

**CREON® 5  
MINIMICROSPHERES® (Pancrelipase Delayed-release Capsules, USP)**

500197 Rev Feb 2006

**PRESCRIBING INFORMATION  
DESCRIPTION**

CREON® 5 Capsules are orally administered and contain pancrelipase (lipase 5,000 USP Units, protease 18,750 USP Units and amylase 16,600 USP Units per capsule) which is of porcine pancreatic origin. Each CREON 5 Capsule is filled with 124 mg of delayed-release MINIMICROSPHERES®.

Inactive ingredients include dibutyl phthalate, dimethicone, hydroxypropylmethylcellulose phthalate, light mineral oil and polyethylene glycol. The capsule shells contain gelatin, red iron oxide, titanium dioxide, yellow iron oxide and FD & C blue No. 2. The capsule imprinting ink contains dimethicone, 2-ethoxyethanol, shellac, soya lecithin, and titanium dioxide.

**CLINICAL PHARMACOLOGY**

The pancreatic enzymes in CREON 5 Capsules are enteric-coated to resist gastric destruction or inactivation. The pancreatic enzymes catalyze the hydrolysis of fats to glycerol and fatty acids, protein into proteoses and derived substances and starch into dextrans and short chain sugars.

**INDICATIONS**

CREON 5 Capsules are indicated for patients with pancreatic exocrine insufficiency as is often associated with:

- 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)

**CONTRAINDICATIONS**

CREON 5 Capsules are contraindicated in the early stages of acute pancreatitis or in patients who are known to be hypersensitive to pork protein.

**WARNINGS**

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

Strictures in the ileo-cecal region and/or ascending colon have been reported in cystic fibrosis patients treated with high doses of high-potency pancreatic enzyme supplements containing 20,000 or greater USP units of lipase per capsule. The underlying mechanism is unknown, but caution should be exercised when doses in excess of 6,000 USP units lipase per kg per meal fail to resolve symptoms, especially in patients with a history of intestinal complications such as meconium ileus equivalent, short bowel syndrome, surgery or Crohn's disease. If symptoms suggestive of gastrointestinal obstruction occur, the possibility of bowel stricture should be investigated including evaluation of pancreatic enzyme therapy.

**PRECAUTIONS**

CREON 5 Capsules MINIMICROSPHERES SHOULD NOT BE CRUSHED OR CHEWED or placed on foods having a pH greater than 5.5. These can dissolve the protective enteric coating resulting in early release of enzymes, irritation of oral mucosa, and/or loss of enzyme activity.

**Information for Patients**

CREON 5 Capsules are a pancreatic enzyme product prescribed to promote improved digestion of foods, especially fat. The prescribed dosage should be taken with each meal and snack or as directed by the physician. The capsules can be swallowed whole, or the contents poured on soft, bland food. Care should be taken to avoid chewing or crushing of the capsule contents, which can result in early release of enzymes, irritation of oral mucosa, and/or loss of enzyme activity. Patients should maintain adequate fluid intake. The prescribed dose range should not be exceeded without calling your doctor.

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

**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 pancrelipase. It is also not known whether pancrelipase can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. CREON 5 Capsules should be given to a pregnant woman only if clearly needed.

**Nursing Mothers**

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when CREON 5 Capsules are administered to a nursing mother.

**ADVERSE REACTIONS**

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

**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 two to four CREON 5 Capsules per meal or snack. **Children Under 6 Years Old**

The exact dosage of CREON 5 Capsules should be selected based on clinical experience for this age group. Patients can be started on one to two capsules per meal or snack.

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 5 MINIMICROSPHERES (Pancrelipase Delayed-release Capsules, USP) are available in a two-piece gelatin capsule (orange opaque top half, blue opaque bottom half) imprinted in white with "SOLVAY" and "1205". Each capsule contains tan-colored delayed-release MINIMICROSPHERES of pancrelipase supplied in bottles of:

100.....NDC 0032-1205-01

250.....NDC 0032-1205-07

CREON 5 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.

Rx only

Manufactured By:  
Solvay Pharmaceuticals GmbH,  
Hannover, Germany

**Marketed by:**

**Solvay Pharmaceuticals, Inc.**

Marietta, GA 30062

500197 Rev Feb 2006

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**CREON® 10  
MINIMICROSPHERES® (Pancrelipase Delayed-release Capsules, USP)**

500198 Rev Feb 2006

**PRESCRIBING INFORMATION  
DESCRIPTION**

CREON® 10 Capsules are orally administered and contain pancrelipase (lipase 10,000 USP Units, protease 37,500 USP Units, and amylase 33,200 USP Units per capsule) which is of porcine pancreatic origin. Each CREON 10 Capsule is filled with 249 mg of delayed-release MINIMICROSPHERES®.

