Melatonin - Sublingual

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MELATONIN - Sublingual 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 - 36 K) For Melatonin products with an oral route of administration, please use the Melatonin-oral monograph. This monograph is intended to serve as a guide to industry for the preparation of Product Licence Applications (PLA) and labels for natural health product market authorization. It is not intended to be a comprehensive review of the medicinal ingredient. Notes Text in parentheses is additional optional information which can be included on the PLA and product label at the applicant's discretion. The solidus (/) indicates that the terms and/or statements are synonymous. Either term or statement may be selected by the applicant. Rules for the application of this monograph when combined with other monographs: Products containing melatonin must not indicate any uses or purposes related to the maintenance/support of good/general health. Products providing a quantity of melatonin that meets the minimum therapeutic dose must indicate a use or purpose associated with melatonin. Date April 26, 2024 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) Preparation(s) N-[2-(5-Methoxy-1H-indol-3-yl)ethyl]acetamide N-Acetyl-5-methoxytryptamine Melatonin Pineal hormone Melatonin Synthetic References: Proper names: RSC 2023; Buscemi et al. 2004; Common names: RSC 2023, Buscemi et al. 2004; Source information: RSC 2023. Route of administration Sublingual 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 sublingual use are indicated in the dosage form drop-down list of the web-based Product Licence Application form for Compendial applications. Note that this list does not include prolonged-release, extended-release or delayed-release dosage forms. Use(s) or Purpose(s) (Used as a) sleep aid (to help promote sleep) (Costello et al. 2014; Wyatt et al. 2006; Brzezinski et al. 2005). Helps (to) increase the total sleep time (aspect of sleep quality) in people suffering from sleep restriction or altered sleep schedule (e.g. shift-work and jet lag) (Zhdanova et al. 2001; Brusco et al. 1999; Sanders et al. 1999; Skene et al. 1999; Garfinkel et al. 1995;Sack et al. 1991). Helps (to) prevent and/or reduce the effects of jet lag/minimize jet lag (e.g. daytime fatigue, sleep disturbance) (for people/if travelling by plane easterly across two or more time zones/flying east over two or more time zones) (Brown et al. 2009; Herxheimer and Petrie 2002; Suhner et al. 1998a; Petrie et al. 1993; Claustrat et al. 1992; Petrie et al. 1989). Helps (to) speed up/reduce the time it takes to fall asleep (sleep onset latency aspect of sleep quality) in people who fall asleep slowly/with delayed sleep phase disorder (van Geijlswijk et al. 2010). Helps (to) re-set the body's sleep-wake cycle (aspect of the circadian rhythm) (van Geijlswijk et al. 2010; Kunz et al. 2004; Sack et al. 2000). Note The above claims can be combined on the product label (e.g. Helps re-set the body's sleep-wake cycle (aspect of the circadian rhythm) and increase the total sleep time (aspect of sleep quality) in people suffering from sleep restriction or altered sleep schedule). Dose(s) Subpopulation(s) Adults 18 years and older Quantity(ies) All uses except jet lag 0.1 - 10 milligrams of melatonin, per day (Brzezinski et al. 2005; IOM 2004; Kayumov et al. 2001; Koda-Kimble 2001; Zhdanova et al. 2001; Brusco et al. 1999; Jean-Louis et al. 1999; Matsumoto 1999; Jorgensen and Witting 1998; Sack et al. 1997; Attenburrow et al. 1996; Zhdanova et al. 1995; Garfinkel 1995; Tzischinsky and Lavie 1994; Dollins et al. 1994; Dahlitz et al. 1991; James et al. 1987). Jet lag 0.5 - 10 milligrams of melatonin, per day (Brown et al. 2009; Herxheimer and Petrie 2002; Suhner et al. 1998a). Direction(s) for use All uses Take as needed, 10 to 30 minutes before bedtime. Place under the tongue until it is dissolved (Abdellah et al. 2023; Bartoli et al. 2012; Naguib and Samarkandi 1999; Jorgensen and Witting 1998). Duration(s) of use No statement required. Risk information Caution(s) and warning(s) Ask a health care practitioner/health care provider/health care professional/doctor/ physician before use if you are taking medications for seizure, blood pressure, to suppress the immune system, to affect mental state or increase sedation, steroids or blood thinners (Wirtz et al. 2008; IOM 2004; Herxheimer and Petrie 2002; Lusardi et al. 2000; Maestroni 1993). Ask a health care practitioner/health care provider/health care professional/doctor/ physician before use if you have a cardiovascular, immune, liver or kidney disease, seizure disorder, asthma or diabetes (Peschke and Mühlbauer 2010; Carrillo-Vico et al. 2005; IOM 2004; der Marderosian and Beuttlers 2003; Sutherland et al. 2003; Calvo et

