CASCARA SAGRADA

This monograph is intended to serve as a guide to industry for the preparation of Product Licence Applications and labels for natural health product market authorization. It is not intended to be a comprehensive review of the medicinal ingredient. It is a referenced document to be used as a labelling standard.

Note: Text in parentheses is additional optional information which can be included on the Product Licence Application and product labels at the applicant's discretion.

Date: October 31, 2008

Proper name(s): *Frangula purshiana* (DC.) J.G. Cooper (Rhamnaceae) (USDA 2004)

Common name(s): Cascara sagrada (McGuffin et al. 2000)

Source material(s): Bark (aged) (Wichtl 2004; Blumenthal et al. 2000)

Route(s) of administration: Oral

Dosage form(s):

- Those suited to the allowable route(s) of administration
- This monograph is not intended to include food-like dosage forms such as bars, chewing gums or beverages.

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

- (Traditionally used in Herbal Medicine as a) stimulant laxative (Williamson 2003; Blumenthal et al. 2000; Moerman 1998; Felter and Lloyd 1983 [1898]).
- (Used in Herbal Medicine for the) short-term relief of occasional constipation (EMEA 2007; Mills and Bone 2005; WHO 2002).
- (Used in Herbal Medicine to) promote(s) bowel movement (by direct action on the large intestine) (EMEA 2007; Sweetman 2007; Blumenthal et al. 2000).

Note: Claims for traditional use must include the term "Herbal Medicine".

Dose(s):

Subpopulation(s): Adults, and adolescents ≥ 11 years (EMEA 2007; Mills and Bone 2005; ESCOP 2003; Berardi et al. 2002)

Quantity(ies):

- Preparations equivalent to 0.25-3 g dried bark, per day (Mills and Bone 2005, ESCOP 2003; Williamson 2003; WHO 2002; Blumenthal et al. 2000; Bradley 1992)
- Preparations equivalent to 10-30 mg of hydroxyanthracene derivatives (calculated as cascaroside A), per day (EMEA 2007; Mills and Bone 2005; ESCOP 2003; Blumenthal et al. 2000)

Directions for use:

- Take two to three times per week. If results are not observed, the frequency of use may be increased up to once daily (EMEA 2007).
- Take a single dose at bedtime (Bradley 1992).
- Take a few hours before or after taking other medications or health products (Repchinsky 2008; Brinker 2001).
- Allow at least 6 to 12 hours for laxative effect to occur (Berardi et al. 2002).
- **Optional** (for products which provide a dosage range)**:** The correct individual dose is the smallest required to produce a comfortable soft-formed stool (EMEA 2007; McGuffin 1997).

See Appendix 1 for examples of appropriate dosage preparations, frequencies of use and directions for use, according to cited references. The purpose of Appendix 1 is to provide guidance to industry.

Duration(s) of use: Consult a health care practitioner for use beyond 7 days (Berardi et al. 2002).

Risk information: Statement(s) to the effect of:

Caution(s) and warning(s):

- Consult a health care practitioner if symptoms persist or worsen.
- Consult a health care practitioner prior to use if you have faecal impaction or symptoms such as abdominal pain, nausea, vomiting or fever (EMEA 2007; Brinker 2001).
- Consult a health care practitioner prior to use if you have a kidney disorder (EMEA 2007; WHO 2002) or are taking cardiac medications such as cardiac glycosides or antiarrhythmic medications (EMEA 2007; Brinker 2001; Blumenthal et al. 2000).

- Consult a health care practitioner prior to use if you are taking thiazide diuretics, corticosteroids, licorice root or other medications or health products which may aggravate electrolyte imbalance (EMEA 2007; WHO 2002; Brinker 2001; Blumenthal et al. 2000).
- Reduce dose or discontinue use if you experience abdominal pain, cramps, spasms and/or diarrhoea (EMEA 2007; WHO 2002; Blumenthal et al. 2000).

Contraindication(s):

- Do not use if you have abnormal constrictions of the gastrointestinal tract, potential or existing intestinal blockage, atonic bowel, appendicitis, inflammatory colon disease such as Crohn's disease or ulcerative colitis, abdominal pain of unknown origin, undiagnosed rectal bleeding, severe dehydration with depleted water or electrolytes (EMEA 2007; WHO 2002) or diarrhoea (Brinker 2001; McGuffin et al. 1997).
- Do not use if you are pregnant or breastfeeding (EMEA 2007; Brinker 2001; Blumenthal et al. 2000).

