1.6 Product Information

1.6.1 Prescribing information (Summary of Product Characteristics)

1. Name of the medicinal product

Tricozole Suspension

2. Qualitative and quantitative composition

Each 5ml contains: Metronidazole benzoate BP equivalent to Metronidazole 125mg.

3. Pharmaceutical form

Oral Suspension

4. Clinical Particulars

4.1 Therapeutic Indications

Tricozole or metronidazole preparations are indicated in the treatment of infections caused by pathogens sensitive/ susceptible to metronidazole as underlined above and specified in the dosage regime below:-

Tricozole or metronidazole preparations are administered orally for various conditions according to the following dosage regimens

1. Treatment of bacterial infections

Adults and children over 10 years: 800mg followed by 400mg at eight hourly intervals

Treatment is usually for 7 days but will depend upon the condition

2. Treatment of anaerobic infections

Children 8 weeks -12 years: 20-30mg/kg /day as a single dose or divided into 7.5mg/kg every 8 hours for 7 days

Children under 8 weeks: 15mg/kg /day as a single dose or divided into 7.5mg/kg every 12hours

3. Treatment of infection caused by Trichomonas

Adults and adolescents: 2g as a single dose, or 200mg three times a day for 7 days, or 400mg twice a day for 5 to 7 days

Both partners should also be treated

Children under 10 years: 40mg / kg as a single dose or 15-30mg /kg/day two to three times daily for 7 days

4. Treatment of non-specific genital infection in women:

400mg twice a day for 7 days, or 2g as a single dose for 5 to 10days

5. Treatment of amoebiasis

Adults and children over 10 years: 400mg -800mg three times a days for 5to 10days

Children 7-10 years: 200mg -400mg three times a day for 5 to 10 days

Children 3-7 years: 1000mg-200mg four times daily for 5-10 days

Children 1-3 years: 100mg -200mg three times daily for 5-10 days or 35-50mg/kg/day in 3 divided doses for 5-10 days

6. Treatment of giardiasis

Adults and children over 10 years: 2g once a day for 3 days, or 400mg three times a day for 5 days or 500mg twice daily for 7-10days

Children 7-10 years: 1g once a day for 3 days

Children 3-7 years: 600mg -800mg once daily for 3 days

Children 1-3 years : 500mg once daily for 3 days or 15-40mg/kg/day divided in two to three doses

7. Treatment of infections of the gums (for 3 days) or teeth (for 3-7days)

Adult and children over 10 years: 200mg three times a day

8. Treatment of infected leg ulcers or pressure sores (7days)

Adults and children over 10years: 400mg three times a day

Treatment of stomach ulcers caused by Helicobacter pylori to be taken as directed by your doctor as part of a course with two other medicines

9. Prevention of infections after surgery

Adults: 1g as a single dose 24hours before surgery then, 400mg at 8 hourly intervals during the 24hours before operation

Children under 12years: 20-30mg/kg as a single dose 1-2 hours before the operation

Newborns with a gestation age less than 40 weeks: A more suitable dosage form should be used

Note: If you are elderly or have liver disease, it is particularly important to take this medicine exactly as directed by the doctor

4.2 Posology and method of administration

Posology

For oral administration.

1. Treatment of bacterial infections

Adults and children over 10 years: 800mg followed by 400mg at eight hourly intervals

Treatment is usually for 7 days but will depend upon the condition

2. Treatment of anaerobic infections

Children 8 weeks -12 years: 20-30mg/kg /day as a single dose or divided into 7.5mg/kg every 8 hours for 7 days

Children under 8 weeks: 15mg/kg /day as a single dose or divided into 7.5mg/kg every 12hours

3. Treatment of infection caused by Trichomonas

Adults and adolescents: 2g as a single dose, or 200mg three times a day for 7 days, or 400mg twice a day for 5 to 7 days

Both partners should also be treated

Children under 10 years: 40mg / kg as a single dose or 15-30mg /kg/day two to three times daily for 7 days

4. Treatment of non-specific genital infection in women:

400mg twice a day for 7 days, or 2g as a single dose for 5 to 10days

5. Treatment of amoebiasis

Adults and children over 10 years: 400mg -800mg three times a days for 5to 10days

Children 7-10 years: 200mg -400mg three times a day for 5 to 10 days

Children 3-7 years: 1000mg-200mg four times daily for 5-10 days

Children 1-3 years: 100mg -200mg three times daily for 5-10 days or 35-50mg/kg/day in 3 divided doses for 5-10 days

6. Treatment of giardiasis

Adults and children over 10 years: 2g once a day for 3 days, or 400mg three times a day for 5 days or 500mg twice daily for 7-10days

Children 7-10 years: 1g once a day for 3 days

Children 3-7 years: 600mg -800mg once daily for 3 days

Children 1-3 years : 500mg once daily for 3 days or 15-40mg/kg/day divided in two to three doses

7. Treatment of infections of the gums (for 3 days) or teeth (for 3-7days)

Adult and children over 10 years: 200mg three times a day

8. Treatment of infected leg ulcers or pressure sores (7days)

Adults and children over 10years: 400mg three times a day

Treatment of stomach ulcers caused by Helicobacter pylori to be taken as directed by your doctor as part of a course with two other medicines

9. Prevention of infections after surgery

Adults: 1g as a single dose 24hours before surgery then, 400mg at 8 hourly intervals during the 24hours before operation

Children under 12years: 20-30mg/kg as a single dose 1-2 hours before the operation

Newborns with a gestation age less than 40 weeks: A more suitable dosage form should be used

Note: If you are elderly or have liver disease, it is particularly important to take this medicine exactly as directed by the doctor

4.3 Contraindications

First trimester of pregnancy and patients with history of hypersensitivity to metronidazole of Nitroimidazole derivatives.

