Caffeine

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CAFFEINE (PDF Version - 130 KB) This monograph is intended to serve as a guide to industry for the preparation of Product Licence Applications (PLAs) and labels for natural health product market authorization. It is not intended to be a comprehensive review of the medicinal ingredient. Notes Text in parentheses is additional optional information which can be included on the 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 on the label. This monograph only supports caffeine as a pure chemical substance and does not support any extract preparations. Uses or Purposes Restrictions when this monograph is combined with other monographs (Class II and III applications): Products containing caffeine from any source (synthetic, isolated or a component of plant material) must not: indicate any uses or purposes related to healthy blood pressure or cardiovascular health at any dose of caffeine except if supported by a monograph for a specific caffeine-containing medicinal ingredient such as green coffee bean extract. indicate any uses or purposes related to nervine/sedative/relaxation, nor contain a sedative at therapeutic dose, at any dose of caffeine. indicate any uses or purposes related to the maintenance/support of good/general health at a daily dose of 40 mg or more total caffeine from all sources. Products providing a total amount of caffeine per day that meets the minimum therapeutic dose (100 mg/day) must indicate a use or purpose associated with caffeine. Products providing more than 400 mg of total caffeine per day cannot make any claims other than the ones listed on this monograph (Class I and II applications), unless additional evidence is provided to support another use specific to caffeine (Class III applications). Date April 25, 2025 Proper name(s), Common name(s), Source information Table 1. Proper name(s), Common name(s), Source information Proper name(s) Common name(s) Source information Source ingredient(s) Source material(s) 1 Part(s) 1,3,7-Trimethylxanthine 3,7-Dihydro-1,3,7-trimethyl-1H-purine-2,6-dione Caffeine Caffeine 2 Caffeine citrate 2 N/A N/A N/A Camellia sinensis Leaf N/A Coffea arabica Coffea canephora Seed N/A Cola acuminata Seed N/A Ilex guayusa Ilex paraguariensis Leaf N/A Paullinia cupana Seed N/A Theobroma cacao Seed References: Proper names: USP-NF 2023; Common name: USP-NF 2023; IOM 2003; Source information: Ashihara and Suzuki 2004; Zajac et al. 2003; Duke 2001; Gennaro 2000. 1 Source materials listed in Table 1 are only allowed if caffeine is isolated and purified from these source materials and has a molecular structure which is identical to that which it had prior to its isolation. This monograph only supports caffeine as a pure chemical substance and does not support any extract preparations. 2 Synthetic. Route of Administration Oral (Higdon and Frei 2006) Dosage Form(s) This monograph does not apply to caffeine added to food. Caffeine is regulated as a food additive when it is added to foods, including beverages, chewing gum, and bars. Questions about using caffeine in food can be sent to the Food Directorate (food-aliment@hc-sc.gc.ca). 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. For caffeinated energy shots, select "liquid (shot)". Note: A caffeinated energy shot is defined as a pre-packaged, ready-to-consume product with a volume of 90 mL or less and meant to be consumed at once (HC 2023, 2013). Use(s) or Purpose(s) All oral dosage forms Helps (temporarily) to support/promote alertness and wakefulness, and to enhance cognitive performance (Christopher et al. 2005; Kamimori et al. 2000; Zwyghuizen-Doorenbos et al. 1990). Helps (temporarily) to support/promote mental sharpness/alertness (Christopher et al. 2005; Kamimori et al. 2000; Zwyghuizen-Doorenbos et al. 1990). Helps (temporarily) to relieve/reduce fatigue, to promote endurance, and to enhance motor performance (Philip et al. 2006; Doherty and Smith 2005; Smith et al. 2005). Helps (temporarily) to enhance (physical) energy (Philip et al. 2006; Doherty and Smith 2005; Smith et al. 2005). Helps (temporarily) to relieve/reduce fatigue/tiredness (Philip et al. 2006; Doherty and Smith 2005; Smith et al. 2005). Oral dosage forms except energy shots (liquid (shot)) Used (temporarily) as a mild diuretic (Shirley et al. 2002; Neuhäuser-Berthold et al. 1997). Notes: The above uses can be combined on the product label (e.g. Helps temporarily to support mental alertness and reduce fatigue). The terms 'Helps' or 'Helps to' can be used interchangeably on the label. Dose(s) Subpopulation(s) Adults 18 years and older Quantity(ies) Mild diuretic 100 - 200 milligrams of caffeine, per single dose; Not to exceed 800 milligrams, per day (Shirley et al. 2002; IOM 2001; Neuhäuser-Berthold et al. 1997). Other uses 100 - 200 milligrams of caffeine, per single dose; Not to exceed 1000 milligrams, per day (FDA 2023; Sawynok 1995;

