

## NATURAL HEALTH PRODUCT

### GLUCOSAMINE SULFATE

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 labels at the applicants' discretion.
- ▶ The solidus (/) indicates that the terms and/or statements are synonymous. Either term or statement may be selected by the applicant.

#### Date

March 11, 2022

#### Proper name(s), Common name(s), Source information

Table 1. Proper name(s), Common name(s), Source information

Proper name(s)	Common name(s)	Source information				
		Source ingredient(s)	Source material(s)	Organism group(s) <sup>1</sup>	Part(s)	Preparation(s)
2-Amino-2-deoxy-D-glucose sulfate	Glucosamine sulfate	▶ Glucosamine Sulfate Potassium Chloride	N/A	▶ Crab ▶ Krill ▶ Lobster ▶ Prawn ▶ Shrimp	Exoskeleton	N/A
		▶ Glucosamine Sulfate Sodium Chloride	▶ <i>Aspergillus flavus var. oryzae</i> ▶ <i>Aspergillus melleus</i> ▶ <i>Aspergillus niger</i> ▶ <i>Aspergillus niger var. awamori</i> ▶ <i>Monascus pilosus</i> ▶ <i>Monascus purpureus</i> ▶ <i>Rhizopus oryzae</i>	N/A	Whole	Fermented

References: Proper name: NLM 2018; Common name: USP 32 2009, Sweetman 2007, Towheed and Anastassiades 2007; Source information: ITIS 2008, Kralovec and Barrow 2008.

<sup>1</sup> The specific organisms used as source material(s) must be indicated in the Animal Tissue Form (ATF); simply indicating "crustaceans" is insufficient.

## 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.

Acceptable dosage forms for oral use are indicated in the dosage form drop-down list of the web-based Product Licence Application form for Compendial applications.

## Use(s) or Purpose(s)

- ▶ Helps to relieve joint pain associated with osteoarthritis (Herrero-Beaumont et al. 2007; Usha and Naidu 2004; Pavelka et al. 2002; Reginster et al. 2001; Thie et al. 2001).
- ▶ Helps to relieve pain associated with osteoarthritis of the knee (Herrero-Beaumont et al. 2007; Usha and Naidu 2004; Pavelka et al. 2002; Reginster et al. 2001).
- ▶ Helps to protect against the deterioration of cartilage (Pavelka et al. 2002; Reginster et al. 2001).
- ▶ A factor in maintaining healthy cartilage and/or joint health (Towheed and Anastassiades 2007; Pavelka et al. 2002; Reginster et al. 2001)

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

Helps protect against the deterioration of cartilage and relieve joint pain associated with osteoarthritis (Herrero-Beaumont et al. 2007; Usha and Naidu 2004; Pavelka et al. 2002; Reginster et al. 2001; Thie et al. 2001)

## Dose(s)

### Subpopulation(s)

Adults 18 years and older

### Quantity(ies)

1,500 milligrams of glucosamine sulfate, per day (Herrero-Beaumont et al. 2007; Pavelka et al. 2002; Reginster et al. 2001)

### Direction(s) for use

No statement required.

### **Duration(s) of use**

Use for at least 4 weeks to see beneficial effects (Mehta et al. 2007; Usha and Naidu 2004; Houpt et al. 1999; Qiu et al. 1998).

### **Risk information**

#### **Caution(s) and warning(s)**

- ▶ Consult a health care practitioner/health care provider/health care professional/doctor/physician if symptoms worsen.
- ▶ Consult a health care practitioner/health care provider/health care professional/doctor/physician prior to use if you are pregnant or breastfeeding (Sivojelezova et al. 2007).

#### **Contraindication(s)**

No statement required.

#### **Known adverse reaction(s)**

No statement required.

### **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**

Must be established in accordance with the requirements described in the *Natural Health Products Regulations* (NHPR).

### **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.



## References cited

Herrero-Beaumont G, Ivorra JAR, Trabado MC, Blanco FJ, Benito P, Martín-Mola E, Paulino J, Marengo JL, Porto A, Laffon A, Araújo D, Figueroa M, Branco J. 2007. Glucosamine sulfate in the treatment of knee osteoarthritis symptoms- a randomized, double-blind, placebo-controlled study using acetaminophen as a side comparator. *Arthritis and Rheumatism* 56(2):555-567.

