added to a small quantity of a soft food (e.g., applesauce, gelatin, etc.) that does not require chewing, and swallowed immediately. Contact of the microsphere with foods having a pH greater than 5.5 can dissolve the protective enteric shell.

#### *Carcinogenesis, Mutagenesis, Impairment of Fertility*

Long-term studies in animals have not been performed to evaluate carcinogenic potential. Methacrylic acid, a minor component of the methacrylic acid copolymer enteric-coating contained in ULTRASE® (pancrelipase) Capsules, has been reported to act as a teratogen in rat embryo cultures. However, the copolymer enteric-coating of ULTRASE® (pancrelipase) Capsules was not mutagenic by the Ames test, and it did not produce chromosome damage in a test for unscheduled DNA synthesis in rat hepatocytes.

#### *Pregnancy: Category C.*

Animal reproduction studies have not been conducted with ULTRASE® (pancrelipase) Capsules. It is not known whether ULTRASE® (pancrelipase) Capsules can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. ULTRASE® (pancrelipase) Capsules should be given to a pregnant woman only if the potential benefit outweighs the potential risk to the fetus.

#### *Nursing Mothers*

It is not known whether ULTRASE® (pancrelipase) is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when ULTRASE® (pancrelipase) Capsules are administered to a nursing mother.

#### ADVERSE REACTIONS:

The most frequently reported adverse reactions to products containing pancrelipase are gastrointestinal in nature. Less frequently, allergic-type reactions have also been observed. Extremely high doses of exogenous pancreatic enzymes have been associated with hyperuricosuria and hyperuricemia when the preparations given were pancrelipase in powdered or capsule form, or pancreatin in tablet form.

Colonic strictures have been reported in cystic fibrosis patients treated with both high- and lower-strength enzyme supplements.<sup>10</sup> A causal relationship has not been established. The possibility of bowel stricture should be considered if symptoms suggestive of gastrointestinal obstruction occur. Since impaired fluid secretion may be a factor in the development of intestinal obstruction, care should be taken to maintain adequate hydration, particularly in warm weather.<sup>11</sup>

“Fibrosing colonopathy” is a term used to describe a condition seen in patients with CF who have taken high amounts of pancreatic enzyme supplements (>6,000 lipase U/kg/meal). At its most advanced, this condition leads to colonic strictures.

1. In whom should one consider the diagnosis of fibrosing colonopathy?
    - a. Patients with cystic fibrosis who have evidence of partial or complete obstruction, bloody diarrhea or chylous ascites.
    - b. Patients who have two of the following three symptoms:
      - abdominal pain
      - ongoing diarrhea
      - poor weight gain
- ESPECIALLY if they have:
- taken >6,000 lipase U/kg/meal
  - age less than twelve years
  - history of meconium ileus
  - prior intestinal surgery
  - history of recurrent DIOS
  - “inflammatory bowel disease”<sup>12</sup>

#### DOSAGE AND ADMINISTRATION:

The enzymatic activity of ULTRASE® (pancrelipase) Capsules is expressed in U.S.P. units. The smallest effective dose should be used. Dosage should be adjusted according to the severity of the exocrine pancreatic insufficiency. Begin therapy with one or two capsules with meals or snacks and adjust dosage according to symptoms. The number of capsules or capsule strength given with meals and/or snacks should be estimated by assessing which dose minimizes steatorrhea and maintains good nutritional status. Dosages should be adjusted according to the response of the patient. Where swallowing of capsules is difficult, they may be opened and the microspheres added to a small quantity of a soft food (e.g., applesauce, gelatin, etc.) that does not require chewing, and swallowed immediately. It is recommended that the total dose of pancrelipase being ingested for a meal or snack be dispersed equally (with fluids) before, during, and after the meal or snack.

