Health Canada Santé Canada

NATURAL HEALTH PRODUCT

SERRAPEPTASE

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 ingredient.

Notes

- 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 September 25, 2018

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)
▸ Serrapeptase Serratiopeptidase	▸ Serrapeptase ▸ Serratiopeptidase	*Serratia marcescens* E-15	Whole cell

References: Proper names: NHPID; Common names:NHPID; Source material: Al-Khateeb and Nusair 2008.

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.

Proteolytic Enzyme

Acceptable dosage forms for the age category listed in this monograph and specified route of administration are indicated in the Compendium of Monographs Guidance Document.

Reduction of symptoms associated with ear, nose and throat infections; Swelling and pain reduction; Mucolytic enzyme

The only acceptable pharmaceutical dosage forms include enteric coated capsules, tablets, granules or similar preparations (Bhagat et al. 2013; Chopra et al. 2009; Balaji SM 2007). The dosage form must be qualified with an additional term to describe the delayed release (e.g. enteric-coated capsules, gastro-resistant tablets, microencapsulated enzymes) (WHO 2011).

Use(s) or Purpose(s)

- Proteolytic enzyme (Martindale 2011).
- Helps to reduce (symptoms such as) pain, quantity of secretion, inability to perceive smell and stuffy nose from ear, nose and/or throat infections (Mazzone et al 1990; Tachibana et al 1984).
- Mucolytic enzyme that helps break down mucous (Nakamura et al 2003; Majima et al 1990; Mazzone et al 1990; Tachibana et al 1984).
- Helps reduce and/or relieve postoperative cheek swelling and/or pain after dental surgery (Al-Khateeb and Nusair 2008; Tachibana et al 1984).

The following combined use(s) or purpose(s) is/are also acceptable:

- Mucolytic enzyme that helps break down mucous to reduce (symptoms such as) pain, quantity of secretion, inability to perceive smell and stuffy nose from ear, nose and/or throat infections (Martindale 2011; Nakamura et al 2003; Majima et al 1990; Mazzone et al 1990; Tachibana et al 1984).
- Proteolytic enzyme that helps reduce and/or relieve postoperative cheek swelling and/or pain after dental surgery (Martindale 2011; Al-Khateeb and Nusair 2008; Tachibana et al 1984).

Dose(s)

Subpopulation(s)

Adults 18 years and older

Quantity(ies)

Proteolytic Enzyme

Not to exceed 120,000 serratiopeptidase units (SU), per day (Martindale 2011).

Reduction of symptoms associated with ear, nose and throat infections; Mucolytic enzyme

60,000-120,000 serratiopeptidase units (SU), per day (Chopra et al. 2009; Nakamura et al. 2003; Majima et al. 1990; Mazzone et al. 1990; Majima et al. 1988; Tachibana et al. 1984).

Swelling and pain reduction

30,000-120,000 serratiopeptidase units (SU), per day (Chopra et al. 2009; Al-Khateeb and Nusair 2008; Tachibana et al. 1984).

Direction(s) for use

Take 2 hours after a meal (Bhagat et al. 2013; Chopra et al. 2009; Mazzone et al. 1990).

Duration(s) of use

Products making a swelling and pain reduction claim (at any dose) and products providing more than 60,000 serratiopeptidase units (SU), per day

Consult a health care practitioner/health care provider/health care professional/doctor/physician for use beyond 7 days (Al-Khateeb and Nusair 2008; Tachibana et al. 1984).

Products providing 60,000 or less serratiopeptidase units (SU), per day

Consult a health care practitioner/health care provider/health care professional/doctor/physician for use beyond 4 weeks (Nakamura et al 2003; Majima et al 1990; Majima et al 1988).

Risk information

Caution(s) and warning(s)

- Consult a health care practitioner/health care provider/health care professional/doctor/physician if symptoms persist or worsen.
- Consult a health care practitioner/health care provider/health care professional/doctor/physician prior to use if you are pregnant, breastfeeding, have a gastrointestinal lesion/ulcer, kidney or liver disorder, or are having surgery (Bhagat et al. 2013; Chopra et al. 2009; Al-Khateeb and Nusair 2008; HSA 2008; Mazzone et al. 1990).
- Consult a health care practitioner/health care provider/health care professional/doctor/physician prior to use if you are taking anticoagulant/blood thinner or anti-inflammatory medications (Bhagat et al. 2013; Chopra et al. 2009; Al-Khateeb and Nusair 2008; Mazzone et al. 1990).