Greden 1974). Energy shots (liquid (shot)) 100 - 200 milligrams caffeine, per single dose (= per shot); Not to exceed 400 milligrams, per day (HC 2023). Direction(s) for use Products providing more than 200 mg caffeine, per day (i.e. to be taken in divided doses or, for shots, if the recommended daily dose includes more than one single dose (= shot) providing more than 100 mg caffeine each) Wait 3 to 4 hours between each dose. Energy shots (liquid (shot)) Do not mix with alcohol (HC 2013). Duration(s) of Use Mild diuretic or products providing more than 400 mg of caffeine, per day For occasional use only (Higdon and Frei 2006; Juliano and Griffiths 2004; Evans and Griffiths 1999) Risk Information Caution(s) and warning(s) Products providing 100 mg to 400 mg caffeine, per day 1 Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you have high blood pressure or glaucoma (Cornelis and El-Sohemy 2007, Chandrasekaran et al. 2005, Noordzij et al. 2005, Avisar et al. 2002, Arya et al. 2000, Jee et al. 1999, Creighton and Stanton 1990). 1 Note: This statement is also required at subtherapeutic quantities for products providing 40 mg or more caffeine per day from all sources for Class II and III applications. Products providing more than 300 mg caffeine, per day Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you are pregnant, breastfeeding, or attempting to conceive (Nawrot et al. 2003). Products providing 400 mg or more caffeine, per day When using this product avoid taking other health products, foods or beverages that contain caffeine and/or increase blood pressure (FDA 2023; Bui et al. 2006; Bouchard et al. 2005; Haller et al. 2005; NIH 2004; Berardi et al. 2002; Vahedi et al. 2000; Zimmerman 1992). Contraindication(s) Products providing more than 400 mg caffeine per day Do not use if you have high blood pressure or glaucoma (Cornelis and El-Sohemy 2007, Chandrasekaran et al. 2005, Noordzij et al. 2005, Avisar et al. 2002, Arya et al. 2000, Jee et al. 1999, Creighton and Stanton 1990). Known adverse reaction(s) All products Stop use and ask a health care practitioner/health care provider/health care professional/doctor/physician if hypersensitivity/allergy occurs (Infante et al. 2003; Hinrichs et al. 2002). Products providing 200 mg or more caffeine, per day Stop use and ask a health care practitioner/health care provider/health care professional/doctor/physician if symptoms such as chest pain and irregular heartbeat occur (Higgins and Babu 2013). Products providing more than 400 mg caffeine, per day Stop use and ask a health care practitioner/health care provider/health care professional/doctor/physician if nervousness, anxiety, insomnia, tremor and/or headache occur (IOM 2001, Zhang 2001, Sawynok 1995). All products except those making a diuretic claim 1 When using this product diuretic effect may occur. 1 Note: This statement is also required at subtherapeutic quantities for products providing 40 mg or more caffeine per day from all sources for Class II and III applications. Non-medicinal ingredients Must be chosen from the current Natural Health Products Ingredients Database (NHPID) and must meet the limitations outlined in the database. Storage conditions Must be established in accordance with the requirements described in the Natural Health Products Regulations . 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. EXAMPLE OF PRODUCT FACTS: Consult the Guidance Document, Labelling of Natural Health Products for more details. 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MEDICINAL INGREDIENT(S)

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

DOSAGE FORM(S)

For caffeinated energy shots, select "liquid (shot)". Note:A caffeinated energy shot is defined as a pre-packaged, ready-to-consume product with a volume of 90 mL or less and meant to be consumed at once (HC 2023, 2013).

