

PANCREATIC ENZYMES

This abbreviated labelling standard (AbLS) is a guide to industry for the preparation of Product Licence Applications (PLAs) and labels for natural health product market authorization. It includes generalized claims and is not intended to be a comprehensive review of the medicinal ingredient. Wording of the claim on the PLA and label must therefore be identical to this AbLS.

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 as provided in the pharmacopoeia.
- To ensure consistent representation of enzyme-containing products, pancreatic enzyme activity must be expressed in USP units in the PLA and label.

Date March 30, 2012

Field	Field content	Reference
Proper and common names	pancreatic enzymes	US FDA 2010 WHO 2011
Source material(s)	bovine (<i>Bos taurus</i> (Bovidae)) pancreas porcine (<i>Sus scrofa</i> (Suidae)) pancreas	BP 2012 Ph.Eur. 2012 Bisby et al. 2011 USP 34
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). 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). This labelling standard is not intended to include foods or food-like dosage forms such as bars, chewing gums or beverages.	Friess et al. 1999 Suarez et al. 1999 Sharpé et al. 1997 WHO 2011
Use(s) or Purpose(s)	Digestive aid. Helps to decrease bloating after high caloric, high fat meals.	Cichoke 2006 Suarez et al. 1999

Field	Field content	Reference
	Digestive aid to help decrease bloating after high caloric, high fat meals. Digestive enzyme.	Suarez et al. 1999
Dose(s)¹	Dose information must include the quantities of both the enzyme preparation and its enzymatic activity: <ul style="list-style-type: none"> • Enzyme preparation (lipase, amylase, and protease) per dosage unit; and • Enzyme activity providing all the following, one to four times per day: <ul style="list-style-type: none"> lipase: 5000 – 10000 USP units amylase: 16600 – 37350 USP units protease: 15625 – 37500 USP units. 	USP 34 Suarez et al. 1999 Domínguez-Muñoz et al. 1997
Sub-population(s)	Adults	
Duration(s) of use	Consult a health care practitioner for use beyond four weeks. For prolonged use, consult a health care practitioner.	Friess et al. 1998
Direction(s) of use	Use the smallest effective dose which controls symptoms.	CPS 2008 Sharpé et al. 1997
	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
	For enteric-coated products: Swallow whole/do not crush or chew.	CPS 2008
	For capsules 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.	Sweetman 2011 CPS 2008
Risk information	Consult a health care practitioner if symptoms persist or worsen.	
	Consult a health care practitioner prior to use if you are pregnant or breastfeeding.	
	Consult a health care practitioner prior to use if you have diabetes.	
	Consult a health care practitioner prior to use if you have pancreatitis, pancreatic exocrine insufficiency or cystic fibrosis.	Halm et al. 1999 Delhayé et al. 1996 Guarner et al. 1993

Field	Field content	Reference
	<p>For products from hog/pig pancreas: Do not use if you are sensitive to pork proteins.</p> <p>For all products: Do not use if you are sensitive to pancreatic enzymes.</p> <p>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).</p>	<p>Sweetman 2011 CPS 2008</p> <p>Friess et al. 1998</p>
Non-medicinal ingredient(s)	Must be chosen from the current <i>Natural Health Products Ingredients Database</i> 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 2012 Ph.Eur. 2012 USP 34
Specification(s)	<p>A Finished Product Specifications Form must accompany the application.</p> <p>The finished product must comply with the requirements of the current NHPD <i>Evidence for Quality of Finished Natural Health Products</i> guidance document.</p> <p>The specifications must include testing for enzymatic activity of the medicinal ingredient at the finished product stage using the assays outlined in the United States Pharmacopeia (USP 34): Pancrelipase – assay for amylase, lipase and protease activity.</p> <p>The medicinal ingredient may comply with the pancreatic enzyme preparation specifications outlined in the following American, British and European pharmacopoeial monographs: USP 34: Pancrelipase BP 2012: Pancreatin Pancreatic extract; Pancreas Powder Ph.Eur. monograph 0350 Ph.Eur. 2012: Pancreas powder / Pancreatis pulvis</p> <p>Overages to compensate for the loss of activity during manufacturing and shelf-life of the finished product are permitted as per the pharmacopoeial standard.</p> <p>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.</p>	

¹. 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):

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

For amylase: 1 Ph. Eur. Unit = 1 BP Unit = 1 FIP Unit ~ 4.15 USP Units
For lipase: 1 Ph. Eur. Unit = 1 BP Unit = 1 FIP Unit ~ 1 USP Unit

References cited

Bisby FA, Roskov YR, Orrell TM, Nicolson D, Paglinawan LE, Bailly N, Kirk PM, Bourgoin T, Baillargeon G, Ouvrard D, editors. Species 2000 & ITIS Catalogue of Life, 15th March 2012 [Internet]. Reading (GB): Species 2000. [Source database: ITIS: The Integrated Taxonomic Information System, Version Apr 2011; Accessed 2012 March 16]. Available from: <http://www.catalogueoflife.org>

BP 2012: British Pharmacopoeia 2012. Volume II. London (GB): The Stationary Office on behalf of the Medicines and Healthcare products Regulatory Agency (MHRA); 2011.

