Kreon 25000

hard gelatine capsules filled with gastro-resistant granules
(= Minimicrospheres™)
300 mg pancreatin (pancreas powder)

Abbott

Read this entire leaflet carefully before you start taking this medicine.
Keep this leaflet. You may need to read it again. If you have questions not answered by this pamphlet, please ask your doctor or pharmacist. This medicine has been prescribed to you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.

Kreon 25 000 is a bicoloured hard gelatine capsule with orange opaque cap and colourless transparent body filled with brownish gastro-resistant pellets (= Minimicrospheres™) for oral administration.
One capsule Kreon 25 000 contains 300 mg pancreatin (pancreas powder, produced from porcine pancreatic tissue) corresponding to

Amylase	18 000	Ph.Eur. units
Lipase	25 000	Ph.Eur. units
Protease	1 000	Ph.Eur. units

Excipients (nonmedicinal ingredients):

Pellet core: macrogol 4000
Pellet coating: hypromellose phthalate, dimethicone 1000, triethyl citrate, cetyl alcohol
Capsule: iron oxides (E 172), titanium dioxide (E 171), sodium lauryl sulphate, gelatine

Indications
Pancreatic enzyme supplements are used for the treatment of children and adults with pancreatic exocrine insufficiency (pancreatic glands do not deliver enough enzymes to digest food).
This condition is often, but not only, found together with the following listed diseases:
- cystic fibrosis
- acute or chronic pancreatitis (inflammation of the pancreas)
- pancreatic surgery (removal of a part or the entire pancreas)
- partial or total gastrectomy (removal of a part or the entire stomach)
- pancreatic cancer
- gastrointestinal bypass surgery
- obstruction of the pancreatic ducts or common bile duct (e.g. from neoplasm)
- Shwachman-Diamond Syndrome (a rare hereditary disorder)

Dosage and administration
Always take Kreon exactly as your doctor has prescribed. If you have any questions, contact your doctor or pharmacist.

The usual dose recommended for children, adolescents and adults with cystic fibrosis is based on weight:
- It will begin with 1 000 lipase units per kg per meal for children less than four years of age and with 500 lipase units per kg per meal for those patients over the age of four.
- Your doctor will adjust the dosage according to the severity of the disease, control of steatorrhoea (fatty stools) and maintenance of good nutritional status.
- For most patients a dose of 10 000 lipase units per kg body weight per day or 4000 lipase units per gram fat intake will suffice.

In other conditions associated with exocrine pancreatic insufficiency:
- Your individual dosage will be determined according to the degree of disturbed digestion and the fat content of the meal. The required dose for a meal ranges from about 25,000 to 80,000 units of lipase and half of the individual dose for snacks.

Always follow your doctor's advice on how much Kreon to take. Your doctor will adjust your dose to your individual needs. If you still have fatty stools or other gastrointestinal symptoms, talk to your doctor.

Always take Kreon during or after a meal or a snack and drink plenty of water. Swallow the capsules whole without crushing or chewing.

When swallowing of capsules is difficult (for instance in small children or elderly patients), you may open the capsules carefully and add the gastro-resistant pellets to small amounts of soft acidic food, such as applesauce, or you can take them with liquid. Swallow the Kreon-soft food mixture immediately without crushing or chewing and drink some water or juice.

It is important to ensure adequate hydration at all times, especially during periods of increased loss of fluids (e.g. diarrhoea and vomiting). Inadequate hydration may aggravate constipation.
Drink plenty of liquid every day.

If you forget to take your medicine, wait until your next meal and take your usual dose. Do not try to make up for the dose that you have missed.

You should take your medicines until your doctor tells you to stop. Many patients will need to take pancreatic enzymes supplements for the rest of their lives.
Do not stop taking Kreon without first talking to your doctor.

Contraindications
Do not take Kreon if you are hypersensitive (allergic) to the active substance (porcine pancreatin, pancreatin derived from pig) or to any of the other ingredients of Kreon (see section "Excipients").

Warnings and special precautions for use
Fibrosing colonopathy (strictures of the large bowel) have been reported in patients with cystic fibrosis taking high doses of pancreatin preparations. This has not been shown in studies with Kreon.

However, if you suffer from cystic fibrosis and take in excess of 10 000 units of lipase per kg per day and experience unusual abdominal symptoms or changes in abdominal symptoms please tell your doctor.

As with all currently marketed products that are made from porcine pancreatin, Kreon comes from pancreatic tissue derived from swine especially bred for food consumption. Although the risk that Kreon will transmit an infectious agent to humans has been reduced by the testing and inactivation of certain viruses during manufacturing, there is a theoretical risk for transmission of a viral disease, including diseases caused by novel or unidentified viruses. The presence of porcine viruses that might infect humans cannot be definitely excluded.
However, no cases of transmission of an infectious illness associated with the use of porcine pancreatic extracts have been reported, whereas they have been used for a long time.

Interactions with other medications
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines including medicines obtained without a prescription.

No interaction studies between this medicinal product and others have been performed.

Pregnancy and lactation
Pregnancy

If you are pregnant or trying to get pregnant please tell your doctor.
He will decide if you should take Kreon and at which dose.

Lactation

No effects on the suckling child are anticipated since animal studies do not point to systemic exposure of the breastfeeding woman to pancreatic enzymes.
If continuation of the treatment with Kreon is required during pregnancy and lactation this medicament should be used in doses sufficient to provide adequate nutritional status.
Kreon can be used while breastfeeding.

Effects on ability to drive and use machines
It is unlikely that Kreon will affect your ability to drive or operate tools or machines.