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

**CLINICAL PHARMACOLOGY**

The pancreatic enzymes in CREON 10 Capsules are enteric-coated to resist gastric destruction or inactivation. The pancreatic enzymes catalyze the hydrolysis of fats to glycerol and fatty acids, protein into proteoses and derived substances and starch into dextrans and short chain sugars.

**INDICATIONS**

CREON 10 Capsules are indicated for patients with pancreatic exocrine insufficiency as is often associated with:

- 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)

**CONTRAINDICATIONS**

CREON 10 Capsules are contraindicated in the early stages of acute pancreatitis or in patients who are known to be hypersensitive to pork protein.

**WARNINGS**

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

Strictures in the ileo-cecal region and/or ascending colon have been reported in cystic fibrosis patients treated with high doses of high-potency pancreatic enzyme supplements containing 20,000 or greater USP units of lipase per capsule. The underlying mechanism is unknown, but caution should be exercised when doses in excess of 6,000 USP units lipase per kg per meal fail to resolve symptoms, especially in patients with a history of intestinal complications such as meconium ileus equivalent, short bowel syndrome, surgery or Crohn's disease. If symptoms suggestive of gastrointestinal obstruction occur, the possibility of bowel stricture should be investigated including evaluation of pancreatic enzyme therapy.

**PRECAUTIONS**

CREON 10 Capsules MINIMICROSPHERES SHOULD NOT BE CRUSHED OR CHEWED or placed on foods having a pH greater than 5.5. These can dissolve the protective enteric coating resulting in early release of enzymes, irritation of oral mucosa, and/or loss of enzyme activity.

**Information for Patients**

CREON 10 Capsules are a pancreatic enzyme product prescribed to promote improved digestion of foods, especially fat. The prescribed dosage should be taken with each meal and snack or as directed by the physician. The capsules can be swallowed whole, or the contents poured on soft, bland food. Care should be taken to avoid chewing or crushing of the capsule contents, which can result in early release of enzymes, irritation of oral mucosa, and/or loss of enzyme activity. Patients should maintain adequate fluid intake. The prescribed dose range should not be exceeded without calling your doctor.

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

**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 pancrelipase. It is also not known whether pancrelipase can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. CREON 10 Capsules should be given to a pregnant woman only if clearly needed.

**Nursing Mothers**

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when CREON 10 Capsules are administered to a nursing mother.

**ADVERSE REACTIONS**

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

**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 to two CREON 10 Capsules per meal or snack.

**Children Under 6 Years Old**

Usual initial starting dosage is up to one CREON 10 Capsule per meal or snack. 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 10 MINIMICROSPHERES (Pancrelipase Delayed-release Capsules, USP) are available in a two-piece gelatin capsule (brown opaque top half, natural transparent bottom half) imprinted in white with "SOLVAY" and "1210". Each capsule contains tan-colored delayed-release MINIMICROSPHERES of pancrelipase supplied in bottles of:

100.....NDC 0032-1210-01

250.....NDC 0032-1210-07

CREON 10 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,  
Hannover, Germany

**Marketed by:**

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Marietta, GA 30062

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

500199 Rev Feb 2006

**PRESCRIBING INFORMATION  
DESCRIPTION**

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

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

**CLINICAL PHARMACOLOGY**

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

**INDICATIONS**

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

- 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)

**CONTRAINDICATIONS**

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

**WARNINGS**

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

Strictures in the ileo-cecal region and/or ascending colon have been reported in cystic fibrosis patients treated with high doses of high-potency pancreatic enzyme supplements containing 20,000 or greater USP units of lipase per capsule. The underlying mechanism is unknown, but caution should be exercised when doses in excess of 6,000 USP units lipase per kg per meal fail to resolve symptoms, especially in patients with a history of intestinal complications such as meconium ileus equivalent, short bowel syndrome, surgery or Crohn's disease. If symptoms suggestive of gastrointestinal obstruction occur, the possibility of bowel stricture should be investigated including evaluation of pancreatic enzyme therapy.

**PRECAUTIONS**

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

**Information for Patients**

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

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

**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 pancrelipase. It is also not known whether pancrelipase can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. CREON 20 Capsules should be given to a pregnant woman only if clearly needed.

**Nursing Mothers**

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

**ADVERSE REACTIONS**

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

**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.

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