Health Canada Santé Canada

ACTIVE HEXOSE CORRELATED COMPOUND - POWDER (AHCC-FD)

For products in granule form, refer to the "ACTIVE HEXOSE CORRELATED COMPOUND - GRANULE (AHCC-FG)" monograph.

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 the statements are synonymous. Either term or statement may be selected by the applicant.

Date November 15, 2012

Proper name(s)

Active hexose correlated compound (Spierings et al. 2007; Matsui et al. 2002)

Common name(s)

- Active hexose correlated compound (Spierings et al. 2007; Matsui et al. 2002)
- AHCC (Spierings et al. 2007; Matsui et al. 2002)

Source material(s)

Freeze-dried mycelium extract of Shiitake (*Lentinula edodes* ((Berk.) Pegler (1976) (Marasmiaceae)) (Fujii et al. 2011; Sumiyoshi et al. 2010)

Route(s) of administration

oral

Dosage form(s)

- The acceptable pharmaceutical dosage form is limited to capsules.

- This monograph is not intended to include foods or food-like dosage forms such as bars, chewing gums or beverages.

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

Antioxidant (Ye et al. 2004, 2003; Wang et al. 2001).

Dose(s)

Subpopulation(s)

adults (≥ 19 years)

Quantity(ies)

Up to 3.6 g Active hexose correlated compound powder (AHCC-FD), per day (Fujii et al. 2011; Cowawintaweewat et al. 2006; Uno et al. 2000)

Directions for use

Take with at least 240 ml liquid (water, milk, fruit juice or similar aqueous beverage). Taking this product with insufficient liquid may result in choking and/or esophageal blockage/obstruction of the throat, esophagus or intestine (US FDA 2009; Matsui et al. 2002).

Duration of use

No statement required.

Risk information Statement to the effect of:

Caution(s) and warning(s):

No statement required.

Contraindication(s):

No statement required.

Known adverse reaction(s):

Symptoms such as nausea and diarrhea have been known to occur; in which case, discontinue use (Sumiyoshi et al. 2010; Matsui et al. 2002).

Non-medicinal ingredients

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

Storage conditions

No statement required.

Specifications

- The finished product must comply with the minimum specifications outlined in the current NHPD *Compendium of Monographs*.
- The medicinal ingredient must comply with the requirements outlined in the *Natural Health Products Ingredients Database* (NHPID).

References cited

Cowawintaweewat S, Manoromana S, Sriplung H, Khuhaprema T, Tongtawe P, Tapchaisri P, Chaicumpa W. Prognostic improvement of patients with advanced liver cancer after active hexose correlated compound (AHCC) treatment. Asian Pacific Journal of Allergy and Immunology 2006;24(1):33-45.

Fujii H, Nishioka N, Simon RR, Kaur R, Lynch B, Roberts A. Genotoxicity and subchronic toxicity evaluation of Active Hexose Correlated Compound (AHCC). Regular Toxicology and Pharmacology 2011;59(2):237-250.

Matsui Y, Uhara J, Satoi S, Kaibori M, Yamada H, Kitade H, Imamura A, Takai S, Kawaguchi Y, Kwon AH, Kamiyama Y. Improved prognosis of postoperative hepatocellular carcinoma patients when treated with functional foods: a prospective cohort study. Journal of Hepatology 2002;37(1):78-86.

Spierings EL, Fujii H, Sun B, Walshe T. A Phase I study of the safety of the nutritional supplement, active hexose correlated compound, AHCC, in healthy volunteers. Journal of Nutritional Science and Vitaminology (Tokyo) 2007;53(6):536-539.

Sumiyoshi Y, Hashine K, Kakehi Y, Yoshimura K, Satou T, Kuruma H, Namiki S, Shinohara N. Dietary administration of mushroom mycelium extracts in patients with early stage prostate cancers managed expectantly: a phase II study. Japanese Journal of Clinical Oncology 2010;40(10):967-972.

Uno K, Kosuna K, Sun B, Fujii H, Wakame K, Chikumaru S, Hosokawa G, Ueda Y. Active Hexose Correlated Compound (AHCC) improves immunological parameters and performance status of patients with solid tumors. Biotherapy 2000;14(3):303-309.

US FDA 2009: United States Food and Drug Administration. 2009. Specific Labeling Requirements for Specific Drug Products. Code of Federal Regulations Title 21, Volume 4 (21CFR201.319). Rockville (MD): United States Department of Health and Human Services, U.S. Food and Drug Administration. [Accessed 2012 March 09]. Available from: http://www.accessdata.fda.gov/

Wang S, Ichimura K, Wakame K. Preventive effects of Active Hexose Correlated Compound (AHCC) on oxidative stress induced by ferric nitrilotriacetate in the rat. Dokkyo Journal of Medical Sciences 2001;28(2-3):745-752.

Ye SF, Ichimura K, Wakame K, Ohe M. Suppressive effects of Active Hexose Correlated Compound on the increased activity of hepatic and renal ornithine decarboxylase induced by oxidative stress. Life Sciences 2003;74(5):593-602.

Ye SF, Wakame K, Ichimura K, Matsuzaki S. Amelioration by active hexose correlated compound of endocrine disturbances induced by oxidative stress in the rat. Endocrine Regulations 2004;38(1):7-13.

References reviewed

Albers R, Antoine JM, Bourdet-Sicard R, Calder PC, Gleeson M, Lesourd B, Samartín S, Sanderson IR, Van Loo J, Vas Dias FW, Watzl B. Markers to measure immunomodulation in human nutrition intervention studies. British Journal of Nutrition 2005;94(3):452-481.

