For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

METROGYL ER®
(Metronidazole Extended Release Tablets USP 600 mg)

COMPOSITION

Each Extended Release film coated tablet contains:
Metronidazole IP……600mg
Excipients…….,q.s.
Colours: Yellow Oxide of Iron, Red Oxide of Iron, Titanium Dioxide IP

DOSAGE FORM

Extended Release Tablet

INDICATIONS

Metronidazole tablets are indicated for the treatment of amoebiasis, urogenital trichomoniasis & giardiasis.

DOSAGE AND METHOD OF ADMINISTRATION

Oral route of administration.

Metronidazole tablets should be swallowed with water (not chewed). It is recommended that the tablets be taken during or after a meal.

Amoebiasis:

Adults and children over 10 years: 600 mg four times daily for 5 days or 600 mg two times daily for 5-10 days or as directed by physician.

Children below 10 years: As directed by physician.

Urogenital trichomoniasis:

Adults and children over 10 years: 600 mg daily for 7 days or as directed by physician.

Children below 10 years: As directed by physician.

Giardiasis:

Adults and children over 10 years: 600 mg two times daily for 5 days or as directed by physician.

Children below 10 years: As directed by physician

USE IN SPECIAL POPULATIONS

Pregnancy and Lactation

There is inadequate evidence of the safety of metronidazole in pregnancy but it has been in wide use for many years without apparent ill consequence. Nevertheless, Metronidazole tablets, like other medicines, should not be given during pregnancy or during lactation unless the physician considers it essential; in these circumstances the short, high-dosage regimens are not recommended.

CONTRAINDICATIONS

Known hypersensitivity to nitroimidazole, metronidazole or any of the excipients

WARNINGS & PRECAUTIONS

Regular clinical and laboratory monitoring (especially leucocyte count) are advised if administration of Metronidazole tablets for more than 10 days is considered to be necessary and patients should be monitored for adverse reactions, such as peripheral or central neuropathy (such as paraesthesia, ataxia, dizziness, convulsive seizures).

Metronidazole should be used with caution in patients with active or chronic severe peripheral and central nervous system disease due to the risk of neurological aggravation.

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.

There is a possibility that after *Trichomonas vaginalis* has been eliminated a gonococcal infection might persist.

The elimination half-life of metronidazole remains unchanged in the presence of renal failure. The dosage of metronidazole therefore needs no reduction. Such patients however retain the metabolites of metronidazole. The clinical significance of this is not known at present.

In patients undergoing haemodialysis metronidazole and metabolites are efficiently removed during an eight-hour period of dialysis. Metronidazole should therefore be re-administered immediately after haemodialysis.

No routine adjustment in the dosage of Metronidazole need be made in patients with renal failure undergoing intermittent peritoneal dialysis (IDP) or continuous ambulatory peritoneal dialysis (CAPD).

Metronidazole is mainly metabolised by hepatic oxidation. Substantial impairment of metronidazole clearance may occur in the presence of advanced hepatic insufficiency. Significant cumulation may occur in patients with hepatic encephalopathy and the resulting high plasma concentrations of metronidazole may contribute to the symptoms of the encephalopathy. Metronidazole should therefore, be administered with caution to patients with hepatic encephalopathy. The daily dosage should be reduced to one third and may be administered once daily.

Patients should be warned that metronidazole may darken urine.

Due to inadequate evidence on the mutagenicity risk in humans, the use of Metronidazole for longer treatment than usually required should be carefully considered

DRUG INTERACTIONS

Patients should be advised not to take alcohol during metronidazole therapy and for at least 48 hours afterwards because of the possibility of a disulfiram-like (antabuse effect) reaction. Psychotic reactions have been reported in patients who were using metronidazole and disulfiram concurrently.

Some potentiation of anticoagulant therapy has been reported when metronidazole has been used with the warfarin type oral anticoagulants. Dosage of the latter may require reducing. Prothrombin times should be monitored. There is no interaction with heparin.

Lithium retention accompanied by evidence of possible renal damage has been reported in patients treated simultaneously with lithium and metronidazole. Lithium treatment should be tapered or withdrawn before administering metronidazole. Plasma concentrations of lithium, creatinine and electrolytes should be monitored in patients under treatment with lithium while they receive metronidazole.

Patients receiving phenobarbital or phenytoin metabolize metronidazole at a much greater rate than normally, reducing the half-life to approximately 3 hours.

Metronidazole reduces the clearance of 5 fluorouracil and can therefore result in increased toxicity of 5 fluorouracil.

