SAFETY DATA SHEET
METRONIDAZOLE TABLETS, USP

Strength: 250 mg, **Pack Size:** HDPE bottle packs of 100, 250 and 500 Tablets
Strength: 500 mg, **Pack Size:** HDPE bottle packs of 50, 100 and 500 Tablets

Revision No.: 00

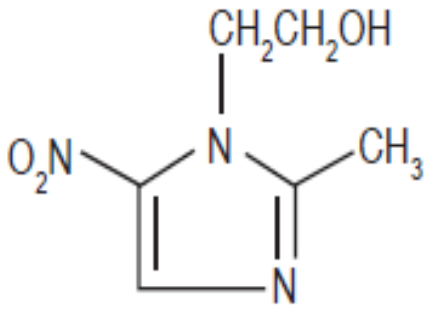
EMERGENCY OVERVIEW

Each Metronidazole Tablets, USP intended for oral administration contains Metronidazole and excipients generally considered to be non- toxic and non-hazardous in small quantities and under conditions of normal occupational exposure.

Section 1. IDENTIFICATION

Identification of the product

Product Name: Metronidazole Tablets, USP 250 mg and 500 mg
Formula: $C_6H_9N_3O_3$
Chemical Name: 2-methyl-5-nitro-1H-imidazole-1-ethanol



Manufacturer / supplier

Company:	**Cadila Healthcare Limited Baddi, India**
Address:	Cadila Healthcare Limited, Swaraj Majra, Judi Kalan, Post - Baddi, Tehsil - Nalagarh, District - Solan, Himachal Pradesh 173205.
Contact for information:	Tel: +91-1795-246841 Fax: +91-1795-246842
Emergency Telephone No.	Tel: +91-1795-246841
Recommended use / Therapeutic Category	Orally /Antibiotic
Restriction on Use / Contraindications:	Metronidazole Tablets is contraindicated in patients with a prior history of hypersensitivity to Metronidazole or other nitroimidazole derivatives. In patients with trichomoniasis, Metronidazole Tablets is contraindicated during the first trimester of pregnancy.

Section 2. HAZARD(S) IDENTIFICATION

Dose and Administration

Dosage should be individualized with careful monitoring of patient response.

Oral Administration:

Trichomoniasis: In the Female:

One-day treatment − Two grams of Metronidazole tablets, given either as a single dose or in two divided doses of one gram each, given in the same day.

Seven-day course of treatment − 250 mg three times daily for seven consecutive days. There is some indication from controlled comparative studies that cure rates as determined by vaginal smears and signs and symptoms, may be higher after a seven-day course of treatment than after a one-day treatment regimen.

Pregnant patients should not be treated during the first trimester. In pregnant patients for whom alternative treatment has been inadequate, the one-day course of therapy should not be used, as it results in higher serum.

In the Male: Treatment should be individualized as it is for the female.

Amebiasis

Adults: For acute intestinal amebiasis (acute amebic dysentery): 750 mg orally three times daily for 5 to 10 days.

For amebic liver abscess: 500 mg or 750 mg orally three times daily for 5 to 10 days.

Pediatric patients: 35 to 50 mg/kg/24 hours, divided into three doses, orally for 10 days.

Anaerobic Bacterial Infections In the treatment of most serious anaerobic infections, intravenous Metronidazole is usually administered initially. The usual adult oral dosage is 7.5 mg/kg every six hours (approx. 500 mg for a 70-kg adult). A maximum of 4 g should not be exceeded during a 24-hour period.

The usual duration of therapy is 7 to 10 days; however, infections of the bone and joint, lower respiratory tract, and endocardium may require longer treatment.

Adverse Effects

The following reactions have been reported during treatment with Metronidazole:

Central Nervous System: The most serious adverse reactions reported in patients treated with Metronidazole have been convulsive seizures, encephalopathy, aseptic meningitis, optic and peripheral neuropathy, the latter characterized mainly by numbness or paresthesia of an extremity. Since persistent peripheral neuropathy has been reported in some patients receiving prolonged administration of Metronidazole, patients should be specifically warned about these reactions and should be told to stop the drug and report immediately to their physicians if any neurologic symptoms occur. In addition, patients have reported headache, syncope, dizziness, vertigo, incoordination, ataxia, confusion, dysarthria, irritability, depression, weakness, and insomnia.

