

**CREON® 20**  
**MINIMICROSPHERES®**  
**(Pancrelipase Delayed-release Capsules, USP)**

R<sub>x</sub> only

1  
2 500199 Rev Feb 2006

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4 **PRESCRIBING INFORMATION**

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6 **DESCRIPTION**

7 CREON® 20 Capsules are orally administered and contain pancrelipase (lipase 20,000 USP  
8 Units, protease 75,000 USP Units and amylase 66,400 USP Units per capsule) which is of  
9 porcine pancreatic origin. Each CREON 20 Capsule is filled with 497 mg of delayed-release  
10 MINIMICROSPHERES®.

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12 Inactive ingredients include dibutyl phthalate, dimethicone, hydroxypropylmethylcellulose  
13 phthalate, light mineral oil and polyethylene glycol. The capsule shells contain gelatin, red iron  
14 oxide, titanium dioxide and yellow iron oxide. The capsule imprinting ink contains dimethicone,  
15 2-ethoxyethanol, shellac, soya lecithin, and titanium dioxide.

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17 **CLINICAL PHARMACOLOGY**

18 The pancreatic enzymes in CREON 20 Capsules are enteric-coated to resist gastric destruction or  
19 inactivation. The pancreatic enzymes catalyze the hydrolysis of fats to glycerol and fatty acids,  
20 protein into proteoses and derived substances and starch into dextrans and short chain sugars.

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22 **INDICATIONS**

23 CREON 20 Capsules are indicated for patients with pancreatic exocrine insufficiency as is often  
24 associated with:

- 25 ● cystic fibrosis  
26 ● chronic pancreatitis  
27 ● post-pancreatectomy  
28 ● post-gastrointestinal bypass surgery (e.g., Billroth II gastroenterostomy)  
29 ● ductal obstruction from neoplasm (e.g., of the pancreas or common bile duct)

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31 **CONTRAINDICATIONS**

32 CREON 20 Capsules are contraindicated in the early stages of acute pancreatitis or in patients  
33 who are known to be hypersensitive to pork protein.

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35 **WARNINGS**

36 Should symptoms of hypersensitivity appear, discontinue medication and initiate symptomatic  
37 and supportive therapy if necessary.

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39 Strictures in the ileo-cecal region and/or ascending colon have been reported in cystic fibrosis  
40 patients treated with high doses of high-potency pancreatic enzyme supplements containing

41 20,000 or greater USP units of lipase per capsule. The underlying mechanism is unknown, but  
42 caution should be exercised when doses in excess of 6,000 USP units lipase per kg per meal fail  
43 to resolve symptoms, especially in patients with a history of intestinal complications such as  
44 meconium ileus equivalent, short bowel syndrome, surgery or Crohn's disease. If symptoms  
45 suggestive of gastrointestinal obstruction occur, the possibility of bowel stricture should be  
46 investigated including evaluation of pancreatic enzyme therapy.

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## 48 **PRECAUTIONS**

49 CREON 20 Capsules MINIMICROSPHERES SHOULD NOT BE CRUSHED OR CHEWED or  
50 placed on foods having a pH greater than 5.5. These can dissolve the protective enteric coating  
51 resulting in early release of enzymes, irritation of oral mucosa, and/or loss of enzyme activity.

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### 53 **Information for Patients**

54 CREON 20 Capsules are a pancreatic enzyme product prescribed to promote improved digestion  
55 of foods, especially fat. The prescribed dosage should be taken with each meal and snack or as  
56 directed by the physician. The capsules can be swallowed whole, or the contents poured on soft,  
57 bland food. Care should be taken to avoid chewing or crushing of the capsule contents, which  
58 can result in early release of enzymes, irritation of oral mucosa, and/or loss of enzyme activity.  
59 Patients should maintain adequate fluid intake. The prescribed dose range should not be  
60 exceeded without calling your doctor.

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62 The most common adverse reactions involve the stomach and intestine including diarrhea,  
63 nausea, vomiting, bloating, constipation, stomach cramps or pain. If these symptoms are  
64 persistent, contact your doctor.

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

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

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### 69 **Pregnancy, Category C**

70 Animal reproduction studies have not been conducted with pancrelipase. It is also not known  
71 whether pancrelipase can cause fetal harm when administered to a pregnant woman or can affect  
72 reproduction capacity. CREON 20 Capsules should be given to a pregnant woman only if clearly  
73 needed.

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### 75 **Nursing Mothers**

76 It is not known whether this drug is excreted in human milk. Because many drugs are excreted in  
77 human milk, caution should be exercised when CREON 20 Capsules are administered to a  
78 nursing mother.

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## 80 **ADVERSE REACTIONS**

81 The most frequently reported adverse reactions to pancreatic enzyme-containing products are  
82 gastrointestinal in nature which may include nausea, vomiting, bloating, cramping, constipation  
83 or diarrhea. Less frequently, allergic-type reactions have also been observed. Very high doses of  
84 pancreatin have been associated with hyperuricosuria and hyperuricemia.

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## **DOSAGE AND ADMINISTRATION**

Clinical experience should dictate initial starting dose. Doses should be taken during meals or snacks, not before or after. Do not take without food.

### **Adults and Children Over 6 Years Old**

Usual initial starting dosage is one CREON 20 Capsule per meal or snack.

### **Children Under 6 Years Old**

The exact dosage of CREON 20 Capsules should be selected based on clinical experience for this age group.

For cystic fibrosis patients, typical doses are 1,500 - 3,000 USP lipase units/kg/meal. Dosage should be adjusted according to the severity of the disease, control of steatorrhea and maintenance of good nutritional status. Doses in excess of 6,000 USP lipase units/kg/meal are not recommended.

Dose increases, if required, should occur with careful monitoring of body weight and stool fat content. When changing strengths of pancreatic enzyme products, care should be taken to maintain equivalent lipase units for each divided dosage.

It is important to ensure adequate hydration of patients at all times while taking pancreatic enzymes.

Where swallowing of capsules is difficult, the capsules may be carefully opened and the MINIMICROSPHERES added to a small amount of soft food, with a pH less than 5.5. The soft food should be swallowed immediately without chewing and followed with a glass of water or juice to insure swallowing.

## **HOW SUPPLIED**

CREON 20 MINIMICROSPHERES (Pancrelipase Delayed-release Capsules, USP) are available in a two-piece gelatin capsule (orange opaque top half, natural transparent bottom half) imprinted in white with "SOLVAY" and "1220". Each capsule contains tan-colored delayed-release MINIMICROSPHERES of pancrelipase supplied in bottles of:

100.....NDC 0032-1220-01  
250.....NDC 0032-1220-07

CREON 20 Capsules must be stored at 25 °C (77 °F); excursions permitted to 15°-30°C (59°-86°F). [See USP Controlled Room Temperature.] PROTECT FROM MOISTURE. DO NOT REFRIGERATE. Dispense in tight, light-resistant containers. For human consumption only.

### **Manufactured By:**

Solvay Pharmaceuticals GmbH,

129 Hannover, Germany

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131 **Marketed by:**

132 **Solvay**

133 **Pharmaceuticals, Inc.**

134 Marietta, GA 30062

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136 500199 Rev Feb 2006

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