Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Creon for Children 5000 Gastro-resistant Granules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 100 mg of gastro-resistant granules (equivalent to one measuring spoonful) contains 60.12mg Pancreatin, containing the following pancreatic enzymes:

Lipase 5,000 Ph. Eur. units
Amylase 3,600 Ph. Eur. units
Protease 200 Ph. Eur. units

Produced from porcine pancreatic tissue.

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Gastro resistant granules
Round, light brown gastro-resistant granules

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of pancreatic exocrine insufficiency.

4.2 Posology and method of administration

Initially 100 mg (5000 lipase units) of gastro-resistant granules (one measure) should be taken with each feed or meal or immediately after. Dose increases, if required, should be added slowly, with careful monitoring of response and symptomatology. The maximum daily dosage should not exceed 10,000 units lipase/kg/day. The required quantity of gastro-resistant granules should be dispensed using the measuring spoon contained in the pack which holds 100 mg.

In young infants, Creon for Children 5000 granules should be mixed with a small amount of infant formula, expressed breast milk or fruit puree and given immediately from a spoon, directly before the feed. The granules should not be added to the baby's bottle.
In weaned infants, granules should be taken with acidic liquids or acidic soft foods but without chewing, directly before the meal. Suitable foodstuffs for use with the granules include apple sauce or yoghurt or fruit juice with a pH less than 5.5(e.g. apple, orange or pineapple juice. Alternatively, the granules can be mixed with a small amount of milk on a spoon and administered to the infant immediately. The granules should not be added to the baby's bottle.
It is important to ensure adequate hydration of patients at all times whilst dosing with Creon.

The daily dose of pancreatic enzymes for most patients should remain below 2500 units of lipase per kilogram per meal (10,000 units per kilogram per day), and higher doses should be used with caution and only if quantitative measures demonstrate substantially improved absorption with such treatment. This applies particularly to young children.

If the granules are mixed with food, it is important that they are taken immediately and the mixture should not be stored, otherwise dissolution of the enteric coating may result. In order to protect the enteric coating, it is important that the granules are not crushed or chewed.
Crushing and chewing of the minimicrospheres or mixing with food or fluid with a pH greater than 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 to ensure that no product is retained in the mouth.
Colonic damage has been reported in patients with cystic fibrosis taking high doses of pancreatic enzyme supplements (see 4.8 Undesirable effects).

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings and precautions for use

Strictures of the ileo-caecum and large bowel (fibrosing colonopathy) have been reported in patients with cystic fibrosis taking high doses of pancreatin preparations. 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 units of lipase/kg/day.

This medicine contains less than 1 mmol sodium (23 mg) per dosage unit, that is to say essentially `sodium-free'.

Traceability
In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

Fertility and pregnancy
For pancreatic enzymes no clinical data on exposed pregnancies are available.
Animal studies show no evidence for any absorption of porcine pancreatic enzymes. Therefore, no reproductive or developmental toxicity is to be expected.
Caution should be exercised when prescribing to pregnant women.
Lactation
No effects on the breast-fed newborns/infants are anticipated since animal studies suggest no systemic exposure of the breast-feeding woman to pancreatic enzymes. Pancreatic enzymes can be used during breast-feeding.

If required during pregnancy or lactation Creon should be used in doses sufficient to provide adequate nutritional status.

4.7 Effects on ability to drive and use machines

Creon has no or negligible influence on the ability to drive or use machines.

4.8 Undesirable effects

In clinical trials, more than 900 patients were exposed to Creon.
The most commonly reported adverse reactions were gastrointestinal disorders and were primarily mild or moderate in severity.
The following adverse reactions have been observed during clinical trials with the below indicated frequencies.

Organ system	Very common ≥ 1/10		Common ≥ 1/100 to < 1/10		Uncommon ≥ 1/1000 to < 1/100	Frequency not known	
Gastrointestinal disorders		Abdominal pain*		nausea, vomiting, constipation, abdominal distention, diarrhoea*		strictures of the ileo-caecum and large bowel (fibrosing	

						colonopathy)	
Skin and subcutaneous tissue disorders					rash	pruritus, urticaria	
Immune system disorders						hypersensitivity (anaphylactic reactions).	

