SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Nutrizym 22

2.

QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains Pancreatin BP 313 mg with not less than the following activities. Lipase 22,000 BP Units, Protease 1,100 BP Units and Amylase 19,800 BP Units.

Excipients with known effect: Castor oil 3.48mg per capsule

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Hard gelatin red and yellow capsule containing enteric coated pancreatin minitablets for oral administration.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the symptomatic relief of pancreatic exocrine insufficiency such as in fibrocystic disease of the pancreas and chronic pancreatitis.

4.2 Posology and method of administration

Posology

Adults (including elderly) and Paediatric population
1-2 capsules with meals and 1 capsule with snacks.

Since the individual response to pancreatin supplements is variable, the number of capsules taken may need to be titrated to the individual according to symptoms and at the discretion of the physician. Dose increase, if required

should be added slowly with careful monitoring of response and symptomatology.

Colonic damage has been reported in patients with cystic fibrosis taking in excess of 10,000 units of lipase/kg/day. The dose of Nutrizym 22 should usually not exceed this dose.

Where a patient is already receiving a lower unit dose enteric coated pancreatic supplement, then Nutrizym 22 may be substituted at 1/2 of the number of capsules normally consumed with the previous preparation.

Method of administration

Capsules should be swallowed whole with water. Where swallowing of capsules proves to be difficult, the minitablets may be removed and taken with water or with a small amount of acidic fluid or soft food, but without chewing. This could be apple sauce or yoghurt or any fruit juice with acidic pH (a pH less than 5.5), e.g. apple, orange or pineapple juice. If the minitablets are mixed with fluid or food, it is important that they are taken immediately and the mixture not stored, otherwise dissolution of the enteric coating may result. In order to protect the enteric coating, it is important that the minitablets are not crushed or chewed. Crushing and chewing of the minitablets or mixing with food or fluid with alkaline pH 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.

Adequate patient hydration should be ensured at all times whilst treating with Nutrizym 22.

4.3 Contraindications

In children aged 15 years and under with cystic fibrosis. Hypersensitivity to the active substance (porcine pancreatin) or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

In several patients with cystic fibrosis (including children), high doses of pancreatin caused fibrosing colonopathy (narrowing of the colon and ileocecal part of the intestine). If symptoms of ileus occur in patients taking pancreatin, fibrosing colonopathy should be considered as potential cause.

Hyperuricaemia and hyperuricosuria have been reported to occur in cystic fibrosis patients; pancreatin extracts contain a small amount of purine which might, in high

doses, contribute to this condition.

Important information about the ingredients of Nutrizym 22

Nutrizym 22 contains castor oil which may cause stomach upset and diarrhoea.

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

4.5 Interactions with other medicaments and other forms of interaction

When given concomitantly:

- Pancreatin may reduce the effect of acarbose and should, therefore, not be taken concomitantly.
- Calcium carbonate and/or magnesium hydroxide may reduce the effect of pancreatin.
- Cimetidine may potentiate the effect of pancreatin.
- Pancreatin may diminish folic acid absorption.
- Long term intake of pancreatin may diminish iron absorption.

4.6 Fertility, Pregnancy and lactation

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 suckling child 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, pancreatin should be used in doses sufficient to provide adequate nutritional status.

4.7 Effects on ability to drive and use machines

Not known.

4.8 Undesirable effects

In clinical trials, more than 900 patients were exposed to pancreatin. 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) including children with cystic fibrosis**, oral mucosa irritation
Skin and subcutaneous tissue disorders			rash	pruritus, urticaria
Immune system disorders				hypersensitivity (anaphylactic reactions including urticaria and angioedema)
Metabolism and nutrition disorders				Hyperuricemia
Renal and urinary disorders				Hyperuricosuria***

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

** See section 4.4 - Special warnings and precautions for use
*** Hyperuricosuria has been reported when high doses of pancreatin have been taken

Allergic reactions mainly, but not exclusively, limited to the skin have been

observed and 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.

As with any pancreatin extract, high doses may cause buccal and perianal irritation, in some cases resulting in inflammation.

Stricture of the ileo-caecum and large bowel, and colitis have been reported in children with cystic fibrosis taking Nutrizym 22 (see section 4.4). Abdominal symptoms (those not usually experienced by the patient) or changes in abdominal symptoms should be reviewed to exclude the possibility of colonic damage - especially if the patient is taking in excess of 10,000 units of lipase/kg/day.

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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Inappropriately large doses could result in abdominal discomfort, nausea, vomiting and perianal irritation or inflammation. Extremely high doses of pancreatin have been reported to be associated with hyperuricosuria and hyperuricaemia. Refer to section 4.8 for the potential side-effects of high doses of pancreatic enzymes in patients with cystic fibrosis.

Supportive measures including stopping enzyme therapy and ensuring adequate rehydration are recommended.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

The active ingredient is a preparation of porcine pancreas with lipase, amylase and protease activity. Lipase enzymes hydrolyse fats to glycerol and fatty acids. Amylase converts starch into dextrins and sugars and protease enzymes change proteins into proteoses and derived substances.

5.2 Pharmacokinetic properties

The active ingredient of Nutrizym 22 is pancreatin which is a substance involved in the digestive process. During the enzymatic degradation of food substances the enzymes themselves are degraded. Any breakdown products are those that would be expected to appear following normal digestion.

5.3 Preclinical safety data

Preclinical data are not available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Uncoated minitablets:
Castor Oil (hydrogenated)
Silicon dioxide, colloidal
Magnesium stearate
Sodium carboxymethylcellulose
Microcrystalline cellulose

Minitablet coating:
Simethicone emulsion
Methacrylic acid copolymer, type C (Eudragit L30D)
Talc
Triethyl citrate

Gelatin capsules:
Titanium dioxide
Iron oxide, red
Iron oxide, yellow
Gelatin

6.2 Incompatibilities

Not known.

6.3 Shelf life

18 months.

6.4 Special precautions for storage

Store below 25 °C in tightly closed containers.

6.5 Nature and contents of container

Polyethylene or polypropylene containers with polyethylene tamper evident closures containing 50, 100, 200 or 500 capsules.

6.6 Special precautions for disposal

Not relevant.

7 MARKETING AUTHORISATION HOLDER

Zentiva Pharma UK Limited,
12 New Fetter Lane,
London,
EC4A 1JP, United Kingdom

8 MARKETING AUTHORISATION NUMBER

PL 17780/1025

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

17 August 1992

10 DATE OF REVISION OF THE TEXT

19/03/2025