CREON® CAPSULES

Pancreatic Extract Enteric-Coated Minimicrospheres

Product Information

NAME OF THE DRUG

Pancreatic Extract

DESCRIPTION

Creon 5,000 Creon 10,000, Creon 25,000 and Creon 40,000 are porcine pancreatic enzyme preparations containing Pancreatic Extract encapsulated in minimicrospheres with a pH-sensitive coating.

Each Creon 5,000 capsule contains Pancreatic Extract 75 mg equivalent to not less than 5,000 BP units lipase, 4,000 BP units amylase and 300 Ph. Eur. units protease. Inactive ingredients include macrogol 4000, paraffin-light liquid, hypromellose phthalate, dimethicone 1000, dibutyl phthalate, gelatin, iron oxide red CI 77491, iron oxide yellow CI 77492 and titanium dioxide.

Each Creon 10,000 capsule contains Pancreatic Extract 150mg equivalent to not less than 10,000 BP units lipase, 8,000 BP units amylase and 600 Ph. Eur. units protease. Inactive ingredients include macrogol 4000, paraffin-light liquid, hypromellose phthalate, dimethicone 1000, dibutyl phthalate, gelatin, iron oxide red CI 77491, iron oxide black CI 77499, iron oxide yellow CI 77492 and titanium dioxide.

Each Creon 25,000 capsule contains Pancreatic Extract 300mg equivalent to not less than 25,000 BP units lipase, 18,000 BP units amylase and 1,000 Ph. Eur. units protease. Inactive ingredients include macrogol 4000, paraffin-light liquid, hypromellose phthalate, dimethicone 1000, dibutyl phthalate, gelatin, iron oxide red CI 77491, iron oxide yellow CI 77492 and titanium dioxide.
Each Creon 40,000 capsule contains Pancreatic Extract 400mg equivalent to not less than 40,000 BP units lipase, 25,000 BP units amylase and 1,600 Ph. Eur. units protease. Inactive ingredients include macrogol 4000, paraffin-light liquid, hypromellose phthalate, dimethicone 1000, dibutyl phthalate, gelatin, iron oxide, titanium dioxide and sodium lauryl sulphate.

	Creon 5,000	Creon 10,000	Creon 25,000	Creon 40,000
Lipase activity (units)	5,000	10,000	25,000	40,000
Amylase activity (units)	4,000	8,000	18,000	25,000
Protease activity (units)	300	600	1,000	1,600

PHARMACOLOGY

Administered orally, pancreatic extract assists in the digestion of proteins, carbohydrates and fats.

Creon has been specially formulated to combine the features of rapid, homogeneous distribution with the chyme in the stomach, with resistance to inactivation by gastric acid and rapid dissolution in the alkaline pH of the duodenum. This is achieved by enteric-coated minimicrospheres which are released in the stomach following dissolution of the gelatin capsule. The minimicrospheres are similar in size to food particles (0.7-1.6mm in diameter), and mix homogeneously with the chyme while being protected from inactivation by gastric acid (pH 1) for up to 2 hours. They pass into the alkaline pH of the duodenum at least as quickly as the food they are intended to digest; here the enteric-coating rapidly dissolves releasing enzymes at the appropriate site.

INDICATIONS

Creon capsules are indicated as pancreatic enzyme replacements in conditions associated with pancreatic exocrine insufficiency (PEI) such as cystic fibrosis, chronic pancreatitis, post pancreatectomy, post-gastrointestinal bypass surgery (eg. Bilroth II gastroenterostomy) and ductal obstruction.

Low dose preparations should be used in preference to high-dose products, but the latter may be considered in patients who may benefit from higher doses and those who are experiencing continued symptoms due to poor compliance.

Agents which increase gastric pH, such as H_2-antagonists and proton pump inhibitors, have been reported to increase the activity of administered pancreatic lipase. This is not an approved indication for these agents. Prescribers should decide, on the basis of published evidence, whether or not to use them in this way.

CONTRAINDICATIONS

Creon Capsules are contraindicated during the early stages of acute pancreatitis and in those patients who are known to be hypersensitive to porcine protein or any of the ingredients.

