

## NATURAL HEALTH PRODUCT

### JOINT HEALTH PRODUCTS

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

March 28, 2024

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

Table 1. Proper name(s), Common name(s), Source information<sup>1</sup>

Proper name(s)	Common name(s)	Source information			
		Source ingredient(s)	Source material(s)	Part(s)	Preparation(s)
<ul style="list-style-type: none"> <li>• <i>all-trans</i>-beta-Carotene</li> <li>• beta-Carotene</li> </ul>	<ul style="list-style-type: none"> <li>• <i>all-trans</i>-beta-Carotene</li> <li>• beta-Carotene</li> </ul>	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



Proper name(s)	Common name(s)	Source information			
		Source ingredient(s)	Source material(s)	Part(s)	Preparation(s)
<i>Boswellia serrata</i>	<ul style="list-style-type: none"> <li>• Boswellia</li> <li>• Indian frankincense</li> <li>• Indian olibanum</li> <li>• Indian olibanum-tree</li> <li>• Shallaki</li> </ul>	N/A	<i>Boswellia serrata</i>	<ul style="list-style-type: none"> <li>• Stem bark oleogum resin</li> <li>• Trunk bark oleogum resin</li> </ul>	Dry
Fruit bromelain	<ul style="list-style-type: none"> <li>• Fruit bromelain</li> <li>• Juice bromelain</li> <li>• Pineapple fruit bromelain</li> </ul>	N/A	<ul style="list-style-type: none"> <li>• <i>Ananas comosus</i> var. <i>bracteatus</i></li> <li>• <i>Ananas comosus</i> var. <i>comosus</i></li> </ul>	Fruit	Isolate
Stem bromelain	<ul style="list-style-type: none"> <li>• Bromelain</li> <li>• Pineapple stem bromelain</li> <li>• Stem bromelain</li> </ul>	N/A	<ul style="list-style-type: none"> <li>• <i>Ananas comosus</i> var. <i>bracteatus</i></li> <li>• <i>Ananas comosus</i> var. <i>comosus</i></li> </ul>	Stem	Isolate
Calcium	Calcium	As per NNHPD Multi-Vitamin/Mineral Supplements monograph	N/A	N/A	As per NNHPD Multi-Vitamin/Mineral Supplements monograph
Chondroitin sulfate <sup>2</sup>	Chondroitin sulfate	Sodium chondroitin sulfate	<ul style="list-style-type: none"> <li>• <i>Anas platyrhynchos</i></li> <li>• <i>Anser anser</i></li> <li>• <i>Bos taurus</i></li> <li>• <i>Cygnus olor</i></li> <li>• <i>Dromaius novaehollandiae</i></li> <li>• <i>Gallus gallus</i></li> <li>• <i>Meleagris gallopavo</i></li> <li>• <i>Numida meleagris</i></li> <li>• <i>Rhea americana</i></li> <li>• <i>Struthio camelus</i></li> <li>• <i>Sus scrofa</i></li> </ul>	Cartilage	Isolate
(1E,6E)-1,7-Bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione	Curcumin	N/A	<i>Curcuma longa</i>	Rhizome	Isolate
		Curcumin	N/A	N/A	Synthetic
Curcuminoids	Curcuminoids	N/A	<i>Curcuma longa</i>	Rhizome	Isolate
<i>Curcuma longa</i>	<ul style="list-style-type: none"> <li>• Common turmeric</li> </ul>	N/A	<i>Curcuma longa</i>	Rhizome	Dry