Aviles H, O'Donnell PM, Orshal JM, Sonnenfeld G. Active Hexose Correlated Compound (AHCC) activates immune function to decrease bacteria load in a murine model of surgical wound infection. The Journal of Immunology 2007;178, S73.

Aviles H, O'Donnell P, Orshal J, Fujii H, Sun B, Sonnenfeld G. Active hexose correlated compound activates immune function to decrease bacterial load in a murine model of intramuscular infection. American Journal of Surgery 2008;195(4):537-545.

Brinker 2010: Brinker F. Final updates and additions for Herb Contraindications and Drug Interactions, 3rd edition, including extensive Appendices addressing common problematic conditions, medications and nutritional supplements, and influences on Phase I, II & III metabolism with new appendix on botanicals as complementary adjuncts with drugs. [Internet]. Sandy (OR): Eclectic Medical Publications. [Last update July 13, 2010; Accessed 2012 May 29]. Available from: http://www.eclecticherb.com/

Brinker F. Herbal Contraindications and Drug Interactions: Plus Herbal Adjuncts With Medicines, expanded 4th Edition. Sandy (OR): Eclectic Medical Publications; 2010.

Gao Y, Zhang D, Sun B, Fujii H, Kosuna K, Yin Z. Active hexose correlated compound enhances tumor surveillance through regulating both innate and adaptive immune responses. Cancer Immunology, Immunotherapy 2006;55(10):1258-1266.

Hirose A, Sato E, Fujii H, Sun B, Nishioka H, Aruoma OI. The influence of active hexose correlated compound (AHCC) on cisplatin-evoked chemotherapeutic and side effects in tumor-bearing mice. Toxicology and Applied Pharmacology 2007;222(2):152-158.

Hoffman G, Wirleitner B, Fuchs D. Potential role of immune system activation-associated production of neopterin derivatives in humans. Inflammation Research 2003;52(8):313-321.

Iqbal M, Giri U, Athar M. Ferric nitrilotriacetate (Fe-NTA) is a potent hepatic tumor promoter and acts through the generation of oxidative stress. Biochemical and Biophysical Research Communications 1995;212(2):557-563.

Kalkan A, Ozden M, Akbulut H. Serum neopterin level in patients with chronic hepatitis B. Japanese Journal of Infectious Diseases 2005;58(2):107-109.

Kawaguchi Y. Improved Survival of Patients with Gastric Cancer or Colon Cancer when treated with Active Hexose Correlated Compound (AHCC): Effect of AHCC on digestive system cancer. Natural Medicine Journal 2009;1(1):1-6.

Kidd PM. The use of mushroom glucans and proteoglycans in cancer treatment. Alternative Medicine Review 2000;5(1):4-27.

Levy AM, Kita H, Phillips SF, Schkade PA, Dyer PD, Gleich GJ, Dubravec VA. Eosinophilia and gastrointestinal symptoms after ingestion of shiitake mushrooms. Journal of Allergy and Clinical Immunology 1998;101(5):613-620.

Mach CM, Fugii H, Wakame K, Smith J. Evaluation of active hexose correlated compound hepatic metabolism and potential for drug interactions with chemotherapy agents. Journal of the Society for Integrative Oncology 2008;6(3):105-109.

Matsushita K, Kuramitsu Y, Ohiro Y, Obara M, Kobayashi M, Li YQ, Hosokawa M. Combination therapy of active hexose correlated compound plus UFT significantly reduces the metastasis of rat mammary adenocarcinoma. Anticancer Drugs 1998;9(4):343-350.

Milner JA. Functional foods: the US perspective. American Journal of Clinical Nutrition 2000;71 (suppl):1654S-1659S.

Nogusa S, Gerbino J, Ritz BW. Low-dose supplementation with active hexose correlated compound improves the immune response to acute influenza infection in C57BL/6 mice. Nutrition Research 2009;29(2):139-143.

NS 2012. Active hexose correlated compound (AHCC) Natural Standard Professional Monograph, Copyright © 2012 [Internet]. [Accessed 2012 May 28]. Available from: http://www.naturalstandard.com

Ritz BW, Nogusa S, Ackerman EA, Gardner EM. Supplementation with active hexose correlated compound increases the innate immune response of young mice to primary influenza infection. The Journal of Nutrition 2006;136:2868-2873.

Sun B, Wakame K, Sato E, Nishioka H, Aruoma OI, Fujii H. The effect of active hexose correlated compound in modulating cytosine arabinoside-induced hair loss, and 6-mercaptopurine- and methotrexate-induced liver injury in rodents. Cancer Epidemiology 2009;33(3-4):293-299.

Terakawa N, Matsui Y, Satoi S, Yanagimoto H, Takahashi K, Yamamoto T, Yamao J, Takai S, Kwon AH, Kamiyama Y. Immunological effect of active hexose correlated compound (AHCC) in healthy volunteers: a double-blind, placebo-controlled trial. Nutrition and Cancer 2008;60(5):643-651.

Wang S, Welte T, Fang H, Chang GJ, Born WK, O'Brien RL, Sun B, Fujii H, Kosuna K, Wang T. Oral administration of active hexose correlated compound enhances host resistance to West Nile encephalitis in mice. Journal of Nutrition 2009;139(3):598-602.

Yagita A, Maruyama S, Wakasugi S, Sukegawa Y. H-2 haplotype-dependent serum IL-12 production in tumor-bearing mice treated with various mycelial extracts. In Vivo 2002;16(1):49-54.

Yin Z, Fujii H, Walshe T. Effects of active hexose correlated compound on frequency of CD4+ and CD8+ T cells producing interferon-γ and/or tumor necrosis factor-α in healthy adults. Human Immunology 2010;71(12):1187-1190.