Joint Health Products, Multiple Ingredient

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JOINT HEALTH PRODUCTS Help on accessing alternative formats, such as Portable Document Format (PDF), Microsoft Word and PowerPoint (PPT) files, can be obtained in the alternate format help section. (PDF Version - 218 KB) This monograph is intended to serve as a guide to industry for the preparation of Product Licence Applications (PLAs) for natural health product market authorization. It is not intended to be a comprehensive review of the medicinal ingredients. 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. This monograph may be used to support single ingredient or multi-ingredient products. However, it is mandatory for joint health products to contain at least one medicinal ingredient from Table 2 at therapeutic dose with its associated claim(s). As enhanced absorption formulations are often used for Turmeric and its constituents, this is a reminder that enhanced absorption dosage forms/formulations are not covered by Natural and Non-prescription Health Products Directorate's monographs and should be submitted as Class III submissions. Date October 25, 2024 Proper name(s), Common name(s), Source information Table 1. Proper name(s), Common name(s), Source information 1 Proper name(s) Common name(s) Source information Source ingredient(s) Source material(s) Part(s) Preparation(s) all-trans -beta-Carotene beta-Carotene all-trans -beta-Carotene beta-Carotene beta-Carotene N/A N/A As per NNHPD Multi- Vitamin/Mineral Supplements monograph Boron Boron As per NNHPD Multi-Vitamin/Mineral Supplements monograph N/A N/A As per NNHPD Multi- Vitamin/Mineral Supplements monograph Boswellia serrata Boswellia Indian frankincense Indian olibanum Indian olibanum-tree Shallaki N/A Boswellia serrata Stem bark oleogum resin Trunk bark oleogum resin Dry Fruit bromelain Fruit bromelain Juice bromelain Pineapple fruit bromelain N/A Ananas comosus var. bracteatus Ananas comosus var. comosus Fruit N/A Stem bromelain Bromelain Pineapple stem bromelain Stem bromelain N/A Ananas comosus var. bracteatus Ananas comosus var. comosus Stem N/A Calcium Calcium As per NNHPD Multi- Vitamin/Mineral Supplements monograph N/A N/A As per NNHPD Multi-Vitamin/Mineral Supplements monograph Chondroitin sulfate 2 Chondroitin sulfate Sodium chondroitin sulfate Anas platyrhynchos Anser anser Bos taurus Cygnus olor Dromaius novaehollandiae Gallus gallus Meleagris gallopavo Numida meleagris Rhea americana Struthio camelus Sus scrofa Cartilage N/A (1E,6E)-1,7-Bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione Curcumin N/A Curcuma longa Rhizome N/A Curcumin N/A N/A Synthetic Curcuminoids Curcuminoids N/A Curcuma longa Rhizome N/A Curcuma longa Common turmeric Curcuma Indian-saffron Jianghuang Turmeric Yellow ginger N/A Curcuma longa Rhizome Dry Harpagophytum procumbens Devil's claw Grapple plant Wood spider N/A Harpagophytum procumbens Secondary root tubers Dry Harpagophytum zeyheri Devil's claw Grapple plant Wood spider N/A Harpagophytum zeyheri Fish oil 3 Fish oil N/A Ammodytidae Carangidae Clupeidae Engraulidae Gadidae 4 Osmeridae Salmonidae Scrombridae Whole N/A 2-Amino-2-deoxy-beta-D-glucopyranose hydrochloride Glucosamine HCl Glucosamine hydrochloride Glucosamine hydrochloride Crab 5 Krill 5 Lobster 5 Prawn 5 Shrimp 5 Exoskeleton N/A Aspergillus flavus var. oryzae Aspergillus melleus Aspergillus niger Aspergillus niger var. awamori Monascus pilosus Monascus purpureus Rhizopus oryzae Whole Fermented 2-Amino-2-deoxy-D-glucose sulfate Glucosamine sulfate Glucosamine sulfate potassium chloride Glucosamine sulfate sodium chloride Crab 5 Krill 5 Lobster 5 Prawn 5 Shrimp 5 Exoskeleton N/A Aspergillus flavus var. oryzae Aspergillus melleus Aspergillus niger Aspergillus niger var . awamori Monascus pilosus Monascus purpureus Rhizopus oryzae Whole Fermented Hyaluronic acid 6 Hyaluronic acid Sodium hyaluronate Gallus gallus Comb N/A Hyaluronic acid Sodium hyaluronate Streptococcus equi Bacterial extracellular capsule Fermented Hydrolyzed collagen 7 Collagen hydrolysate Hydrolyzed collagen N/A Bovine Bovine skin/hide split N/A Porcine Bone Skin Fish Bone Skin Chicken Cartilage Magnesium Magnesium As per NNHPD Multi-Vitamin/Mineral Supplements monograph N/A N/A As per NNHPD Multi-Vitamin/Mineral Supplements monograph Manganese Manganese Dimethyl sulfone Methylsulfonylmethane Sulfonylbismethane Methylsulfo-nylmethane MSM Dimethyl sulfone N/A N/A Synthetic Vitamin A Vitamin A As per NNHPD Multi-Vitamin/Mineral Supplements monograph N/A N/A As per NNHPD Multi-Vitamin/Mineral Supplements monograph Vitamin C Vitamin C Vitamin D Vitamin D Vitamin D 2 Vitamin D Vitamin D 3 Vitamin K 1 Vitamin K