#### *SUGGESTIONS FOR THE USE OF PANCREATIC ENZYMES IN CYSTIC FIBROSIS*<sup>12</sup>

1. Patients should be receiving optimal diet for age and clinical status, recognizing that those with failure to thrive or malnutrition require additional calories and other nutrients for catch-up growth.
2. Nutrition assessment should be a part of routine clinical evaluations.
3. Initial dosing of pancreatic enzyme supplements should begin with 500 lipase U/kg/meal using enteric-coated microsphere products.
4. Patients should be reassessed 2-4 weeks after initiation of therapy. The following items should be assessed:
  - Clinical status, e.g., abdominal symptoms and exam;
  - Nutritional intake and growth (height, weight, head circumference);
  - Character of stools - greasy, oily (for information, not for decision making);
  - Quantitative 72-hour fecal fat when indicated but not less than annually (perform on a normal diet for age);
  - Fat soluble vitamin measures.
5. Corollaries to dosing suggestions:
  - a. Dose may be altered in a stepwise fashion according to the response of the patient (see 4. above).
  - b. Dose approaching 2,000 lipase U/kg/meal would indicate the need for further investigation (see below). Patients presently on higher doses should be reevaluated; either immediately decrease the dose or titrate down to a lower dose range at, or below, 2,000 lipase U/kg/meal. Doses >6,000 lipase U/kg/meal have been associated with colonic strictures.
  - c. Pancreatic supplements mixed with applesauce or other acidic food substances should be administered immediately, not stored.
  - d. Enteric-coated microspheres should not be crushed.
  - e. Enzyme doses (as lipase U/kg/meal) tend to decrease with advancing age.
  - f. Patients should accept only product brands prescribed by their physician.
  - g. Adjustment of dosage is the responsibility of the physician. Patients should be advised not to adjust doses without consulting their physician. Changes in product or dosage may require an adjustment period.
  - h. Complaints transmitted by phone should be investigated thoroughly before dose is adjusted. If indicated, this investigation should include 72-hour fecal fat testing.
  - i. Pancreatic supplements should be stored in a cool, dry place and checked regularly for expiration date.

#### HOW SUPPLIED:

*ULTRASE® (pancrelipase) Capsules*

Gelatin capsules (opaque white and opaque white), imprinted “ULTRASE”. Bottles of 100 (NDC 58914-045-10).

Store at controlled room temperature, between 15°C and 25°C (59°F and 77°F), in a dry place. Do not refrigerate.

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## Rx only

REV. June 2005

Marketed as ULTRASE® by:  
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## ULTRASE® MT

(‘ul-trās)  
**(pancrelipase) Capsules**  
**Enteric-Coated Minitablets**

## Prescribing Information

### DESCRIPTION:

ULTRASE® MT (pancrelipase) Capsules are orally administered capsules containing enteric-coated minitablets of porcine pancreatic enzyme concentrate, predominantly pancreatic lipase, amylase, and protease.

*Each ULTRASE® MT12 Capsule is orally administered and contains 223 mg of enteric-coated minitablets of porcine pancreatic concentrate containing:*

Lipase.....	12,000 U.S.P. Units
Amylase.....	39,000 U.S.P. Units
Protease.....	39,000 U.S.P. Units

*Each ULTRASE® MT18 Capsule is orally administered and contains 333 mg of enteric-coated minitablets of porcine pancreatic concentrate containing:*

Lipase.....	18,000 U.S.P. Units
Amylase.....	58,500 U.S.P. Units
Protease.....	58,500 U.S.P. Units

*Each ULTRASE® MT20 Capsule is orally administered and contains 371 mg of enteric-coated minitablets of porcine pancreatic concentrate containing:*

Lipase.....	20,000 U.S.P. Units
Amylase.....	65,000 U.S.P. Units
Protease.....	65,000 U.S.P. Units

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

### CLINICAL PHARMACOLOGY:

ULTRASE® MT (pancrelipase) Capsules are designed to prevent inactivation by gastric acid thereby resulting in the delivery of high levels of biologically active enzymes into the duodenum. The enzymes catalyze the hydrolysis of fats into glycerol and fatty acids, starch into dextrins and sugars, and protein into proteoses and derived substances.