RISK INFORMATION

Caution(s) and warning(s) Products providing 100 mg to 400 mg caffeine, per day1 Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you have high blood pressure or glaucoma (Cornelis and El-Sohemy 2007, Chandrasekaran et al. 2005, Noordzij et al. 2005, Avisar et al. 2002, Arya et al. 2000, Jee et al. 1999, Creighton and Stanton 1990). 1Note:This statement is also required at subtherapeutic quantities for products providing 40 mg or more caffeine per day from all sources for Class II and III applications. Products providing more than 300 mg caffeine, per day Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you are pregnant, breastfeeding, or attempting to conceive (Nawrot et al. 2003). Products providing 400 mg or more caffeine, per day When using this product avoid taking other health products, foods or beverages that contain caffeine and/or increase blood pressure (FDA 2023; Bui et al. 2006; Bouchard et al. 2005; Haller et al. 2005; NIH 2004; Berardi et al. 2002; Vahedi et al. 2000; Zimmerman 1992). Contraindication(s) Products providing more than 400 mg caffeine per day Do not use if you have high blood pressure or glaucoma (Cornelis and El-Sohemy 2007, Chandrasekaran et al. 2005, Noordzij et al. 2005, Avisar et al. 2002, Arya et al. 2000, Jee et al. 1999, Creighton and Stanton 1990). Known adverse reaction(s) All products Stop use and ask a health care practitioner/health care provider/health care professional/doctor/physician if hypersensitivity/allergy occurs (Infante et al. 2003; Hinrichs et al. 2002). Products providing 200 mg or more caffeine, per day Stop use and ask a health care practitioner/health care provider/health care professional/doctor/physician if symptoms such as chest pain and irregular heartbeat occur (Higgins and Babu 2013). Products providing more than 400 mg caffeine, per day Stop use and ask a health care practitioner/health care provider/health care professional/doctor/physician if nervousness, anxiety, insomnia, tremor and/or headache occur (IOM 2001, Zhang 2001, Sawynok 1995). All products except those making a diuretic claim1 When using this product diuretic effect may occur. 1Note:This statement is also required at subtherapeutic quantities for products providing 40 mg or more caffeine per day from all sources for Class II and III applications.

NON-MEDICINAL INGREDIENTS

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

STORAGE CONDITION(S)

Must be established in accordance with the requirements described in theNatural Health Products Regulations.

SPECIFICATIONS

The finished product specifications must be established in accordance with the requirements described in the Natural and Non-prescription Health Products Directorate (NNHPD) Quality of Natural Health Products Guide.The medicinal ingredient must comply with the requirements outlined in the NHPID.

REFERENCES

1Source materials listed in Table 1 are only allowed if caffeine is isolated and purified from these source materials and has a molecular structure which is identical to that which it had prior to its isolation. This

monograph only supports caffeine as a pure chemical substance and does not support any extract preparations.2Synthetic.

Proper name(s)	Common name(s)	Source information		
Source ingredient(s)	Source material(s)1	Part(s)		
1,3,7-Trimethylxanthine3,7-Dihydro-1,3,7-trimethyl-1H-purine-2,6-dione	Caffeine1	Caffeine2Caffeine citrate2	N/A	N/A
N/A	Camellia sinensis	Leaf		
N/A	Coffea arabicaCoffea canephora	Seed		
N/A	Cola acuminata	Seed		
N/A	Ilex guayusaIlex paraguariensis	Leaf		
N/A	Paullinia cupana	Seed		
N/A	Theobroma cacao	Seed		