1 Vitamin K 2 Vitamin K 2 Willow bark Willow bark N/A Salix alba Salix daphnoides Salix purpura Salix x fragilis Bark Young branch bark Dry 1 References: Proper names: NIHa 2023, RSC 2023, USP-NF 2023, USDA 2023, Martindale 2012, Ph.Eur. 2012, , ICIDH 2008, Kralovec and Barrow 2008, Towheed and Anastassiades 2007, IUBMB 1992. Common names: NIHa 2023, RSC 2023, USP-NF 2023, PPRC 2015, BP 2012, Martindale 2012, Ph.Eur. 2012, Goel et al. 2008, ICIDH 2008, Kralovec and Barrow 2008, Towheed and Anastassiades 2007, Boon and Smith 2004, McGuffin et al. 2000, Moskowitz 2000, IUBMB 1992, Deodhar et al. 1980. Source information: ITIS 2023, NIHb 2023, RSC 2023, USDA 2023, USP-NF 2023, Froese and Pauly. 2018, EMA 2017, PPRC 2015, Martindale 2012, Ph.Eur. 2012, Schauss et al. 2012, Sitanggang et al. 2012, EP 2011, FCC 8 2012, Khan and Abourashed 2010, Evans 2009, Yoshida et al. 2009, Goel et al. 2008, Kalman et al. 2008, Kralovec and Barrow 2008, Sato and Iwaso 2008, Chmielowski et al. 2007, Schrieber and Gareis 2007, Dahiya et al 2006, Chong et al. 2005, Boon and Smith 2004, Wichtl 2004, Baziwane and He 2003, ESCOP 2003, Barnes et al. 2002, Sato et al. 2002, Blumenthal et al. 2000, BHC 1992, Deodhar et al. 1980. 2 Cartilage must be derived from healthy and domestic animals used for food by humans (USP-NF 2023). 3 Corresponds to oil from the whole body of one or more of species of the families listed in Table 1 in its natural and/or concentrated triglyceride/triacylglycerol form and/or its concentrated esterified form (BP 2023; Ph.Eur. 2023; Froese and Pauly 2022). The species common names and not the family could be listed on the label. 4 For fish oils including species of Gadidae as a source material, the vitamin A and D content should be tested to ensure that the daily maximum amounts meet the Multi-Vitamin/Mineral Supplements monograph for each age group. 5 The specific organisms used as source material(s) must be indicated in the Animal Tissue Form (ATF); simply indicating "crustaceans" is insufficient. 6 The stabilizing salt (i.e. sodium) if present should be indicated. 7 For the purpose of this monograph, hydrolyzed collagen has no jelling power and is soluble in cold water (Schrieber and Gareis 2007; Moskowitz 2000). The average molecular weight of hydrolyzed collagen is approximately 4 kDa (i.e. 2-6 kDa) (Moskowitz 2000; Oesser et al. 1999). 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) Refer to Tables 2 and 3. Notes: It is mandatory for all products to cite at least one use or purpose statement from Table 2. A use or purpose statement is acceptable only if at least one medicinal ingredient associated with that statement is present at a dose at or above the minimum daily dose listed in Table 2. Medicinal ingredients which do not meet the minimum daily dose for a use or purpose statement will be considered as acceptable complementary medicinal ingredients in product formulations. For multi-ingredient products: To prevent the product from being represented as a "traditional medicine", any indicated traditional use claim must refer to the specific medicinal ingredient(s) and recognized traditional system of medicine from which the claim originates when 1) both traditional and modern claims are present or 2) when claims originate from multiple systems of traditional medicine (e.g., Turmeric is traditionally used in Herbal Medicine to help relieve joint pain). When ALL of the medicinal ingredients (MIs) in the product are used within the SAME identified system of traditional medicine AND the product makes ONLY traditional claims, listing of MIs in the traditional claim(s) is not required. Dose(s) Subpopulation(s) Adults 18 years and older Quantity(ies) Refer to Tables 2 and 3. Note: When 'decoction' or 'infusion' is listed as an acceptable method of preparation, 'decoction concentrate' or 'infusion concentrate' is also allowed. It also applies to standardized methods of preparation. Table 2 . Joint health uses or purposes and associated daily doses Medicinal ingredients Uses or purposes 1 Methods of preparation Dose/day Single dose Minimum 2 Maximum 3 Maximum single dose 3 Boswellia serrata Helps relieve joint pain and swelling associated with osteoarthritis of the knee. Standardized Extracts 999 mg extracts standardized to 40% boswellic acid 999 mg extracts standardized to 40% boswellic acid 333 mg extracts standardized to 40% boswellic acid Chondroitin sulfate Helps relieve (joint) pain associated with osteoarthritis (of the knee). N/A 800 mg 1,200 mg N/A Curcumin Helps relieve joint pain and inflammation. N/A 1,200 mg 1,200 mg 400 mg Curcuminoids Helps relieve joint pain and inflammation. N/A 1,500 mg Optional: The potency constituent, curcumin, can be included 1,500 mg Optional: The potency constituent, curcumin, can be included 500 mg Turmeric (concentrated extracts) Helps relieve joint pain and inflammation. Standardized Extracts Extract standardized to 75% curcuminoids or more; Providing 1,500 mg curcuminoids Optional: The potency constituent, curcumin, can be included Extract standardized to 75% curcuminoids or more; Providing 1,500 mg curcuminoids Optional: The potency constituent, curcumin, can be included Extract standardized to 75% curcuminoids or more; Providing 500 mg curcuminoids Turmeric (native extracts) 4 (Traditionally) used in Herbal Medicine (as an anti-inflammatory) to help relieve joint pain. Dry, Powdered, Non-Standardized Extracts (Dry extract*, Tincture, Fluid extract, Decoction, Infusion) 1,000 mg dried rhizome; For dry extracts, maximum ratio is 10:1 9,000 mg dried rhizome; For dry extracts, maximum ratio is 10:1 N/A Standardized Extracts Extracts providing up to 35% curcuminoids and a Quantity crude equivalent of 1,000 mg dried rhizome Optional: The potency constituent, curcumin, can be included Extracts providing up to 35% curcuminoids and a Quantity crude equivalent of 9,000 mg dried rhizome Optional: The potency constituent, curcumin, can be

included Devil's claw Used in Herbal Medicine to help relieve joint pain associated with osteoarthritis. Dry, Powdered, Non-Standardized Extracts (Dry extract*, Tincture, Fluid extract, Decoction, Infusion) 600 mg dried secondary root tubers 7,500 mg dried secondary root tubers N/A Fish oil 5 In conjunction with conventional therapy, helps reduce the pain of rheumatoid arthritis in adults. Standardized fixed oil 2,800 mg eicosapentaenoic acid (EPA) + docosahexaenoic acid (DHA) with a EPA:DHA ratio of 0.5:1-2:1 5,000 mg EPA + DHA with a EPA:DHA ratio of 0.5:1-2:1 N/A Glucosamine hydrochloride Helps maintain healthy cartilage/joint health. N/A 1,500 mg 2,000 mg N/A Glucosamine sulfate Helps relieve joint pain associated with osteoarthritis (of the knee). Helps protect against the deterioration of cartilage. A factor in maintaining healthy cartilage and/or joint health. N/A 1,500 mg 1,500 mg N/A Hyaluronic acid Helps support joint health. N/A 48 mg (sourced from Gallus gallus comb) 120 mg (sourced from Gallus gallus comb) N/A 120 mg (sourced from microbial fermentation) 200 mg (sourced from microbial fermentation) Hydrolyzed collagen Helps reduce joint pain associated with osteoarthritis. Helps reduce osteoarthritis-related joint pain. Helps manage/in the management of joint pain. N/A 1,200 mg 10,000 mg N/A Methylsulfonylmethane (MSM) Helps relieve (joint) pain associated with osteoarthritis (of the knee). N/A 1,500 mg 6,000 mg 2,000 mg Willow bark Used in Herbal Medicine to relieve minor joint pain (due to osteoarthritis). Dry, Powdered, Non-Standardized Extracts (Dry extract, Tincture, Fluid extract, Decoction, Infusion) 3,000 mg dried (young branch) bark 9,000 mg dried (young branch) bark 3,000 mg dried (young branch) bark Standardized Extracts Extract providing up to 15% total salicin equivalent to 45 mg total salicin Extract providing up to 15% total salicin equivalent to 240 mg total salicin Extract providing up to 15% total salicin equivalent to 120 mg total salicin 1 At least two of the following references were consulted per use or purpose: EMA 2017; Bruyère et al. 2012; Benito-Ruiz et al. 2009; Yoshida et al. 2009; Clark et al. 2008; Winston and Kuhn 2008; Herrero-Beaumont et al. 2007; Mazières et al. 2007; Sontakke et al. 2007; Towheed and Anastassiades 2007; Kim et al. 2006; Mills and Bone 2005; Uebelhart et al. 2004; Usha and Naidu 2004; Braham et al. 2003; ESCOP 2003; Hoffmann 2003; Kimmatkar et al. 2003; Pavelka et al. 2002; Sato et al. 2002; Mazières et al. 2001; Reginster et al. 2001; Thie et al. 2001; Blumenthal et al. 2000; Mills and Bone 2000; Volker et al. 2000; Houpt et al. 1999; Bourgeois et al. 1998; Bucsi and Poor 1998; Uebelhart et al. 1998; Sköldstam et al. 1992; Deodhar et al. 1980. 2 At least one of the following references was consulted per minimum dose: EMA 2017; Bruyère et al. 2012; Benito-Ruiz et al. 2009; WHO 2009; Yoshida et al. 2009; Clark et al. 2008; Kalman et al. 2008; Herrero-Beaumont et al. 2007; Mezieres et al. 2007; Sontakke et al. 2007; Fitzpatrick 2005; Mills and Bone 2005; Boon and Smith 2004; Uebelhart et al. 2004; Usha and Naidu 2004; Wichtl 2004; ESCOP 2003; Hoffmann 2003; Kimmatkar et al. 2003; Williamson 2003; Barnes et al. 2002; Pavelka et al. 2002; Mezieres et al. 2001; Reginster et al. 2001; Blumenthal et al. 2000; Volker et al. 2000; Houpt et al. 1999; Bucsi and Poor 1998; Uebelhart et al. 1998; Deodhar et al. 1980. 3 At least one of the following references was consulted per maximum dose: EMA 2017; Bruyère et al. 2012; Benito-Ruiz et al. 2009; WHO 2009; Clark et al. 2008; Sato et Iwaso 2008; Herrero-Beaumont et al. 2007; Sontakke et al. 2007; Hathcock and Shao 2006; Kim et al. 2006; Mills and Bone 2005; Boon and Smith 2004; Wichtl 2004; Braham et al. 2003; ESCOP 2003; Kimmatkar et al. 2003; Williamson 2003; Barnes et al. 2002; Pavelka et al. 2002; Sato et al. 2002; Reginster et al. 2001; Blumenthal et al. 2000; Bourgeois et al. 1998; US FDA 1997; BHC 1992; Deodhar et al. 1980. 4 Turmeric: Refer to the Turmeric monograph for more information on native extracts. 5 Fish oil: The EPA:DHA ratio for fish oil must be between 0.5:1 and 2:1 (Volker et al. 2000; Sköldstam et al. 1992) and potency must be expressed as the quantity (mg) and/or percent (%) of EPA and DHA (% w/w) relative to the total quantity of fish oil. *Note: For Devil's claw and Turmeric, solvents allowed for the method of preparation "Non-standardized extracts (Dry extract)" as part of this monograph are ethanol and/or water only. The following claims are only acceptable in addition to at least one claim from Table 2 above. A joint health product cannot contain only ingredients and claims from Table 3. Table 3. Additional uses or purposes (optional) and associated daily doses Medicinal ingredients Uses or purposes 1 Methods of preparation Dose/day Single dose Minimum 2 Maximum 3 Maximum/ single dose 3 beta-Carotene Provitamin A/Source of vitamin A to help in the development and maintenance of bones. Helps in the development and maintenance of bones. N/A 390 µg 18,000 µg N/A Boron 4 Helps maintain healthy calcium metabolism. N/A 0.7 mg 3.36 mg 4 N/A Fruit Bromelain 5 Stem Bromelain 5 Used in herbal medicine to help relieve minor pain, swelling and inflammation. N/A 480,000 FCC papain units (PU) 5 130,000,000 FCC PU 5 45,000,000 FCC PU Calcium Adequate calcium (and vitamin D) (throughout life) as part of a healthy diet, (along with physical activity) may help prevent bone loss/osteoporosis (in peri- and postmenopausal women) (in later life). Adequate calcium (and vitamin D) (throughout life) as part of a healthy diet, (along with physical activity) may reduce the risk of developing osteoporosis (in peri- and postmenopausal women) (in later life). As part of a healthy diet (when taken with Vitamin D) may help prevent bone loss/osteoporosis. Helps in the development and maintenance of bones. Helps maintain/support bone health. N/A 65 mg 1,500 mg N/A Magnesium Helps in the development and maintenance of bones. N/A 20 mg 500 mg N/A Manganese Helps in the development and maintenance of bones. N/A 0.13 mg 9 mg N/A Vitamin A Helps in the development and maintenance of bones. Helps build strong bones N/A 65 µg RAE all-trans Retinol: 3,003 µg RAE N/A all-trans Retinyl acetate: 3,000 µg RAE

