

285 MM

Metrogyl® Tablets 200 mg  
Metrogyl® Tablets 400 mg

METRONIDAZOLE TABLETS BP 200 mg  
METRONIDAZOLE TABLETS BP 400 mg

**DESCRIPTION:**  
Metrogyl (Metronidazole) is an oral synthetic antiprotozoal and antibacterial agent.

**PRODUCT DESCRIPTION:**  
Metrogyl Tablets 200 mg: Pink, round, biconvex film coated tablets.  
Metrogyl Tablets 400 mg: Orange, round, biconvex film coated tablets.

**Composition:**  
Each film coated tablet contains: Metronidazole BP 200 mg / 400 mg.

**PHARMACOLOGICAL ACTION:**  
**MECHANISM OF ACTION:**  
Metronidazole diffuses into aerobic and anaerobic bacteria equally well, but in the former it remains unchanged while in the later it is reduced. As a result of biochemical reduction in the cell, the concentration of unchanged drug is reduced and this probably creates a gradient which promotes further uptake of the drug into anaerobic organisms, the nitro group of Metronidazole is reduced in anaerobic bacteria and protozoa by the pyruvate phosphoroclastic reaction, in which the drug acts as a preferential electron acceptor. Oxygen markedly reduces the uptake of Metronidazole in experiments using certain anaerobic protozoa, suggesting that this process depends on reducing power inside the cell. The selective uptake and specificity of Metronidazole for anaerobes may be because their redox process are different from those aerobes; it has been assumed that the product of reduction of the nitro group of Metronidazole interacts with the DNA with ultimate inhibition of nucleic acid synthesis and subsequent cell death. Moreover Metronidazole has been shown to inhibit DNA synthesis and degrade existing DNA in Clostridium bifermentans.

**PHARMACOKINETICS:**  
Disposition of Metronidazole in the body is similar for both oral and intravenous dosage forms, with an average elimination half-life in healthy humans of eight hours. The major route of elimination of Metronidazole and its metabolites is via the Urine (60 to 80% of the dose), with fecal excretion accounting for 6 to 15% of the dose. The metabolites that appear in the urine result primarily form side-chain oxidation (1-(beta hydroxyethyl)-2-hydroxymethyl -5-nitroimidazole and 2-methyl-5-nitroimidazole-1-yl-acetic acid) and glucuronide conjugation, with unchanged metronidazole accounting for approximately 20% of the total. Renal clearance of metronidazole is approximately 10ml/min/1.73 m 2. Metronidazole is the major component appearing in the plasma, with lesser quantities of the 2 –hydroxymethyl metabolite also being present. Less than 20% of the circulating metronidazole is bound to plasma proteins. Both the parent compound and the metabolite process In vitro bactericidal activity against most strains of anerobic bacteria and in vitro trichomonacidal activity. Metronidazole appears in cerebrospinal fluid, saliva, and breast milk in concentrations similar to those found in plasma. Bactericidal concentrations of Metronidazole have also been detected in pus form hepatic abscesses. Following administration metronidazole is well absorbed with peak plasma concentrations occurring between one and two hours after administration. Plasma concentrations of Metronidazole are proportional to the administered dose. Oral administration 250 mg, 500 mg, or 2,000 mg produced peak plasma concentrations of bioavailability differences between males and females; however, because of weight differences, the resulting plasma levels in males are generally lower. Decreased renal function does not alter the single dose pharmacokinetics of metronidazole. However, plasma clearance of metronidazole is decreased patients with decreased liver function.

**INDICATIONS:**  
Symptomatic Trichomoniasis  
Asymptomatic Trichomoniasis  
Intestinal Amoebiasis  
Amoebic Liver Abscess  
Anaerobic Bacterial Infections  
Intra-Abdominal Infections  
Skin and Skin Structure Infections  
Gynaecologic Infections  
Bacterial Septicemia  
Bone and Joint Infections  
Central Nervous Systems (CNS) Infections  
Lower Respiratory Tract Infections  
Endocarditis

**DOSAGE**  
In elderly patients the pharmacokinetics of metronidazole may be altered and therefore monitoring of serum levels may be necessary to adjust the metronidazole dosages accordingly.