Houpt JB, McMillan R, Wein C, Paget-Dellio SD. 1999. Effect of glucosamine hydrochloride in the treatment of pain of osteoarthritis of the knee. *Journal of rheumatology* 26(11):2423-2430.

ITIS 2008: Integrated Taxonomic Information System. Taxon Based on Biological Information System [online]. Canadian Biodiversity Information Facility, Government of Canada. [Accessed 2018 June 19]. Available from: <https://www.itis.gov/>

Kralovec A, Barrow CJ. 2008. Glucosamine Production and Health Benefits. In: *Marine Nutraceuticals and Functional Foods*. Colin Barrow and Fereidoon Shahidi, editors, pp198-227. Boca Raton (FL): CRC Press, Taylor and Francis Group.

Mehta K, Gala J, Bhasale S, Naik S, Modak M, Thakur H, Deo N, Miller MJ. 2007. Comparison of glucosamine sulfate and a polyherbal supplement for the relief of osteoarthritis of the knee: a randomized controlled trial. *BMC Complementary and alternative Medicine* 31(7):34.

NLM 2018: United States National Library of Medicine. ChemIDplus advanced [online]. Chemical name. RN: 000-00-0. Bethesda (MD): Specialized Information Services, United States National Library of Medicine, National Institutes of Health, United States Department of Health & Human Services. [Accessed 2018 June 19]. Available from: <https://chem.nlm.nih.gov/chemidplus/>

Pavelka K, Gatterova J, Olejarova M, Machacek S, Giacovelli G, Rovati LC. 2002. Glucosamine sulfate use and delay of progression of knee osteoarthritis: a 3-year, randomized, placebocontrolled, double-blind study. *Archives of Internal Medicine* 162(18):2113-2123.

Qiu GX, Gao SN, Giacovelli G, Rovati L, Stenikar I. 1998. Efficacy and safety of glucosamine sulfate versus ibuprofen in patients with knee osteoarthritis. *Arzneimittelforschung* 48:460474.

Reginster JY, Deroisy R, Rovati LC, Lee RL, Lejeune E, Bruyere O, Giacovelli G, Henrotin Y, Dacre JA, Gossett C. 2001. Long-term effects of glucosamine sulfate on osteoarthritis progression: a randomized, placebo-controlled clinical trial. *The Lancet* 357:251-256.

Sivojelezova A, Koren G, Einarson A. 2007. Glucosamine Use in Pregnancy: An Evaluation of Pregnancy Outcome. *Journal of Women's Health* 16(3):345-348.

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

Thie NM, Prasad NG, Major PW. 2001. Evaluation of glucosamine sulfate compared to ibuprofen for the treatment of temporomandibular joint osteoarthritis: a randomized double blind controlled 3 month clinical trial. *The Journal of Rheumatology* 28:1347-1355.

Towheed, TE, Anastassiades T. 2007. Glucosamine Therapy for Osteoarthritis: An Update. *The Journal of Rheumatology* 34(9):1787-1790.

Usha PR, Naidu MU. 2004. Randomized, double-blind, parallel, placebo-controlled study of oral glucosamine, methylsulfonylmethane and their combination in osteoarthritis. *Clinical Drug Investigation* 24(6):353-363.

USP 32 2009: United States Pharmacopeial Convention. 2009. United States Pharmacopeia and the National Formulary (USP 32 - NF 27). Rockville (MD): The United States Pharmacopeial Convention.

### References reviewed

ACR 2005: American College of Rheumatology: Osteoporosis drug may delay joint destruction in knee osteoarthritis (press release) [online]. Atlanta (GA). [Accessed 2008 August 21]. Available from: <http://www.rheumatology.org/press/2005/bucklandwright.asp>

Adams ME. 1999. Hype about glucosamine. *The Lancet* 354(9176):354:353.

