1.5 Product Information: METRONEN TABLETS

1.5.1 Prescribing information (Summary of products characteristics):

1. Name of the Medicinal Product: METRONEN TABLETS

Strength: Each uncoated tablet contains Metronidazole BP 200mg

Pharmaceutical form: Tablet

2. Qualitative and Quantitative composition:

Qualitative composition:

Sr. No.	Ingredient	Specification	Uses
1	Metronidazole	BP	Active
2	Lactose	BP	Diluents
3	Maize starch (Mixing)	BP	Diluents
4	Microcrystalline cellulose	BP	Diluents
5	Maize starch (Paste)	BP	Binder
6	Povidone K30	BP	Binder
7	Sodium methyl paraben	BP	Antimicrobial preservative
8	Sodium propyl paraben	BP	Antimicrobial preservative
9	Colour Tartrazine supra	BP	Colour
10	Magnesium stearate	BP	Lubricant

Quantitative composition:

Sr. No.	Ingredient	Specification	Quantity mg per tablet
1	Metronidazole	BP	200.00
2	Lactose	BP	20.00
3	Maize starch (Mixing)	BP	46.40
4	Microcrystalline cellulose	BP	20.00
5	Maize starch (Paste)	BP	28.00
6	Povidone K30	BP	4.00
7	Sodium methyl paraben	BP	0.80
8	Sodium propyl paraben	BP	0.40
9	Colour Tartrazine supra	BP	0.20
10	Magnesium stearate	BP	0.20

3. Pharmaceutical form: Tablet

4. Clinical particular's:

4.1 Therapeutic indication:

Symptomatic Trichoniasis, asymptomatic Trichomoniasis, intestinal amoebiasis, amoebic liver abscess, anaerobic bacterial infections, intra-abdominal infections, skin and skin structure infections, Central Nervous System (CNS) infections, lower respiratory tract infections, Endocarditis.

4.2 Posology and method of administration:

Trichomoniasis:

Adults: 200 mg every 8 hours for 7 days or 400-500 mg every 12 hours for 5-7 days or 2 g as a single dose.

Children:

1-3 years: 50 mg every 8 hours for 7 days, 3-7 years: 100 mg every 12 hours, 7-12 year: 100 mg every 8 hours

AMOEBIASIS

Adults:

For acute intestinal amoebiasis (acute amoebic dysentery): 750 mg orally three times daily for 5 to 10 days.

For amoebic 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

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.

Method of Administration: Oral route.

4.3 Contraindication:

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

4.4 Special warning and precaution for use:

Convulsive seizures and peripheral neuropathy, the latter characterized mainly by numbness or paraesthesia of an extremity, have been reported in patients treated with Metronidazole. Metronidazole should be administered with caution to patients with central nervous system diseases.

4.5 Interactions with other medicinal products and other forms of interactions:

Patients should be advised not to take alcohol during therapy and for at least 48 hours afterwards because of the possibility of a disulfiram-like (antabuse effects) reaction.

Psychotic reactions have been reported in patients who were using Metronidazole and disulfiram concurrently.
Metronidazole can cause potentiation of anti-coagulant therapy when 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 metabolise 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 co administration is necessary.
Plasma levels of busulfan may be increased by Metronidazole which may lead to severe busulfan toxicity.

Additional information on special populations:
Not Applicable

Paediatric population:
Not Applicable

4.6 Fertility, 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, 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.

4.7 Effects on ability to drive and use machines:
Patients should be warned about the potential for drowsiness, dizziness, confusion, hallucinations, convulsions or transient visual disorders, and advised not to drive or operate machinery if these symptoms occur.

4.8 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, and pancytopenia

Not known: leucopenia.

Immune system disorders:

Rare: anaphylaxis,

Not known: angioedema, 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: diplopia, myopia, in most cases transient.

Not known: optic neuropathy/neuritis

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: abnormal liver function tests, cholestatic hepatitis, 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.
Musculoskeletal, connective tissue and bone disorders:
Very rare: myalgia, arthralgia.
Renal and urinary disorders:
Very rare: darkening of urine (due to metronidazole metabolite).

4.9 Overdose and Treatment:

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 over dosage. In cases of suspected massive overdose, symptomatic and supportive treatment should be instituted.

5. Pharmacological Properties:

5.1 Pharmacodynamic properties:

Metronidazole is active against a wide range of pathogenic micro-organisms 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.

5.2 Pharmacokinetic properties:

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.

5.3 Preclinical safety data:

Metronidazole has been shown to be carcinogenic in the mouse and in the rat following chronic oral administration however similar studies in the hamster have given negative results. Epidemiological studies have provided no clear evidence of an increased carcinogenic risk in humans.

Metronidazole has been shown to be mutagenic in bacteria in vitro. In studies conducted in mammalian cells in vitro as well as in rodent or humans in vivo, there was inadequate evidence of a mutagenic effect of Metronidazole, with some studies reporting mutagenic effects, while other studies were negative.

6. Pharmaceutical Particulars:

6.1 List of excipients

Metroren Tablet contains the following excipients:
Lactose, Maize starch (Mixing), Microcrystalline cellulose, Maize starch (Paste), Povidone K30, Sodium methyl paraben, Sodium propyl paraben, Colour Tartrazine supra, Magnesium stearate.

6.2 Incompatibilities

None known

6.3 Shelf life

24 months

6.4Special precaution for storage

Store in a cool, dry place below 30°C. Protect from light. Keep out of reach of children.

6.5 Nature and contents of container

10 tablets are packed in Aluminium/transparent PVC blister; such ten blisters are packed in a unit carton along with literature insert.

6.6Special precautions for disposal

No special precaution.

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESSES:

Marketing Authorization Holder:
Rene Industries Ltd
Address : PO Box 6034, Plot No.680, Kamuli, Kireka, Kampala, Uganda.

Manufactured by:
Rene Industries Ltd
Address : PO Box 6034, Plot No.680, Kamuli, Kireka, Kampala, Uganda.

8. MARKETING AUTHORISATION NUMBER:
Not Applicable

9. DATE OF FIRST REGISTRATION/RENEWAL OF THE REGISTRATION:
Not Applicable

10. DATE OF REVISION OF THE TEXT:
Not Applicable

11. DOSIMETRY (IF APPLICABLE):
Not Applicable

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE):
Not Applicable