Proper name(s)	Common name(s)	Source information			
		Source ingredient(s)	Source material(s)	Part(s)	Preparation(s)
	<ul style="list-style-type: none"> <li>• Curcuma</li> <li>• Indian-saffron</li> <li>• Jianghuang</li> <li>• Turmeric</li> <li>• Yellow ginger</li> </ul>				
<i>Harpagophytum procumbens</i>	<ul style="list-style-type: none"> <li>• Devil's claw</li> <li>• Grapple plant</li> <li>• Wood spider</li> </ul>	N/A	<i>Harpagophytum procumbens</i>	Secondary root tubers	Dry
<i>Harpagophytum zeyheri</i>	<ul style="list-style-type: none"> <li>• Devil's claw</li> <li>• Grapple plant</li> <li>• Wood spider</li> </ul>	N/A	<i>Harpagophytum zeyheri</i>		
Fish oil <sup>3</sup>	Fish oil	N/A	<ul style="list-style-type: none"> <li>• Ammodytidae</li> <li>• Carangidae</li> <li>• Clupeidae</li> <li>• Engraulidae</li> <li>• Gadidae<sup>4</sup></li> <li>• Osmeridae</li> <li>• Salmonidae</li> <li>• Scrombridae</li> </ul>	Whole	N/A
2-Amino-2-deoxy-beta-D-glucopyranose hydrochloride	<ul style="list-style-type: none"> <li>• Glucosamine HCl</li> <li>• Glucosamine hydrochloride</li> </ul>	Glucosamine hydrochloride	<ul style="list-style-type: none"> <li>• Crab<sup>5</sup></li> <li>• Krill<sup>5</sup></li> <li>• Lobster<sup>5</sup></li> <li>• Prawn<sup>5</sup></li> <li>• Shrimp<sup>5</sup></li> </ul>	Exoskeleton	Isolate
			<ul style="list-style-type: none"> <li>• <i>Aspergillus flavus</i> var. <i>oryzae</i></li> <li>• <i>Aspergillus melleus</i></li> <li>• <i>Aspergillus niger</i></li> <li>• <i>Aspergillus niger</i> var. <i>awamori</i></li> <li>• <i>Monascus pilosus</i></li> <li>• <i>Monascus purpureus</i></li> <li>• <i>Rhizopus oryzae</i></li> </ul>	Whole	Fermented
2-Amino-2-deoxy-D-glucose sulfate	Glucosamine sulfate	<ul style="list-style-type: none"> <li>• Glucosamine Sulfate</li> <li>• Potassium Chloride</li> </ul>	<ul style="list-style-type: none"> <li>• Crab<sup>5</sup></li> <li>• Krill<sup>5</sup></li> <li>• Lobster<sup>5</sup></li> <li>• Prawn<sup>5</sup></li> <li>• Shrimp<sup>5</sup></li> </ul>	Exoskeleton	Isolate

Proper name(s)	Common name(s)	Source information			
		Source ingredient(s)	Source material(s)	Part(s)	Preparation(s)
		<ul style="list-style-type: none"> <li>• Glucosamine Sulfate</li> <li>• Sodium Chloride</li> </ul>	<ul style="list-style-type: none"> <li>• <i>Aspergillus flavus</i> var. <i>oryzae</i></li> <li>• <i>Aspergillus melleus</i></li> <li>• <i>Aspergillus niger</i></li> <li>• <i>Aspergillus niger</i> var. <i>awamori</i></li> <li>• <i>Monascus pilosus</i></li> <li>• <i>Monascus purpureus</i></li> <li>• <i>Rhizopus oryzae</i></li> </ul>	Whole	Fermented
Hyaluronic acid <sup>6</sup>	Hyaluronic acid	Sodium hyaluronate	<i>Gallus gallus</i>	Comb	Isolate
		<ul style="list-style-type: none"> <li>• Hyaluronic acid</li> <li>• Sodium hyaluronate</li> </ul>	<i>Streptococcus equi</i>	Bacterial extracellular capsule	Fermented
Hydrolyzed collagen <sup>7</sup>	<ul style="list-style-type: none"> <li>• Collagen hydrolysate</li> <li>• Hydrolyzed collagen</li> </ul>	N/A	Bovine	Bovine skin/ hide split	N/A
			Porcine	<ul style="list-style-type: none"> <li>• Bone</li> <li>• Skin</li> </ul>	
			Fish	<ul style="list-style-type: none"> <li>• Bone</li> <li>• Skin</li> </ul>	
			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				
<ul style="list-style-type: none"> <li>• Dimethyl sulfone</li> <li>• Methylsulfonyl methane</li> <li>• Sulfonylbismethane</li> </ul>	<ul style="list-style-type: none"> <li>• Methylsulfonylmethane</li> <li>• MSM</li> </ul>	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	<ul style="list-style-type: none"> <li>• Vitamin D</li> <li>• Vitamin D<sub>2</sub></li> </ul>				
	<ul style="list-style-type: none"> <li>• Vitamin D</li> <li>• Vitamin D<sub>3</sub></li> </ul>				