4.4 Special Warnings and Precautions for Use

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

There is the 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 (IPD) 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 encephalopathy.

Metronidazole should be administered with caution to patients with hepatic encephalopathy. The daily dosage may be reduced to one third and may be administered once daily.

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.

Patients should be warned that metronidazole may darken urine.

Due to inadequate evidence on the mutagenicity risk in humans (see section 5.3), the use of Metronidazole for longer treatment than usually required should be carefully considered.

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.

4.5 Interaction with other medicinal products and other forms of Interaction

Metronidazole potentiates anticoagulant effect of warfarin and other coumarin anticoagulants. Drugs that induce microsomal liver enzymes such as phenytoin or phenobarbitone will accelerate elimination of metronidazole resulting in reduced plasma concentrations while those drugs that decrease the activity of the enzymes such as cimetidine will have the opposite effect

4.6 Pregnancy and Lactation

There is inadequate evidence of the safety of metronidazole in pregnancy. Metronidazole should not therefore be given during pregnancy or during lactation unless the physician considers it essential, in these circumstances short, high dosage regimes are not recommended.

A significant amount of metronidazole is found in breast milk and breast feeding should be avoided after a large dose. This could give a bitter taste to the milk.

4.7 Effects on Ability to Drive and Use Machines

None unknown

4.8 Undesirable Effects

4.9 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

4.10 Overdose and treatment

Below are the symptoms of overdose

- Nervous system effects, including seizures and encephalopathy (abnormal brain function).

Symptoms can include:

- Convulsions (sudden movements caused by tightening of your muscles)
- Dizziness
- Headache
- Confusion
- Ataxia (loss of control of body movements)

5. Pharmacological properties

5.1 Pharmacodynamic properties

ATC Code: P01AB01

Metronidazole is a 5-nitroimidazole derivative with a fairly broad antimicrobial activity. Metronidazole has cidal activity against anaerobic protozoa which includes Balantidium *coli,Blastocystis hominis,Trichomonas vaginalis,Entamoeba Histolytica, Glardia intestinalis (formerly G lamblia)* and the causative organisms of acute ulcerative gingivitis. Metronidazole has bactericidal activity against all obligate anaerobic bacteria and some facultative anaerobic bacteria. Clostridia and susceptible strains of Eubacterium are among the anaerobic Gram positive bacilli sensitive to metronidazole. Anaerobic Gram positive cocci sensitive to metronidazole include peptococci and peptostreptococci. The facultative anaerobes that are sensitive to metronidazole are Gardnerella vaginalis, Helicobacter'pylori and some spirochaetes.

5.2 Pharmacokinetic properties

Metronidazole is completely and promptly absorbed when given orally, the plasma concentration having a linear relationship with the dose for doses between 200-2000mg. About 10% of the metronidazole is bound to plasma proteins. It has a half-life of about 8 hours in the plasma and repeated doses every 6-8 hours results in some accumulation. It is widely distributed in the body and penetrates well into most body tissues and fluids, which include vagina secretions, seminal secretions, saliva, breast milk and celebralspinal fluid. Over 50% if systemic metronidazole is metabolized in the liver into two major metabolites both of which have antitrichomonal activity. A good percentage of the drug is excreted unchanged in urine.

Metronidazole is thought to be concentrated in susceptible cells and organisms into chemically reactive reduced forms, which give rise to cytotoxic products.

Reduced forms of metronidazole have been shown to cause loss of helical structure and strand breakage in DNA thus impairing its function. Mutagenic effects of metronidazole and its ability to potentiate the effects of radiation on hypoxic tumour cells is probably due to the reduced forms

5.3 Preclinical safety data

Not applicable

6. Pharmaceutical Particulars

6.1 List of Excipients

- Sodium Methyl Paraben
- Sodium Propyl Paraben
- Xanthan Gum
- Colloidal Silicon Dioxide
- Sodium Saccharin
- Polysorbate 80
- Strawberry Essence
- Citric Acid
- Sodium CMC
- Silicon Emulsion
- Tartrazine Colour
- Purified Water

6.2 Incompatibilities

None known.

6.3 Shelf Life

36 months from the date of manufacture

6.4 Special Precautions for Storage

Store below 30°C in a dry place.

6.5 Nature and Contents of Container

Yellow, viscous, homogenous free flowing suspension. Packed in 100ml /60ml amber glass/PET bottle and contained in a unit box with literature insert

6.6 Special precaution for disposal and other handling

Not applicable

MODULE 1	:	ADMINISTRATIVE INFORMATION & PRODUCT INFORMATION

7 Marketing Authorization Holder and Manufacturing Site Addresses
Marketing Authorization Holder:

Company Name: LABORATORY & ALLIED LTD

Address: Plot No. 209/10349, Opposite Sameer Business Park, Next to Libra House, Mombasa road, P.O. Box 42875 GPO 00100, Nairobi,

Country : Kenya

Telephone : +254 20 8040306

Telefax : +254 20 8040309

E-Mail : info@laballied.com.

Manufacturing Site Address:

Company Name: LABORATORY & ALLIED LTD

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Country : Kenya

Telephone : +254 20 8040306

Telefax : +254 20 8040309

E-Mail : info@laballied.com

8 Marketing Authorization Number:
KENYA: H2013/CTD923/136

9 Date of first Registration/ Renewal of the Registration:
KENYA: 25/03/2013

10 Date of revision of the text:
April 2019