SUMMARY PRODUCT CHARACTERISTICS (SmPC)

1. NAME OF THE MEDICINAL PRODUCT

DIAZOLE SUSPENSION

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml contains:

Diloxanide Furoate BP.....125 mg

Metronidazole Benzoate BP

Eq. to Metronidazole .....100 mg

Flavored Syrupy Base.....q.s

Color: Tartrazine

Excipients of known effect (s): Each 5mL contains Sodium Methyl Hydroxy 11.0 mg, Benzoate Sodium Propyl Hydroxy Benzoate 2.20mg, and Bronopol 2.20mg

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Oral Suspension

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

Acute amoebiasis, Chronic amoebiasis, Hepatic amoebiasis and other systemic diseases due to E. histolytica, Giardiasis.

4.2.Posology and Method of Administration

Posology

A: **Prophylaxis***:* against anaerobic infection- chiefly in the context of abdominal (especially colorectal) and gynaecological surgery.
Dosage: 200mg at 8-hourly intervals during the 24 hours preceding the operation, followed by postoperative intravenous or rectal administration until the patient is able to take Metronidazole

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

Elderly: Caution is advised in the elderly, particularly at high doses, although there is limited information available on modification of drug.

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

B: **Treatment of established anaerobic infection:**
400mg followed by 200mg at 8-hourly intervals.

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

Children < 8 weeks of age: 15mg/kg as a single dose daily or divided into 7.5mg/kg every 12 hours.

In newborns with a gestation age <40 weeks, accumulation of metronidazole can occur during the first week of life, which is why the concentrations of metronidazole in serum should preferably be monitored after a few days of therapy.

Method of administration
Oral Suspension by mouth.

4.3. Contraindications

Hypersensitivity to Diazole Suspension is a contraindication. In addition, diazole suspension should not be used if you have the following conditions:
Alcohol, Alcohol intoxication, Habit of drinking too much alcohol, Liver disease, Lower seizure threshold, Seizures, Tingling or pain of hands or feet.

4.4. Special Warnings and Precautions for Use

Before using diazole Suspension, inform your doctor about your current list of medications, over the counter products (e.g. vitamins, herbal supplements, etc.), allergies, pre-existing diseases, and current health conditions (e.g. pregnancy, upcoming surgery, etc.). Some health conditions may make you more susceptible

to the side-effects of the drug. Take as directed by your doctor or follow the direction printed on the product insert. Dosage is based on your condition. Tell your doctor if your condition persists or worsens. Important counselling points are listed below.
- Breastfeeding, Children less than 2 years of age, Dermatitis, Extra-intestinal amebiasis, Peripheral neuropathy, Pregnancy, Symptomatic intestinal amebiasis, Systemic metronidazole.

4.5. Interaction with Other Medicinal Products and Other Forms of Interaction

If you use other drugs or over-the-counter products at the same time, the effects of Diazole Suspension may change. This may increase your risk for side effects or cause your drug not to work properly. Tell your doctor about all the drugs, vitamins, and herbal supplements you are using, so that your doctor can help you prevent or manage drug interactions. Diazole Suspension may interact with the following drugs and products:
- Alcohol, Anticoagulants, Antimicrobials, Cyclosporin, Cimetidine, Fluorouracil, Lithium, Phenobarbital or phenytoin, Phenytoin.

4.6. Pregnancy and Lactation

There is inadequate evidence of the safety of metronidazole and diloxanide furoate in pregnancy. Metronidazole and diloxanide furoate 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 and diloxanide furoate 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 machine:

N/A

4.8. Undesirable Effects

The following is a list of possible side-effects that may occur from all constituting ingredients of diazole Suspension. This is not a comprehensive list. These side effects are possible, but do not always occur. Some of the side-effects may be rare but serious. Consult your doctor if you observe any of the following side-effects, especially if they do not go away.

- Anorexia, Headache, Dizziness, Flatulence, Vomiting, Nausea, Diarrhoea, Abdominal cramps, Pruritus, Urticaria, Diarrhea, Fever, Joint or muscle pain, Brain disease, Unpleasant metallic taste, Furred tongue, Gastrointestinal disturbances, Darkening of urine, Blurred or double vision, Numbness, Upset stomach, Pain in your eyes, Feeling sick and weak, Skin rashes, Redness, Loss of appetite, Sleepiness or dizziness, Tingling, Fits, Confusion, Hallucinations, Metallic taste, Dryness of mouth, Disease affecting nerves, Hypersensitivity reactions, diazole Suspension may also cause side-effects not listed here.

If you notice other side-effects not listed above, contact your doctor for medical advice. You may also report side-effects to your local food and drug administration authority.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the National Regulatory Authority pharmacovigilance reporting channels.

4.9. Overdose

- Do not use more than prescribed dose. Taking more medication will not improve your symptoms; rather they may cause poisoning or serious side-effects. If you suspect that you or anyone else who may have overdosed of diazole Suspension, please go to the emergency department of the closest hospital or nursing home. Bring a medicine box, container, or label with you to help doctors with necessary information.

- Do not give your medicines to other people even if you know that they have the same condition or it seems that they may have similar conditions. This may lead to overdosage.
- Please consult your physician or pharmacist or product package for more information.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic Properties

Pharmacotherapeutic group: Antibiotic and Amoebicide

ATC codes: **Metronidazole - J01XD01 and**

Diloxanide furoate - P01AC01

Metronidazole

Metronidazole treats amebiasis, trichomoniasis, and giardiasis, exerting both antibacterial and antiprotozoal activities. Metronidazole is an effective treatment for some anaerobic bacterial infections. Metronidazole has shown antibacterial activity against the majority of obligate anaerobes, however, during in vitro studies, it does not demonstrate significant action against facultative anaerobes or obligate aerobes. The nitro group reduction of metronidazole by anaerobic organisms is likely responsible for the drug's antimicrobial cytotoxic effects, causing DNA strand damage to microbes.