**Trichomoniasis:**  
Metronidazole is given orally either as a single 2-g dose, as a 2-day course of 800 mg in the morning and 1.2 g in the evening, or as a 7-day course of 600 mg to 1 g daily in two or three divided doses. Sexual partners should also be treated.

**Amoebiasis:**  
Metronidazole is given in oral doses of 400 to 800 mg three times daily for 5 to 10 days.

**Anaerobic Bacterial Infections:**  
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 gm 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.

**WARNINGS:**  
Convulsive Seizures and Peripheral Neuropathy: Convulsive seizures and peripheral neuropathy, the later characterized mainly by numbness or paresthesia of an extremity, have been reported in patients treated with metronidazole. The appearance of abnormal

neurologic signs demands the prompt discontinuation of Metrogyl therapy. Metrogyl should be administered with caution to patients with central nervous system diseases, Cases of severe hepatotoxicity / acute hepatic failure, including cases with a fatal outcome with very rapid onset after treatment initiation in patients with Cockayne syndrome have been reported with products containing metronidazole for systemic use. In this population, metronidazole should therefore be used after careful benefit-risk assessment and only if no alternative treatment is available. Liver function tests must be performed just prior to the start of therapy, throughout and after end of treatment until liver function is within normal ranges, or until the baseline values are reached. If the liver function tests become markedly elevated during treatment, the drug should be discontinued  
Patients with Cockayne syndrome should be advised to immediately report any symptoms of potential liver injury to their physician and stop taking metronidazole.

**CONTRAINDICATIONS:**  
Metrogyl is contraindicated in patients with a prior history of hypersensitivity to metronidazole or other nitroimidazole derivatives. In patients with trichomoniasis, Metrogyl is contraindicated during the first trimester of pregnancy.

**PRECAUTIONS:**  
General: Patients with severe hepatic diseases metronidazole metabolizes slowly, with resultant accumulation of metronidazole and its metabolites in the plasma. Accordingly for such patients, doses below those usually recommended should be administered cautiously. In known or previously recognized candidiasis Metrogyl may prevent more prominent symptoms during therapy and requires treatment with a candidicidal agent.

Pregnancy: Metronidazole crosses the placental barrier and enters the fetal circulation rapidly. Reproduction studies have been performed in rats at doses up to five times the human close and have revealed no evidence of impaired fertility or harm to the fetus due to Metronidazole.

Nursing Mothers: Because of the potential for tumorigenicity shown for metronidazole in mouse and rat studies, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the concentration similar to those found in plasma.

Paediatric Use: Safety and effectiveness in children have not been established. except for the treatment of amoebiasis.

**SIDE EFFECTS:**  
The following reactions have also been reported during treatment with Metrogyl (Metronidazole)  
Mouth: A sharp unpleasant metallic taste is not unusual.  
Hematopoietic: Reversible neutropenia (leukopenia), rarely, reversible thrombocytopenia.  
Cardiovascular: Flattening of the T-wave may be seen in electrocardiographic tracings.  
Central Nervous System: Convulsive seizures, peripheral neuropathy, dizziness, vertigo, in-coordination, ataxia, confusion, irritability, depression, weakness, and insomnia.  
Hypersensitivity: Urticaria, erythematous rash, flushing, nasal congestion, dryness of the mouth (or vagina or vulva) and fever, Renal: Dysuria, cystitis, polyuria, incontinence, and a sense of pelvic pressure.