all-trans Retinyl palmitate: 3,022 µg RAE Vitamin C Helps in the development and maintenance of bones. Helps in collagen formation to maintain/support healthy bones. N/A 6 mg 2,000 mg N/A Vitamin D Helps in the development and maintenance of bones. Vitamin D intake, when combined with sufficient calcium, a healthy diet, and regular exercise, may reduce the risk of developing osteoporosis. N/A 1 µg 25 µg N/A Vitamin K 1 Vitamin K 2 and total Vitamin K 1 + K 2 Helps in the maintenance of bones. N/A 6 µg 120 µg N/A 1 At least two of the following references were consulted per use or purpose: HC 2018; Hunt 2012; FDA 2008; Tang et al. 2007; IOM 2006; NAMS 2006; Shils et al. 2006; Devirian and Volpe 2003; Brown and Josse 2002; Walker et al. 2002; Groff and Gropper 2000; NIH 2001; Blumenthal 1998; IOM 1997; Nielsen et al. 1987. 2 At least one of the following references was consulted per minimum daily dose: HC 2018; Hunt 2012; IOM 2006; Walker et al. 2002; Blumenthal 1998. 3 At least one of the following references was consulted per maximum daily dose: HC 2018; Hunt 2012; IOM 2006; Kerkhoffs et al. 2004; Singer et al. 2001. 4 Boron: Specific rule for boron for products providing more than 0.7 mg of boron per day. Refer to the 'Notes" section below. 5 Fruit bromelain/Stem bromelain: One papain unit (PU) is defined as that quantity of enzyme that liberates the equivalent of 1 microgram of tyrosine per hour under the conditions of the assay (FCC 8 2012). One gelatin digestion unit (GDU) is approximately equivalent to 15,000 FCC papain unit (1 GDU ≈ 15,000 FCC PU). Dose information may include the quantities of both the enzyme preparation and its enzymatic activity. The enzymatic activity quantity may be indicated in the Quantity/Unit field and its quantity of enzyme preparation in mg or ml in the Additional Quantity/Unit field. Notes: The above uses can be combined on the product label (e.g. Helps maintain joint health and reduce joint pain associated with osteoarthritis). The terms 'Helps' or 'Helps to' can be used interchangeably on the label. Specific rule for products providing more than 0.7 mg of boron per day: in order to ensure a favorable risk-benefit profile, a product providing elemental boron at doses in excess of 0.7 mg and up to the maximum limit of 3.36 mg per day must: be a joint health product; contain at least one medicinal ingredient from Table 2; and make only the specified joint pain/health claims from Table 2. In addition, the claim associated with boron 'Helps maintain healthy calcium metabolism' can be included. Other health products such as multi-vitamin/mineral supplements must not provide more than the maximum limit of 0.7 mg elemental boron per day. Direction(s) for use Table 4. Direction(s) for use Medicinal ingredients Daily dose Directions for use 1 Boron 0.7 mg or more boron when the claim associated with boron is made and if the product formulation does not also contain amounts of vitamin D and calcium that meet the minimum doses from the NNHPD Multi-Vitamin/Mineral Supplement monograph. Take with vitamin D and calcium. Fruit Bromelain Stem Bromelain All doses (Optional) Take with food. Calcium All doses Take with food, a few hours before or after taking other medications or health products. Methylsulfonylmethane (MSM) 1,500 mg or more MSM Take with food. Avoid taking at bedtime. 1 The following references were consulted for the directions for use: Boron: Devirian and Volpe 2003; Zittermann 2003; Calcium: Sweetman 2015, IOM 2011, ASHP 2005; MSM: Kim et al. 2006. Combination rules For multi-ingredient products containing fruit bromelain and stem bromelain, the combined proteolytic activity should not exceed the maximum proteolytic activity of 130,000,000 FCC PU per day and 45,000,000 FCC PU per single dose. The same combination rule applies with combination of fruit bromelain and/or stem bromelain with papain. The finished product should not exceed a total amount of curcuminoids of 500 mg per dose and 1500 mg per day. The finished product should not exceed a total amount of curcumin of 400 mg per dose and 1200 mg per day. The daily dose for glucosamine hydrochloride in combination with glucosamine sulfate is subject to the following limitations: the sum of the percentages of their individual maximum daily doses must not exceed 120%; [(e.g. a product providing a daily dose of 2000 mg glucosamine hydrochloride (100% of the 2000 mg maximum daily dose) + 300 mg glucosamine sulfate (20% of the 1500 mg maximum daily dose) would be acceptable (100%+20%=120%)]. Duration(s) of use Notes A minimum duration of use statement is required for all products citing use or purpose statements associated with boswellia, chondroitin sulfate, devil's claw, glucosamine (hydrochloride and sulfate), hydrolyzed collagen or methylsulfonylmethane (MSM). If more than one duration of use statement is indicated for a particular product formulation, only the shortest applicable duration of use statement is required on the PLA and product label. For example, a product citing use or purpose statements for chondroitin sulfate and glucosamine hydrochloride need only include the following duration of use statement on the product label: "Use for at least 1 month to see beneficial effects." A maximum duration of use statement is required for all products containing bromelain or willow bark. If the maximum duration of use is shorter than the minimum duration of use to see beneficial effects, the associated claim cannot be included. Minimum duration(s) of use Table 5. Minimum duration(s) of use Medicinal ingredients Minimum durations of use 1 Hydrolyzed collagen Use for at least 5 months to see beneficial effects. Chondroitin sulfate Use for at least 3 months to see beneficial effects. Devil's claw Use for at least 2-3 months to see beneficial effects. Boswellia Use for at least 2 months to see beneficial effects. Glucosamine hydrochloride Use for at least 1 month to see beneficial effects. Glucosamine sulfate Methylsulfonylmethane (MSM) 1 At least one of the following references was consulted per duration of use: Bruyère et al. 2012; Benito-Ruiz et al. 2009; Clark et al. 2008; Bjordal et al. 2007; Mehta et al. 2007; Sontakke et al. 2007; Kim et al. 2006; Usha and Naidu 2004; ESCOP 2003; Kimmatkar et al. 2003; Houpt et al. 1999; Qiu

