

FRUIT BROMELAIN

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.

Date March 30, 2012

Field	Field content	Reference
Proper name(s)	fruit bromelain	IUBMB 1992
Common name(s)	fruit bromelain/ pineapple fruit bromelain/ juice bromelain	IUBMB 1992
Source material(s)	pineapple (<i>Ananas comosus</i> (L.) Merr. var. <i>comosus</i> (Bromeliaceae)) fruit	USDA 2011
Route(s) of administration	Oral	
Dosage form(s)	<p>The acceptable pharmaceutical dosage forms include, but are not limited to capsules, chewables (e.g. gummies, tablets), liquids, powders, strips or tablets.</p> <p>This AbLS is not intended to include foods or food-like dosage forms such as bars, chewing gums or beverages.</p>	
Use(s) or Purpose(s)	Digestive enzyme	
Dose(s)	<p>Dose information must include the quantities of both the enzyme preparation and its enzymatic activity:</p> <ul style="list-style-type: none"> • Enzyme preparation providing up to 600 mg per day; not to exceed 300 mg per dose; and • Enzyme activity providing up to 20 250 000 FCC PU^{1,2} per day³; not to exceed 10 125 000 FCC PU per dose. 	<p>Kerkhoffs et al. 2004; Walker et al. 2002; Singer et al. 2001; Klein and Kullich 2000; Gutfreund et al. 1978</p> <p>Glade et al. 2001; Gutfreund et al. 1978</p>
Sub-population(s)	Adults	
Duration(s) of use	For prolonged use, consult a health care practitioner.	
Direction(s) of	Take with food/meal.	

Field	Field content	Reference
use	Consult a health care practitioner prior to use if you are pregnant or breastfeeding.	
Risk information	Consult health care practitioner prior to use if you have gastrointestinal lesions/ulcers, are taking anticoagulant agents, anti-inflammatory agents or antibiotics or before having surgery.	Sweetman 2011 Brinker 2010 Blumenthal et al. 2000
	Hypersensitivity/allergy has been known to occur, in which case discontinue use.	Sweetman 2011 Brinker 2010 Murray and Pizzorno 2006 Blumenthal et al. 2000 Baur and Fruhmman 1979
	Nausea, vomiting, and diarrhoea have been known to occur, in which case discontinue use (and consult a health care practitioner).	Sweetman 2011 Brien et al. 2006 Blumenthal et al. 2000
Non-medicinal ingredient(s)	Must be chosen from the current NHPD <i>Natural Health Products Ingredients Database</i> and must meet the limitations outlined in the database.	
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 assay outlined in the Food Chemicals Codex (FCC 7) : PLANT PROTEOLYTIC ACTIVITY.</p> <p>Details of the manufacturing of the enzyme at the raw material stage should include fermentation medium, isolation process and the percent purity of the medicinal ingredient.</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. FCC 7: one papain unit (PU) is defined as that quantity of enzyme that liberates the equivalent of 1 µg of tyrosine per hour under the conditions of the assay.
- ². One gelatin digestion unit (GDU) is approximately equivalent to 15 000 FCC papain unit (1 GDU ≈ 15 000 FCC PU).
- ³. For multi-ingredient products containing both Papain and Bromelain, the combined proteolytic activity should not exceed the maximum proteolytic activity of 7 200 000 FCC PU per day (as per the NHPD Papain AbLS).

References cited

Baur X, Fruhmann G. Allergic reactions, including asthma, to the pineapple protease bromelain following occupational exposure. *Clinical Allergy* 1979;9(5):443-450.

Blumenthal M, Goldberg A, Brinckmann J, editors. *Herbal Medicine: Expanded Commission E Monographs*. Boston (MA): Integrative Medicine Communications; 2000.

Brien S, Lewith G, Walker AF, Middleton R, Prescott P, Bundy R. Bromelain as an adjunctive treatment for moderate-to-severe osteoarthritis of the knee: a randomized placebo-controlled pilot study. *QJM: An International Journal of Medicine* 2006;99(12): 841-850.

