

NEW ZEALAND DATA SHEET

PANZYTRAT 25,000 modified release capsule

Pancrelipase

1 PRODUCT NAME

PANZYTRAT 25,000

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each PANZYTRAT 25,000 capsule contains pancreatin from porcine pancreas with the following enzyme activities:

Lipase	25,000 Ph Eur Units
Amylase	22,000 Ph Eur Units
Protease	1,250 Ph Eur Units

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

PANZYTRAT capsules contain white-grey enteric-coated microtablets with a characteristic odour. PANZYTRAT 25,000 capsules are of size "0" elongated with a chestnut-coloured opaque cap and natural transparent body.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

PANZYTRAT is indicated for patients with exocrine pancreatic enzyme deficiency such as (but not restricted to):

- Cystic fibrosis
- Chronic pancreatitis
- Post-pancreatectomy
- Post-gastrointestinal bypass surgery e.g. Billroth II gastroenterostomy
- Ductal obstructions from neoplasm e.g. of the pancreas or common bile duct

4.2 Dose and method of administration

The dosage should be adjusted to suit the individual severity of the pancreatic insufficiency.

Unless otherwise prescribed by the physician the following dose levels apply for PANZYTRAT 25,000:

in infants up to 18 months	- 2 capsules daily (corresp. to 50,000 lipase units)
in children	- 4 capsules daily (corresp. to 100,000 lipase units)
in adults	- 6 capsules daily (corresp. to 150,000 lipase units)

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Some patients may require much higher doses than those shown here. Where there is total pancreatic insufficiency the entire daily requirement for lipase must be substituted, generally up to 400,000 lipase units daily.

Particular care should be taken in the case of cystic fibrosis patients to ensure that the dose does not exceed the enzyme dose required for adequate fat absorption, taking into account the size and composition of meals. Any increases in the dose should be conducted under medical supervision and with the aim of improving symptoms (e.g. steatorrhoea, abdominal pain). A daily enzyme dose of 15,000-20,000 lipase units per kilogram of body weight should not be exceeded.

The capsules should be taken unchewed at meal times with plenty of liquid, preferably non-alkaline (fruit juice, for example). The daily dose should be spread out over the day. Patients unable to take the capsules whole – e.g. following gastrectomy – may open the capsules and swallow the unchewed contents.

It is important to ensure adequate hydration at all times for patients being treated with PANZYTRAT. Although the duration of treatment may be unlimited, regular review by an appropriate specialist is recommended during long-term use.

4.3 Contraindications

- Acute pancreatitis or acute exacerbations of chronic pancreatic diseases
- Hypersensitivity to pork protein or to any of the ingredients of the formulation. Hypersensitivity reactions to pork protein include symptoms such as sneezing, lachrymation and skin rashes.

4.4 Special warnings and precautions for use

Stricture formation in the ileo-caecal region and/or ascending colon has been reported in children with cystic fibrosis who were under treatment with high potency enzyme supplements. If symptoms suggestive of gastrointestinal obstruction occur, the possibility of bowel stricture should be considered and if necessary, the patient referred to an appropriate specialist.

There is a risk of gastrointestinal intolerance and allergic reactions in patients allergic to porcine products.

An adequate dietary intake with proper balance of protein, fat and carbohydrate should be used in conjunction with pancrelipase. In patients with deficient pancreatic bicarbonate secretion, antacid supplementation may be required for control of steatorrhoea. It is important that any antacid supplementation should not be taken concomitantly with PANZYTRAT capsules as the alkali may destroy the enteric coat. At least one hour should elapse between the administration of antacid and PANZYTRAT capsules.

The active enzymes contained in PANZYTRAT may damage the oral mucosa if released in the oral cavity (e.g. by chewing). Therefore, the capsules or its contents must be swallowed whole and not be chewed. Contact of the enteric-coated beads of microtablets with foods having a pH above 5.5 can dissolve the protective enteric shell.

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Caution should be exercised when this product is administered to patients with gout, renal impairment or hyperuricemia. PANZYTRAT contains purines that may increase blood uric acid levels.

4.5 Interaction with other medicines and other forms of interaction

Folic acid

Folic acid absorption may be reduced by the ingestion of pancreatin-containing agents. Folic acid supplementation may therefore be necessary. Monitoring of folic acid levels is therefore recommended.

Acarbose, miglitol

Pancreatic enzymes may attenuate the effect of acarbose and miglitol. Monitoring of the antidiabetic effect on the patient's blood sugar level is recommended when these medicines are used in combination.

4.6 Fertility, pregnancy and lactation

Pregnancy

PANZYTRAT may be taken during pregnancy after consideration of the risks and benefits by the treating physician. No harmful effects are anticipated, since systemic exposure to PANZYTRAT is negligible.

Breast-feeding

There is no evidence to suggest that PANZYTRAT could be harmful during lactation, since the systemic exposure is negligible.

Fertility

No information available.