al. 2002; Herxheimer and Petrie 2002; Sutherland et al. 2002; Cagnacci et al. 2001a; Arangino et al. 1999; Sheldon 1998; Maestroni 1993). When using this product avoid taking with alcohol or products that cause drowsiness (Herxheimer and Petrie 2002; Holliman and Chyka 1997). When using this product avoid driving or using machinery for 5 hours (Avery et al. 1998; Suhner et al. 1998b). Ask a health care practitioner/health care provider/health care professional/doctor/physician if sleeplessness persists for more than 4 weeks (chronic insomnia) (Buscemi et al. 2004; IOM 2004; Dipiro et al. 2002). Contraindication(s) Do not use if you are pregnant or breastfeeding (IOM 2004). Known adverse reaction(s) Stop use if allergy occurs or if you experience headache, confusion, or nausea (Herxheimer and Petrie 2002). 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 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. References cited Abdellah SA, Raverot V, Gal C, Guinobert I, Bardo V, Blondeau C, Claustrat B. Bioavailability of melatonin after administration of an oral prolonged-release tablet and an immediate-release sublingual spray in healthy male volunteers. Drugs in R&D 2023;23:257-265. Arangino S, Cagnacci A, Angiolucci M, Vacca AMB, Longu G, Volpe A, Melis GB. Effects of melatonin on vascular reactivity, catecholamine levels, and blood pressure in healthy men. 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Lissoni P, Barni S, Mandala M, Ardizzoia A, Paolorossi F, Vaghi M, Longarini R, Malugani F, Lusardi P, Piazza E, Fogari R. Cardiovascular effects of melatonin in hypertensive patients well controlled by nifedipine: a 24-hour study. British Journal of Clinical Pharmacology 2000;49:423427. Lissoni P, Barni S, Mandalà M, Ardizzoia A, Paolorossi F, Vaghi M, Longarini R, Malugani F, Tancini G. Decreased toxicity and increased efficacy of cancer chemotherapy using the pineal hormone melatonin in metastatic solid tumour patients with poor clinical status. European Journal of Cancer 1999;35(12):1688-1692. Mundey K, Benloucif S, Harsanyi K, Dubocovich ML, Zee PC. Phase-dependent treatment of delayed sleep phase syndrome with melatonin. Sleep 2005;28(10):1271-1278. Neri B, De Leonardis V, Gemelli MT, Di Loro F, Mottola A. Ponchietti R, Raugei A, Cini G. Melatonin as biological response modifier in cancer patients. Anticancer Research 1998;18:1329-1332. Ninomiya T, Iwatani N, Tomoda A, Miike T. 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Neuro-Psychopharmacology & Biological Psychiatry 2007;31:1-11. Pires MLN, Benedito-Silva AA, Pinto L, Souza L, Vismari L, Calil HM. Acute effects of low doses of melatonin on the sleep of young healthy subjects. Journal of Pineal Research 2001;31:326-332. Pizzorno Jr JEP, Murray MT. Textbook of Natural Medicine. 3rd edition, Volume 1. St-Louis (MI): Churchill Livingstone Elsevier; 2006. Reid KJ, Zee PC. Circadian rhythm sleep disorders. Handbook of Clinical Neurology 2011;99:963-977. Reiter RJ, Calvo JR, Karbownik M, Qi W, Tan DX. Melatonin and its relation to the immune system and inflammation. Annals of the New York Academy of Sciences 2006;917:376-386. Sletten TL, Vincenzi S, Redman JR, Lockley SW, Rajaratnam SMW. Timing of sleep and its relationship with the endogenous melatonin rhythm. Frontiers in neurology 2010;1:137. Suhner A, Schlagenhauf P, Johnson R, Tschopp A, Steffen R. Comparative study to determine the optimal melatonin dosage form for the alleviation of jet lag. Chronobiology International 1998;15(6):655-656. Tancini G. Decreased toxicity and increased efficacy of cancer chemotherapy using the pineal hormone melatonin in metastatic solid tumor patients with poor clinical status. European Journal of Cancer 1999;35:1688-1692. Vijayalaxmi CRT Jr, Reiter RJ, Herman TS. Melatonin: from basic research to cancer treatment clinics. Journal of Clinical Oncology 2002;20:2575-2601. Voordouw BCG, Euser R, Verdonk RER, Alberda BT, De Jong FH, Drogendijk AC, Fauser BCJM, Cohen M. Melatonin and melatonin-progestin combinations alter pituitary-ovarian function in women and can inhibit ovulation. Journal of Clinical Endocrinology and Metabolism 1992;74(1):108-117. Zawilska JB, Nowak JZ. Melatonin: from biochemistry to therapeutic applications. Polish Journal of Pharmacology 1999;51:3-23. Zee PC. Shedding light on the effectiveness of melatonin for circadian rhythm sleep disorders. Sleep 2010;33(12):1581-1582 Zee PC. Shedding light on the effectiveness of melatonin for circadian rhythm sleep disorders. Commentary on van Geijlswijk et al. The use of exogenous melatonin in delayed sleep phase disorder: a meta-analysis. Sleep 2010;33:1605-1614. Zee PC, Goldstein CA. Treatment of shift work disorder and jet lag. Current Treatment Options in Neurology 2010;12(5):396-411. Zhdanova IV, Wurtman RJ, Morabito C, Piotrovska VR, Lynch HJ. Effects of low oral doses of melatonin, given 2-4 hours before habitual bedtime, on sleep in normal young humans. Sleep. 1996 Jul 1;19(5):423-31. Zhdanova IV and RJ Wurtman 1997. Efficacy of melatonin as a sleep-promoting agent. Journal of Biological Rhythms 12(6):644-650. Report a problem on this page Date modified: 2019-03-01

