

Scientific Name: Melatonin Other Names: MEL, MLT, N-acetyl-5-methoxytryptamine

## Who is this for?

### Uses

In the United States, supplemental melatonin is mostly for the short-term relief of sleep disturbances -- especially jet lag. Results from several controlled studies show that melatonin taken before, during, and after long-distance travel may lessen or prevent sleep disruption. In addition, melatonin may be associated with less daytime drowsiness than prescription sleeping pills. Although it is not approved as a regular prescription drug, melatonin does have a special orphan drug designation from the U.S. Food and Drug Administration (FDA). An orphan drug has extremely limited uses, such as for the treatment of a rare disease. Melatonin is prescribed as an orphan drug for blind individuals who suffer from sleep disturbances because their daily rhythm is distorted by the lack of light-and-dark effects that help to regulate sleeping cycles in sighted individuals. Melatonin is also available as a dietary supplement without a prescription.

For about 15 years, melatonin supplementation has been studied extensively -- mainly in Europe -- for treating cancer. In studies conducted in laboratory animals or human cancer cell cultures, melatonin appeared to keep some types of tumors from spreading as rapidly as untreated tumors. Several studies have also been conducted in humans with advanced tumors. In general, supplemental melatonin appeared to help prevent or delay the spread of tumors for many of these individuals, but much more study is needed to confirm this finding. In animal studies, certain cancers, such as leukemia, may have been worsened by supplemental melatonin. For the treatment of cancer, melatonin is most often injected into muscle tissue, but injectable melatonin is not available for use in the United States.

Melatonin may have additional positive effects. In recent studies, melatonin has shown some value for easing the withdrawal from benzodiazepine drugs for individuals who have become dependent on those drugs. Other studies show that melatonin supplements may also be useful in helping individuals who are trying to stop smoking. It has also shown some effectiveness in lowering blood pressure levels in several human studies and reducing blood cholesterol levels in limited animal studies. Other recent research indicates that melatonin is concentrated in certain cells (which may also produce natural melatonin) in the stomach and intestines, where it may help prevent damage caused when non-steroidal anti-inflammatory drugs are taken on a long-term basis. In one study, supplemental melatonin may have prevented cluster headaches in individuals susceptible to having that type of headache. Because very high oral doses of melatonin are believed to decrease fertility for women, some inconclusive research has been done into its use as a contraceptive. In other studies, a liquid form of melatonin was applied to the skin to serve as protection from ultraviolet light and sunburn. In laboratory animals, melatonin may help to prevent the development of Type 1 diabetes. While clinical research continues for the use of melatonin in these and many other conditions, no definitive results prove that melatonin is effective for any of them.

## When should I be careful taking it?

Although melatonin may be given in hospitals to premature infants at risk of developing lung problems, the use of supplemental melatonin for children is not recommended.

Because naturally-produced melatonin has a role in the development of sexual organs, melatonin supplementation could interfere with normal sexual development.

In high doses, melatonin may hamper the ability to get pregnant by decreasing female fertility. Women who are trying to conceive should not take melatonin. Because it is not known how melatonin affects pregnant women or the fetus, melatonin should be avoided during pregnancy.

Melatonin is broken down in the liver, so individuals with known or suspected liver diseases should avoid taking it. If liver function is diminished, high levels of melatonin could build up in the blood, possibly leading to unwanted side effects.

Melatonin may promote both immune response and inflammation, making it inappropriate for individuals with autoimmune conditions. Various autoimmune conditions include:

- Crohn's disease
- Multiple Sclerosis
- Psoriasis
- Rheumatoid Arthritis
- Systemic Lupus Erythematosus
- Type 1 diabetes

### Precautions

Some reliable evidence suggests that melatonin supplementation can worsen symptoms for individuals with depression. People who have depression or bipolar disorder should use it only with the supervision of a health professional.

Melatonin can cause drowsiness, so individuals who operate heavy machinery or perform other tasks that require alertness should avoid its use.

Women who are breast-feeding should avoid taking melatonin because not enough is known about its potential effects on infants.

In animal studies, melatonin has decreased the activity of the thyroid gland. Although similar effects have not been seen in humans, individuals with thyroid conditions should consult a health professional before taking melatonin.