Brinker F. Final Updates and Additions to Herb Contraindications and Drug Interactions, 3rd edition [Internet]. Sandy (OR): Eclectic Medical Publications. [Last update July 13, 2010; Accessed 2012 March 28]. Available from: <http://www.eclecticherb.com/emp/updatesHCDI.html>

FCC 7: Food Chemicals Codex, Seventh edition. Rockville (MD): The United States Pharmacopeial Convention; 2012.

Glade MJ, Kendra D, Kaminski MV. Improvement in protein utilization in nursing-home patients on tube feeding supplemented with an enzyme product derived from *Aspergillus niger* and bromelain. *Nutrition* 2001;17(4):348-350.

Gutfreund AE, Taussig SJ, Morris AD. Effect of oral bromelain on blood pressure and heart rate of hypertensive patients. *Hawaii Medical Journal* 1978;37(5):143-146.

IUBMB 1992: IUBMB Enzyme Nomenclature [Internet]. London (GB): Queen Mary, University of London. [fruit bromelain: CAS 9001-00-7, EC 3.4.22.33 created 1965 as EC 3.4.4.24, transferred 1972 to EC 3.4.22.4, part transferred 1992 to EC 3.4.22.33; Accessed 2012 March 28]. Available from: <http://www.chem.qmul.ac.uk/iubmb/enzyme/EC3/4/22/33.html>

Kerkhoffs GM, Struijs PA, de Wit C, Rahlfs VW, Zwipp H, van Dijk CN. A double blind, randomised, parallel group study on the efficacy and safety of treating acute lateral ankle sprain with oral hydrolytic enzymes. *British Journal of Sports Medicine* 2004;38;431-435.

Klein G, Kullich W. Short-term treatment of painful osteoarthritis of the knee with oral enzymes: a randomised, double-blind study versus diclofenac. *Clinical Drug Investigation* 2000;19(1):15-23.

Murray MT, Pizzorno JE. Bromelain. In: Pizzorno JE, Murray MT, editors. *Textbook of Natural Medicine*, Third edition, volume 1. St. Louis (MI): Churchill Livingstone Elsevier; 2006. p. 791-795.

Singer F, Singer C, Oberleitner H. Phlogenzym versus diclofenac in the treatment of activated osteoarthritis of the knee. A double-blind prospective randomized study. *International Journal of Immunotherapy* XVII 2001;(2/3/4):135-141.

Sweetman SC, editor. Martindale: The Complete Drug Reference [Internet]. London (GB): Pharmaceutical Press. [Bromelains: syn: EC 3.4.22.33, CAS: 9001-00-7, latest modification 10 Oct 2011; Accessed 2012 March 28]. Available from: <http://www.medicinescomplete.com>

USDA 2011: United States Department of Agriculture, Agricultural Research Service, National Genetic Resources Program. Germplasm Resources Information Network (GRIN) [Internet]. Beltsville (MD): National Germplasm Resources Laboratory. [*Ananas comosus* (L.) Merr. var. *comosus* (Bromeliaceae): last updated 16-Jun-2011; Accessed 2012 March 28]. Available from: http://www.ars-grin.gov/cgi-bin/npgs/html/tax_search.pl

Walker AF, Bundy R, Hicks SM, Middleton RW. Bromelain reduces mild acute knee pain and improves well-being in a dose-dependent fashion in an open study of otherwise health adults. *Phytomedicine* 2002;9:681-686.

References reviewed

Baur X. Studies on the specificity of human IgE-antibodies to the plant proteases papain and bromelain. *Clinical & Experimental Allergy* 1979;9(5):451-457.

Berardi RR, Kroon LA, McDermott JH, Newton GD, Oszko MA, Popovich NG, Remington TL, Rollins CJ, Shimp LA, Tietze KJ, editors. *Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care*, 15th edition. Washington (DC): APhA Publications; 2006.

Evidence for Quality of Finished Natural Health Products, Version 2.0 [Internet]. 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>

Repchinsky C, editor-in-chief. *Patient Self-Care: Helping Patients Make Therapeutic Choices*, 1st edition. Ottawa (ON): Canadian Pharmacists Association; 2002.