MEDICINAL INGREDIENT(S)

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 theNatural Health Products Regulations.

DOSAGE FORM(S)

Acceptable dosage forms for sublingual use are indicated in the dosage form drop-down list of the web-based Product Licence Application form for Compendial applications. Note that this list does not include prolonged-release, extended-release or delayed-release dosage forms.

USE(S) OR PURPOSE(S)

Products providing a quantity of melatonin that meets the minimum therapeutic dose must indicate a use or purpose associated with melatonin.

DOSE(S)

Zhdanova IV, Wurtman RJ, Regan MM, Taylor JA, Shi JP, Leclair OU. Melatonin treatment for age-related insomnia. Journal of Clinical Endocrinology and Metabolism 2001;86(10):4727-4730.

RISK INFORMATION

Caution(s) and warning(s) Ask a health care practitioner/health care provider/health care professional/doctor/ physician before use if you are taking medications for seizure, blood pressure, to suppress the immune system, to affect mental state or increase sedation, steroids or blood thinners (Wirtz et al. 2008; IOM 2004; Herxheimer and Petrie 2002; Lusardi et al. 2000; Maestroni 1993).Ask a health care practitioner/health care provider/health care professional/doctor/ physician before use if you have a cardiovascular, immune, liver or kidney disease, seizure disorder, asthma or diabetes (Peschke and Mühlbauer 2010; Carrillo-Vico et al. 2005; IOM 2004; der Marderosian and Beuttlers 2003; Sutherland et al. 2003; Calvo et al. 2002; Herxheimer and Petrie 2002; Sutherland et al. 2002; Cagnacci et al. 2001a; Arangino et al. 1999; Sheldon 1998; Maestroni 1993).When using this product avoid taking with alcohol or products that cause drowsiness (Herxheimer and Petrie 2002; Holliman and Chyka 1997).When using this product avoid driving or using machinery for 5 hours (Avery et al. 1998; Suhner et al. 1998b).Ask a health care practitioner/health care provider/health care professional/doctor/physician if sleeplessness persists for more than 4 weeks (chronic insomnia) (Buscemi et al. 2004; IOM 2004; Dipiro et al. 2002). Contraindication(s) Do not use if you are pregnant or breastfeeding (IOM 2004). Known adverse reaction(s) Stop use if allergy occurs or if you experience headache, confusion, or nausea (Herxheimer and Petrie 2002).

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 theNatural Health Products Regulations.

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) QualityThe medicinal ingredient must comply with the requirements outlined in the NHPID. EXAMPLE OF PRODUCT FACTS:

REFERENCES

Route of administration Sublingual

Proper name(s)	Common name(s)	Source Information	
Source ingredient(s)	Preparation(s)		
N-[2-(5-Methoxy-1H-indol-3-yl)ethyl]acetamide	N-Acetyl-5-methoxytryptamine	Melatonin	Synthetic