# What side effects should I watch for?

## Major Side Effects

Melatonin can affect the normal body production or the supplemental use of certain hormones. Blood levels of human growth hormone may be increased, while luteinizing hormone may be decreased. Other hormones may be affected, too. Laboratory tests for these hormones may be inaccurate if the tests are performed during the same time frame melatonin is taken. Be sure your doctor knows that you take melatonin.

## Less Severe Side Effects

Other side effects reported by individuals taking melatonin include:

- Abdominal cramps
- Confusion
- Daytime drowsiness
- Depression
- Dizziness
- Fatigue
- Headache

- Irritability
- Low blood pressure
- Nausea
- Vomiting

# What interactions should I watch for?

# Prescription Drugs

Studies have revealed that melatonin may interfere with the blood pressure-lowering effects of nifedipine GITS (Procardia XL). As a result, blood pressure was not controlled. Another medication used for blood pressure, verapamil (Calan, Isoptin, Verelan), reduced the effectiveness of melatonin when they were taken at the same time. Whether melatonin and other high blood pressure medicines interact is not known. If you take medicine for high blood pressure, talk to your doctor or pharmacist before you take melatonin.

Fluvoxamine (Luvox), an antidepressant, is known to increase natural melatonin production and it may also increase blood levels of melatonin if it is taken at the same time as melatonin supplements. If fluvoxamine and melatonin are taken together, the risk for side effects of melatonin may be increased. Other antidepressant medications may also interact with melatonin. If you take an antidepressant, do not take melatonin.

Because it can enhance immune system function, melatonin may interfere with the effects of drugs used to suppress the immune system after organ transplants or in other conditions. Taking melatonin is not recommended for patients who take drugs such as:

- azathioprine (Imuran)
- corticosteroids
- cyclosporine (Neoral, Sandimmune)
- daclizumab (Zenapak)
- mycophenolate (CellCept)
- sirolimus (Rapamune)
- tacrolimus (Prograf)

Melatonin opposes the action of natural corticosteroids and corticosteroid drugs, which are used for a wide range of inflammatory conditions including arthritis, asthma, cancer, eye conditions, and skin infections. When supplemental melatonin is taken at the same time as corticosteroids, the effects of the corticosteroid may be decreased. It is best not to take melatonin and corticosteroids at the same time. Commonly prescribed corticosteroids include:

- beclomethasone (Beconase, Beclovent, Vancenase, Vanceril)
- dexamethasone (Decadron)
- hydrocortisone
- methylprednisolone (Medrol)
- prednisolone
- prednisone (Deltasone, Orasone)
- triamcinolone (Azmacort, Nasacort)

When melatonin is used with prescription drugs that promote sleepiness, the effects of the drug may be exaggerated, resulting in sedation or mental impairment. Prescription drugs that may cause sleepiness include:

- Anticonvulsants such as carbamazepine (Tegretol), phenytoin (Dilantin), and valproic acid (Depakote)
- Barbiturates such as phenobarbital
- Benzodiazepines such as alprazolam and diazepam (Valium)
- Drugs for insomnia such as zaleplon (Sonata) and zolpidem (Ambien)

 Tricyclic antidepressants such as amitriptyline, amoxapine, doxepin and nortriptyline

In animal studies, melatonin has increased the anti-seizure effects of the anticonvulsant drugs, carbamazepine (Tegretol) and phenytoin (Dilantin).

## **Non-prescription Drugs**

The sleep-producing effects of over-the-counter products containing diphenhydramine can be enhanced by taking melatonin at the same time. Diphenhydramine is contained in many over-the-counter sleep aids as well as in some cough and cold products, therefore caution should be used when taking these medications with melatonin because excessive drowsiness may result.

# Herbal Products

Melatonin may cause excessive sedation if taken with sedating herbs such as:

- Catnip
- Hops
- Kava
- St. John's Wort
- Valerian

# Foods

In several small studies of humans, caffeine has been shown to reduce the amounts of melatonin that the body produces naturally and also to block supplemental melatonin.

No other interactions between melatonin and foods have been reported, but drinking alcohol at the same time as taking melatonin may result in increased drowsiness.