A note on convulsions and neuropathy and carcinogenesis

It is important to be aware of the risk of peripheral neuropathy and convulsions associated with metronidazole, especially at higher doses. If convulsions or numbness of an extremity occur, discontinue the drug immediately. Metronidazole has been found to be carcinogenic in mice and rats. The relevance to this effect in humans is unknown. It is advisable to only administer metronidazole when clinically necessary and only for its approved indications.

Diloxanide Furoate

Diloxanide is a luminal amebicide, however the mechanism of action of diloxanide is unknown. Diloxanide destroys the trophozoites of E. histolytica that eventually form into cysts. The cysts are then excreted by persons infected with asymptomatic amebiasis. Diloxanide furoate is a prodrug, and is hydrolyzed in the gastrointestinal tract to produce diloxanide, the active ingredient.

5.2. Pharmacokinetic Properties

Metronidazole

Absorption: After the intravenous infusion of a 1.5g dose, peak concentration was reached within 1 hour and was peak level of 30-40 mg/L.[16] When a multiple-dose regimen of 500mg three times a day administered intravenously, steady-state concentrations were achieved within about 3 days and peak concentration was measured at 26 mg/L.[16] When administered orally in the tablet form, metronidazole is absorbed entirely absorbed, showing a bioavailability of greater than 90%.[7] One resource indicates that Cmax after a single oral dose of 500mg metronidazole ranges from 8 to 13 mg/L, with a Tmax of 25 minutes to 4 hours. The AUC following a single 500mg oral dose of metronidazole was 122 ± 10.3 mg/L • h.[7]

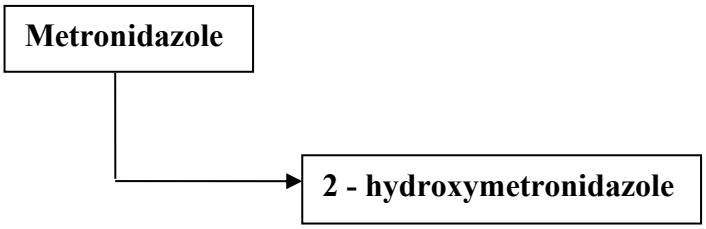
A note on the absorption of topical preparations

Insignificant percutaneous absorption of metronidazole occurs after the application of 1% metronidazole cream topically. Healthy volunteers applied one 100 mg dose of 14C-labelled metronidazole 2% cream to unbroken skin. After 12 hours, metronidazole was not detected in the plasma. Approximately 0.1% to 1% of the administered metronidazole was measured in the urine and feces.

Metabolisam: Metronidazole undergoes hepatic metabolism via hydroxylation, oxidation, and glucuronidation. The metabolism of metronidazole yields 5 metabolites. The hydroxy metabolite, 1-(2-hydroxy-ethyl)-2-hydroxy methyl-5-nitroimidazole, is considered the major active metabolite. Unchanged metronidazole is found in the plasma along with small amounts of its 2-hydroxymethyl metabolite. Several metabolites of metronidazole are found in the urine. They are primarily a product of side-chain oxidation in addition to

glucuronide conjugation. Only 20% of the dose found in the urine is accounted for by unchanged metronidazole. The two main oxidative metabolites of metronidazole are hydroxy and acetic acid metabolites.

Hover over products below to view reaction partners



Elimination: Metronidazole and metabolites are 60 to 80% eliminated in the urine, and 6-15% excreted in the feces.

Diloxanide Furoate

Absorption**:** Bioavailability is 90% (in diloxanide parental form), however diloxanide furoate is slowly absorbed from the gastrointestinal tract.

Metabolism: Hydrolyzed to furoic acid and diloxanide, which undergoes extensive glucuronidation (99% of diloxanide occurs as glucuronide and 1% as free diloxanide in the systemic circulation).

Elimination: Renal (90%, rapidly excreted as glucuronide metabolite). 10% is excreted in the feces as diloxanide.

5.3. Preclinical safety data

N/A

6. PHARMACEUTICAL PARTICULARS

6.1. List of Excipients

- Xanthan gum

- Sodium Methyl Hydroxybenzoate
- Sodium Propyl Hydroxybenzoate
- Bronopol
- Sucrose
- Glycerin
- Sorbitol Solution 70%
- Polysorbate-80 (Tween-80)
- Colloidal Silicon Dioxide
- Citric Acid
- Colour: Tartrazine FCF
- ESS: Mixed fruit S3212
- Purified Water

6.2. Incompatibilities:
Not Applicable

6.3. Shelf Life:
36 Months

6.4. Special Precautions for Storage:
Store at a temperature not exceeding 30^0C. Protect from light.

6.5. Nature and Contents of Container
100 ml suspension packed in a PET amber bottle affixed with a coded label has batch number, manufacturing date and expiry date packed in unit box with an insert and 10 ml measuring cap.

7. MARKETING AUTHORIZATION HOLDER

Marketing Authorization Holder:
NATIONAL PHARMACY LIMITED
P.O.BOX 17843 – 005, NAIROBI

Manufactured by:
ZAIN PHARMA LIMITED
Plot No. 209/13741,
Colchester Park, Go down No. 1,2,3,
P.O. Box 100167-00101
Nairobi, Kenya.

8. Marketing authorization number(s)

H2025/CTD9231/21071

9. Date of first authorization/renewal of the authorization

25 ay 2026

10. Date of revision of the text

Date of review: 12.04.2021