Patients receiving ciclosporin are at risk of elevated ciclosporin serum levels. Serum ciclosporin and serum creatinine should be closely monitored when coadministration is necessary.

Plasma levels of busulfan may be increased by metronidazole which may lead to severe busulfan toxicity.

UNDESIRABLE EFFECTS

The frequency of adverse events listed below is defined using the following convention:
Very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000), not known (cannot be estimated from the available data).
Serious adverse reactions occur rarely with standard recommended regimens. Clinicians who contemplate continuous therapy for the relief of chronic conditions, for periods longer than those recommended, are advised to consider the possible therapeutic benefit against the risk of peripheral neuropathy.

Blood and lymphatic system disorders:

Very rare: agranulocytosis, neutropenia, thrombocytopenia, pancytopenia

Not known: leucopenia.

Immune system disorders:

Rare: anaphylaxis

Not known: angiodema, urticaria, fever.

Metabolism and nutrition disorders:

Not known: anorexia.

Psychiatric disorders:

Very rare: psychotic disorders, including confusion and hallucinations.

Not known: depressed mood

Nervous system disorders:

Very rare:

- encephalopathy (eg. confusion, fever, headache, hallucinations, paralysis, light sensitivity, disturbances in sight and movement, stiff neck) and subacute cerebellar syndrome (eg. ataxia, dysathria, gait impairment, nystagmus and tremor) which may resolve on discontinuation of the drug.
- drowsiness, dizziness, convulsions, headaches

Not known:

- during intensive and/or prolonged metronidazole therapy, peripheral sensory neuropathy or transient epileptiform seizures have been reported. In most cases neuropathy disappeared after treatment was stopped or when dosage was reduced.
- aseptic meningitis

Eye disorders:

Very rare: vision disorders such as diplopia and myopia, which, in most cases, is transient.

Not known: optic neuropathy/neuritis

Ear and labyrinth disorders:

Not known: hearing impaired/hearing loss (including sensorineural), tinnitus

Gastrointestinal disorders:

Not known: taste disorders, oral mucositis, furred tongue, nausea, vomiting, gastro-intestinal disturbances such as epigastric pain and diarrhoea.

Hepatobiliary disorders:

Very rare:

- increase in liver enzymes (AST, ALT, alkaline phosphatase), cholestatic or mixed hepatitis and hepatocellular liver injury, jaundice and pancreatitis which is reversible on drug withdrawal.
- cases of liver failure requiring liver transplant have been reported in patients treated with metronidazole in combination with other antibiotic drugs.

Skin and subcutaneous tissue disorders:

Very rare: skin rashes, pustular eruptions, pruritis, flushing

Not known: erythema multiforme, Stevens-Johnson syndrome or toxic epidermal necrolysis, fixed drug eruption

Musculoskeletal, connective tissue and bone disorders:

Very rare: myalgia, arthralgia.

Renal and urinary disorders:

Very rare: darkening of urine (due to metronidazole metabolite).

OVERDOSE

Single oral doses of metronidazole, up to 12g have been reported in suicide attempts and accidental overdoses. Symptoms were limited to vomiting, ataxia and slight disorientation. There is no specific antidote for metronidazole overdosage. In cases of suspected massive overdose, symptomatic and supportive treatment should be instituted.

PHARMACODYNAMIC AND PHARMACOKINETIC PROPERTIES

Pharmacodynamics

Pharmacotherapeutic group: Antibacterials for systemic use, ATC code: J01X D01
Metronidazole has antiprotozoal and antibacterial actions and is effective against Trichomonas vaginalis and other protozoa including Entamoeba histolytica and Giardia lamblia and against anaerobic bacteria

Pharmacokinetics

Metronidazole is rapidly and almost completely absorbed on administration of Metronidazole tablets; peak plasma concentrations occur after 20 min to 3 hours.

The half-life of metronidazole is 8.5 ± 2.9 hours. Metronidazole can be used in chronic renal failure; it is rapidly removed from the plasma by dialysis. Metronidazole is excreted in milk but the intake of a suckling infant of a mother receiving normal dosage would be considerably less than the therapeutic dosage for infants.

STORAGE AND HANDLING INSTRUCTIONS

Protect from light & moisture.

PACKAGING INFORMATION

Blister of 10 tablets

Manufactured in India by:
J. B. Chemicals & Pharmaceuticals Ltd.
At: Plot No. 215-219, GIDC Industrial Area,
Panoli – 394 116.
® Regd. Trade Mark

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