PRECAUTIONS

Fibrosing Colonopathy

Fibrosing colonopathy has been reported in cystic fibrosis patients treated with some high potency enzyme supplements. The mechanism of injury is unknown. Doses in excess of 10,000 BP units lipase/kg/day should be used with caution. Patients who use doses in excess of 10,000 BP units lipase/kg/day and who develop new symptoms or have a medical history of gastrointestinal complications should be reviewed regularly (e.g. by ultrasound).

Check The Following Before Use

Neither the capsules nor the minimicrospheres should be crushed or chewed. In the case of difficulty in swallowing the capsules, the capsules may be carefully opened and the enteric-coated minimicrospheres taken with liquid during the intake of food, or shaken onto soft food that does not require chewing, and swallowed immediately. Food having pH of more than 5.5 can dissolve the protective enteric-coating of the minimicrospheres.

Other

The presence of porcine parvovirus cannot be totally excluded in medicines containing extracts of pancreatic powder of porcine origin. However, there is no evidence of transmission of this virus to humans or of causing illness in humans. The presence of other porcine viruses also cannot be definitively excluded. However, no cases of transmission of an infectious illness associated with the use of porcine pancreatic powder extracts have been reported.

Use In Pregnancy

Safe use in pregnancy has not been established. Therefore, Creon Capsules should not be used in the first trimester of pregnancy unless, in the judgement of the physician, the expected benefits outweigh the potential hazards.

Use During Lactation

It is not known whether any of the components of Creon 5,000 Creon 10,000, Creon 25,000 or Creon 40,000 are excreted in breast milk or have a harmful effect on the newborn. Therefore, Creon 5,000 Creon 10,000, Creon 25,000 and Creon 40,000 should only be used by breast feeding mothers if the expected benefits outweigh the potential risks.

Interactions with Other Drugs

Antacids should not be taken concomitantly with Creon Capsules as the alkaline pH may break down the enteric-coating. Should antacid administration be considered necessary, it is recommended that at least one hour elapse between the intake of antacids and any Creon Capsules.

ADVERSE REACTIONS

Diarrhoea, abnormal stools, constipation, abdominal discomfort, nausea and allergic or hypersensitivity reaction of the skin have been reported infrequently.

Bowel stricture formation has occasionally been reported in children with cystic fibrosis taking high lipase pancreatic enzyme supplements, and should be considered if abdominal symptoms develop *(See Precautions).*

DOSAGE AND ADMINISTRATION

The dosage should be individually titrated, and depends on the severity of the disease, and the composition of food.

Initially one Creon 5,000, Creon 10,000, or Creon 25,000 capsule with every meal and snack.

Infants and children with cystic fibrosis: 1,500 - 6,000 lipase BP units/kg body weight/meal.

The maximum recommended dose of lipase in infants and children is 20,000 BP units per kg body weight in 24 hours.

Dose increases should be added slowly with adequate hydration at all times (approx. 100 mL of fluid with each dose).

The daily dose for most patients should not exceed 10,000 lipase units/kg of body weight.

It is important to ensure adequate hydration at all times, especially during periods of increased loss of fluids. Inadequate hydration may aggravate constipation.

Patients requiring higher dosages should be reviewed regularly and should be monitored with ultrasound.

The capsules can be swallowed whole with 100 mL of water, or for each administration they may be opened and the granules taken with fluid or soft food, but without chewing. If the granules are mixed with food it is important that they are taken immediately, otherwise dissolution of the enteric coating may result.

OVERDOSAGE

Extremely high doses of pancreatin have been reported to be associated with hyperuricosuria and hyperuricaemia.

PRESENTATION

Creon 5,000: Opaque light brown/colourless-transparent capsule containing brownish minimicrospheres in bottles of 100 (AUST R 80973)

Creon 10,000: Opaque dark brown/colourless-transparent capsule containing brownish minimicrospheres in bottles of 100 (AUST R 67949)

Creon 25,000: Opaque light brown/colourless-transparent capsule containing brownish minimicrospheres in bottles of 100 (AUST R 67248)

Creon 40,000: Opaque brown/colourless-transparent capsule containing brownish minimicrospheres in bottles of 100 capsules (AUST R 143137).

STORAGE CONDITIONS

Store below 25^{o}C. In warmer climates it may be necessary to store the product in the refrigerator**.** Keep out of reach of children.

SPONSOR
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