### INDICATIONS AND USAGE:

ULTRASE® MT (pancrelipase) Capsules are indicated for patients with partial or complete exocrine pancreatic insufficiency caused by:

- Cystic fibrosis (CF)
- Chronic pancreatitis due to alcohol use or other causes
- Surgery (pancreatico-duodenectomy or Whipple's procedure, with or without Wirsung duct injection, total pancreatectomy)
- Obstruction (pancreatic and biliary duct lithiasis, pancreatic and duodenal neoplasms, ductal stenosis)
- Other pancreatic disease (hereditary, post traumatic and allograft pancreatitis, hemochromatosis, Shwachman's Syndrome, lipomatosis, hyperparathyroidism)
- Poor mixing (Billroth II gastrectomy, other types of gastric bypass surgery, gastrinoma)

Pancrelipase capsules are effective in controlling steatorrhea.<sup>1-9</sup>

### CONTRAINDICATIONS:

Pancrelipase capsules are contraindicated in patients known to be hypersensitive to pork protein. Pancrelipase capsules are contraindicated in patients with acute pancreatitis or with acute exacerbations of chronic pancreatic diseases.

### WARNINGS:

Should hypersensitivity occur, discontinue medication and treat symptomatically.

### PRECAUTIONS:

#### General

TO PROTECT ENTERIC COATING, MINITABLETS MUST NOT BE CRUSHED OR CHEWED. Where swallowing of capsules is difficult, they may be opened and the minitablets added to a small quantity of a soft food (e.g., applesauce, gelatin, etc.) that does not require chewing, and swallowed immediately. Contact of the minitabulet with foods having a pH greater than 5.5 can dissolve the protective enteric shell.

#### Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals have not been performed to evaluate carcinogenic potential.

#### Pregnancy: Category C.

Animal reproduction studies have not been conducted with ULTRASE® MT (pancrelipase) Capsules. It is not known whether ULTRASE® MT (pancrelipase) Capsules can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. ULTRASE® MT (pancrelipase) Capsules should be given to a pregnant woman only if the potential benefit outweighs the potential risk to the fetus.

#### Nursing Mothers

It is not known whether ULTRASE® MT (pancrelipase) is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when ULTRASE® MT (pancrelipase) Capsules are administered to a nursing mother.

## ADVERSE REACTIONS:

The most frequently reported adverse reactions to products containing pancrelipase are gastrointestinal in nature. Less frequently, allergic-type reactions have also been observed. Extremely high doses of exogenous pancreatic enzymes have been associated with hyperuricosuria and hyperuricemia when the preparations given were pancrelipase in powdered or capsule form, or pancreatin in tablet form.

In two clinical studies with ULTRASE® MT in 193 patients with cystic fibrosis, the adverse events described were all gastrointestinal in nature and may actually represent symptoms of the underlying disease, such as abdominal pain/cramps (5.7%), diarrhea (3.6%), and greasy stools and flatulence (1.5% each). In a postmarketing trial with another enteric-coated formulation, 160 adverse events occurred in the 15,711 patients (0.97%) evaluated.<sup>10</sup> The most frequent events reported were diarrhea, skin reaction, and abdominal discomfort (0.2% each).

Colonic strictures have been reported in cystic fibrosis patients treated with both high- and lower-strength enzyme supplements.<sup>11</sup> A causal relationship has not been established. The possibility of bowel stricture should be considered if symptoms suggestive of gastrointestinal obstruction occur. Since impaired fluid secretion may be a factor in the development of intestinal obstruction, care should be taken to maintain adequate hydration, particularly in warm weather.<sup>12</sup>

“Fibrosing colonopathy” is a term used to describe a condition seen in patients with CF who have taken high amounts of pancreatic enzyme supplements (>6,000 lipase U/kg/meal). At its most advanced, this condition leads to colonic strictures.

