MELATONIN - SUBLINGUAL

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 (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 are synonyms or that the statements are synonymous. Either term or statement may be selected by the applicant.

**Date**
May 14, 2013

**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**
sublingual (Buscemi et al. 2004)

**Dosage form(s)**
Those pharmaceutical dosage forms suited to sublingual administration.
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. 2001).
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 2001)
  - immune system disease (der Marderosian and Beutters 2009; Carrillo-Vico et al. 2005; IOM 2004; Calvo et al. 2002; GAO 2001; Maestrioni 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 medications (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**

Andrade C, Srihari BS, Reddy KP, Chandramma L. Melatonin in medically ill patients with


Suhner A, Schlagenauf P, Johnson R, Tschopp A, Steffen R. Comparative study to determine the optimal melatonin dosage form for the alleviation of jet lag. Chronobiology International


Sutherland ER, Martin RJ, Ellison MC, Kraft M. Immunomodulatory effects of melatonin in asthma. American Journal of respiratory and critical care medicine 2002;166:1055-1061.

Sutherland ER, Ellison MC, Kraft M, Martin RJ. Elevated serum melatonin is associated with the nocturnal worsening of asthma. Journal of Allergy and Clinical Immunology 2003;112(3):513-517.


References reviewed


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).