Proper name(s)	Common name(s)	Source information			
		Source ingredient(s)	Source material(s)	Part(s)	Preparation(s)
Vitamin K <sub>1</sub>	Vitamin K <sub>1</sub>				
Vitamin K <sub>2</sub>	Vitamin K <sub>2</sub>				
Willow bark	Willow bark	N/A	<ul style="list-style-type: none"> <li>• <i>Salix alba</i></li> <li>• <i>Salix daphnoides</i></li> <li>• <i>Salix purpurea</i></li> <li>• <i>Salix x fragilis</i></li> </ul>	<ul style="list-style-type: none"> <li>• Bark</li> <li>• Young branch bark</li> </ul>	Dry

<sup>1</sup>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.

<sup>2</sup>Cartilage must be derived from healthy and domestic animals used for food by humans (USP-NF 2023).

<sup>3</sup>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.

<sup>4</sup>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.

<sup>5</sup>The specific organisms used as source material(s) must be indicated in the Animal Tissue Form (ATF); simply indicating “crustaceans” is insufficient.

<sup>6</sup>The stabilizing salt (i.e. sodium) if present should be indicated.

<sup>7</sup>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 <sup>1</sup>	Methods of preparation	Dose/day		Single dose
			Minimum <sup>2</sup>	Maximum <sup>3</sup>	Maximum single dose <sup>3</sup>
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).	Isolate	800 mg	1,200 mg	N/A
Curcumin	Helps relieve joint pain and inflammation.	Isolate	1,200 mg	1,200 mg	400 mg
Curcuminoids	Helps relieve joint pain and inflammation.	Isolate	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) <sup>4</sup>	(Traditionally) used in Herbal Medicine 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	Extracts providing up to 35% curcuminoids and a Quantity crude equivalent of	



Medicinal ingredients	Uses or purposes <sup>1</sup>	Methods of preparation	Dose/day		Single dose
			Minimum <sup>2</sup>	Maximum <sup>3</sup>	Maximum single dose <sup>3</sup>
			Optional: The potency constituent, curcumin, can be included	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 <sup>5</sup>	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.	Isolate	1,500 mg	2,000 mg	N/A
Glucosamine sulfate	<ul style="list-style-type: none"> <li>Helps relieve joint pain associated with osteoarthritis (of the knee).</li> <li>Helps protect against the deterioration of cartilage.</li> <li>A factor in maintaining healthy cartilage and/or joint health.</li> </ul>	Isolate	1,500 mg	1,500 mg	N/A
Hyaluronic acid	Helps support joint health.	Isolate	48 mg (sourced from <i>Gallus gallus</i> comb)	120 mg (sourced from <i>Gallus gallus</i> comb)	N/A
			120 mg (sourced from microbial fermentation)	200 mg (sourced from microbial fermentation)	





Medicinal ingredients	Uses or purposes <sup>1</sup>	Methods of preparation	Dose/day		Single dose
			Minimum <sup>2</sup>	Maximum <sup>3</sup>	Maximum single dose <sup>3</sup>
Hydrolyzed collagen	<ul style="list-style-type: none"> <li>• Helps reduce joint pain associated with osteoarthritis.</li> <li>• Helps reduce osteoarthritis-related joint pain.</li> <li>• Helps manage/in the management of joint pain.</li> </ul>	Isolate	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

<sup>1</sup>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.