Gastrointestinal: The most common adverse reactions reported have been referable to the gastrointestinal tract, particularly nausea, sometimes accompanied by headache, anorexia, and occasionally vomiting; diarrhea; epigastric distress; and abdominal cramping and constipation.
Mouth: A sharp, unpleasant metallic taste is not unusual. Furry tongue, glossitis, and stomatitis have occurred; these may be associated with a sudden overgrowth of *Candida* which may occur during therapy.
Dermatologic: Erythematous rash and pruritus.
Hematopoietic: Reversible neutropenia (leukopenia); rarely, reversible thrombocytopenia.
Cardiovascular: Flattening of the T-wave may be seen in electrocardiographic tracings.
Hypersensitivity: Urticaria, erythematous rash, Stevens-Johnson Syndrome, toxic epidermal necrolysis, flushing, nasal congestion, dryness of the mouth (or vagina or vulva), and fever.
Renal: Dysuria, cystitis, polyuria, incontinence, and a sense of pelvic pressure. Instances of darkened urine have been reported by approximately one patient in 100,000. Although the pigment which is probably responsible for this phenomenon has not been positively identified, it is almost certainly a metabolite of Metronidazole and seems to have no clinical significance.
Other: Proliferation of *Candida* in the vagina, dyspareunia, decrease of libido, proctitis, and fleeting joint pains sometimes resembling "serum sickness." Rare cases of pancreatitis, which generally abated on withdrawal of the drug, have been reported. Patients with Crohn's disease are known to have an increased incidence of gastrointestinal and certain extraintestinal cancers. There have been some reports in the medical literature of breast and colon cancer in Crohn's disease patients who have been treated with Metronidazole at high doses for extended periods of time. A cause and effect relationship has not been established. Crohn's disease is not an approved indication for Metronidazole tablets.

Over Dose Effect

Single oral doses of Metronidazole, up to 15 g, have been reported in suicide attempts and accidental overdoses. Symptoms reported include nausea, vomiting, and ataxia. Oral Metronidazole has been studied as a radiation sensitizer in the treatment of malignant tumors.
Neurotoxic effects, including seizures and peripheral neuropathy, have been reported after 5 to 7 days of doses of 6 to 10.4 g every other day.

Contraindications

Metronidazole Tablets is contraindicated in patients with a prior history of hypersensitivity to Metronidazole or other nitroimidazole derivatives.
In patients with trichomoniasis, Metronidazole Tablets is contraindicated during the first trimester of pregnancy.

Pregnancy Comments

There are no adequate and well-controlled studies of Metronidazole in pregnant women.

There are published data from case-control studies, cohort studies, and 2 meta-analyses that include more than 5000 pregnant women who used Metronidazole during pregnancy. Many studies included first trimester exposures. One study showed an increased risk of cleft lip, with or without cleft palate, in infants exposed to Metronidazole in-utero; however, these findings were not confirmed. In addition, more than ten randomized placebo-controlled clinical trials enrolled more than 5000 pregnant women to assess the use of antibiotic treatment (including Metronidazole) for bacterial vaginosis on the incidence of preterm delivery. Most studies did not show an increased risk for congenital anomalies or other adverse fetal outcomes following Metronidazole exposure during pregnancy. Three studies conducted to assess the risk of infant cancer following Metronidazole exposure during pregnancy did not show an increased risk; however, the ability of these studies to detect such a signal was limited.

Metronidazole crosses the placental barrier and its effects on the human fetal organogenesis are not known. Reproduction studies have been performed in rats, rabbits, and mice at doses similar to the maximum recommended human dose based on body surface area comparisons. There was no evidence of harm to the fetus due to Metronidazole.

Pregnancy Category Pregnancy Category B

Section 3. COMPOSITION / INFORMATION ON INGREDIENTS

Component	Exposure Limit	CAS No.
Principle Component:		
Metronidazole	Not Found	443-48-1
Inactive Ingredients:		
Colloidal silicon dioxide	Not Found	7631-86-9
Hypromellose	Not Found	9004-65-3
Low-substituted hydroxypropyl cellulose	Not Found	9004-64-2
Microcrystalline Cellulose	Not Found	9004-34-6
Stearic acid	Not Found	57-11-4
Additionally each tablet contains Opadry II white 02F580003 which contains		
Hypromellose	Not Found	9004-65-3
Polyethylene glycol	Not Found	25322-68-3
Talc	Not Found	14807-96-6
Titanium Dioxide	Not Found	13463-67-7

Section 4. FIRST -AID MEASURES

Inhalation	Remove to fresh air. If discomfort occurs or persists, get medical attention.
Skin contact	Remove contaminated clothing and shoes. Wash skin with soap and plenty of water. If irritation occurs or persists, get medical attention. Wash clothing and shoes before reuse.
Eye contact	Immediately flush eyes with plenty of water. If irritation occurs or persists, get medical attention.
Ingestion	If large quantities of this material are swallowed, get medical attention immediately. If swallowed, rinse mouth with water (only if the person is conscious). Do not induce vomiting unless directed by medical personnel. Never give anything by mouth to an unconscious person.