Albert SG, Oiknine RF, Parseghian S, Mooradian AD, Haas MJ, McPherson T. 2007. The effect of glucosamine on Serum HDL cholesterol and apolipoprotein AI levels in people with diabetes. *Diabetes Care* 30(11):2800-2803.

Anderson JW, Nicolosi RJ, Borzelleca JF. 2005. Glucosamine effects in humans: a review of effects on glucose metabolism, side effects, and safety considerations and efficacy. *Food and Chemical Toxicology* 43(2):187-201.

Audimoolam VK, Bhandari S. 2006. Transhepatic venous access as an alternative for Tesio catheter in the case of a patient on haemodialysis with antiphospholipid syndrome. *Nephrology Dialysis Transplantation* 21(7):2031-2033.

Bassleer C, Rovati L, Franchimont P. 1998. Stimulation of proteoglycan production by glucosamine sulfate in chondrocytes isolated from human osteoarthritic articular cartilage in vitro. *Osteoarthritis and Cartilage* 6(6):427-434.

Bijlsma JW, Lafeber FP. 2008. Glucosamine sulfate in osteoarthritis: the jury is still out. *Annals of Internal Medicine* 148(4):315-316.

Bisby FA, Roskov YR, Orrell TM, Nicolson D, Paglinawan LE, Bailly N, Kirk PM, Bourgoin T, van Hertum J, editors. 2008. Species 2000 & ITIS Catalogue of Life: 2008 Annual Checklist. Digital Resource [online database]. Reading (UK): Species 2000. [Accessed 2008 August 21].

Available from: <http://www.catalogueoflife.org/annual-checklist/2008/>

Cargill Acidulants 2004. "Proposal for making a "Substantial Equivalence" notification for Non-Shellfish Glucosamine Hydrochloride under regulation (EC) No. 258/97 for the European Parliament and the Council of Jan 27, 1997 concerning novel foods and novel food ingredients" [online]. Eddyville (IA). [Accessed 2008 August 21]. Available from: <http://www.food.gov.uk/multimedia/pdfs/glucosamine1.pdf>

Clegg DO, Reda DJ, Harris CL, Klein MA, O'Dell JR, Hooper MM, Bradley JD, Bingham CO 3<sup>rd</sup>, Weisman MH, Jackson CG, Lane NE, Cush JJ, Moreland LW, Schumacher HR Jr, Oddis CV, Wolfe F, Molitor JA, Yocum DE, Schnitzer TJ, Furst DE, Sawitzke AD, Shi H, Brandt KD, Delafuente JC. 2000. Glucosamine in the treatment of osteoarthritis. *Complementary and Alternative Therapies for Rheumatic Diseases II* 26(1):1-11.

Dudek A, Raczkiwicz-Papierska A, Tlustochowicz W. 2007. Efficacy of glucosamine sulfate treatment in patients with osteoarthritis. *Polski Merkuriusz Lekarski : Organ Polskiego Towarzystwa Lekarskiego* 22(129):204-207.

Felson DT. 2006. Glucosamine and chondroitin sulfate in knee osteoarthritis: where now? *Nature Clinical Practice. Rheumatology* 2(7):356-357.

Frestedt JL, Walsh M, Kuskowski MA, Zenk JL. 2008. A natural mineral supplement provides relief from knee osteoarthritis symptoms: a randomized controlled pilot trial. *Nutrition Journal* 17(7):9.

Fulop N, Marchase RB, Chatham JC. 2007. Role of Protein O-linked N-acetyl-glucosamine in mediating cell function and survival in the cardiovascular system. *Cardiovascular Research* 73(2):288-297.

Gray HC, Hutcheson PS, Slavin RG. 2004. Is glucosamine safe in patients with seafood allergy? *The Journal of Allergy and Clinical Immunology* 114(2): 456-460.

Hayes M, Carney B, Slater J, Brück W. 2008. Mining marine shellfish wastes for bioactive molecules: chitin and chitosan--Part A: extraction methods. *Biotechnology Journal* 3(7):871-877.

