

## METROZOLE

Tablets & Suspension

### Composition

#### Metrozole Suspension

Each teaspoonful (5 ml) contains Metronidazole (as benzoyl) 125 mg

#### Metrozole 250 Tablets

Each tablet contains Metronidazole 250 mg.

#### Metrozole 500 Tablets

Each tablet contains Metronidazole 500 mg.

### Action

Metronidazole is an antiprotozoal agent; anaerobic antibacterial agent.

Metrozole is active against a wide range of pathogenic microorganisms notably species of *Bacteroides*, *Fusobacteria*, *Clostridia*, *Eubacteria*, *anaerobic cocci* and *Gardnerella vaginalis*. It is also active against *Trichomonas*, *Entamoeba histolytica*, *Giardia lamblia* and *Balantidium coli*. It is suggested that unchanged metronidazole penetrates the protozoan cell, where the nitro group is reduced to a hydroxyl or amine group that reacts with DNA and stops nucleic acid synthesis.

### Pharmacokinetics

#### Absorption

Metrozole is rapidly and almost completely absorbed after oral administration leading to peak serum levels after 20 minutes to 3 hours. The bioavailability of metronidazole in Metrozole suppositories is 60-80%. Effective blood concentrations are achieved 5-12 hours after the first suppository and are maintained by the recommended 8 hourly regimen.

#### Distribution

Metronidazole is widely distributed into most body tissues and fluids where it achieves concentrations similar to those in plasma. Metronidazole is not protein bound to any significant degree. Metronidazole is metabolised by oxidation in the liver to a number of metabolites, one of which (the hydroxy metabolite) has some antibacterial activity.

#### Elimination

The elimination half-life of metronidazole is 7-8 hours, and that of the hydroxyl metabolite slightly longer. About 55 to 80 percent of an administered dose is excreted in the urine as nitro-containing compounds, of which unchanged metronidazole and the hydroxymethyl homologue each comprise about one third. The fate of the remainder is unknown.

Metronidazole should be administered with caution to patients with advanced hepatic insufficiency. Metronidazole can be used in chronic renal failure; it is rapidly removed from the plasma by dialysis. Metronidazole is excreted in breast milk but the intake of a suckling infant of a mother receiving normal dosage would be considerably less than the therapeutic dosage for infants.

## Indications

### Trichomoniasis

#### *Symptomatic Trichomoniasis*

Metrozole is indicated for the treatment of symptomatic trichomoniasis in women and men, when the presence of the trichomonad has been confirmed by appropriate laboratory procedures.

#### *Asymptomatic Trichomoniasis*

Metrozole is indicated in the treatment of asymptomatic women, when the organism is associated with endocervicitis, cervicitis or cervical erosion.

#### *Asymptomatic Consorts*

Trichomoniasis vaginalis infection is a venereal disease. Therefore, asymptomatic sexual partners of treated patients should be treated simultaneously if the organism has been found to be present, in order to prevent reinfection of the partner. During the treatment, it is recommended that the patient refrain from sexual intercourse, or the male partner use a condom to avoid reinfection.

### Amebiasis

Metrozole is indicated in the treatment of acute intestinal amebiasis (amebic dysentery) and amebic liver abscess.

## Contraindications

- Known hypersensitivity to metronidazole or any of the ingredients in the tablets.
- Pregnancy - metronidazole should not be used in the first trimester in patients with trichomoniasis or bacterial vaginosis.
- Breast feeding should be discontinued for 12-24 hours when single high dose (e.g. 2g) therapy is used.

## Warnings & Precautions

This drug should be used with care in patients with evidence or history of blood dyscrasia. Mild leukopenia has been observed during administration. However, no persistent hematological abnormalities attributable to the drug have been observed. Total and differential leukocyte counts are recommended prior to, and following, therapy.

Metronidazole should be administered with care to patients receiving corticosteroids, or patients predisposed to edema.

### Convulsive Seizures and Peripheral Neuropathy

Convulsive seizures and peripheral neuropathy, the latter characterized mainly by numbness or paresthesia of an extremity, have been reported in patients treated with Metronidazole. Should any abnormal neurological sign appear, prompt discontinuation of therapy is warranted. As a rule, caution should be exercised when Metronidazole is administered to patients with central nervous system disorders.

### Use in Impaired Hepatic Function

Patients with severe hepatic disease metabolize Metronidazole slowly and therefore, accumulation of the drug and its metabolites may occur. Doses below those usually recommended should be administered, with caution.

### **Use in Paediatrics**

Safety and efficacy in children have not been established, except for the treatment of amebiasis.

## **Fertility, pregnancy and lactation**

### **Pregnancy**

#### *Category B*

Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women.

### **Nursing Mothers**

Safety of use in nursing mothers has not been established. Following oral administration, Metronidazole is secreted in breast milk in concentrations similar to those attained in plasma. The half-life in breast milk is about 9-10 hours. A nursing mother should express and discard any breast milk produced while on the drug, and resume nursing 24-48 hours after the drug is discontinued. Therefore, a decision should be made whether to discontinue the drug or to discontinue breastfeeding taking into account the importance of the drug to the mother.