et al. 1998. Maximum duration(s) of use Products containing bromelain Ask a health care practitioner/health care provider/health care professional/doctor/physician for prolonged use Products containing willow bark Ask a health care practitioner/health care provider/health care professional/doctor/physician for use beyond 6 weeks (Beer and Wegener 2008; Biegert et al. 2004). Risk Information Caution(s) and warning(s) Products providing more than 2.8 g of hydrolyzed collagen per day or any other medicinal ingredient from Table 2 at any dose (except products containing willow bark requiring a contraindication) Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you are pregnant or breastfeeding. (Joint) pain (and swelling) associated with osteoarthritis or rheumatoid arthritis Ask a health care practitioner/health care provider/health care professional/doctor/physician if symptoms worsen. Joint inflammation/anti-inflammatory/minor pain, swelling and inflammation relief Ask a health care practitioner/health care provider/health care professional/doctor/physician if symptoms persist or worsen. Products containing following medicinal ingredients Table 6. Caution(s) and warning(s) Medicinal ingredients Daily dose Cautions and warnings 1 beta-Carotene More than 6,000 µg Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you are a tobacco smoker. Boron More than 0.7 mg Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you have been diagnosed with estrogen-dependant cancer or have a kidney disorder. Fruit Bromelain Stem Bromelain All doses Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you have gastrointestinal lesions/ulcers or are having a surgery. Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you are taking blood thinners, anti-inflammatory agents or antibiotics. Curcumin/Curcuminoids/Turmeric (concentrated extracts) All doses Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you are taking blood thinners. Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you have a biliary disorder. Fish oil and willow bark combined All doses Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you are having a surgery. Manganese More than 5 mg Ask a health care practitioner/health care provider/health care professional/doctor/physician before if you have a liver disorder. Turmeric (native extracts) All doses Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you have a biliary disorder. Vitamin K 1 and/or K 2 All doses Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you are taking blood thinners. Willow bark All doses Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you have asthma or peptic ulcer disease. Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you are taking blood thinners or products containing salicylates (such as acetylsalicylic acid or non-steroidal anti-inflammatory drugs). 1 The following references were consulted for the caution and warning statements: beta-Carotene: Touvier et al. 2005; Omenn et al. 1996; ATBC 1994; Boron: Usuda et al. 1996; Nielsen et al. 1992; Fruit/Stem Bromelain: Martindale 2011; Brinker 2010; Blumenthal et al. 2000; Curcumin: Brinker 2010; ESCOP 2003; McGuffin et al. 1997 ; Curcumin : Brinker 2010; Mills and Bone 2005; ESCOP 2003; McGuffin et al. 1997; Fish oil and willow bark combined: Block et al. 2012, 2013; Larson et al. 2008; Manganese: IOM 2006; IOM 2001; Krieger et al. 1995; Turmeric: Brinker 2010; ESCOP 2003; McGuffin et al. 1997; Vitamin K1, K2: ASHP 2005; Franco et al 2004; IOM 2001; Hansten et al 1997; Willow bark: EMA 2017. Contraindication(s) Products containing willow bark Do not use if you are pregnant or breastfeeding (EMA 2017; Brinker 2010; Wichtl 2004; ESCOP 2003; Barnes et al. 2002; Blumenthal et al. 2000). Do not use if you are allergic to salicylates (EMA 2017; Brinker 2010; Wichtl 2004, ESCOP 2003; Barnes et al. 2002; Blumenthal et al. 2000). Known adverse reaction(s) Products containing boswellia and/or bromelain Stop use if hypersensitivity/allergy occurs (Martindale 2011; Brinker 2010; WHO 2009; Murray and Pizzorno 2006; Blumenthal et al. 2000; Baur and Fruhmann 1979). Products containing boswellia, bromelain, hydrolyzed collagen, methylsulfonylmethane and/or willow bark When using this product you may experience gastrointestinal discomfort/disturbances (EMA 2017; Martindale 2011; Brinker 2010; Sontakke et al. 2007; Brien et al. 2006; Wichtl 2004; ESCOP 2003; Kimmatkar et al. 2003; Barnes et al. 2002; Blumenthal et al. 2000; McGuffin 2000; Moskowitz 2000). Products providing more than 350 mg magnesium per day When using this product you may experience diarrhoea (IOM 2006 , IOM 1997). Non-medicinal ingredients Must be chosen from the current Natural Health Products Ingredients Database (NHPID) and must meet the limitations outlined in that database. Storage conditions Must be established in accordance with the requirements described in the Natural Health Products Regulations. Products containing fish oil, except those encapsulated Refrigerate after opening (Wille and Gonus 1989). Products containing fish oil (information for industry; not for labelling) To be packaged in airtight container, protected from light (Ph.Eur. 2023; USP-NF 2023). Products containing hydrolyzed collagen (information for industry; optional for labelling depending on the packaging) To be protected from heat and moisture (Ph.Eur. 2023). 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. Ingredients sourced from bovine tissues In order to minimize the risk of Transmissible Spongiform Encephalopathies (TSEs) from products sourced from bovine tissues, product licence applicants must have a veterinary certificate on file and must ensure that the following criteria have been met (Ph.Eur. 2023): Source animal is fit for human consumption; Source material can be traced back to the herd or animal; Avoidance of cross-contamination with high-infectivity tissues is ensured during sourcing; Manufacturing procedures that are known to reduce infectivity are implemented (e.g. procedures that are in accordance with those outlined in Chapter 5.02.08 of the European Pharmacopoeia 2012 'Minimising the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products'). Fish oil Peroxide, anisidine, and totox values of fish oil and omega-3 fatty acids derived from fish oil must be in accordance with the methods set out by the Association of Analytical Community (AOAC) and/or Pharmacopoeial analytical methods. These specifications are necessary to ensure the oxidative stability of the fish oil and the omega-3 fatty acids derived from fish oil (HC 2015). The maximum peroxide value (PV) must be 5 mEq/kg, the maximum anisidine value (AV) must be 20 while the maximum Totox value must be 26 (calculated as 2 X PV + AV). The dioxins, polychlorinated dibenzo-para-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs); the dioxin-like polychlorinated biphenyls (dioxin-like PCBs; and the polychlorinated biphenyls (PCBs) are contaminants in oils from marine sources. Testing for these contaminants are required. As indicated in the Quality of Natural Health Products Guide, testing should be performed using appropriate analytical methods, such as method No. 1613 revision B of the Environmental Protection Agency for PCDDs and PCDFs and method No. 1668B of the Environmental Protection Agency for chlorinated biphenyl congeners. Licence holders are advised to consult the Commission of the European Communities documents on dioxins and dioxin-like PCB contaminants in marine oil for further information. Refer to the Quality of Natural Health Products Guide for more information on the acceptable limits of dioxins and dioxin-like PCBs For fish oils including Gadidae as a source material, the vitamin A and D content should be tested to ensure that their respective daily maximum amounts meet the Multi-Vitamin/Mineral Supplements monograph for each age group. Bromelain Details of the manufacturing of the enzyme at the raw material stage should include fermentation medium, and the isolation process of the medicinal ingredient. 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 Food Chemicals Codex (FCC): PLANT PROTEOLYTIC ACTIVITY. 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. Chondroitin sulfate The medicinal ingredient must either: i. Comply with the specifications outlined in the Chondroitin Sulfate Sodium Monographs published in the British or European Pharmacopoeiae, or the United States Pharmacopoeia or, ii. Be cited in an approved NHP Master File, authorized by a letter of access issued to the applicant by the NHP Master File's registered owner Hyaluronic acid Information pertaining to the molecular weight of the hyaluronic acid must be available upon request for characterization (e.g. Certificate of Analysis, Technical Data Sheet, Product Information, etc). The average molecular weight of hyaluronic acid obtained from Gallus gallus comb must be 800 kDa. The average molecular weight of sodium hyaluronate from Streptococcus equi must be 900 kDa. Information regarding Method of preparation must be provided upon request For all products obtained through microbial fermentation, the species of Streptococcus used must be provided upon request and should be substantiated by the evidence. Information regarding manufacturing processes that reduce or eliminate pyrogenic or inflammatory components of the cell wall must be submitted upon request. The content of sulfated glycosaminoglycans, nucleic acids, protein, and microbial contamination derived from this ingredient must be in accordance with the methods set out by the European Pharmacopoeia: Sulfated glycosaminoglycans: maximum 1%, if the ingredient is extracted from Gallus gallus comb Nucleic acids: the absorbance of solution at 260 nm is maximum 0.5 Protein: maximum 0.3% Microbial contamination: Total Aerobic Microbial Count of 10 2 CFU/g Hydrolyzed Collagen For the purpose of this monograph, hydrolyzed collagen has no jelling power and is soluble in cold water (Schrieber and Gareis 2007; Moskowitz 2000). The average molecular weight of hydrolyzed collagen is approximately 4 kDa (i.e. 2-6 kDa) (Moskowitz 2000; Oesser et al. 1999). EXAMPLE OF PRODUCT FACTS: Consult the Guidance Document, Labelling of Natural Health Products for more details. References cited ASHP 2005: American Society of Health-System Pharmacists. 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MEDICINAL INGREDIENT(S)