Cichoke AJ. Pancreatic Enzymes. In: Pizzorno JE, Murray MT, editors. Textbook of Natural Medicine, Third edition, volume 1. St. Louis (MI): Churchill Livingstone Elsevier; 2006. p. 1131-1146.

CPS 2008: Compendium of Pharmaceuticals and Specialties: The Canadian Drug Reference for Health Professionals. Ottawa (ON): Canadian Pharmacists Association; 2008.

Delhaye M, Meuris S, Gohimont AC, Buedts K, Cremer M. Comparative evaluation of a high lipase pancreatic enzyme preparation and a standard pancreatic supplement for treating exocrine pancreatic insufficiency in chronic pancreatitis. *European Journal of Gastroenterology and Hepatology* 1996;8:699-703.

Domínguez-Muñoz JE, Birckelbach U, Glasbrenner B, Sauerbruch T, Malfertheiner P. Effect of oral pancreatic enzyme administration on digestive function in healthy subjects: comparison between two enzyme preparations. *Alimentary Pharmacology and Therapeutics* 1997;11(2):403-408.

Ferrone M, Raimondo M, Scolapio JS. Pancreatic enzyme pharmacotherapy. *Pharmacotherapy* 2007;27(6):910-920.

Friess H, Kleeff J, Malfertheiner P, Müller MW, Homuth K, Büchler MW. Influence of high-dose pancreatic enzyme treatment on pancreatic function in healthy volunteers. *International Journal of Pancreatology* 1998;23(2):115-123.

Guarner L, Rodríguez R, Guarner F, Malagelada JR. Fate of oral enzymes in pancreatic insufficiency. *Gut* 1993;34:708-712.

Halm U, Löser C, Löhr M, Katschinski M, Mössner J. A double-blind, randomized, multicentre, crossover study to prove equivalence of pancreatin minimicrospheres versus microspheres in exocrine pancreatic insufficiency. *Alimentary Pharmacology and Therapeutics* 1999;13(7):951-957.

Ph.Eur. 2012: European Pharmacopoeia, 7th edition. Strasbourg (FR): Directorate for the Quality of Medicines and HealthCare of the Council of Europe (EDQM), 2012.

Scharpé S, Uyttenbroeck W, Samyn N. Pancreatic Enzyme Replacement. In: Lauwers A, Scharpé S, editors. Pharmaceutical Enzymes. London (GB): Taylor & Francis, Inc; 1997. p. 187-221.

Suarez F, Levitt MD, Adshead J, Barkin JS. Pancreatic supplements reduce symptomatic response of healthy subjects to a high fat meal. Digestive Diseases and Sciences 1999;44(7):1317-1321.

Sweetman SC, editor. Martindale: The Complete Drug Reference [Internet]. London (GB): Pharmaceutical Press; 2011. [Pancreatic enzymes: latest modification 09-Apr-2011; Accessed 2012 March 16]. Available from: <http://www.medicinescomplete.com>

US FDA 2010: Postmarket Drug Safety Information for Patients and Providers. Updated Questions and Answers for Healthcare Professionals and the Public: Use an Approved Pancreatic Enzyme Product (PEP), Page last updated: 05/24/2010. [Internet] [Accessed 2012 March 16]. Available from: <http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm204745.htm>

USP 34: United States Pharmacopeia and the National Formulary (USP 34 - NF 29). Rockville (MD): The United States Pharmacopeial Convention; 2011.

WHO 2011: WHO Model List of Essential Medicines, 17th edition, March 2011 [Internet]. [Accessed 2012 March 16]. Available from: <http://www.who.int/medicines/publications/essentialmedicines/en/index.html>

References reviewed

Evidence for Quality of Finished Natural Health Products, Version 2.0. Ottawa (ON): Natural Health Products Directorate, Health Canada; 2007. [Accessed 2011 August 2]. Available from: <http://www.hc-sc.gc.ca/dhp-mps/prodnatur/legislation/docs/eq-paq-eng.php>