**INTERACTION WITH OTHER MEDICAMENTS:**  
Metronidazole has been reported to potentiate the anticoagulant effect of warfarin and other oral coumarin anticoagulants, resulting in a prolongation of prothrombin time. This possible drug interaction should be considered when metronidazole is prescribed for patients on this type of anticoagulant, therapy. The simultaneous administration of drugs that induce micorsomal liver enzymes, such as phenytoin or Phenobarbital, may accelerate the elimination of metronidazole, resulting in reduced plasma levels; impaired clearance of pheytoin has also been reported. The simultaneous administration of drugs that decrease microsomal liver enzyme activity, such as cimetidine, may prolong the half-life and decrease plasma clearance of metronidazole. In patients stabilized on relatively high doses of serum lithium, short-term cases, signs of lithium toxicity. Serum lithium and serum creatinine levels should be precede clinical symptoms of lithium intoxication. Alcoholic beverages should not be consumed during Metronidazole therapy and for at least one day afterward because abdominal cramps, nausea, vomiting, headaches, and flushing may occur. Psychotic reactions have been reported in alcoholic patients who are using metronidazole and disulfiram concurrently. Metronidazole should not be given to patients who have taken disulfiram within the last two weeks.

**SYMPTOMS AND TREATMENT OF OVERDOSE:**  
Single oral doses of metronidazole, upto 15 g have been reported in suicide attempts and accidental overdoses. Symptoms reported include nausea, vomiting, and ataxia. Oral Metronidazole has been studies 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 every other day. Treatment: there is no specific antidote for metronidazole overdose: therefore management of the patient should consist of symptomatic and supportive therapy.

**STORAGE:**  
Store below 30 °C in a cool, dry place. Protect from light.

**Shelf Life:** 5 years

**PRESENTATION:**  
Monocarton 10 x10 tablets  
Secondary outer carton of 10 x (10 x 10 tablets).

 Manufactured by :  
**UNIQUE PHARMACEUTICAL LABORATORIES**  
(A Div. of J. B. Chemicals & Pharmaceuticals Ltd.)  
Plot No. 215-219, G.I.D.C Industrial Area, Panoli-394 116, Gujarat, India  
® Regd. Trade Mark

Product Registration Holder and Imported by:  
UNIMED SDN BHD  
No.53, Jalan Tembaga, SD 5/2B, Bandar Sri Damansara,  
52200 Kuala Lumpur, Malaysia.

**Revision Date:** 02.10.20 **130110**

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| SAP Code : 130110                                                                                                                         | Country : Malaysia                | Mfg. Location : UPL Panoli TI-10          | Product Name : Metrogyl 200/400 Tab                                                                                                        |                      |
| Packaging Material : Leaflet                                                                                                              | Existing / Reference Art : 122512 | Version No.: 5                            | Date : 23.11.2021                                                                                                                          |                      |
| Dimension : (L) 285 x (B) 110 mm (± 1 mm tolerance)                                                                                       |                                   | Size After Folding : 110 x 36 mm (+/-1mm) | Core Dia : NA                                                                                                                              |                      |
| Reel Dia : NA                                                                                                                             | Varnish / Lamination : NA         | Folding Pattern : 3 Horizontal Folds      | Print Repeat Length : NA                                                                                                                   |                      |
| Specification : White maplitho paper                                                                                                      |                                   | Pantone : Black<br><div></div>            |                                                                                                                                            |                      |
| Grammage: 56 ± 5% gm/m²                                                                                                                   |                                   |                                           |                                                                                                                                            |                      |
| Thickness : NA                                                                                                                            |                                   |                                           |                                                                                                                                            |                      |
| Other Test : NA                                                                                                                           |                                   |                                           |                                                                                                                                            |                      |
| Reason for Change :Change in Text matter as per customer requirement                                                                      |                                   |                                           | <div>J. B. CHEMICALS &amp; PHARMACEUTICALS LTD.</div> |                      |
| File Path : X:\Artworks\Prakash\Malaysia\Metrogyl 400 mg Tablets V-1\open file\130110 Metrogyl 200 & 400 mg Tablet Leaflet - Malaysia.cdr |                                   |                                           |                                                                                                                                            |                      |
| Artist : Gajanan Khade                                                                                                                    | Initiated by                      | Checked by                                | Approved by                                                                                                                                | Approved by          |
| Sign & Date                                                                                                                               |                                   |                                           |                                                                                                                                            |                      |
| Designation                                                                                                                               | Executive - PDD                   | Manager - PDD                             | Regulatory Affairs                                                                                                                         | V. P. (Supply Chain) |