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.This monograph may be used to support single ingredient or multi-ingredient products. However, it is mandatory for joint health products to contain at least one medicinal ingredient from Table 2 at therapeutic dose with its associated claim(s).As enhanced absorption formulations are often used for Turmeric and its constituents, this is a reminder that enhanced absorption dosage forms/formulations are not covered by Natural and Non-prescription Health Products Directorate's monographs and should be submitted as Class III submissions. DateOctober 25, 2024

USE(S) OR PURPOSE(S)

Medicinal ingredientsUses or purposes1Methods of preparationDose/daySingle doseMinimum2Maximum3Maximum single dose3 Boswellia serrataHelps relieve joint pain and swelling associated with osteoarthritis of the knee.Standardized Extracts999 mg extracts standardized to 40% boswellic acid999 mg extracts standardized to 40% boswellic acid333 mg extracts standardized to 40% boswellic acidChondroitin sulfateHelps relieve (joint) pain associated with osteoarthritis (of the knee).N/A800 mg1,200 mgN/ACurcuminHelps relieve joint pain and inflammation.N/A1,200 mg1,200 mg400 mgCurcuminoidsHelps relieve joint pain and inflammation.N/A1,500 mgOptional: The potency constituent, curcumin, can be included1,500 mgOptional: The potency constituent, curcumin, can be included500 mgTurmeric(concentrated extracts)Helps relieve joint pain and inflammation.Standardized ExtractsExtract standardized to 75% curcuminoids or more; Providing 1,500 mg curcuminoidsOptional: The potency constituent, curcumin, can be includedExtract standardized to 75% curcuminoids or more; Providing 1,500 mg curcuminoidsOptional: The potency constituent, curcumin, can be includedExtract standardized to 75% curcuminoids or more; Providing 500 mg curcuminoidsTurmeric(native extracts)4(Traditionally) used in Herbal Medicine (as an anti-inflammatory) to help relieve joint pain.Dry, Powdered, Non-Standardized Extracts (Dry extract*, Tincture, Fluid extract, Decoction, Infusion)1,000 mg dried rhizome; For dry extracts, maximum ratio is 10:19,000 mg dried rhizome; For dry extracts, maximum ratio is 10:1N/AStandardized ExtractsExtracts providing up to 35% curcuminoids and a Quantity crude equivalent of 1,000 mg dried rhizomeOptional: The potency constituent, curcumin, can be includedExtracts providing up to 35% curcuminoids and a Quantity crude equivalent of 9,000 mg dried rhizomeOptional: The potency constituent, curcumin, can be includedDevil's clawUsed in Herbal

Medicine to help relieve joint pain associated with osteoarthritis.Dry, Powdered, Non-Standardized Extracts (Dry extract*, Tincture, Fluid extract, Decoction, Infusion)600 mg dried secondary root tubers7,500 mg dried secondary root tubersN/AFish oil5In conjunction with conventional therapy, helps reduce the pain of rheumatoid arthritis in adults.Standardized fixed oil2,800 mg eicosapentaenoic acid (EPA) + docosahexaenoic acid (DHA) with a EPA:DHA ratio of 0.5:1-2:15,000 mg EPA + DHA with a EPA:DHA ratio of 0.5:1-2:1N/AGlucosamine hydrochlorideHelps maintain healthy cartilage/joint health.N/A1,500 mg2,000 mgN/AGlucosamine sulfateHelps relieve joint pain associated with osteoarthritis (of the knee).Helps protect against the deterioration of cartilage.A factor in maintaining healthy cartilage and/or joint health.N/A1,500 mg1,500 mgN/AHyaluronic acidHelps support joint health.N/A48 mg (sourced fromGallus galluscomb)120 mg (sourced fromGallus galluscomb)N/A120 mg (sourced from microbial fermentation)200 mg (sourced from microbial fermentation)Hydrolyzed collagenHelps reduce joint pain associated with osteoarthritis.Helps reduce osteoarthritis-related joint pain.Helps manage/in the management of joint pain.N/A1,200 mg10,000 mgN/AMethylsulfonylmethane (MSM)Helps relieve (joint) pain associated with osteoarthritis (of the knee).N/A1,500 mg6,000 mg2,000 mgWillow barkUsed in Herbal Medicine to relieve minor joint pain (due to osteoarthritis).Dry, Powdered, Non-Standardized Extracts (Dry extract, Tincture, Fluid extract, Decoction, Infusion)3,000 mg dried (young branch) bark9,000 mg dried (young branch) bark3,000 mg dried (young branch) barkStandardized ExtractsExtract providing up to 15% total salicin equivalent to 45 mg total salicinExtract providing up to 15% total salicin equivalent to 240 mg total salicinExtract providing up to 15% total salicin equivalent to 120 mg total salicin