1. In whom should one consider the diagnosis of fibrosing colonopathy?
  - a. Patients with cystic fibrosis who have evidence of partial or complete obstruction, bloody diarrhea or chylous ascites.
  - b. Patients who have two of the following three symptoms:
    - abdominal pain
    - ongoing diarrhea
    - poor weight gain

ESPECIALLY if they have:

  - taken >6,000 lipase U/kg/meal
  - age less than twelve years
  - history of meconium ileus
  - prior intestinal surgery
  - history of recurrent DIOS
  - “inflammatory bowel disease”<sup>13</sup>

## DOSAGE AND ADMINISTRATION:

The enzymatic activity of ULTRASE® MT (pancrelipase) Capsules is expressed in U.S.P. units. The smallest effective dose should be used. Dosage should be adjusted according to the severity of the exocrine pancreatic insufficiency. Begin therapy with one or two capsules with meals or snacks and adjust dosage according to symptoms. The number of capsules or capsule strength given with meals and/or snacks should be estimated by assessing which dose minimizes steatorrhea and maintains good nutritional status. Dosages should be adjusted according to the response of the patient. Where swallowing of capsules is difficult, they may be opened and the minitabets added to a small quantity of a soft food (e.g., applesauce, gelatin, etc.) that does not require chewing, and swallowed immediately. It is recommended that the total dose of pancrelipase being ingested for a meal or snack be dispersed equally (with fluids) before, during, and after the meal or snack.

## SUGGESTIONS FOR THE USE OF PANCREATIC ENZYMES IN CYSTIC FIBROSIS<sup>13</sup>

1. Patients should be receiving optimal diet for age and clinical status, recognizing that those with failure to thrive or malnutrition require additional calories and other nutrients for catch-up growth.
2. Nutrition assessment should be a part of routine clinical evaluations.
3. Initial dosing of pancreatic enzyme supplements should begin with 500 lipase U/kg/meal using enteric-coated minitabets products
4. Patients should be reassessed 2-4 weeks after initiation of therapy. The following items should be assessed:
  - Clinical status, e.g., abdominal symptoms and exam;
  - Nutritional intake and growth (height, weight, head circumference);
  - Character of stools - greasy, oily (for information, not for decision making);
  - Quantitative 72-hour fecal fat when indicated but not less than annually (perform on a normal diet for age);
  - Fat soluble vitamin measures.
5. Corollaries to dosing suggestions:
  - a. Dose may be altered in a stepwise fashion according to the response of the patient (see 4. above).
  - b. Dose approaching 2,000 lipase U/kg/meal would indicate the need for further investigation (see below). Patients presently on higher doses should be reevaluated; either immediately decrease the dose or titrate down to a lower dose range at, or below, 2,000 lipase U/kg/meal. Doses >6,000 lipase U/kg/meal have been associated with colonic strictures.
  - c. Pancreatic supplements mixed with applesauce or other acidic food substances should be administered immediately, not stored.
  - d. Enteric-coated minitabets should not be crushed.
  - e. Enzyme doses (as lipase U/kg/meal) tend to decrease with advancing age.
  - f. Patients should accept only product brands prescribed by their physician.
  - g. Adjustment of dosage is the responsibility of the physician. Patients should be advised not to adjust doses without consulting their physician. Changes in product or dosage may require an adjustment period.
  - h. Complaints transmitted by phone should be investigated thoroughly before dose is adjusted. If indicated, this investigation should include 72-hour fecal fat testing.
  - i. Pancreatic supplements should be stored in a cool, dry place and checked regularly for expiration date.

## HOW SUPPLIED:

**ULTRASE® MT12 (pancrelipase) Capsules**

Gelatin capsules (white and yellow), imprinted “ULTRASE MT12”. Bottles of 100 (NDC 58914-002-10).

**ULTRASE® MT18 (pancrelipase) Capsules**

Gelatin capsules (gray and white), imprinted “ULTRASE MT18”. Bottles of 100 (NDC 58914-018-10).

**ULTRASE® MT20 (pancrelipase) Capsules**

Gelatin capsules (light gray and yellow), imprinted “ULTRASE MT20”. Bottles of 100 (NDC 58914-004-10), and bottles of 500 (NDC 58914-004-50).

Store at controlled room temperature, between 15°C and 25°C (59°F and 77°F), in a dry place. Do not refrigerate.

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Rx only

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**AXCAN SCANDIPHARM INC.**

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www.axcan.com



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