Some interactions between herbal products and medications can be more severe than others. The best way for you to avoid harmful interactions is to tell your doctor and/or pharmacist what medications you are currently taking, including any over-the-counter products, vitamins, and herbals. For specific information on how melatonin interacts with drugs, other herbals, and foods and the severity of those interactions, please use our <u>Drug Interactions Checker</u> to check for possible interactions.

## Should I take it?

Melatonin is a hormone primarily produced naturally by the pineal gland of mammals. In humans, the pineal gland is a very small organ located in the brain. Sensitive to light, it produces melatonin only during darkness -- with production increasing approximately an hour or two before an individual's customary sleeping times and then decreasing before usual awakening times. It is now believed that other body tissues, such as the retinas, also produce small amounts of melatonin. Children begin producing melatonin at about 3 months of age. Its production increases until about age 20 and then drops off as individuals age. By age 80, natural melatonin levels are estimated at 20% of their peak levels. Melatonin production also appears to be reduced in conditions such as dementia, which are usually associated with aging.

In humans, melatonin affects daily cycles, also called circadian rhythms, such as sleep and temperature. In other mammals, melatonin plays a role in seasonal changes such as hibernation. Melatonin also seems to promote growth and sexual maturity and it may assist in maintaining balance. Low levels of melatonin have been associated with depression, fibromyalgia, insomnia, some seizure disorders, and other conditions.

Supplemental melatonin should be synthetic -- derived from sources that are not animal

or human. In the past, some melatonin products were made from animal tissue, which carried the risk of possible contamination with viruses and other toxins. Because of concerns with contamination and safety, Japan currently prohibits the sale of melatonin supplements and Britain restricts their use.

#### **Dosage and Administration**

In the United States, supplemental melatonin is most readily available as capsules and tablets -- some in controlled-release forms that deliver measured doses of melatonin over extended periods of time. It also comes in a tablet that dissolves under the tongue. Dosing recommendations vary considerably, with a wide range between 0.1 mg and 10 mg used in studies for various conditions. However, to promote sleep, doses over 0.5 mg generally were no more effective than lower doses. In clinical studies, melatonin has been used for as long as 9 months, but most commonly it is used for a few days at a time. Common recommendations for its use include:

- For insomnia: 0.3 mg to 5 mg at bedtime.
- For jet lag: 0.5 mg to 5 mg at bedtime for up to 5 days, beginning on the day before the trip.
- For smoking cessation: 0.3mg taken 3 to 4 hours after the last cigarette.
- For benzodiazepine withdrawal: 2 mg controlled-release daily at bedtime for 6 weeks as the benzodiazepine dose is gradually decreased.

If you choose to use melatonin, follow exactly the directions on the package of the product you purchase.

#### Summary

In the United States, melatonin is used mainly for regulating disturbed sleep that may be caused by traveling across multiple time zones or changing shifts at work.

Melatonin may also have some usefulness for treating some types of cancer, helping individuals dependent on benzodiazepines to withdraw from therapy, and helping smokers quit smoking. Other uses may include preventing both cluster headaches and sunburn. However, it has not yet been found effective for any of these uses.

# Risks

Women who are pregnant or breast-feeding, or who are trying to conceive should not use melatonin supplements. Melatonin may affect fertility in women trying to conceive, and not enough is known about its potential effects on fetal and infant development and growth to recommend it for pregnant or breast-feeding women. Because natural melatonin appears to have an effect on sexual development, supplemental melatonin should not be given to children. Melatonin should also be avoided by individuals with liver conditions, because it may accumulate in the blood -- possibly causing side effects. Individuals with depressive disorders should only use supplemental melatonin if a doctor recommends it because melatonin may cause or worsen symptoms of depression. Because melatonin can cause drowsiness, individuals who take it should be careful when performing tasks that require alertness.

## Side Effects

Melatonin may affect the body's production and use of some hormones.

In addition, it can cause:

- Abdominal cramps, nausea, or vomiting
- Confusion, drowsiness, or dizziness
- Headache or irritability
- Low blood pressure

## Interactions

Melatonin may interfere with the effectiveness of:

- Antidepressants
- Corticosteroids
- Drugs for high blood pressure
- Immunosuppressants
- Sedatives

Melatonin may also increase sleepiness caused by some prescription, non-prescription, and herbal products and by alcohol.

Caffeine may decrease the effectiveness of melatonin.

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