HC 2007: Health Canada. Canada Vigilance Online Database: CADRMP Online Query. Ottawa (ON): Drugs and Health Products, Health Canada. [Accessed 2009 August 21]. Available from: [http://205.193.93.51/CADRMP/index\\_e.jsp](http://205.193.93.51/CADRMP/index_e.jsp)

Hughes R, Carr A. 2002. A randomized, double-blind, placebo-controlled trial of glucosamine sulphate as an analgesic in osteoarthritis of the knee. *Rheumatology (Oxford)* 41(3):279-284.

Jimenez SA, Dodge GR. 1997. The effects of glucosamine sulfate on human chondrocyte gene expression. *Osteoarthritis and Cartilage* 5 (Suppl A): 72.



Marshall PD, Poddar S, Tweed EM, Brandes L. 2006. Clinical inquiries: Do glucosamine and chondroitin worsen blood sugar control in diabetes? *The Journal of Family Practice* 55(12):1091-1093.

Masson E, Lagarde M, Wiernsperger N, El Bawab S. 2006. Hyperglycemia and glucosamine-induced mesangial cell cycle arrest and hypertrophy: Common or independent mechanisms? *IUBMB life* 58(7):381-388.

Masson E, Wiernsperger N, Lagarde M, Bawab SE. 2005. Involvement of gangliosides in glucosamine-induced proliferation decrease of retinal pericytes. *Glycobiology* 15(6):585-591.

McAlindon T, Formica M, LaValley M, Lehmer M, Kabbara K. 2004. Effectiveness of glucosamine for symptoms of knee osteoarthritis: results from an internet-based randomized double-blind controlled trial. *The American Journal of Medicine* 117(9):643-649.

Merriam-Webster Online Dictionary. 2008. [online]. Merriam-Webster, Incorporated. [Accessed 2008 August 21]. Available from: <http://www.merriam-webster.com/dictionary/shellfish>

Moskowitz RW, Williams HJ. 2006. Glucosamine, chondroitin sulphate, and the two in combination for painful knee osteoarthritis. *The New England Journal of Medicine* 354(8):795-808.

Muniyappa R, Karne RJ, Hall G, Cranson SK, Bronstein JA, Ver MR, Hortin GL, Quon MJ. 2006. Oral Glucosamine for 6 weeks at Standard Doses Does Not Cause or Worsen Insulin Resistance or Endothelial Dysfunction in Lean or Obese Subjects. *Diabetes* 55:3142-3150.

Nakamura H, Masuko K, Yudoh K, Kato T, Kamada T, Kawahara T. 2007. Effects of glucosamine administration on patients with rheumatoid arthritis. *Rheumatology International* 27(3):213-218.

Nakamura M, Barberi AJ, Antonetti DA, LaNoue KF, Robinson KA, Buse MG, Gardner TW. 2001. Excessive Hexosamines Block the Neuroprotective Effect of Insulin and Induce Apoptosis in retinal Neurons. *The Journal of Biological Chemistry* 270(23):43748-48755.

Noack W, Fischer M, Förster KK, Rovati LC, Setnikar I. 1994. Glucosamine sulfate in osteoarthritis of the knee. *Osteoarthritis and Cartilage* 2(1):51-59.

Ossendza RA, Grandval P, Chinoune F, Rocher F, Chapel F, Bernardini D. 2007. Hépatite aiguë cholestatique à la Glucosamine forte®. *Gastroentérologie clinique et biologique* 31(4):449-450.

Ostojic SM, Arsic M, Prodanovic S, Vukovic J, Zlatanovic M. 2007. Glucosamine administration in athletes: effects on recovery of acute knee injury. *Research in Sports Medicine* 15(2):113-124.

Persiani S, Roda E, Rovati LC, Locatelli M, Giacovelli G, Roda A. 2005. Glucosamine oral bioavailability and plasma pharmacokinetics after increasing doses of crystalline glucosamine



sulfate in man. *Osteoarthritis and Cartilage* 13(12):1041-1049.

Rashad S, Revell P, Hemingway A, Low F, Rainsford K, Walker F. 1989. Effect of non-steroidal anti-inflammatory drugs on the course of osteoarthritis. *The Lancet* 14(2)(8668):914-915.