<sup>2</sup>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.

<sup>3</sup>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.

<sup>4</sup>**Turmeric:** Refer to the Turmeric monograph for more information on native extracts.

<sup>5</sup>**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 <sup>1</sup>	Methods of preparation	Dose/day		Single dose
			Minimum <sup>2</sup>	Maximum <sup>3</sup>	Maximum/single dose <sup>3</sup>
beta-Carotene	<ul style="list-style-type: none"> <li>• Provitamin A/Source of vitamin A to help in the development and maintenance of bones.</li> <li>• Helps in the development and maintenance of bones.</li> </ul>	N/A	390 µg	18,000 µg	N/A
Boron <sup>4</sup>	Helps maintain healthy calcium metabolism.	N/A	0.7 mg	3.36 mg <sup>4</sup>	N/A
Fruit Bromelain <sup>5</sup> Stem Bromelain <sup>5</sup>	Used in herbal medicine to help relieve minor pain, swelling and inflammation.	Isolate	480,000 FCC papain units (PU) <sup>5</sup>	130,000,000 FCC PU <sup>5</sup>	45,000,000 FCC PU
Calcium	<ul style="list-style-type: none"> <li>• 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).</li> <li>• 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).</li> <li>• As part of a healthy diet (when taken with Vitamin D) may help prevent bone loss/osteoporosis.</li> <li>• Helps in the development and maintenance of bones.</li> </ul>	N/A	65 mg	1,500 mg	N/A

Medicinal ingredients	Uses or purposes <sup>1</sup>	Methods of preparation	Dose/day		Single dose
			Minimum <sup>2</sup>	Maximum <sup>3</sup>	Maximum/single dose <sup>3</sup>
	<ul style="list-style-type: none"> <li>Helps maintain/support bone health.</li> </ul>				
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	<ul style="list-style-type: none"> <li>Helps in the development and maintenance of bones.</li> <li>Helps build strong bones.</li> </ul>	N/A	65 µg RAE	<i>all-trans</i> Retinol: 3,003 µg RAE <i>all-trans</i> Retinyl acetate: 3,000 µg RAE <i>all-trans</i> Retinyl palmitate: 3,022 µg RAE	N/A
Vitamin C	<ul style="list-style-type: none"> <li>Helps in the development and maintenance of bones.</li> <li>Helps in collagen formation to maintain/support healthy bones.</li> </ul>	N/A	6 mg	2,000 mg	N/A
Vitamin D	<ul style="list-style-type: none"> <li>Helps in the development and maintenance of bones.</li> <li>Vitamin D intake, when combined with sufficient calcium, a healthy diet, and regular exercise, may reduce the risk of developing osteoporosis.</li> </ul>	N/A	1 µg	25 µg	N/A
Vitamin K <sub>1</sub> Vitamin K <sub>2</sub> and total Vitamin K <sub>1</sub> + K <sub>2</sub>	Helps in the maintenance of bones.	N/A	6 µg	120 µg	N/A

<sup>1</sup>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.

<sup>2</sup>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.

<sup>3</sup>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.

<sup>4</sup>**Boron:** Specific rule for boron for products providing more than 0.7 mg of boron per day. Refer to the 'Notes' section below.

<sup>5</sup>**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 <sup>1</sup>
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.
<ul style="list-style-type: none"> <li>• Fruit Bromelain</li> <li>• Stem Bromelain</li> </ul>	All doses (Optional)	Take with food.
Calcium	All doses	Take with food, a few hours before or after taking other medications or natural health products.
Methylsulfonylmethane (MSM)	1,500 mg or more MSM	<ul style="list-style-type: none"> <li>• Take with food.</li> <li>• Avoid taking at bedtime.</li> </ul>

<sup>1</sup>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 <sup>1</sup>
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.



