

NATURAL HEALTH PRODUCT

PANCREATIC ENZYMES

This monograph is intended to serve as a guide to industry for the preparation of Product Licence Applications (PLAs) and labels for natural health product market authorization. It is not intended to be a comprehensive review of the medicinal ingredients.

Notes

- ▶ The term “pancreatic enzymes” is used as a collective term for various enzyme preparations derived from animal pancreas. For pharmacopoeial grade ingredients, the applicant must use the proper name and common name of the enzyme as provided in the pharmacopoeia. Table 1 in the Appendix indicates the differences in the amounts of the enzyme activities of amylase, lipase and protease for Pancreatic Extract, Pancreatic Powder, Pancreatin and Pancrelipase.
- ▶ To ensure consistent representation of enzyme-containing products, pancreatic enzyme activity must be expressed in USP units in the PLA and label.
- ▶ Text in parentheses is additional optional information which can be included on the PLA and product label at the applicant’s discretion.
- ▶ The solidus (/) indicates that the terms and/or the statements are synonymous. Either term or statement may be selected by the applicant.

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Proper name(s)

Pancreatic enzymes (WHO 2011; US FDA 2010)

Common name(s)

- ▶ Pancreatic enzymes (WHO 2011; US FDA 2010)
- ▶ Pancreatic extract/powder (BP 2012; Ph.Eur. 2012)
- ▶ Pancreatin (BP 2012; USP 35)
- ▶ Pancrelipase (USP 35)

Source material(s)

- ▶ Bovine (*Bos taurus* (Bovidae)) pancreas (BP 2012; Ph.Eur. 2012; USP 35; Bisby et al. 2011)
- ▶ Porcine (*Sus scrofa* (Suidae)) pancreas (BP 2012; Ph.Eur. 2012; USP 35; Bisby et al. 2011)

Route(s) of administration

Oral

Dosage form(s)

- ▶ The only acceptable pharmaceutical dosage forms are delayed-release capsules, tablets, or granules (e.g. enteric-coated tablets, capsules containing enteric-coated granules/(mini)microspheres) (Friess et al. 1999; Suarez et al. 1999; Sharpé et al. 1997).
- ▶ The dosage form must be qualified with an additional term to describe the delayed release (e.g. enteric-coated capsules, gastro-resistant tablets, microencapsulated pancreatic enzymes) (WHO 2011).
- ▶ This monograph is not intended to include foods or food-like dosage forms such as bars, chewing gums or beverages.

Use(s) or Purpose(s) Statement(s) to the effect of

- ▶ Digestive aid (Cichoke 2006).
- ▶ Digestive aid to help decrease bloating after high caloric, high fat meals (Suarez et al. 1999).
- ▶ Digestive enzyme (Cichoke 2006).
- ▶ Helps to decrease bloating after high caloric, high fat meals (Suarez et al. 1999).

Dose(s)

Subpopulation(s)

Adults (≥ 18 years)

Quantity(ies)

Dose information must include the quantities of both the enzyme preparation and its enzymatic activity:

- ▶ Enzyme preparation (lipase, amylase, and protease) per dosage unit;
and
- ▶ Enzyme activity providing all the following (USP 35; Suarez et al. 1999; Domínguez-Muñoz et al. 1997):
 - amylase: $1.7 \times 10^4 - 1.49 \times 10^5$ USP amylase units per day, not to exceed 3.7×10^4 USP units per single dose
 - lipase: $5.0 \times 10^3 - 4.0 \times 10^4$ USP lipase units per day, not to exceed 2.0×10^4 USP units per single dose
 - protease: $1.6 \times 10^4 - 1.25 \times 10^5$ USP protease units per day, not to exceed 3.8×10^4 USP units per single dose

Note

Pharmacopoeial units other than USP may be represented on the label as additional information. The following approximate conversion factors can be used to convert the activities of pancreatic enzymes into USP units (Scharpé et al. 1997):

Amylase: 1 Ph. Eur. Unit = 1 BP Unit = 1 FIP Unit ~ 4.15 USP Units

Lipase: 1 Ph. Eur. Unit = 1 BP Unit = 1 FIP Unit ~ 1 USP Unit

Protease: 1 Ph. Eur. Unit = 1 BP Unit = 1 FIP Unit ~ 62.5 USP Units

Directions for use

All products

- ▶ Take with or immediately before a meal/food (Ferrone et al. 2007; Suarez et al. 1999; Friess et al. 1998; Domínguez-Muñoz et al. 1997).
- ▶ Use the smallest effective dose which controls symptoms (CPS 2008; Sharpé et al. 1997).

