APPROVED
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INSTRUCTION
for medical use

FIRULIN 10000

Composition:
active substance: pancreatin;
1 hard capsule contains pancreatin 150 mg in gastro-resistant granules with enzymatic activity: lipase 10000 Ph. Eur. units, amylase 8000 Ph. Eur. units, protease 600 Ph. Eur. units;
excipients: macrogol 8000, hypromellose, hypromellose phthalate, triethyl citrate, dimethicone;
hard capsule: gelatin, purified water, iron oxide yellow (E 172), iron oxide red (E 172), iron oxide black (E 172), titanium dioxide (E 171), sodium lauryl sulfate.

Pharmaceutical form. Hard capsules with gastro-resistant granules.
Main physical and chemical properties: size 1 hard gelatin capsule with opaque brown cap and clear colorless body filled with gastro-resistant brown granules.

Pharmacotherapeutic group. Digestives, including enzymes. Multienzymes.
ATC code: A09A A02.

Pharmacological properties
Pharmacodynamics
FIRULIN 10000 contains porcine pancreatin formulated as enteric-coated (acid-resistant) granules within gelatin capsules. The capsules dissolve rapidly in the stomach releasing plenty of granules, a multi-dose principle which is designed to achieve good mixing with the chyme, emptying from the stomach together with the chyme and after release, good distribution of enzymes within the chyme. When the granules 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
Treatment with pancreatin significantly improves the symptoms of pancreatic exocrine insufficiency including stool consistency, abdominal pain, flatulence, and stool frequency, independent of the underlying disease in patients with pancreatic exocrine insufficiency.

Preclinical safety data
Preclinical data show no relevant acute, sub chronic or chronic toxicity. Studies on genotoxicity, carcinogenicity or toxicity to reproduction have not been performed.

Pharmacokinetic properties

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.

Clinical characteristics

Indications

Treatment of pancreatic exocrine insufficiency in pediatric and adult patients caused by various diseases and conditions given below, but not limited to:

- chronic pancreatitis;
- pancreatectomy;
- gastrectomy;
- gastrointestinal bypass surgery (e.g. Billroth II gastroenterostomy);
- Shwachman-Diamond Syndrome;
- status after an attack of acute pancreatitis and initiation of enteral or oral feeding.

Contraindications

Hypersensitivity to the active substance, to pork (allergy to pork) or to any other component of the medicinal product.
Acute hepatitis.
Mechanical jaundice.
Intestinal obstruction.

Interaction with other medicinal products and other forms of interaction

Iron. With the simultaneous use of pancreatin with iron preparations, the absorption of the latter may be reduced.
Folic acid. Absorption of folic acid may be reduced in patients taking pancreatin, so monitoring of folic acid levels is recommended during concomitant use.
Acarbose, miglitol. Pancreatin may reduce the effectiveness of acarbose and miglitol. Therefore, monitoring of patient blood glucose levels is recommended during coadministration.

Special warnings and precautions for use

Strictures of the ileo-caecum and large bowel (fibrosing colonopathy) have been reported in patients taking high doses of pancreatin. As a precaution, unusual abdominal symptoms or changes in abdominal symptoms should be medically assessed to exclude the possibility of fibrosing colonopathy, especially if the patient is taking in excess of 10000 Ph. Eur. units of lipase/kg/day (see “Adverse reactions” section).
There is a theoretical risk for transmission of porcine 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.
It should be used with caution in patients with renal failure, hyperuricemia.
The drug should not be used for acute or chronic pancreatitis in the exacerbation phase until the patient is transferred to enteral feeding.
<u>Excipients</u>
This medicine contains less than 0.00022 mmol sodium per capsule, that is to say essentially ‘sodium-free’.

Pregnancy and lactation
There are no adequate data from the use of pancreatin in pregnant women. Animal studies are insufficient with respect to effects on pregnancy and embryonal/fetal development, parturition and postnatal development. The potential risk for humans is unknown. FIRULIN 100000 should not be used during pregnancy or lactation except in certain cases when, in the opinion of the healthcare practitioner, the potential benefits outweigh the potential risks.

Effects on ability to drive and use machines
The drug has no or negligible influence on the ability to drive and use machines.