Medicinal ingredients	Minimum durations of use <sup>1</sup>
Glucosamine hydrochloride	Use for at least 1 month to see beneficial effects.
Glucosamine sulfate	
Methylsulfonylmethane (MSM)	

<sup>1</sup>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 <sup>1</sup>
beta-Carotene	More than 6,000 µg	<b>Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you are a tobacco smoker.</b>
Boron	More than 0.7 mg	<b>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.</b>
<ul style="list-style-type: none"> <li>• Fruit Bromelain</li> <li>• Stem Bromelain</li> </ul>	All doses	<ul style="list-style-type: none"> <li>• <b>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.</b></li> <li>• <b>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.</b></li> </ul>
Curcumin	All doses	<ul style="list-style-type: none"> <li>• <b>Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you are taking blood thinners.</b></li> <li>• <b>Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you have a biliary disorder.</b></li> </ul>
Fish oil and willow bark combined	All doses	<b>Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you are having a surgery.</b>
Manganese	More than 5 mg	<b>Ask a health care practitioner/health care provider/health care professional/doctor/physician before if you have a liver disorder.</b>
Turmeric	All doses	<b>Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you have a biliary disorder.</b>
Vitamin K <sub>1</sub> and/or K <sub>2</sub>	All doses	<b>Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you are taking blood thinners.</b>
Willow bark	All doses	<ul style="list-style-type: none"> <li>• <b>Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you have asthma or peptic ulcer disease.</b></li> <li>• <b>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).</b></li> </ul>

<sup>1</sup>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 Fruhmam 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):

  - i. Source animal is fit for human consumption;
  - ii. Source material can be traced back to the herd or animal;
  - iii. Avoidance of cross-contamination with high-infectivity tissues is ensured during sourcing;
  - iv. 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*
  - i. 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  $2 \times PV + AV$ ).
  - ii. 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
- iii. 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*
    - i. Details of the manufacturing of the enzyme at the raw material stage should include fermentation medium, and the isolation process of the medicinal ingredient.
    - ii. 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.
    - iii. 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*
    - i. 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.
    - ii. Information regarding Method of preparation must be provided upon request
    - iii. 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.
    - iv. 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*
    - i. For the purpose of this monograph, hydrolyzed collagen has no jelling power and is soluble in cold water (Schrieber and Gareis 2007; Moskowitz 2000).
    - ii. 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.

<b>Product Facts</b>	
<b>Medicinal ingredients</b> in each capsule	
Curcumin ( <i>Curcuma longa</i> – rhizome)	XX mg
Hydrolyzed collagen (Porcine – bone)	XX mg
Calcium	XX mg
<b>Uses</b>	
<ul style="list-style-type: none"> <li>• Help relieve joint pain and inflammation.</li> <li>• Helps to reduce joint pain associated with osteoarthritis.</li> <li>• Helps in the development and maintenance of bones.</li> </ul>	
<b>Warnings</b>	
<b>If applicable<sup>1</sup>:</b>	
<b>Allergens: food allergen, gluten (gluten source), sulphites</b>	
<b>Contains aspartame</b>	
<b>Ask a health care practitioner before use if</b> • you are pregnant or breastfeeding • you are taking blood thinners • you have a biliary disorder.	
<b>When using this product</b> you may experience gastrointestinal discomfort.	
<b>Ask a health care practitioner if</b> symptoms persist or worsen.	
<b>Directions</b>	
Adults 18 years and older: • Take X capsule(s), X time(s) a day • Take with food, a few hours before or after taking other medications or natural health products • Use for at least 5 months to see beneficial effects <sup>2</sup> .	
<b>Other information</b>	
(Add storage information)	
<b>Non-medicinal ingredients</b>	
List all NMIs	
<b>Questions?</b> (Call) 1-XXX-XXX-XXXX	

<sup>1</sup> This section can be removed from the table if the product contains no allergen or aspartame.

<sup>2</sup> The qualifier ‘For joint pain associated with osteoarthritis:’ may be included on the label to inform consumers.

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