Undesirable effects
Like all medicines, Kreon may cause side effects, although not everybody experiences them.
If you notice any side effects not mentioned in this leaflet, or if any of the side effects gets serious, please inform your doctor or pharmacist.

In clinical trials more than 600 patients with pancreatic exocrine insufficiency due to cystic fibrosis, chronic pancreatitis, and pancreatic surgery received Kreon.

The most common side effects were gastrointestinal disorders which were mostly mild or moderate.

The side effects experienced by patients treated with Kreon, participating in clinical trials, are given below. The frequencies of these study related side effects are ranked according to the following:

Very Common:	Between 10 and 100 cases in 100 treated patients
Common:	Between 1 and 10 cases in 100 treated patients
Uncommon:	Less than one case in 100 treated patients

Gastrointestinal disorders

Very common: Abdominal pain (which occured as often or even less often as during the use of a placebo).
Common: Nausea (the feeling sick), vomiting, constipation, abdominal distention (bloating) and diarrhea (the last was observed similar or less frequently compared to placebo)
Gastrointestinal disorders are mainly associated with the underlying disease.

Skin and subcutaneous tissue disorders

Uncommon: rash.
Unknown frequency: Pruritus (severe itching) and urticaria (hives) have been additionally identified as adverse reactions during post-approval use. Because these reactions were reported spontaneously from a population of uncertain size, it is not possible to reliably estimate their frequency.

Multiple clinical trials were conducted in other patient populations: HIV, acute pancreatitis (inflammation of the pancreas), diabetes mellitus. No additional adverse drug reactions were identified compared to the above three patient groups.

Children
No specific side effects were found. In children with cystic fibrosis frequency, type and severity of side effects were similar to those in adults.

Overdose
Extremely high doses of pancreatin (the active ingredient in Kreon) have been reported to be associated with hyperuricosuria and hyperuricaemia (an excess of uric acid in the urine and in the blood).

If you have taken too much Kreon, you should drink plenty of water and consult your doctor immediately.

Pharmacodynamics
The following is a detailed description of how the active ingredient of Kreon works. For further explanations please consult your doctor.

Pharmacotherapeutic group: Multienzymes (amylase, lipase, protease)

Kreon contains porcine pancreatin (pancreatin derived from pig) formulated as enteric-coated (acid-resistant) minimicrospheres within gelatine capsules.
The capsules dissolve rapidly in the stomach releasing hundreds of minimicrospheres. This multi-dose principle is designed to achieve good mixing of this medicine with the chyme, emptying from the stomach together with the chyme and after release into the intestines, good distribution of enzymes within the chyme.
When the minimicrospheres reach the small intestine the coating rapidly disintegrates (at pH > 5.5) to release enzymes with lipolytic, amylolytic and proteolytic activity to ensure the digestion of fats, starches and proteins. The products of pancreatic digestion are then either absorbed directly, or following further hydrolysis by intestinal enzymes.

Clinical efficacy:

Overall 23 studies investigating the efficacy of Kreon in patients with pancreatic exocrine insufficiency have been conducted. Seven of these were either placebo or baseline controlled studies performed in patients with cystic fibrosis, chronic pancreatitis or post-surgical conditions.
In all randomized, placebo-controlled, efficacy studies, the pre-defined primary objective was to show superiority of Kreon over placebo on the primary efficacy parameter, the coefficient of fat absorption (CFA).
In all performed studies, irrespective of etiology, marked improvement was also shown in disease specific symptomatology (e.g. stool frequency, stool consistency, flatulence and abdominal pain).

Paediatric population:

In cystic fibrosis (CF) the efficacy of Kreon over placebo was demonstrated in three placebo-controlled studies, performed in paediatric and young adult CF patients and in one baseline-controlled study in infants. Overall, 118 patients were investigated in these trials. The data indicate that there is no difference in effect as measured by CFA due to the age of subjects.

Pharmacokinetics
The following is a detailed description of how the active ingredients of Kreon are metabolized by the body. For further explanations please consult your doctor.

Animal studies showed no evidence for absorption of intact enzymes and therefore classical pharmacokinetic studies have not been performed. Pancreatic enzyme supplements do not require absorption to exert their effects. On the contrary, their full therapeutic activity is exerted from within the lumen of the gastrointestinal tract. Furthermore, they are proteins, and as such undergo proteolytic digestion while passing along the gastrointestinal tract before being absorbed as peptides and amino acids.

Incompatibilities
Not applicable.

Shelf life and storage conditions
Kreon 25 000 can be stored for up to 3 years.

The in-use shelf life (after first opening of the bottle) is 3 months.

Do not use the medicine after the expiry date stated on the carton.

Do not store above 25°C.

Store in the original package and keep the container tightly closed in order to protect from moisture.

Keep this medicine out of the reach and sight of children.

Pack sizes
Kreon comes in 20, 50, or 100 capsules per pack (not all pack sizes may be marketed).
The bottle is made of HDPE.

Further information
Any unused product or waste material should be disposed of in accordance with local requirements.

The information in this leaflet is limited. For further information, please contact your doctor or pharmacist.

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March 2010

Manufactured by:
Abbott Products GmbH
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THIS MEDICATION

is a product which affects your health and its use contrary to instructions is dangerous to you.
Strictly follow the doctor's prescription, the method of use and the instructions of the pharmacist who sold you the medication.
- The doctor and the pharmacist are the experts in medicines, their benefits and risks.
- Do not interrupt the period of treatment prescribed without talking to your doctor first.
- Do not repeat the same prescription without first consulting your doctor.
- Keep all medications out of reach of children.

Council of Arab Health Ministers,
Union of Arab Pharmacists.