## **Adverse Reactions**

### **Central Nervous System**

Convulsive seizures and peripheral neuropathies are the most serious adverse reactions encountered. Peripheral neuropathies are characterized mainly by numbness or paresthesia of an extremity.

Less serious adverse reactions include dizziness, vertigo, in coordination, ataxia, confusion, irritability, depression, weakness, insomnia, headache, syncope.

### **Gastrointestinal**

Nausea sometimes accompanied by headache, anorexia, vomiting, diarrhea, epigastric distress, abdominal cramping, constipation, proctitis, sharp unpleasant metallic taste, a modification of the taste of alcoholic beverages, furry tongue, glossitis and stomatitis (may be associated with a sudden overgrowth of Candida).

### **Hematological**

Reversible neutropenia (leukopenia) and, rarely, reversible thrombocytopenia.

### **Renal/ Genitourinary**

Dysuria, cystitis, polyuria, incontinence, sense of pelvic pressure, dyspareunia. Darkened urine has been reported, though it seems to have no clinical significance.

### **Cardiac**

Flattening of the T-wave may be seen in ECG tracings.

### **Hypersensitivity**

Urticaria, erythematous rash, flushing, nasal congestion, dryness of the mouth, fever.

### **Other**

Dyspareunia, decrease of libido, proctitis, fleeting joint pains sometimes resembling serum sickness.

## Drug Interactions

### *Metronidazole/ Coumarin Anticoagulants*

Metronidazole potentiates the anticoagulant effect of warfarin and other coumarin anticoagulants, resulting in a prolongation of prothrombin time.

### *Metronidazole/ Disulfiram*

Concurrent use with disulfiram may result in an acute psychotic reaction or confusional state caused by the combined toxicity. Metronidazole should not be given to patients who have taken disulfiram within two weeks prior to Metronidazole treatment.

### *Metronidazole/ Cimetidine*

The simultaneous administration of drugs that decrease microsomal liver enzyme activity, such as cimetidine, may prolong the half-life of Metronidazole and decrease its plasma clearance.

### *Metronidazole/ Lithium*

In patients stabilized on relatively high doses of lithium, short-term Metronidazole therapy has been associated with elevation of serum lithium and, in a few cases, signs of lithium toxicity. Serum lithium and serum creatinine levels should be obtained several days after initiation of Metronidazole therapy, to detect any increase that may precede clinical symptoms of lithium intoxication.

### *Metronidazole/ Phenobarbital/ Phenytoin*

The antimicrobial effectiveness of Metronidazole may be decreased when administered concurrently with phenobarbital or with phenytoin, probably due to increased Metronidazole metabolism. A higher dose of the anti-infective may be required.

### *Metronidazole/ Alcohol*

Consumption of alcoholic beverages during Metronidazole therapy may cause abdominal cramps, nausea, vomiting, headache and flushing.

## Diagnostic Interference

Metronidazole interferes with serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), lactate dehydrogenase (LDH), triglycerides, and hexokinase glucose level determinations, resulting in false decreased values.

## Dosage and Administration

In elderly patients, the pharmacokinetics of Metronidazole may be altered. Therefore, monitoring of serum levels may be necessary to adjust the Metronidazole dosage accordingly.

## Trichomoniasis

### *Women*

#### *1-Day Treatment*

2 grams orally, given either as a single dose or in two equal divided doses on the same day.

If a pregnant patient is treated during the second or third trimester, 1-day treatment should not be used, as it results in higher serum levels that reach the fetal circulation.



### *7-Day Treatment*

250 mg orally, 3 times a day for 7 consecutive days.

There is some indication from controlled comparative studies that cure rates, as determined by vaginal smears, signs and symptoms may be higher after a 7-day course of treatment than after a 1-day treatment regimen.

A 7-day course of treatment may minimize re infection of the female long enough to treat sexual contacts.

Single-dose treatment can assure compliance, especially if administered under supervision, in those patients who cannot be relied upon to continue the 7-day regimen.

When repeat courses of the drug are required, it is recommended that an interval of 4-6 weeks elapse between courses, and that the presence of the trichomonad be confirmed by appropriate laboratory measures.

### *Men*

250 mg orally twice daily (morning and evening) for 10 days. The dose may be increased and the duration of treatment prolonged, if necessary.

## **Amebiasis**

### *Acute Intestinal Amebiasis*

750 mg orally, 3 times daily for 5-10 days.

### *Amebic Liver Abscess*

500-750 mg orally, 3 times daily for 5-10 days. This therapy does not obviate the need for aspiration or drainage of pus.

### *Children*

35-50 mg/kg body weight/day, divided into 3 oral doses over 24 hours, for 10 days.

## **Over Dosage**

Over Dosage, symptoms manifested by Nausea, vomiting and ataxia.

There is no specific antidote to Metronidazole. Management consists of symptomatic and supportive therapy. Early gastric lavage may be helpful.

## **Presentation**

### **Metrozole Suspension**

Bottle of 120 ml.

### **Metrozole 250mg Tablets**

Box of 20 tablets.

### **Metrozole 500 mg Tablets**

Box of 20 tablets.