MELATONIN - ORAL

For Melatonin products with a sublingual route of administration, please use the Melatonin-sublingual monograph.

This monograph is intended to serve as a guide to industry for the preparation of Product Licence Applications (PLAs) and labels for natural health product market authorization. It is not intended to be a comprehensive review of the medicinal ingredient.

Notes
› Text in parentheses is additional optional information which can be included on the PLA and product label at the applicant’s discretion.
› The solidus (/) indicates that the terms and/or the statements are synonymous. Either term or statement may be selected by the applicant.

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Proper name(s)
› N-[2-(5-Methoxy-1H-indol-3-yl)ethyl]acetamide (Martindale 2012; Merck 2012)
› N-Acetyl-5-methoxytryptamine (Martindale 2012; Merck 2012)

Common name(s)
Melatonin (Merck 2012; Buscemi et al. 2004)

Source material(s)
Melatonin (Merck 2012)

Route(s) of administration
oral (Buscemi et al. 2004)

Dosage form(s)
› The acceptable pharmaceutical dosage forms include, but are not limited to capsules, chewables (e.g. gummies, tablets), liquids, powders, strips or tablets.
› This monograph is not intended to include foods or food-like dosage forms such as bars, chewing gums or beverages.
Use(s) or Purpose(s) Statement(s) to the effect of

- 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, jet lag) (Zhdanova et al. 2001; Shamir et al. 2000; Skene et al. 1999; Brusco et al. 1999; Sanders et al. 1999; Dolberg et al. 1998; Garfinkel et al. 1995; Haimov et al. 1995; Sack et al. 1991).

- Helps to prevent and/or reduce the effects of jet lag (e.g. daytime fatigue, sleep disturbance) for people travelling by plane easterly across two or more time zones (Brown et al. 2009; Herxheimer and Petrie 2009; Suhner et al. 1998a; Petrie et al. 1993; Claustrat et al. 1992; Petrie et al. 1989).

- Helps to reduce the time it takes to fall asleep (sleep onset latency aspect of sleep quality) in people 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).

Dose(s) Statement(s) to the effect of

Subpopulation(s)

adults (≥ 19 years) (IOM 2004)

Quantity(ies)

All uses except jet lag:

Jet lag:
0.5-10 mg, per day (Brown et al. 2009; Herxheimer and Petrie 2009; Suhner et al. 1998a)

Directions for use

All uses:
Do not drive or use machinery for 5 hours after taking melatonin (Avery et al. 1998; Suhner et al. 1998b).

All uses except jet lag:
Take once a day, at or before bedtime (Murray et al. 2006; Kayumov et al. 2001; Zhdanoya et al.
Jet lag:
Take once a day at bedtime after darkness has fallen, while travelling, and at destination until adaptation to the new daily pattern (Brown et al. 2009; Herxheimer and Petrie 2009).

See Appendix 1 for examples of dosage preparations, frequencies of use and directions for use, according to cited references. The purpose of Appendix 1 is to provide guidance to industry.

**Duration of use**

Statement(s) to the effect of

All uses except jet lag:
For use beyond 4 weeks, consult a health care practitioner (Buscemi et al. 2004; IOM 2004).

Jet lag:
For occasional short-term use (Herxheimer and Petrie 2009).

**Risk information**

Statement(s) to the effect of

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

All uses except jet lag:
If symptoms persist for more than 4 weeks (chronic insomnia), consult your health care practitioner (Buscemi et al. 2004; IOM 2004; Dipiro et al. 2002).

All uses:
- Consumption with alcohol, other medications or natural health products with sedative properties is not recommended (Herxheimer and Petrie 2009; Holliman and Chyka 1997).
- If you have one of the following conditions, consult a health care practitioner prior to use:
  - asthma (Sutherland et al. 2003; Sutherland et al. 2002)
  - cardiovascular disease (IOM 2004; Scheer et al. 2004; Cagnacci et al. 2001b; GAO 2001; Lusardi et al. 2000; Arangino et al. 1999)
  - chronic kidney disease (IOM 2004)
  - depression (der Marderosian and Beuttlers 2009; IOM 2004; GAO 2001; Carman et al. 1976)
  - diabetes or hypoglycaemia (Peschke and Mühlbauer 2010; Cagnacci et al. 2001a; GAO 2001).
  - hormonal disorder (IOM 2004; Cagnacci et al. 2001b; GAO 2011).
  - immune system disease (der Marderosian and Beutters 2009; Carrillo-Vico et al. 2005; IOM 2004; Calvo et al. 2002; GAO 2001; Maestroni 1993)
  - liver disease (IOM 2004)
  - migraines (IOM 2004)
  - seizure disorders (Herxheimer and Petrie 2009; IOM 2004; Sheldon 1998)
If you are taking one of the following medications, consult a health care practitioner prior to use:

- anticoagulant (Herxheimer and Petrie 2009; Wirtz et al. 2008)
- anticonvulsant (IOM 2004)
- blood pressure medications (Herxheimer and Petrie 2009; Scheer et al. 2004; Lusardi et al. 2000)
- immunosuppressive medications (Lissoni et al. 1999; Maestroni 1993)
- sedative, hypnotic or psychotropic medications (IOM 2004; Holliman and Chyka 1997)
- steroids (GAO 2001)

Contraindication(s)

If you are pregnant or breastfeeding, do not use this product (IOM 2004).

Known adverse reaction(s)

- Mild gastrointestinal symptoms (nausea, vomiting, or cramping) have been known to occur in which case, discontinue use (Herxheimer and Petrie 2009).
- Rare allergic reactions have been known to occur in which case, discontinue use (Herxheimer and Petrie 2009).

Non-medicinal ingredients

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

Storage conditions

Statement(s) to the effect of

No statement required.

Specifications

- The finished product specifications must be established in accordance with the requirements described in the NHPD *Quality of Natural Health Products Guide*.
- The medicinal ingredient must comply with the requirements outlined in the *Natural Health Products Ingredients Database* (NHPID). In addition, the medicinal ingredient may comply with the specifications outlined in the Melatonin monograph of the British Pharmacopoeia.

References cited


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Zee PC. Shedding light on the effectiveness of melatonin for circadian rhythm sleep disorders. Sleep 2010;33(12):1581-1582


Appendix 1: Examples of dosage preparations, frequencies of use and directions for use

All uses except jet lag:


Direction for use

All uses:

- Take once a day at or before bedtime (Murray et al. 2006; Kayumov et al. 2001; Zhdanova et al. 2001).
- Do not drive or use machinery for 5 hours after taking melatonin (Avery et al. 1998; Suhner et al. 1998b).

Jet lag:

0.5-10 mg, per day (Brown et al. 2009; Herxheimer and Petrie 2009; Suhner et al. 1998a)

Direction for use

- Take once a day at bedtime after darkness has fallen, while travelling and at the destination until adaptation to the new daily pattern (Herxheimer and Petrie 2009).
- Do not drive or use machinery for 5 hours after taking melatonin (Avery et al. 1998; Suhner et al. 1998b).