Health Canada Santé Canada

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 pharmocopoeia. Table 2 in the Specification section indicates the differences in the amounts of the enzyme activities of amylase, lipase and protease for Pancreatic Extract, 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 statements are synonymous. Either term or statement may be selected by the applicant.

Date April 29, 2019

Proper name(s), Common name(s), Source material(s)

Table 1. Proper name(s), Common name(s), Source material(s)

Proper name(s)	Common name(s)	Source material(s)	
		Proper name(s)	Part(s)
Pancreatic enzymes	Pancreatic enzymes	▸ *Bos taurus* ▸ *Sus scrofa*	Pancreas
Pancreatic extract	Pancreatic extract		
Pancreatin	Pancreatin		
Pancrelipase	Pancrelipase		

References: Proper names: BP 2019, USP 41 2018, Ph.Eur. 2016, WHO 2011, US FDA 2010; Common names: BP 2019, USP 41 2018, Ph.Eur. 2016, WHO 2011, US FDA 2010; Source materials: BP 2019, USP 41 2018, Ph.Eur. 2016, Bisby et al. 2011.

Route of administration

Oral

Dosage form(s)

This monograph excludes foods or food-like dosage forms as indicated in the Compendium of Monographs Guidance Document.

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).

Use(s) or Purpose(s)

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

Dose(s)

Subpopulation(s)

Adults 18 years and older

Quantity(ies)

Enzyme preparation providing all the following enzyme activities (USP 41 2018; Suarez et al. 1999; Domínguez-Muñoz et al. 1997):

- Amylase: 17,000 to 149,000 USP amylase units per day, not to exceed 37,000 USP units per single dose
- Lipase: 5,000 to 40,000 USP lipase units per day, not to exceed 20,000 USP units per single dose
- Protease: 16,000 to 125,000 USP protease units per day, not to exceed 38,000 USP units per single dose

Notes

- Dose information must include the quantities of both the enzyme preparation and its enzymatic activity as potency.
- 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

Direction(s) 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).

Encapsulated products containing granules/(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(s) of use

Consult a health care practitioner/health care provider/health care professional/doctor/physician for use beyond 4 weeks (Friess et al. 1998).

Risk information

Caution(s) and warning(s)

All products

Consult a health care practitioner/health care provider/health care professional/doctor/ physician prior to use if you are pregnant, breastfeeding, have diabetes, pancreatitis, pancreatic exocrine insufficiency or cystic fibrosis (Halm et al. 1999; Delhaye et al. 1996; Guarner et al. 1993).

Digestive aid/Decrease bloating

Consult a health care practitioner/health care provider/health care professional/doctor/physician if symptoms persist or worsen.

Contraindication(s)

All products

Do not use this product if you are sensitive to pancreatic enzymes (Martindale 2011; CPS 2008).

Products from Sus scrofa pancreas

Do not use this product if you are sensitive to pork proteins (Martindale 2011; CPS 2008).

Known adverse reaction(s)

Stop use and consult a health care practitioner/health care provider/health care professional/ doctor/physician if nausea, vomiting, abdominal pain/epigastric pain and/or heartburn occur (Friess et al. 1998).

Non-medicinal ingredients

Must be chosen from the current Natural Health Products Ingredients Database (NHPID) and must meet the limitations outlined in the database.

Storage conditions

Store in a tightly closed, light-resistant container in a cool, dry place (BP 2019; USP 41 2018; Ph.Eur. 2016).

Specifications

- The finished product specifications must be established in accordance with the requirements described in the Natural and Non-prescription Health Products Directorate (NNHPD) Quality of Natural Health Products Guide.
- The medicinal ingredient must comply with the requirements outlined in the NHPID.
- The specifications must include testing for enzymatic activity of the medicinal ingredient at the 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.
- 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.
- In addition, the medicinal ingredient proper name and common name should be determined by the pharmacopoeial amounts of amylolytic, lipolytic and proteolytic activities for

Pancreatin, Pancreatic extract and Pancrelipase according to the British, European and U.S. pharmacopoeias (Table 2).

Table 2. 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 2019	Pancreatin	24 FIP	20 FIP	1.4 FIP
USP 41 2018	Pancreatin	25 USP	2 USP	25 USP
BP 2019	Pancreatic extract[2]	12 Ph. Eur.	15 Ph. Eur.	1 Ph. Eur.
Ph.Eur. 2016	Pancreas extract (powder)[2]	12 Ph. Eur.	15 Ph. Eur.	1.0 Ph. Eur.
USP 41 2018	Pancrelipase	100 USP	24 USP	100 USP

1. Minimum amounts
2. Cross-referenced within the respective pharmacopoeias. The proper and common name 'Pancreatic extract' should be used for both BP 2019 and Ph.Eur 2016.

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