Enteric-coated products

Swallow whole/ Do not crush or chew (CPS 2008).

Capsule products containing (mini)microspheres and delayed-release granules

(For individuals who experience difficulties swallowing capsules, the capsules may be opened and) the granules/(mini)microspheres may be mixed with soft food or fluid. Use immediately after mixing (Martindale 2011; CPS 2008).

Duration of use

Consult a health care practitioner for use beyond four weeks (Friess et al. 1998).

Risk information

Statement(s) to the effect of

Caution(s) and warning(s)

- ▶ If you have diabetes, consult a health care practitioner prior to use.
- ▶ If you have pancreatitis, pancreatic exocrine insufficiency or cystic fibrosis, consult a health care practitioner prior to use (Halm et al. 1999; Delhaye et al. 1996; Guarner et al. 1993).
- ▶ If you are pregnant or breastfeeding, consult a health care practitioner prior to use.
- ▶ If symptoms persist or worsen, consult a health care practitioner.

Contraindication(s)

All products

If you are sensitive to pancreatic enzymes, do not use this product (Martindale 2011; CPS 2008).

Products from hog/pig pancreas

If you are sensitive to pork proteins, do not use this product (Martindale 2011; CPS 2008).

Known adverse reaction(s)

Nausea, vomiting, abdominal pain/epigastric pain and/or heartburn have been known to occur, in which case discontinue use (and consult a health care practitioner) (Friess et al. 1998).

Non-medicinal ingredients

Must be chosen from the current NHPD *Natural Health Products Ingredients Database* and must meet the limitations outlined in the database.

Storage conditions Statement(s) to the effect of

Store in a tightly closed, light-resistant container in a cool, dry place (BP 2012; Ph.Eur. 2012; USP 35).

Specifications

- ▶ The finished product specifications must be established in accordance with the requirements described in the NHPD *Quality of Natural Health Products Guide*.
- ▶ The medicinal ingredient must comply with the requirements outlined in the *Natural Health Products Ingredients Database* (NHPID).
- ▶ The specifications must include testing for enzymatic activity of the medicinal ingredient at appropriate stages of formulation and manufacturing using the assay outlined in the current United States Pharmacopeia (USP):
 - Pancrelipase – assay for amylase, lipase and protease activity.
- ▶ The medicinal ingredient may comply with the pancreatic enzyme preparation specifications outlined in the current British, European and United States pharmacopoeial monographs:
 - BP: Pancreatin; Pancreatic Extract¹
 - Ph.Eur.: Pancreas powder / Pancreatis pulvis
 - USP: Pancrelipase

Note

¹ Pancreatic extract is cross-referenced to Pancreas Powder, Ph.Eur. monograph 0350

- ▶ Overages to compensate for the loss of activity during manufacturing and shelf-life of the finished product are permitted as per the pharmacopoeial standard.
- ▶ Where published methods are not suitable for use, manufacturers will use due diligence to ensure that the enzymes remain active to the end of the shelf life indicated on the product label.

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Appendix 1 Pharmacopoeial information

The following table shows the different amounts of amylolytic, lipolytic and proteolytic activities for Pancreatin, Pancreatic extract and Pancrelipase according to the British, European and U.S. pharmacopoeias.

Table 1 Amylase, lipase and protease activity units per milligram of pancreas preparation according to the British, European and U.S. pharmacopoeias

Pharmacopoeia	Enzyme	Units of Activity ¹		
		Amylase	Lipase	Protease
BP 2012	Pancreatin	24 FIP	20 FIP	1.4 FIP
USP 35	Pancreatin	25 USP	2 USP	25 USP
BP 2012	Pancreatic extract ²	12 Ph. Eur.	15 Ph. Eur.	1 Ph. Eur.
Ph.Eur. 2012	Pancreas powder ²	12 Ph. Eur.	15 Ph. Eur.	1.0 Ph. Eur.
USP 35	Pancrelipase	100 USP	24 USP	100 USP

1. Minimum amounts

2. Cross-referenced within the respective pharmacopoeias