*Gastrointestinal disorders are mainly associated with the underlying disease. Similar or lower incidences compared to placebo were reported for abdominal pain and diarrhoea.

Strictures of the ileo-caecum and large bowel (fibrosing colonopathy) have been reported in patients with cystic fibrosis taking high doses of pancreatin preparations, see section 4.4 Special warnings and precautions for use.
Allergic reactions mainly but not exclusively limited to the skin have been observed and identified as adverse reactions during postapproval use. Because these reactions were reported spontaneously from a population of uncertain size, it is not possible to reliably estimate their frequency.

Paediatric population
No specific adverse reactions were identified in the paediatric population. Frequency, type and severity of adverse reactions were similar in children with cystic fibrosis 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. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Website: www.hpra.ie

4.9 Overdose

Extremely high doses of panreatin have been reported to be associated with hyperuricosuria and hyperuricaemia.
Supportive measures including stopping enzyme therapy and ensuring adequate rehydration are recommended.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Multienzymes (amylase, lipase, protease), ATC code:A09A A02
Creon for Children 5000 contains porcine pancreatin formulated as enteric-coated (acid-resistant) minimicrospheres, a multi-dose principle which is designed to achieve good mixing with the chyme, emptying from the stomach altogether with the chyme and after release, 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 30 studies investigating the efficacy of Creon (Creon capsules with 10000, 25000 or 40000 Ph. Eur units of lipase and Creon 5000) in patients with pancreatic exocrine insufficiency have been conducted. Ten of these were placebo 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 Creon over placebo on the primary efficacy parameter, the coefficient of fat absorption (CFA).
The coefficient of fat absorption determines the percentage of fat that is absorbed into the body taking into account fat intake and fecal fat excretion. In the placebo-controlled PEI studies, the mean CFA (%) was higher with Creon treatment (83.0%) as compared to placebo (62.6%). In all studies, irrespective of the design, the mean CFA (%) at the end of the treatment period with Creon was similar to the mean CFA values for Creon in the placebo controlled studies.
Treatment with Creon improves the symptoms of pancreatic exocrine insufficiency including stool consistency, abdominal pain, flatulence and stool frequency, independent of the underlying disease.

Paediatric population

In cystic fibrosis (CF) the efficacy of Creon was demonstrated in 288 paediatric
patients covering an age range from newborns to adolescents. In all studies, the mean end-of treatment CFA values exceeded 80% on Creon comparably in all paediatric age groups.

Creon 5000 has been specifically developed to offer a dosage form for infants and children. One baseline-adjusted specific study performed over 8 weeks in infants demonstrated that
Creon 5000 was effective regarding the improvement of CFA and stool fat excretion as well as fecal energy loss after two weeks of treatment.
This study was designed mainly to evaluate the efficacy of Creon 5000 in 12 infants, aged 1-23 months. The analysis of the results showed that the primary efficacy parameter, CFA, significantly increased from a baseline mean of 58.0% to a mean of 84.7% (mean increase 26.7%, p = 0.0013, paired t-test). Height and weight increased, but the weight for height percentile remained nearly constant and close to 100%.

5.2 Pharmacokinetic properties

Pharmacokinetic data are not available as the enzymes act locally in the gastro-intestinal tract. After exerting their action, the enzymes are digested themselves in the intestine.

5.3 Preclinical safety data

None stated

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hypromellose phthalate
Macrogol 4000
Triethyl citrate
Cetyl alcohol
Dimethicone

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.
12 weeks after first opening

6.4 Special precautions for storage

Do not store above 25°C.
Keep the container tightly closed in order to protect from moisture.

6.5 Nature and contents of container

Glass container with LDPE cap.
Containers hold 20 g of gastro-resistant granules.
The dosing spoon is made of Polystyrol. One dosing spoon measures 100mg Creon granules.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Viatris Healthcare Limited
Damastown Industrial Park
Mulhuddart
Dublin 15
Dublin
Ireland

8 MARKETING AUTHORISATION NUMBER

PA23355/006/003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 23rd June 2006

Date of last renewal: 23rd June 2011

10 DATE OF REVISION OF THE TEXT

July 2023