Contraindication(s)

No statement required.

Known adverse reaction(s)

Stop use if rash, difficulty breathing, hypersensitivity and/or severe allergy occur (Bhagat et al. 2013; Balagi 2007).

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

No statement required.

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.
- Details of the manufacturing of the enzyme at the raw material stage should include fermentation medium and the isolation process of the medicinal ingredient.
- No traces of any antibiotics or their residues, should be detectable in the finished product.
- The medicinal ingredient may comply with the specifications outlined in the Japanese Pharamcopia (JP XVI) : Serrapeptase.
- 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 Japanese Pharmacopia (JP XVI) : Serrapeptase.
- Where published methods are not suitable for use, manufacturers will use due diligence to ensure that the enzymes remain active to the end of their shelf life indicated on the product label.

References cited

Al-Khateeb TH and Nusair Y. Effect of the proteolytic enzyme serrapeptase on swelling, pain and trismus after surgical extraction of mandibular third molars. International Jounal of Oral Maxillofacial Surgery 2008;37:264-268.

Balaji SM. Textbook of Oral & Maxillofacial Surgery. Elsevier India; 2007.

Bhagat S, Agarwal M and Roy V. Serratiopeptidase : A systemic review of the existing evidence. International Journal of Surgery 2013;11(3):209-217

Chopra D, Rehan HS, Mehra P, et al. A randomized, double-blind, placebo-controlled study comparing the efficacy and safety of paracetamol, serratiopeptidase, ibuprofen and betamethasone using the dental impaction pain model. International Journal of Oral Maxillofacial Surgery 2009;38:350-355.

HSA 2006: Singapore Health Sciences Authority Safety-related Product Label Amendments (September 2006). [Accessed 2016 January 8]. Available from: http://www.hsa.gov.sg/content/hsa/en/Health_Products_Regulation/Safety_Information_and_Product_Recalls/Safety-related_Product_Label_Amendments/2006/September.html#Serratiopeptidase.

Majima Y, Hirata K, Takeuchi K et al. Effects of orally administered drugs on dynamic viscoelasticity of human nasal mucus. The American Review of Respiratory Disease 1990;141(1):79-83.

Majima Y, Inagaki M, Hirata K, et al. The effect of an orally administered proteolytic enzyme on the elasticity and viscosity of nasal mucus. Archives of Oto-rhino-laryngology 1988;244:355-359.

Martindale 2011: Sweetman SC, editor. 2011. Martindale: The Complete Drug Reference. [Internet]. London (GB): Pharmaceutical Press. [Serrapeptase: CAS 37312-62-2; 95077-02-4, latest modification: 2011 October 10; Accessed 2018 August 10]. Available from: http://www.medicinescomplete.com.

Mazzone A, Catalani M, Costanzo M, et al. Evaluation of serratia peptidase in acute or chronic inflammation of otorhinolaryngology pathology : a multicentre, double-blind, randomized trial versus placebo. Journal of International Medical Research 1990;18:379-388.

Nakamura S, Hashimoto Y, Mikami M, Yamanaka E, Soma T, Hino M, Azuma A, Kudoh S. Effect of the proteolytic enzyme serrapeptase in patients with chronic airway disease. Respirology 2003 Sep;8(3):316-20.

Tachibana M, Mizukoshi O, Harada Y, et al. A multi-centre, double-blind study of serrapeptase versus placebo in post-antrotomy buccal swelling. Pharmatherapeutica 1984;3(8):526-530.

References reviewed

Evidence for Quality of Finished Natural Health Products, Version 2.0 [Internet]. Ottawa (ON): Natural Health Products Directorate, Health Canada. 2015. [Accessed 2016 January 8]. Available from: http://www.hc-sc.gc.ca/dhp-mps/prodnatur/legislation/docs/eq-paq-eng.php.

JP XVI : Japanese Pharmacopia. Ministry of Health, Labour and Welfare; 2011.