4.7 Effects on ability to drive and use machines

No or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

	Uncommon* (1/1,000 to <1/100)	Not known** (frequency cannot be estimated from the available data)
Immune system disorders		Type I hypersensitivity (urticaria, sneezing, lacrimation increased, bronchospasm), gastrointestinal tract irritation
Metabolism and nutrition disorders	Decreased appetite	
Nervous system disorders	Dizziness, balance disorder	
Respiratory, thoracic and mediastinal disorders	Rhinitis	

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	Uncommon* (1/1,000 to <1/100)	Not known** (frequency cannot be estimated from the available data)
Gastrointestinal disorders	Diarrhoea, abdominal pain, nausea, vomiting, dyspepsia (pyrosis, heartburn), stomatitis	Ileal stenosis, colonic stenosis, ileus (cases from the literature, both promoted during high-dose therapy in patients with cystic fibrosis)
Skin and subcutaneous tissue disorders	Erythema	
General disorders and administration site conditions	Malaise	

*Based on analysis of adverse events in published clinical studies involving 953 patients, whereby it has not been possible to assess causality in every case. All data are Preferred Terms (MedDRA Version 13.1, English version), categorised according to decreasing frequency of adverse events.

** Undesirable effects known from many years of pancreatin use.

Malabsorption

The following may also be symptoms of continuing malabsorption, which may consequently necessitate dose adjustment by the doctor: anorexia, diarrhoea, abdominal pain, nausea, vomiting, dyspepsia (pyrosis, heartburn), malaise.

Intestinal strictures

Underlying intestinal strictures may be responsible for symptoms of abdominal pain, vomiting and nausea, particularly in patients with cystic fibrosis (see **Warnings and Precautions**).

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions <https://nzphvc.otago.ac.nz/reporting/>

4.9 Overdose

Accidental or intentional ingestion of an overdose of PANZYTRAT has not been reported. For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: digestives, including enzymes (multienzymes)

ATC code: A09AA02

As well as containing lipase, α -amylase and proteases (e.g. trypsin and chymotrypsin), which are excretory pancreatic enzymes pancreas powder (pancreatin) also contains other enzymes, as well as other ancillary agents without any enzymatic activity. Digestive potency is determined by enzymatic activity and the pharmaceutical form.

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Enzymatic lipase activity and the number of proteases (e.g. trypsin) play an essential role, whilst amylolytic activity is only significant in the treatment of cystic fibrosis, as cleavage of nutritional polysaccharides is still unaffected even in cases of chronic pancreatitis.

Pancreatic lipase cleaves fatty acids from a triacylglyceride molecule at Positions 1 and 3. Absorption of the resultant free fatty acids and 2-monoglycerides is rapid and mainly takes place from the upper small intestine, assisted by bile acids. Like human pancreatic lipase, porcine pancreatic lipase is acid-unstable, with the result that its lipolytic activity is irreversibly inactivated at a pH value of <4.

Trypsin is activated from trypsinogen autocatalytically or by enterokinase in the small intestine and, as an endopeptidase, cleaves peptide bonds in which lysine and arginine are involved. For trypsin, feedback inhibition of stimulated pancreatic secretion – caused by activated trypsin – is assumed to occur in the upper small intestine. This effect is attributed to the analgesic action of pancreatin preparations, which has been described in a few studies.

As an endoamylase, α -amylase cleaves glucose-containing polysaccharides very rapidly, so that its activity is still generally sufficient even when secretory activity of the pancreas is considerably reduced as a result of disease.

5.2 Pharmacokinetic properties

At physiological conditions protection of the medicine is necessary in order to prevent the enzymes contained (lipases, proteases, amylases) from being destroyed by gastric acid. This is achieved by gastro-resistant coating of the micro tablets contained in the capsules.

After intake of the capsules the micro tablets are released during the stomach passage. Synchronous intake of food provides the steady mixing of the micro tablets with the chyme. The micro film tablets dissolve after leaving the stomach at pH > 5.5 and the active substance is released into the chyme.

Pancreatin and the enzymes contained therein are not absorbed from the gastrointestinal tract. They are eliminated through the stool or largely degraded or denatured by digestive juice or bacteria. The resulting amino acids and short-chain peptides can be taken up by the body.

5.3 Preclinical safety data

No information available.

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6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal silicon dioxide	Methacrylic acid – ethyl acrylate copolymer
Crospovidone	Microcrystalline cellulose
Gelatin	Purified talc
Glycol montanate	Simeticone
Iron oxide black	Titanium dioxide
Iron oxide red	Triethyl citrate
Magnesium stearate	

It has been agreed that PANZYTRAT 25,000 is acceptable for both Jewish and Muslim patients when used as a medicine.

6.2 Incompatibilities

None

6.3 Shelf life

36 months from date of manufacture or 6 months once opened. The product should not be used after the expiry date stated on the package.

6.4 Special precautions for storage

PANZYTRAT should be stored at or below 25°C in a dry place. Keep the container tightly closed.

6.5 Nature and contents of container

PANZYTRAT 25,000 capsules in glass bottles of 100.

6.6 Special precautions for disposal

Not applicable

7 MEDICINE SCHEDULE

Prescription Medicine

8 SPONSOR

Pharmaco (NZ) Ltd
4 Fisher Crescent
Mt Wellington
Auckland 1060
Telephone: 09 377 3336

9 DATE OF FIRST APPROVAL

24 May 1991

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10 DATE OF REVISION OF THE TEXT

Nov 2017

[CCDS 01/2011]

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
All	Reformatted to new SPC format