DOSE(S)

Medicinal ingredientsUses or purposes1Methods of preparationDose/daySingle doseMinimum2Maximum3Maximum single dose3 Boswellia serrataHelps relieve joint pain and swelling associated with osteoarthritis of the knee.Standardized Extracts999 mg extracts standardized to 40% boswellic acid999 mg extracts standardized to 40% boswellic acid333 mg extracts standardized to 40% boswellic acidChondroitin sulfateHelps relieve (joint) pain associated with osteoarthritis (of the knee).N/A800 mg1,200 mgN/ACurcuminHelps relieve joint pain and inflammation.N/A1,200 mg1,200 mg400 mgCurcuminoidsHelps relieve joint pain and inflammation.N/A1,500 mgOptional: The potency constituent, curcumin, can be included1,500 mgOptional: The potency constituent, curcumin, can be included500 mgTurmeric(concentrated extracts)Helps relieve joint pain and inflammation.Standardized ExtractsExtract standardized to 75% curcuminoids or more; Providing 1,500 mg curcuminoidsOptional: The potency constituent, curcumin, can be includedExtract standardized to 75% curcuminoids or more; Providing 1,500 mg curcuminoidsOptional: The potency constituent, curcumin, can be includedExtract standardized to 75% curcuminoids or more; Providing 500 mg curcuminoidsTurmeric(native extracts)4(Traditionally) used in Herbal Medicine (as an anti-inflammatory) to help relieve joint pain.Dry, Powdered, Non-Standardized Extracts (Dry extract*, Tincture, Fluid extract, Decoction, Infusion)1,000 mg dried rhizome; For dry extracts, maximum ratio is 10:19,000 mg dried rhizome; For dry extracts, maximum ratio is 10:1N/AStandardized ExtractsExtracts providing up to 35% curcuminoids and a Quantity crude equivalent of 1,000 mg dried rhizomeOptional: The potency constituent, curcumin, can be includedExtracts providing up to 35% curcuminoids and a Quantity crude equivalent of 9,000 mg dried rhizomeOptional: The potency constituent, curcumin, can be includedDevil's clawUsed in Herbal Medicine to help relieve joint pain associated with osteoarthritis.Dry, Powdered, Non-Standardized Extracts (Dry extract*, Tincture, Fluid extract, Decoction, Infusion)600 mg dried secondary root tubers7,500 mg dried secondary root tubersN/AFish oil5In conjunction with conventional therapy, helps reduce the pain of rheumatoid arthritis in adults.Standardized fixed oil2,800 mg eicosapentaenoic acid (EPA) + docosahexaenoic acid (DHA) with a EPA:DHA ratio of 0.5:1-2:15,000 mg EPA + DHA with a EPA:DHA ratio of 0.5:1-2:1N/AGlucosamine hydrochlorideHelps maintain healthy cartilage/joint health.N/A1,500 mg2,000 mgN/AGlucosamine sulfateHelps relieve joint pain associated with osteoarthritis (of the knee).Helps protect against the deterioration of cartilage.A factor in maintaining healthy cartilage and/or joint health.N/A1,500 mg1,500 mgN/AHyaluronic acidHelps support joint health.N/A48 mg (sourced fromGallus galluscomb)120 mg (sourced fromGallus galluscomb)N/A120 mg (sourced from microbial fermentation)200 mg (sourced from microbial fermentation)Hydrolyzed collagenHelps reduce joint pain associated with osteoarthritis.Helps reduce osteoarthritis-related joint pain.Helps manage/in the management of joint pain.N/A1,200 mg10,000 mgN/AMethylsulfonylmethane (MSM)Helps relieve (joint) pain associated with osteoarthritis (of the knee).N/A1,500 mg6,000 mg2,000 mgWillow barkUsed in Herbal Medicine to relieve minor joint pain (due to

osteoarthritis).Dry, Powdered, Non-Standardized Extracts (Dry extract, Tincture, Fluid extract, Decoction, Infusion)3,000 mg dried (young branch) bark9,000 mg dried (young branch) bark3,000 mg dried (young branch) barkStandardized ExtractsExtract providing up to 15% total salicin equivalent to 45 mg total salicinExtract providing up to 15% total salicin equivalent to 240 mg total salicinExtract providing up to 15% total salicin equivalent to 120 mg total salicin

RISK INFORMATION

Caution(s) and warning(s) Products providing more than 2.8 g of hydrolyzed collagen per day or any other medicinal ingredient from Table 2 at any dose (except products containing willow bark requiring a contraindication) Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you are pregnant or breastfeeding. (Joint) pain (and swelling) associated with osteoarthritis or rheumatoid arthritis Ask a health care practitioner/health care provider/health care professional/doctor/physician if symptoms worsen. Joint inflammation/anti-inflammatory/minor pain, swelling and inflammation relief Ask a health care practitioner/health care provider/health care professional/doctor/physician if symptoms persist or worsen. Products containing following medicinal ingredients Table 6. Caution(s) and warning(s)Medicinal ingredientsDaily doseCautions and warnings1beta-CaroteneMore than 6,000 µgAsk a health care practitioner/health care provider/health care professional/doctor/physician before use if you are a tobacco smoker.BoronMore than 0.7 mgAsk a health care practitioner/health care provider/health care professional/doctor/physician before use if you have been diagnosed with estrogen-dependant cancer or have a kidney disorder.Fruit BromelainStem BromelainAll dosesAsk a health care practitioner/health care provider/health care professional/doctor/physician before use if you have gastrointestinal lesions/ulcers or are having a surgery.Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you are taking blood thinners, anti-inflammatory agents or antibiotics.Curcumin/Curcuminoids/Turmeric (concentrated extracts)All dosesAsk a health care practitioner/health care provider/health care professional/doctor/physician before use if you are taking blood thinners.Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you have a biliary disorder.Fish oil and willow bark combinedAll dosesAsk a health care practitioner/health care provider/health care professional/doctor/physician before use if you are having a surgery.ManganeseMore than 5 mgAsk a health care practitioner/health care provider/health care professional/doctor/physician before if you have a liver disorder.Turmeric (native extracts)All dosesAsk a health care practitioner/health care provider/health care professional/doctor/physician before use if you have a biliary disorder.Vitamin K1and/or K2All dosesAsk a health care practitioner/health care provider/health care professional/doctor/physician before use if you are taking blood thinners.Willow barkAll dosesAsk a health care practitioner/health care provider/health care professional/doctor/physician before use if you have asthma or peptic ulcer disease.Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you are taking blood thinners or products containing salicylates (such as acetylsalicylic acid or non-steroidal anti-inflammatory drugs).

NON-MEDICINAL INGREDIENTS

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

STORAGE CONDITION(S)

Must be established in accordance with the requirements described in theNatural Health Products Regulations. Products containing fish oil, except those encapsulated Refrigerate after opening (Wille and Gonus 1989). Products containing fish oil (information for industry; not for labelling) To be packaged in airtight container,

protected from light (Ph.Eur. 2023; USP-NF 2023). Products containing hydrolyzed collagen (information for industry; optional for labelling depending on the packaging) To be protected from heat and moisture (Ph.Eur. 2023).