Known adverse reaction(s): Hypersensitivity has been known to occur; in which case, discontinue use (EMEA 2007).

Non-medicinal ingredients: Must be chosen from the current NHPD *List of Acceptable Non-medicinal Ingredients* and must meet the limitations outlined in the list.

Specifications:

- Must comply with the minimum specifications outlined in the current *Compendium of Monographs*.
- Bark must be dried and aged for a minimum of one year (Wichtl 2004; Blumenthal et al. 2000) or heated and dried to induce artificial aging to allow oxidation of the anthrones (Blumenthal et al. 2000). For example, the bark may be heated in hot air at 80-100°C for several hours (Wichtl 2004).
- The medicinal ingredient may comply with the specifications outlined in the pharmacopoeial monographs listed in Table 1 below.

Table 1: Cascara sagrada monographs published in the British, European and United States Pharmacopoeiae

Pharmacopoeia	Monograph
British Pharmacopoeia (BP)	Cascara Standardized Cascara Dry Extract
European Pharmacopoeia (Ph. Eur.)	Cascara Cascara Dry Extract, Standardised
United States Pharmacopoeia (USP)	Cascara Sagrada Cascara Sagrada Extract Cascara Tablets

References cited:

Berardi RR, DeSimone EM, Newton GD, Oszko MA, Popovich NG, Rollins CJ, Shimp LA, Tietze KJ, editors. 2002. Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care, 13th edition. Washington (DC): American Pharmaceutical Association.

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

Bradley PR, editor. 1992. British Herbal Compendium: A Handbook of Scientific Information on Widely Used Plant Drugs, Volume 1. Bournemouth (UK): British Herbal Medicine Association.

Brinker F. 2001. Herb Contraindications and Drug Interactions, 3rd edition. Sandy (OR): Eclectic Medical Publications.

BP 2008: British Pharmacopoeia, Volume II. London (UK): The Stationary Office, on behalf of the Medicines and Healthcare products Regulatory Agency (MHRA).

EMEA 2007. European Medicines Agency. Community Herbal Monograph on *Rhamnus Purshianus* D.C., cortex (on line). London (UK): EMEA Committee on Herbal Medicinal Products (HMPC), 31 October 2007. Available from: http://www.emea.europa.eu/pdfs/human/hmpc/rhamni_purshianae_cortex/51357906enfin.pdf [Accessed 1 August 2008].

ESCOP 2003: ESCOP Monographs: The Scientific Foundation for Herbal Medicinal Products, 2nd edition. Exeter (UK): European Scientific Cooperative on Phytotherapy and Thieme.

Felter HW, Lloyd JU. 1983. King's American Dispensatory, Volume 1, 18th edition. Sandy (OR): Eclectic Medical Publications [Reprint of 1898 original].

McGuffin M, Kartesz JT, Leung AY, Tucker AO, editors. 2000. Herbs of Commerce, 2nd edition. Silver Spring (MD): American Herbal Products Association.

Mills S, Bone K. 2005. The Essential Guide to Herbal Safety. St. Louis (MO): Elsevier Churchill Livingstone.

Moerman DE. 1998. Native American Ethnobotany. Portland (OR): Timber Press.

Ph. Eur. 2008: European Pharmacopoeia, 6th edition, Volume 1. Strasbourg (France): Directorate for the Quality of Medicines and HealthCare of the Council of Europe (EDQM).

Repchinsky C, editor. 2008. Compendium of Pharmaceuticals and Specialties. The Canadian Drug Reference for Health Professionals. Ottawa (ON): Canadian Pharmacists Association.

Sweetman SC, editor. 2007. Martindale: The Complete Drug Reference, 35th edition. London (UK): Pharmaceutical Press.

USDA 2004: United States Department of Agriculture, Agricultural Research Service, National Genetic Resources Program. Germplasm Resources Information Network (GRIN) [online database]. *Frangula purshiana* (DC.) J.G. Cooper. Beltsville (MD): National Germplasm Resources Laboratory. Available from: http://www.ars-grin.gov/cgi-bin/npgs/html/tax_search.pl [Accessed 30 July 2008).

USP 31: 2008. United States Pharmacopeia and the National Formulary (USP 31 - NF 26). Rockville (MD): United States Pharmacopeial Convention, Inc.

WHO 2002: World Health Organization. WHO Monographs on Selected Medicinal Plants, Volume 2. Geneva (CHE): World Health Organization.

