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Zolen™ DS Tablets / Zolen™ Suspension

(Diloxanide Furoate + Metronidazole) / (Diloxanide Furoate + Metronidazole Benzoate)

QUALITATIVE AND QUANTITATIVE COMPOSITION

Zolen™ DS Tablets	Zolen™ Suspension
Each film coated tablet contains:	Each 10ml contains: Diloxanide Furoate USP..... 250mg
Diloxanide Furoate USP 500mg	Metronidazole Benzoate BP.....320mg
Metronidazole BP.....400mg	equivalent to Metronidazole 200mg

Zolen™ is indicated in the treatment of amoebiasis offering therapeutic benefits. It is a combination of diloxanide and metronidazole, a luminal ameobicide. **Zolen™** thus contains a potent and comprehensive therapy for all forms of amoebiasis.

PHARMACEUTICAL FORM
Tablets and Suspension

CLINICAL PARTICULARS
THERAPEUTIC INDICATIONS:
Acute amoebic dysentery, chronic intestinal amoebiasis, giardiasis, hepatic amoebiasis and other systemic diseases due to E. histolytica.

POSOLOGY AND METHOD OF ADMINISTRATION:
Tablets: The recommended dosage of **Zolen™ DS** for adults is 1 tablet thrice daily for 5 days or as prescribed by the physician.

In refractory cases the treatment can be up to continued 10 days, if prescribed by the physician.
Prolonged administration e.g. as a prophylaxis is not recommended.

Suspension: The recommended dosage for:
Children aged one to 5 years:
5ml (one teaspoonful) thrice daily for 5 days or as prescribed by the physician.

Children aged 5 to 12 years:
5-10ml (one-two teaspoonfuls) thrice daily for 5 days or as prescribed by the physician.

Adults and children over 12 years:
10-20ml (two-four teaspoonfuls) thrice daily for 5 days or as prescribed by the physician.
In refractory cases the treatment can be continued up to 10 days, if prescribed by the physician.
Prolonged administration e.g. as a prophylaxis is not recommended.

CONTRAINDICATIONS:
- Hypersensitivity to the active substance or to any of the excipients.
- Avoid during pregnancy and breast feeding.
- Prolonged administration for e.g. as a prophylactic is not recommended.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE:
Metronidazole:
- Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take **Zolen™ DS** tablets as this product contains lactose.
- Patients should abstain from alcohol for at least 48 hours following discontinuation of therapy with metronidazole. A disulfiram-like reaction with hypotension and flushing has occurred.
- Caution is advised in patients with porphyria.
- Metronidazole tablets should not be used in patients with blood dyscrasias or with active non-infectious disease of the central nervous system. High doses of metronidazole may mask the presence of syphilis.
- Caution in patients with epilepsy or those who have had seizures as high doses of metronidazole can induce seizures. Consideration of the therapeutic benefit against the risk of peripheral neuropathy is advised with continuous therapy for chronic conditions.
- Regular clinical and laboratory surveillance are advised if treatment continues for more than 10 days.
- Use with caution in the second and third trimester when used to treat trichomoniais or bacterial vaginosis.

Renal:
- The elimination half-life of metronidazole remains unchanged in the presence of renal failure. The dosage of metronidazole, therefore, needs no reduction.
- In patients undergoing hemodialysis metronidazole and metabolites are efficiently removed during an eight-hour period of dialysis. Metronidazole should, therefore, be re-administered immediately after hemodialysis. 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).

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTIONS:
Metronidazole: Interactions to be used with caution:
Lithium: 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 concentration of lithium, creatinine, and electrolytes should be monitored in patients under treatment with lithium while they receive metronidazole.
- **Anticoagulants:** 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. No interactions have been reported with anticoagulants of the heparin type. However, anticoagulant activity should be routinely monitored with these products.
- Disulfiram like reaction.
- Psychotic reactions have been reported.
- Immunosuppressants: Patients receiving cyclosporine are at risk of elevated cyclosporine serum levels. Serum cyclosporine and serum creatinine should be closely monitored when co administration is necessary.

Pharmacokinetic Interactions:
- **Antiepileptics:** Patients receiving phenobarbital metabolise metronidazole at a much greater rate than normally, reducing the half-life to approximately 3 hours. Metronidazole inhibits metabolism of phenytoin (increases plasma-phenytoin concentration). Primidone accelerates the metabolism of metronidazole causing reduced plasma concentrations.
- **Cytotoxics:** Metronidazole inhibits metabolism of fluorouracil. Therefore, increased toxicity of fluorouracil can result. Plasma levels of busulfan may be increased by metronidazole which may lead to severe busulfan toxicity.
- **Ulcer-healing drugs:** Cimetidine inhibits the metabolism of metronidazole (increases plasma-metronidazole concentration).
- **Oestrogens:** broad spectrum antibiotics possibly reduce the contraceptive effect.
- **Drug-lab modifications:** Aspartate amino transferase assays may give spuriously low values in patients taking metronidazole, depending on the method used.

