SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Metrozol 400 mg Tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 400 mg of Metronidazole.

Excipients with known effect: Lactose BP 96.00 mg per tablet.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Uncoated tablet.

Product description: Yellow, circular, flat bevelled edge tablet embossed 'COSMOS' on one side and MZ 400 with a breakline on the other side. The breakline is not intended for division of the tablet into two equal doses. The tablet should be swallowed whole and should not be broken or chewed.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

It is indicated in the prophylaxis and treatment of infections in which anaerobic bacteria have been identified or are suspected to be the cause.

1. The prevention of post-operative infections due to anaerobic bacteria, particularly species of Bacteroides and anaerobic streptococci.

2. The treatment of septicaemia, bacteraemia, peritonitis, brain abscess, necrotising pneumonia, osteomyelitis, puerperal sepsis, pelvic abscess, pelvic cellulitis, and post-operative wound infections from which pathogenic anaerobes have been isolated.

3. Urogenital trichomoniasis in the female (trichomonal vaginitis) and in the male.

4. Bacterial vaginosis (also known as non-specific vaginitis, anaerobic vaginosis or Gardnerella vaginitis).

5. All forms of amoebiasis (intestinal and extra-intestinal disease and that of symptomless cyst passers).

6. Giardiasis.

7. Acute ulcerative gingivitis.

8. Anaerobically-infected leg ulcers and pressure sores.

9. Acute dental infections (e.g. acute pericoronitis and acute apical infections).

4.2 Posology and method of administration

Posology

Prophylaxis against anaerobic infection: Chiefly in the context of abdominal (especially colorectal) and gynaecological surgery.

Adults: 400 mg 8 hourly during 24 hours immediately preceding operation followed by postoperative intravenous or rectal administration until the patient is able to take tablets.

Children: Children < 12 years: 20-30 mg/kg as a single dose given 1-2 hours before surgery. Newborns with a gestation age < 40 weeks: 10 mg/kg body weight as a single dose before operation.

Anaerobic infections: The duration of a course of treatment is about 7 days but it will depend upon the seriousness of the patient's condition as assessed clinically and bacteriologically.

Treatment of established anaerobic infection:

Adults: 800 mg followed by 400 mg 8 hourly.

Children > 8 weeks to 12 years of age: The usual daily dose is 20-30 mg/kg/day as a single dose or divided into 7.5 mg/kg every 8 hours. The daily dose may be increased to 40 mg/kg, depending on the severity of the infection. Duration of treatment is usually 7 days.

Children < 8 weeks of age: 15 mg/kg as a single dose daily or divided into 7.5 mg/kg every 12 hours. In newborns with a gestation age < 40 weeks, accumulation of metronidazole can occur during the first week of life, therefore the concentrations of metronidazole in serum should preferably be monitored after a few days of therapy.

Method of Administration

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

4.3 Contraindications

Known hypersensitivity to nitroimidazoles, metronidazole or any of the excipients.

4.4 Special warnings and precautions for use

Regular clinical and laboratory monitoring (especially leucocyte count) are advised if administration of 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.

Cases of severe bullous skin reactions such as Stevens Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) or acute generalised exanthematous pustulosis (AGEP) have been reported with metronidazole. If symptoms or signs of SJS, TEN or AGEP are present, Metrozol treatment must be immediately discontinued.

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.

Metrozol contains lactose and therefore patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

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 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.

4.6 Fertility, pregnancy and lactation

Pregnancy

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 Metrozol, like other medicines, should not be given during pregnancy unless considered essential by a physician.

Lactation

Metrozol is contraindicated during lactation unless the physician considers it essential; in these circumstances the short, high-dosage regimens are not recommended.

Fertility

No evidential data disputing fertility safety.

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

Blood and lymphatic system disorders: Very rare: agranulocytosis, neutropenia, thrombocytopenia, 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 (e.g. confusion, fever, headache, hallucinations, paralysis, light sensitivity, disturbances in sight and movement, stiff neck) and subacute cerebellar syndrome (e.g. ataxia, dysarthria, 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.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are requested to report any suspected adverse reactions via the Pharmacy and Poisons Board, Pharmacovigilance Electronic Reporting System (PvERS):

https://pv.pharmacyboardkenya.org

4.9 Overdose

Single oral doses of metronidazole, up to 12 g, 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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Therapeutic class: Antibiotic and antiprotozoal drug.

ATC code: J01XD01.

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.

5.2 Pharmacokinetic properties

Metronidazole is rapidly and almost completely absorbed on administration of Metrozol tablets; peak plasma concentrations occur after 20 minutes 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

human in vivo studies, 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

- Lactose BP
- Maize starch BP
- Potassium sorbate BP
- Tartrazine yellow colour
- Stearic acid BP
- Aerosil BP
- Microcrystalline cellulose BP

Coating:

- Hypromellose BP
- Ethyl cellulose BP
- Diethyl phthalate BP
- Titanium dioxide BP
- Tartrazine yellow lake colour
- Isopropyl alcohol BP
- Dichloromethane BP
- Carnauba wax NF

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 30°C. Protect from light and moisture.

6.5 Nature and contents of container

PVC/Alu foil packed in blisters in unit cartons with literature insert. Available in pack sizes of 10 x 10 tablets and 1000 tablets.

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorization Holder

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8. Marketing Authorization Number

H1988/444/2671

9. Date of First Registration/Renewal of Registration

Date of First Registration: 10th July 1986

10. Date of Revision of Text

December 2025