Reginster JY. 2007. The efficacy of glucosamine sulfate in osteoarthritis: financial and nonfinancial conflict of interest. *Arthritis and Rheumatism* 56(7):2105-2110.

Reichelt A, Förster KK, Fischer M, Rovati LC, Setnikar I. 1994. Efficacy and safety of intramuscular glucosamine sulfate in osteoarthritis of the knee. A randomised, placebocontrolled, double-blind study. *Arzneimittelforschung* 44(1):75-80.

Robertson LA, Kim AJ, Werstuck GH. 2006. Mechanisms linking diabetes mellitus to the development of atherosclerosis: a role for endoplasmic reticulum stress and glycogen synthase kinase-3. *Canadian Journal of Physiology and Pharmacology* 84(1):39-48.

Rozendaal RM, Koes BW, van Osch GJ, Uitterlinden EJ, Garling EH, Willemsen SP, Ginai AZ, Verhaar JA, Weinans H, Bierma-Zeinstra SM. 2008. Effect of glucosamine sulfate on hip osteoarthritis: a randomized trial. *Annals of Internal Medicine* 148(4):268-277.

Runkel DR, Cupp MJ. 1999. Glucosamine sulfate use in osteoarthritis. *American journal of health-system pharmacy: American Journal of Health-System Pharmacy* 56(3):267-269.

Sandy JD, Gamett D, Thompson V, Verscharen C. 1998. Chondrocyte-mediated catabolism of aggrecan: aggrecanase-dependent cleavage induced by interleukin-1 or retinoic acid can be inhibited by glucosamine. *The Biochemical Journal* 335 (Pt 1):59-66.

Schuster E, Dunn-Coleman N, Frisvad JC, Van Dijck PW. 2002. On the safety of *Aspergillus niger*--a review. *Applied Microbiology and Biotechnology* 59(4-5):426-435.

Scroggie DA, Albright A, MD Harris. 2003. The effect of glucosamine-chondroitin supplementation on glycosylated haemoglobin levels in patients with type 2 diabetes mellitus: a placebo-controlled, double-blinded, randomized clinical trial. *Archives of Internal Medicine* 163(13): 1587-1590.

Tannis AJ, Barban J, Conquer JA. 2004. Effect of glucosamine supplementation on fasting and non-fasting plasma glucose and serum insulin concentrations in healthy individuals. *Osteoarthritis and Cartilage* 12(6):506-511.

The Arthritis and Glucosamine Information Centre. Glucosamine Side effects. Raleigh (NC): DTC Health. [Accessed 2008 August 21]. Available from: <http://www.glucosaminearthritis.org/glucosamine/glucosamine-side-effects.html>.

Towheed TE, Maxwell L, Anastassiades TP, Shea B, Houpt J, Robinson V, Hochberg MC, Wells G. 2005. Glucosamine therapy for treating osteoarthritis. *Cochrane database of systematic reviews* (2):CD002946.



Viad SC, LaValley MP, McAlindon TE, Felson DT. 2007. Glucosamine for pain in osteoarthritis: why do trial results differ? *Arthritis and rheumatism* 56(7):2267-2277.

Villacis J, Rice TR, Bucci LR, El-Dahr JM, Wild L, Demerell D, Soteres D, Lehrer SB. 2006. Do shrimp-allergic individuals tolerate shrimp-derived glucosamine? *Clinical and experimental allergy : Journal of the British Society for Allergy and Clinical Immunology* 36(11):1457-1461.

Williams HJ. 2006. Glucosamine, chondroitin sulfate, and the two in combination for painful knee osteoarthritis. *The New England Journal of Medicine* 354(8):795-808.

Yu JG, Boies SM, and JM Olefsky. 2003. The effect of oral glucosamine sulphate on insulin sensitivity in human subjects. *Diabetes Care* 26(6): 1941-1942.

Zachara NE, Hart GW. 2006. Cell signaling, the essential role of O-GlcNAc!. *Biochimica et biophysica acta* 1761(5-6):599-617.