FERTILITY, PREGNANCY AND LACTATION:
There is inadequate evidence of the safety of metronidazole in pregnancy. Metronidazole should not be given during pregnancy or during lactation unless it is considered essential.

UNDESIRABLE EFFECTS:
- **Hypersensitivity:** Urticaria , Itching, rashes , anaphylaxis.
- **Gastrointestinal (GI) System:** Anorexia, metallic taste, dry mouth nausea, vomiting, abdominal distress/ flatulence, diarrhoea, looseness of stool.
- **Central Nervous system:** Headache, confusion, dizziness, vertigo, hallucinations, encephalopathy (rare), light sensitivity, disturbances in sight and movement, stiff neck) and subacute cerebellar syndrome (e.g. ataxia, dysathria, gait impairment, nystagmus and tremor) which may resolve in discontinuation of the drug, drowsiness, dizziness, convulsions.
- **Blood Disorders:** Agranulocytosis, neutropenia, thrombocytopenia, pancytopenia, leucopenia.
- **Eye Disorders:** Diplopia, myopia (very rare).
- **Musculoskeletal, connective tissue and bone disorders:** Myalgia, arthralgia.

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OVERDOSAGE:
Early gastric lavage is recommended for gross overdosage. There is no specific treatment.

PHARMACOLOGICAL PROPERTIES
MECHANISM OF ACTION:
Metronidazole has antiprotozoan and antibacterial effects. It effects against Trichomonas vaginalis, Gardnerella vaginalis and other protazoa including Entamoeba histolytica, Gardia lamblia and anaerobic bacteria.
Diloxanide is Luminal ameobicide. The mechanism of action of diloxanide is unknown.This agent destroys the trophozoites of E. histolytica that eventually form into cysts. The cysts are then excreted by persons infected with asymptomatic ameobiasis.

Absorption: Metronidazole is readily absorbed following administration by mouth and bioavailability is 90-100%. Peak plasma concentrations occur after 20 minutes to 3 hours. Absorption may be delayed, but is not reduced overall, by administration with food.
Diloxanide furoate is slowly absorbed from the gastrointestinal tract and can therefore provide an adequate concentration of the medication in the intestinal lumen for a long period of time, however, the parent compound, diloxanide, is rapidly absorbed and has a bioavailability of approximately 90%.

Distribution: Metronidazole is widely distributed. It appears in most body tissues and fluids. It also crosses the placenta and rapidly enters foetal circulation. No more than 20% is bound to plasma proteins.

Biotransformation: Metronidazole is metabolised in the liver by side-chain oxidation and glucuronide formation. The half-life of metronidazole is 6.5 ± 2.9 hours. The half-life of metronidazole is reported to be longer in neonates and in patients with severe liver disease.
Diloxanide furoate is largely hydrolyzed into diloxanide and furoic acid in the intestinal lumen before being absorbed. The absorbed diloxanide is extensively conjugated with glucuronic acid, this conjugate being inactive. 99% of diloxanide occurs as glucuronide and 1% as free diloxanide in the systemic circulation.

Elimination: The majority of a dose of metronidazole is excreted in the urine, mainly as metabolites; a small amount appears in the feces.
Approximately 90% of diloxanide is rapidly excreted in the urine as the glucuronide metabolite. Fecal is about 10%.

SHELF LIFE:
See expiry on the pack.

AVAILABILITY
Zolen™ DS tablets in a pack of 15's
Zolen™ suspension in a pack of 90ml

INSTRUCTIONS
Dosage: As advised by the physician.
To be sold on the prescription of registered medical practitioner.
Keep out of reach of children.
Avoid exposure to heat, light, humidity and freezing.
Store between 15 to 30°C.
Improper storage may deteriorate the medicine.

زولن ڈی ایس ٹیبلٹ (ڈائلوگزنائیڈ فیوریٹ + میٹرونیڈازول)
زولن سسپینشن (ڈائلوگزنائیڈ فیوریٹ + میٹرونیڈازول بینزویٹ)

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔
بچوں کی پہنچ سے دور رکھیں۔
دوا کو دھوپ، گرمی، نمی اور منجمد ہونے سے محفوظ ۱۵ سے ۳۰ ڈگری سینٹی گریڈ کے درمیان میں رکھیں ورنہ دوا خراب ہو جائیگی۔

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