Administration and dosage
Method of administration
It is recommended to take the drug during or immediately after meals.
The capsules and granules should be swallowed intact, without crushing or chewing, with enough fluid during or after each meal or snack.
When swallowing of capsules is difficult (e.g. small children or elderly patients), the capsules may be carefully opened and the granules added to acidic soft food (pH < 5.5) that does not require chewing, or taken with acidic liquid (pH < 5.5). This could be apple sauce or yoghurt or fruit juice with a pH < 5.5, e.g. apple, orange or pineapple juice.
If the granules are mixed with liquid or food, it is important that they are taken immediately. The mixture should not be stored.
Crushing and chewing of the granules or mixing with food or fluid with a pH > 5.5 can disrupt the protective enteric coating. This can result in early release of enzymes in the oral cavity and may lead to reduced efficacy and irritation of the mucous membranes.
Care should be taken that no product is retained in the mouth.
It is important to ensure adequate hydration of patients at all times whilst dosing pancreatin, especially during periods of increased loss of fluids. Inadequate hydration may aggravate constipation.
Any mixture of the granules with food or liquids should be used immediately and should not be stored.
Dosage
The posology aims at individual needs and depends on the severity of the disease and the composition of food.
Therapy should be initiated at the lowest recommended dose and gradually increased with careful monitoring of the patient's response, symptoms and nutritional status. Patients should be instructed not to increase the dosage on their own. Changes in dosage may require an adjustment period of several days.
Adults
The usual initial dose is from 10000 to 25000 Ph. Eur. units lipase during each main meal. However, some patients will need higher doses to eliminate steatorrhea and maintain proper nutritional status. According to generally accepted clinical practice, it is believed that at least 20000 to 50000 Ph. Eur. lipase units should be taken with food. The dose for the main meals (breakfast, lunch, or dinner) can range from 25000 to 80000 Ph. Eur. lipase units; and with additional snack between main meals, it should be half of the individual dose.
Children (from birth to 18 years)
Dosage and duration of treatment for children are determined by the doctor individually.
Duration of treatment
The duration of the treatment course is determined by the doctor depending on the nature and course of the disease.

Children
FIRULIN 10000 can be used in children (see "Administration and dosage" section).

Overdose
Very high doses of pancreatin have been associated with hyperuricosuria and hyperuricaemia.
Supportive measures including stopping enzyme therapy and ensuring adequate rehydration are recommended.

Adverse effects
The most commonly reported adverse reactions were gastrointestinal disorders, primarily mild or moderate in severity, and were mainly associated with the underlying disease.
The frequency category of adverse effects is defined as follows: very common (≥ 1/10); common (≥ 1/100, < 1/10); uncommon (≥ 1/1000, < 1/100); rare (≥ 1/10000, < 1/1000); very rare (< 1/10000); frequency not known (cannot be estimated from available data).
Gastrointestinal disorders:
very common – abdominal pain*;
common – nausea, vomiting, constipation, flatulence, diarrhea*;
very rare – change in bowel habits, irritation of the skin around the mouth or anus, especially after taking high doses;
frequency not known – strictures of the ileo-caecum and large bowel (fibrosing colonopathy)**.
Skin and subcutaneous tissue disorders:
uncommon – rash;
frequency not known – itching, urticaria.
Immune system disorders:
frequency not known – allergic reactions of the immediate type***, hypersensitivity (anaphylactic reactions and reactions with localization in the gastrointestinal tract).
Influence on the results of laboratory and functional tests:
frequency not known – hyperuricemia, hyperuricosuria, folic acid deficiency.

* Similar or lower incidences compared to placebo were reported.
** Strictures of the ileo-caecum and large bowel (fibrosing colonopathy) have been reported in patients taking high doses of pancreatin preparations (see "Special warnings and precautions for use" section).
*** Allergic reactions were mainly skin reactions (rash, urticaria), among other manifestations there were sneezing, lacrimation, bronchospasm, dyspnea.

Children
No specific adverse reactions were identified in the pediatric population. Frequency, type, and severity of adverse reactions were similar in children as compared to adults.
Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Medical and pharmaceutical workers, as well as patients or their legal representatives are asked to report any suspected adverse reactions and lack of effectiveness of the medicinal product through the Pharmacovigilance Automated Information System at: https://aisf.dec.gov.ua.

Shelf life. 2 years.

Storage conditions
Store in original packing at temperature below 25°C.
Keep out of reach of children.

Package. 10 capsules in a blister, 2 or 10 blisters in a cardboard package.

Conditions of supply. Without prescription.

Manufacturer. KUSUM HEALTHCARE PVT LTD.

Location of manufacturer and its address of business activity.
Plot No. M-3, Indore Special Economic Zone, Phase-II, Pithampur, Distt. Dhar, Madhya Pradesh, Pin 454774, India.

Date of last revision.