Wichtl M, editor. 2004. Herbal Drugs and Phytopharmaceuticals: A Handbook for Practice on a Scientific Basis, 3rd edition. Stuttgart (D): Medpharm GmbH Scientific Publishers.

Williamson EM. 2003. Potter's Herbal Cyclopaedia: The Authoritative Reference work on Plants with a Known Medical Use. Saffron Walden (UK): The C.W. Daniel Company Limited.

References reviewed:

Barnes J, Anderson LA, Philipson JD. 2002. Herbal Medicines: A Guide for Healthcare Professionals, 2nd edition. London (UK): The Pharmaceutical Press.

BHP 1996: British Herbal Pharmacopoeia. Bournemouth (UK): British Herbal Medicine Association.

BHP 1983: British Herbal Pharmacopoeia. Cowling (UK): British Herbal Medical Association.

Ellingwood F. 1983. American Materia Medica, Therapeutics and Pharmacognosy. Sandy (OR): Eclectic Medical Publications [Reprint of 1919 original].

FDA 1985: Unites States Food and Drug Administration. Laxative Drug Products for Over-the-Counter Human Use; Tentative Final Monograph. Proposed Rules sections 334.10 and 334.52. Federal Register Volume 50, Number 10, Tuesday, January 15, 1985. Available from: http://www.fda.gov/cder/otcmonographs/category_sort/laxative.htm [Accessed 2008-07-31].

Gruenwald J, Bendler T, Jaenicke C, editors. 2004. PDR for Herbal Medicines, 3rd edition. Montvale (NJ): Medical Economics Company.

HC 1997. Health Canada. TPD/NHPD Category IV Labelling Standard, Stimulant Laxatives [online]. Ottawa (ON): Therapeutic Products Directorate, Health Canada. Available from: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/label-etiquet-pharm/laxstimu-eng.php [Accessed 26 August 2008].

HC 1994. Health Canada. TPD/NHPD Category IV Labelling Standard, General Laxatives [online]. Ottawa (ON): Therapeutic Products Directorate, Health Canada. Available from: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/label-etiquet-pharm/laxat-eng.php [Accessed 26 August 2008].

Hoffmann D. 2003. Medical Herbalism: The Science and Practice of Herbal Medicine. Rochester (VT): Healing Arts Press.

Mills S, Bone K. 2000. Principles and Practice of Phytotherapy. Toronto (ON): Churchill Livingstone.

Pray WS. 2006. Non-Prescription Product Therapeutics, 2nd edition. New York (NY): Lippincott Williams & Wilkins

Remington JP, Woods HC, editors. 1918. The Dispensatory of the United States of America [online] 20th edition. Abridged; botanicals only. Bisbee (AZ): Scanned by Michael Moore, director, The Southwest School of Botanical Medicine. Available from: http://www.swsbm.com/Dispensatory/USD-1918-complete.pdf [Accessed 2 August 2008].

Repchinsky 2002: Canadian Pharmacists Association. Patient Self-Care. Helping Patients Make Therapeutic Choices. Ottawa (ON): Canadian Pharmacists Association.

Wiersema J, León B. 1999. World Economic Plants: A Standard Reference. Boca Raton (FL): CRC Press LLC.

Appendix 1: Examples of appropriate dosage preparations, frequencies of use and directions for use

Dried bark:

- 0.3-1 g dried bark, per day (Mills and Bone 2005; ESCOP 2003)
- 1-2.5 g powdered bark, per day (Williamson 2003)
- 0.5-2.5 g dried bark, per day (WHO 2002)
- 1-2 g cut or powdered aged bark, per day (Blumenthal et al. 2000)
- 0.25-1 g dried bark, per day (Bradley 1992)

Infusion:

- 0.3-2 g dried bark, per day (Mills and Bone 2005)
- 1.5-2 g dried bark, per day (ESCOP 2003)
- 1-2 g dried bark, per day (Blumenthal et al 2000)

Directions for use: Pour 150 ml of boiling water over dried bark and infuse for 10-15 minutes (Blumenthal et al 2000).

Tincture: 1.5-3 g, per day
(1:2, 3-6 ml) (Mills and Bone 2005)

Preparations providing the following quantities of hydroxyanthracene derivatives (calculated as cascaroside A):

- 10-30 mg, per day (EMEA 2007)
- 20-30 mg, per day (Mills and Bone 2005; ESCOP 2003)
- 20-30 mg, per day (Blumenthal et al. 2000)