Section 5. FIRE FIGHTING MEASURES

Flash Point	Not applicable
Extinguishing Media	Water, Carbon Dioxide, Dry Chemical, Foam.
Unusual Fire and Explosion Hazards	Toxic emissions may be given off in a fire.
Fire Fighting Instructions	Wear NIOSH/MSHA approved positive pressure, self-contained breathing apparatus and full protective turn out gear. Use caution in approaching fire. Use water to keep fire exposed containers cool.

Section 6. ACCIDENTAL RELEASE MEASURES

Spill Clean Up Procedures	Use proper personal protective equipment and clothing. Shut off the source of the spill or leak if it is safe to do so. Scoop or shovel spilled material into a suitable labeled open head drum. Secure the drum cover and move the container to a safe holding area. Wash spill area thoroughly with soapy water.
Treatment and Disposal	Decontaminate equipment. Dispose of protective clothing with spilled material.
Environmental precautions	Avoid release to the environment. Prevent further leakage or spillage if safe to do so. Avoid discharge into drains, water courses or onto the ground. Inform appropriate managerial or supervisory personnel of all environmental releases.

Section 7. HANDLING AND STORAGE

Storage	Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature]. Protect from light. Dispense in a tight, light resistant container (USP).

Precautions for safe handling	Avoid contact with eyes. Avoid breathing dust. Use with adequate ventilation. When handling, use proper personal protective equipment. Wash thoroughly after handling. Keep container tightly closed when not in in use. Store in a dry area at room temperature.

Section 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Respiratory Protection	Use a NIOSH/MSHA approved respirator if there is a risk of exposure to dust/fume at levels exceeding the exposure limits. No personal respiratory protective equipment normally required.
Skin protection	For prolonged or repeated skin contact use suitable protective gloves.
Eye/face protection	If contact is likely, safety glasses with side shields are recommended.
Protective Clothing	Protective clothing is not normally necessary, however it is good practice to use apron.
Biological limit values	No biological exposure limits noted for the ingredient(s).
Exposure guidelines	General ventilation normally adequate.
Thermal hazards	Wear appropriate thermal protective clothing, when necessary.
General hygiene considerations	Always observe good personal hygiene measures, such as washing after handling the material and before eating, drinking, and/or smoking. Routinely wash work clothing and protective equipment to remove contaminants. For advice on suitable monitoring methods, seek guidance from a qualified environment, health and safety professional.
Engineering controls	Engineering controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.

Section 9. PHYSICAL AND CHEMICAL PROPERTIES

Physical state	Tablets
Color	White to off white
Odor	Odorless
Pure/Mixture	Mixture

Section 10. STABILITY AND REACTIVITY

Stability	Normally stable but formation of toxic gases is possible during heating or in case of fire.
Incompatibility materials to avoid	Strong Oxidizing agents
Polymerization	No
Conditions of Polymerization	Will not occur

Section 11. TOXICOLOGICAL INFORMATION

Metronidazole
Irritation Skin

May cause skin reaction.

Reproductive

Metronidazole failed to produce any adverse effects on fertility or testicular function in male rats at doses up at 400 mg/kg/day (similar to the maximum recommended clinical dose, based on body surface area comparisons) for 28 days. However, rats treated at the same dose for 6 weeks or longer were infertile and showed severe degeneration of the seminiferous epithelium in the testes as well as marked decreases in testicular spermatid counts and epididymal sperm counts. Fertility was restored in most rats after an eight week, drug-free recovery period. There was no evidence of harm to the fetus due to Metronidazole.

Teratogenicity, Carcinogenicity and Mutagenicity

Reproduction studies have been performed in rats, rabbits, and mice at doses similar to the maximum recommended human dose based on body surface area comparisons. There was no evidence of harm to the fetus due to Metronidazole.

Tumors affecting the liver, lungs, mammary, and lymphatic tissues have been detected in several studies of Metronidazole in rats and mice, but not hamsters. Two lifetime tumorigenicity studies in hamsters have been performed and reported to be negative.

Metronidazole has shown mutagenic activity in in vitro assay systems including the Ames test. Studies in mammals in vivo have failed to demonstrate a potential for genetic damage.

Section 12. ECOLOGICAL INFORMATION

Do not allow product to enter drinking water supplies, waste water or soil.

Section 13. DISPOSAL CONSIDERATION

Disposal Recommendations Dispose the waste in accordance with all applicable Federal, State and local laws.

Section 14. TRANSPORT INFORMATION

The product is not hazardous when shipping via air (IATA), ground (DOT), or sea (IMDG).

Section 15. REGULATORY INFORMATION

Generic Medicine, ANDA Number 206560

Section 16. OTHER INFORMATION

Additional Information

NFPA Rating: These ratings are based on NFPA code 704 and are intended for use by emergency personnel to determine the immediate hazards of a material
Health……..0
Fire……..0
Reactivity…0

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