METAPHARMACEUTICAL IND SL
Josep Plà, 163, 2n 5a / Tel. 933 089 976 / info@metapharmaceutical.com

Technical Data sheet

MELATONINA BP FARMA		
DESCRIPTION DCI: MELATONIN		DESCRIPTION DOE: MELATONINA
CAS Nº: 73-31-4	EC Nº: 200-797-7	AEMPS CODE: 90496A
MOL. WEIGHT: 232,278	MOL. FORMULA:: C13H16N2O2	ARTICLE CODE: 009613

ATTRIBUTES	SHOULD BE
Characters	
Appearance	A white to off-white crystalline powder
Solubility	Slightly soluble in water, soluble in acetone, ethyl acetate and methanol
Melting point	117 ºC
Identification	Complies
Related substances	
5-Metoxytriptamine	=< 0.5 %
Unknown impurities	=< 0.1 %
Total impurities	=< 1 %
Water	=< 0.3 %
Sulfated ash	=< 0.1 %
Assay	98.0 - 102.0 %
Residual solvents	
Ethyl acetate	=< 5000 ppm
Ethanol	=< 5000 ppm
Methylene chloride	=< 600 ppm
Pyridine	=< 200 ppm

COMPLIES WITH

British Pharmacopoeia 2018

STORAGE

Store at room temperature and in the original container, in a cool and well-ventilated place. Store away from sources of heat,

REMARKS

Melatonine is subjected to the requirements of the ICH Q3D "Elemental Impurities" guideline.

Certificates of residual solvents, allergens, non-GMO and BSE-TSE are available upon request.

Properties and uses
It is a neurohormone produced by the pineal gland from tryptophan. It intervenes in the inhibition of gonadal development and in the control of estrus. It also acts on changes in skin color, for protective purposes. There seems to be a diurnal rhythm of melatonin secretion: it secretes in the hours of darkness and can influence the sleep pattern. Its effect on insomnia, jet lag, and depressive tratornos has been studied.
In adults, the absorption of ingested melatonin is complete and may decrease up to 50% in older people. Food affects both the rate of absorption and the serum concentration of melatonin. The kinetics are linear in a dose range between 2 and 8 mg and the bioavailability of approximately 15% since it undergoes a significant first-pass effect. The binding to plasma proteins is 60%, most of it to albumin, alpha1 acid glycoprotein and high density lipoprotein (HDL). The main route of metabolism is hepatic via the cytochrome P450 system and the corresponding isoenzymes CYP1A1, CYP1A2 and possibly also CYP2C19. The inactive metabolites and a small proportion of unchanged melatonin (2%) have an elimination half-life of 3.5-4 h and are excreted renally in the form of sulfated and glucuronic conjugates. In monotherapy, Melatonin is indicated in the short-term treatment of primary insomnia characterized by poor quality sleep in patients over 55 years of age.

Dosage
It is usually an orally administered substance in the form of modified release tablets. The recommended dose is one tablet of 2 mg, once a day, 1-2 hours before going to sleep, after having eaten a food. Continue this dosing schedule for three weeks.

Technical Data sheet

MELATONINA BP FARMA		
DESCRIPTION DCI: MELATONIN		DESCRIPTION DOE: MELATONINA
CAS Nº: 73-31-4	EC Nº: 200-797-7	AEMPS CODE: 90496A
MOL. WEIGHT: 232,278	MOL. FORMULA:: C13H16N2O2	ARTICLE CODE: 009613

Side effects
Adverse reactions reported during clinical trials are very varied: nervous (migraine, nervousness, dizziness), digestive (dry mouth, abdominal pain, constipation, hyperbilirubinemia), and others (hyperhidrosis, asthenia, weight gain, etc ...)).
During the clinical trials, the administration of doses much higher than the therapeutic ones (300 mg of melatonin) did not give adverse reactions of clinical importance. In case of overdose it would be possible to wait for the onset of drowsiness that would be resolved within 12 hours after ingestion, which is why no special treatment would be necessary.

Contraindications
It should not be used in patients with autoimmune diseases, renal failure, or liver failure. It should be used with caution in situations where drowsiness may entail a risk to safety, such as driving vehicles or operating machinery.

Precautions
There are no clinical data referring to the use of melatonin in pregnancy, therefore and although studies in animals do not show teratogenic effects, use in this state is not recommended. Endogenous melatonin has been detected in breast milk, which is why it is suspected that exogenous administration could also be excreted, therefore, use during breastfeeding is not recommended.

Interactions
Melatonin is metabolized by the cytochrome P450 system, therefore interactions will occur with drugs that use this same route: inhibitors of metabolism (fluvoxamine, methoxallen, cimetidine, estrogens, quinolones ...) and inducers of metabolism (phenobarbital, carbamazepine, tobacco ...). Effects on endogenous melatonin levels caused by different types of drugs are also known: agonists and adrenergic antagonists, opioid agonists and antagonists, antidepressants, prostaglandin inhibitors, benzodiazepines, tryptophan and alcohol.