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.Ingredients sourced from bovine tissuesIn order to minimize the risk of Transmissible Spongiform Encephalopathies (TSEs) from products sourced from bovine tissues, product licence applicants must have a veterinary certificate on file and must ensure that the following criteria have been met (Ph.Eur. 2023):Source animal is fit for human consumption;Source material can be traced back to the herd or animal;Avoidance of cross-contamination with high-infectivity tissues is ensured during sourcing;Manufacturing procedures that are known to reduce infectivity are implemented (e.g. procedures that are in accordance with those outlined in Chapter 5.02.08 of the European Pharmacopoeia 2012 'Minimising the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products').Fish oilPeroxide, anisidine, and totox values of fish oil and omega-3 fatty acids derived from fish oil must be in accordance with the methods set out by the Association of Analytical Community (AOAC) and/or Pharmacopoeial analytical methods. These specifications are necessary to ensure the oxidative stability of the fish oil and the omega-3 fatty acids derived from fish oil (HC 2015). The maximum peroxide value (PV) must be 5 mEq/kg, the maximum anisidine value (AV) must be 20 while the maximum Totox value must be 26 (calculated as 2 X PV + AV).The dioxins, polychlorinated dibenzo-para-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs); the dioxin-like polychlorinated biphenyls (dioxin-like PCBs; and the polychlorinated biphenyls (PCBs) are contaminants in oils from marine sources. Testing for these contaminants are required. As indicated in the Quality of Natural Health Products Guide, testing should be performed using appropriate analytical methods, such as method No. 1613 revision B of the Environmental Protection Agency for PCDDs and PCDFs and method No. 1668B of the Environmental Protection Agency for chlorinated biphenyl congeners. Licence holders are advised to consult the Commission of the European Communities documents on dioxins and dioxin-like PCB contaminants in marine oil for further information. Refer to the Quality of Natural Health Products Guide for more information on the acceptable limits of dioxins and dioxin-like PCBsFor fish oils including Gadidae as a source material, the vitamin A and D content should be tested to ensure that their respective daily maximum amounts meet the Multi-Vitamin/Mineral Supplements monograph for each age group.BromelainDetails of the manufacturing of the enzyme at the raw material stage should include fermentation medium, and the isolation process of the medicinal ingredient.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 Food Chemicals Codex (FCC): PLANT PROTEOLYTIC ACTIVITY.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.Chondroitin sulfateThe medicinal ingredient must either: i. Comply with the specifications outlined in the Chondroitin Sulfate Sodium Monographs published in the British or European Pharmacopoeiae, or the United States Pharmacopoeia or, ii. Be cited in an approved NHP Master File, authorized by a letter of access issued to the applicant by the NHP Master File's registered ownerHyaluronic acidInformation pertaining to the molecular weight of the hyaluronic acid must be available upon request for characterization (e.g. Certificate of Analysis, Technical Data Sheet, Product Information, etc). The average molecular weight of hyaluronic acid obtained fromGallus galluscomb must be 800 kDa. The average molecular weight of sodium hyaluronate fromStreptococcusequi must be 900 kDa.Information regarding Method of preparation must be provided upon requestFor all products obtained through microbial fermentation, the species ofStreptococcusused must be provided upon request and should be substantiated by the evidence. Information regarding manufacturing processes that reduce or eliminate pyrogenic or inflammatory components of the cell wall must be submitted upon request.The content of sulfated glycosaminoglycans, nucleic acids, protein, and microbial contamination derived from this ingredient must be in accordance with the methods set out by the European Pharmacopoeia:Sulfated glycosaminoglycans: maximum 1%, if the ingredient is extracted fromGallus galluscombNucleic acids: the absorbance of solution at 260 nm is maximum 0.5Protein: maximum 0.3%Microbial contamination: Total Aerobic Microbial Count of 102CFU/gHydrolyzed CollagenFor the purpose of this monograph, hydrolyzed collagen has no jelling power and is soluble in cold water (Schrieber and Gareis

2007; Moskowitz 2000).The average molecular weight of hydrolyzed collagen is approximately 4 kDa (i.e. 2-6 kDa) (Moskowitz 2000; Oesser et al. 1999).

REFERENCES

2Cartilage must be derived from healthy and domestic animals used for food by humans (USP-NF 2023). 3Corresponds to oil from the whole body of one or more of species of the families listed in Table 1 in its natural and/or concentrated triglyceride/triacylglycerol form and/or its concentrated esterified form (BP 2023; Ph.Eur. 2023; Froese and Pauly 2022). The species common names and not the family could be listed on the label. 4For fish oils including species of Gadidae as a source material, the vitamin A and D content should be tested to ensure that the daily maximum amounts meet the Multi-Vitamin/Mineral Supplements monograph for each age group. 5The specific organisms used as source material(s) must be indicated in the Animal Tissue Form (ATF); simply indicating "crustaceans" is insufficient. 6The stabilizing salt (i.e. sodium) if present should be indicated. 7For the purpose of this monograph, hydrolyzed collagen has no jelling power and is soluble in cold water (Schrieber and Gareis 2007; Moskowitz 2000). The average molecular weight of hydrolyzed collagen is approximately 4 kDa (i.e. 2-6 kDa) (Moskowitz 2000; Oesser et al. 1999).

name(s)	Source information		
erial(s)	Part(s)	Preparation(s)	
a-Carotenebeta-Carotene	beta-Carotene	N/A	N/A
	As per NNHPD Multi-Vitamin/Mineral Supplements monograph	N/A	N/A
dian frankincenseIndian olibanumN/A	Indian olibanum-treeShallaki	Boswellia serrata	Stem bark oleogum resinTrunk
ainJuice bromelainPineapple fruitN/A	Bromelain	Ananas comosusvar.bracteatusAnanas comosusvar.comosus	Fruit
ineapple stem bromelainStem bromelain	N/A	Ananas comosusvar.bracteatusAnanas comosusvar.comosus	Stem
	As per NNHPD Multi- Vitamin/Mineral Supplements monograph	N/A	N/A
sulfate	Sodium chondroitin sulfate	Anas platyrhynchosAnser anserBos taurusCygnus olorGallus gallusDromaiusnovaeholla	Cartilage
ene-3,5-dione	N/A	Curcuma longa	Rhizome
	N/A	Synthetic	
ds	N/A	Curcuma longa	Rhizome
rmericCurcumaIndian-saffronJiangHuang	N/A	Curcuma longa	Rhizome
Grapple plantWood spider	N/A	Harpagophytum procumbens	Secondary root tubers
Grapple plantWood spider	N/A	Harpagophytum zeyheri	
	N/A	AmmodytidaeCarangidaeClupeidaeEngraulidaeGadidae4OsmeridaeSalmon	
e HClGlucosamine hydrochloride	Glucosamine hydrochloride	Crab5Krill5Lobster5Prawn5Shrimp5	Exoskeleton
s nigerAspergillus nigervar.awamoriMonascus	FermentedMonascus pilosusMonascus purpureusRhizopus oryzae		
e sulfate	Glucosamine sulfate potassium chlorideGlucosamine sulfate sodium chloride	Crab5Krill5Lobster5Prawn5Shrimp5	Exoskeleton
s nigerAspergillus nigervar. awamoriMonascus	FermentedMonascus pilosusMonascus purpureusRhizopus oryzae		
acid	Sodium hyaluronate	Gallus gallus	Comb
us equi	Bacterial extracellular capsule	Fermented	
drolysateHydrolyzed collagen	N/A	Bovine	Bovine skin/hide split

