METAPHARMACEUTICAL IND SL
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Technical Data sheet

METRONIDAZOL (PH.EUR)		
DESCRIPTION DCI: METRONIDAZOLE	DESCRIPTION DOE: METRONIDAZOL	
CAS Nº: 443-48-1	EC Nº: 207-136-1	AEMPS CODE: 1966A
MOL. WEIGHT: 171.20	MOL. FORMULA:: C6H9N3O3	ARTICLE CODE: 1294

ATTRIBUTES	SHOULD BE
Appearance	White or yellowish, crystalline powder
Solubility	Slightly soluble in water, in acetone, in alcohol and in methylene chloride
Identification C	Complies
Appearance of solution	Not more opalescent than ref. susp. II and not more intensely coloured than ref. sol. GY6
Related substances	
Any impurity	=< 0.1 %
Total impurities	=< 0.2 %
Loss on drying	=< 0.5 %
Sulfated ash	=< 0.1 %
Assay	99.0 - 101.0 %
Residual solvents	
Ethylene oxide	=< 1 ppm
Ethanediol	=< 620 ppm
Microbial contamination	
TAMC	=< 1000 CFU/g
TYMC	=< 100 CFU/g
Staphylococcus aureus	Absence
Escherichia coli	Absence
Pseudomonas aeruginosa	Absence
Bacterial endotoxines	=< 0.35 EU/mg

COMPLIES WITH

European Pharmacopoeia 9.0

STORAGE

Keep the container thightly closed. Store it in a cool and dry place.

REMARKS

Metronidazole 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
Metronidazole is a nitroimidazole antibiotic active against protozoa, helminths, and anaerobic bacteria. It works by altering the DNA of the susceptible germs and preventing their synthesis. Metronidazole is rapidly absorbed after oral administration with an approximate bioavailability of 100%. The rectal bioavailability is 60-80%, and the vaginal route is 20-25%. It is widely distributed in most tissues and fluids, including bile, saliva, bones, seminal fluid, vaginal secretions, breast milk, etc ... Most of it is excreted in urine, especially in the form of metabolites, and in small amounts in faeces. It crosses the placental barrier and quickly passes into the fetal circulation. It binds a maximum of 20% to plasma proteins. It is metabolized in the liver by oxidation of the side chain and formation of the glucuronide. The elimination half-life is about 8 h. It is active against Trichomonas vaginalis, Entamoeba histolytica, Giardia lamblia, Gardnerella vaginalis, Helicobacter pylori, Balantidium coli, Blastocystis hominis, Bacteroides, Clostridium, and some spirochetes. It is indicated in:

- Trichomoniasis: is an agent of choice in genital infections by trichomonas in men and women.
- Non-specific vaginitis.

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- Amebiasis: it is also an agent of choice for this pathology.
- Balantidiasis.
- Giardiasis.
- Acute dental infections.
- Acne rosacea.
- Decubitus ulcers.
- Acute necrotizing ulcerative gingivitis or Vincent's infection.
- Gastroduodenal ulcers: in combination with other drugs. -Anaerobic infections of the abdominal cavity.
- Pseudomembranous colitis.
- Perioral dermatitis.
- Prophylaxis of some surgical infections.

It is administered orally (in capsules or tablets), rectally (suppositories), vaginally (ovules or vaginal tablets), and topically (gels or creams). Orally, it can be administered with food or after meals. Topically, it is incorporated in gels or emulsions with an O / W or W / O sign.

Dosage

- Nonspecific trichomoniasis and vaginitis: a single dose of 2 g orally, or 200-250 mg / 8 h or 400-500 mg / 12 h for 7 days. You can also administer 500 mg ovules for 20 days.
- Amebiasis and balantidiasis: 400-800 mg / 8 h orally for 5-10 days (in children normally 35-50 mg / Kg / day in several doses).
- Giardiasis and acute dental infections: 2 g / 24 h orally for 3 days, or 400 mg / 8 h for 5 days, or 500 mg / 12 h for 7-10 days (in children normally 15 mg / Kg / day in several shots).
- Acne rosacea: 200 mg / 12 h orally and 0.75 - 2% topically.
- Decubitus ulcers: 400 mg / 8 h orally for 7 days, and also 1% via topical. - Acute necrotizing ulcerative gingivitis and dental infections: 200 mg / 8 h orally for 3 days.
- Gastroduodenal ulcers: 400 mg / 8-12 h for 7 days. - Anaerobic infections: 800 mg initial oral followed by 400 mg / 8 h for 7 days. Intravenous route 500 mg / 8 h.

Side effects

The adverse effects of metronidazole are a function of the dose and duration of treatment. The most frequent are gastrointestinal disorders, especially nausea and metallic taste, which sometimes accompany headache, anorexia, and vomiting. In addition, diarrhea, constipation, dry mouth, saguaral tongue, glossitis, and stomatitis may occur, being associated with cases of pseudomembranous colitis and pancreatitis. In addition, peripheral neuropathy may appear, usually presenting with numbness and tingling of the extremities and epileptic seizures. Other symptoms in the CNS are weakness, dizziness, ataxia, drowsiness, insomnia, depression, or confusion. Moderate transient leukopenia, skin rashes and pruritus, and anaphylactic reactions may occur. Other side effects include urethral disorders and darkening of urine, as well as elevations in liver enzymes. Intravenously, it can cause thrombophlebitis. Vaginal urethral burning, vaginal itching, vaginitis, urinary continence, and cystitis. It can stain the urine red or brown, although this has no pathological significance.

Contraindications

Diseases of the central nervous system. Avoid administration during pregnancy (especially in the first trimester) and during breastfeeding.

Precautions

Contraindicated in allergy to nitroimidazoles. It should be used with caution in patients with blood dyscrasias or CNS disorders. When therapy exceeds 10 days, treatment should be discontinued if signs of peripheral neuropathy or CNS toxicity appear. Reduce dose in patients with severe liver disease. Rectally, metronidazole is absorbed more slowly and therefore suppositories are not recommended in case of serious infections. During the treatment should be avoided drinking alcohol because it can produce a reaction antabús.

Interactions

The simultaneous use of metronidazole and disulfiram can cause acute psychosis or mental confusion. Reactions have been described when administered with pharmaceutical preparations containing alcohol. It can potentiate the effect and toxicity of

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oral anticoagulants, phenytoin, lithium, and 5-fluorouracil, while its action and toxicity can be increased by cimetidine and reduced by barbiturates.

Other observations
It is thermolabile and photosensible.