	As per NNHPD Multi-Vitamin/Mineral Supplements	N/A	N/A
mylmethaneMSM	Dimethyl sulfone	N/A	N/A
	As per NNHPD Multi-Vitamin/Mineral Supplements	N/A	N/A
tamin D2			
	N/A	Salix albaSalix daphnoidesSalix purpuraSalix fragilis	Bark, young branch bark

urposes1	Methods of preparation	Dose/day	Single dose
	Maximum single dose3		
e joint pain and swelling associated with osteoarthritis of the knee.	Standardized Extracts	999 mg extracts standardized to 40% boswellic acid	999 mg extracts standardized
e (joint) pain associated with osteoarthritis (of the knee).	N/A	800 mg	1,200 mg
e joint pain and inflammation.	N/A	1,200 mg	1,200 mg
e joint pain and inflammation.	N/A	1,500 mgOptional: The potency constituent, curcumin, can be included	1,500 mg Optional: The potenc
e joint pain and inflammation.	Standardized Extracts	Extract standardized to 75% curcuminoids or Extract standardized to 95% cur	Extract standardized to 75% cur
y) used in Herbal Medicine (as an Anti-Inflammatory, Non-Steroidal Anti-Rheumatic) to help relieve joint pain associated with osteoarthritis.	Dry Powdered, Non-Standardized Extracts (Dry extract, Tincture, Fluid extract, Decoction, Infusion)	1,000 mg dried rhizome; Fluid extract, Decoction, Infusion: 1:1	2,000 mg dried rhizome; For d
viding up to 35% curcuminoids and a Quantity rhizomeOptional: The potency constituent, curcumin, can be included	Extracts providing up to 35% curcuminoids and a Quantity crude equivalent of 1,000 mg dried rhizomeOptional: The potency constituent, curcumin, can be included	Quantity crude equivalent of 9,000 mg dried	
bal Medicine to help relieve joint pain associated with osteoarthritis.	Dry Powdered, Non-Standardized Extracts (Dry extract, Tincture, Fluid extract, Decoction, Infusion)	600 mg dried secondary root	7,500 mg dried secondary roo
on with conventional therapy, helps to reduce the pain of rheumatoid arthritis in adults.	Standardized fixed oil	2,800 mg eicosapentaenoic acid (EPA) + docosahexaenoic acid (DHA) with a EPA:DHA ratio of 0.5:1-2:1	5,000 mg EPA + DHA with a EPA:DHA r
ain healthy cartilage/joint health.	N/A	1,500 mg	2,000 mg
e joint pain associated with osteoarthritis (of the knee).Helps protect against the deterioration of cartilage.A factor in maintaining healthy cartilage and/or jo	N/A	1,500 mg	1,500 mg
ort joint health.	N/A	48 mg (sourced fromGallus galluscomb)	120 mg (sourced fromGallus g
urced from microbial fermentation)			
e joint pain associated with osteoarthritis.Helps reduce osteoarthritis-related joint pain	N/A	1,200 mg Helps manage/in the management of joint pain	10,000 mg
e (joint) pain associated with osteoarthritis (of the knee).	N/A	1,500 mg	6,000 mg
bal Medicine to relieve minor joint pain, Powdered, Non-Standardized Extracts (Dry extract, Tincture, Fluid extract, Decoction, Infusion)		3,000 mg dried (young branch bar	9,000 mg dried (young branch
iding up to 15% total salicin equivalent to 45 mg total salicin	Extract providing up to 15% total salicin equivalent to 240 mg total salicin	Extract providing up to 15% total salicin equivalent to 120 mg total salicin	

s or purposes1	Methods of preparation	Dose/day	Single dose
mum3	Maximum/ single dose3		
itamin A/Source of vitamin A to help in the de bones.Helps in the development and maintenance of bones.	N/A	390 µg	18,000 µg
s maintain healthy calcium metabolism.	N/A	0.7 mg	3.36 mg4
d in herbal medicine to help relieve minor pain	N/A	480,000 FCC papain units (PU)5	130,000,000 FCC PU5
quate calcium (and vitamin D) (throughout life) with physical activity) may help prevent bone loss/osteoporosis (in peri- and postmenopausal women) (in later life).Adequate calcium (and vitamin D) (throughout life) as part of a healthy diet, (along with physical activity) may reduce the risk of developing osteoporosis (in peri- and postmenopausal women) (in later life).As part of a healthy diet (when taken with Vitamin D) may help prevent bone loss/osteoporosis.Helps in the development and maintenance of bones.	N/A) as part of a healthy diet, (along	65 mg Helps maintain/support bone health.	1,500 mg
s in the development and maintenance of bones.	N/A	20 mg	500 mg
s in the development and maintenance of bones.	N/A	0.13 mg	9 mg
s in the development and maintenance of bones.	N/A.Helps build strong bones	65 µg RAE	all-transRetinol: 3,003 µg R
s in the development and maintenance of bones.	N/A.Helps in collagen formation to maintain/support healthy bones.	6 mg	2,000 mg
s in the development and maintenance of bones. exercise, may reduce the risk of developing osteoporosis.	N/A.Vitamin D intake, when combined with sufficient calcium, a healthy diet, and regular	1 µg	25 µg
s in the maintenance of bones.	N/A	6 µg	120 µg

Medicinal ingredients	Daily dose	Directions for use1
Boron	0.7 mg or more boron when the claim associated with boron is made and the product formulation does not also contain amounts of vitamin D and calcium that meet the minimum doses NNHPD Multi-Vitamin/Mineral Supplement monograph.	Take with vitamin D and calcium
Fruit BromelainStem Bromelain	All doses (Optional)	Take with food.
Calcium	All doses	Take with food, a few hours before or after taking oth products.
Methylsulfonylmethane (MSM)	1,500 mg or more MSM	Take with food.Avoid taking at bedtime.

Medicinal ingredients	Minimum durations of use1
Hydrolyzed collagen	Use for at least 5 months to see beneficial effects.
Chondroitin sulfate	Use for at least 3 months to see beneficial effects.
Devil's claw	Use for at least 2-3 months to see beneficial effects.
Boswellia	Use for at least 2 months to see beneficial effects.
Glucosamine hydrochloride	Use for at least 1 month to see beneficial effects.

Glucosamine sulfate	
Methylsulfonylmethane (MSM)	

Medicinal ingredients	Daily dose	Cautions and warnings1
beta-Carotene	More than 6,000 µg	Ask a health care practitioner/health care provider/health ca professional/doctor/physician before use if you are a tobacco smoker.
Boron	More than 0.7 mg	Ask a health care practitioner/health care provider/health ca professional/doctor/physician before use if you have been diagnosed with es disorder.
Fruit BromelainStem Bromelain	All doses	Ask a health care practitioner/health care provider/health ca professional/doctor/physician before use i or are having a surgery.Ask a health care pr professional/doctor/physician before use i anti-inflammatory agents or antibiotics.
Curcumin/Curcuminoids/Turmeric (concentrated extracts)	All doses	Ask a health care practitioner/health care provider/health ca professional/doctor/physician before use i professional/doctor/physician before use i
Fish oil and willow bark combined	All doses	Ask a health care practitioner/health care provider/health ca professional/doctor/physician before use if you are having a surgery.
Manganese	More than 5 mg	Ask a health care practitioner/health care provider/health ca professional/doctor/physician before if you have a liver disorder.
Turmeric (native extracts)	All doses	Ask a health care practitioner/health care provider/health ca professional/doctor/physician before use if you have a biliary disorder.
Vitamin K1and/or K2	All doses	Ask a health care practitioner/health care provider/health ca professional/doctor/physician before use if you are taking blood thinners.
Willow bark	All doses	Ask a health care practitioner/health care provider/health ca professional/doctor/physician before use i professional/doctor/physician before use i products containing salicylates (such as acetylsalic anti-inflammatory drugs).