1.6.1.1 Name of the medicinal Product

1.6.1.1.1 strength

TINIDAZOLE TABLETS

1.6.1.1.2 Pharmaceutical Form

Oral Tablet

1.6.1.2 Qualitative and Quantitative Composition

1.6.1.2.1 Qualitative declaration

Tinidazole BP

1.6.1.2.2 Quantitative declaration

Sr. No.	Ingredients	Specifications	Label Claim (mg/Tablet)	Reason for Inclusion
1.	Tinidazole	BP	500.000	Anti Parasitic
2.	Lactose (Lactose Monohydrate)	BP	60.000	Diluent
3.	Povidone (P.V.P K-30)	BP	10.000	Binder
4.	Maize starch	BP	30.000	Diluent
5.	Sodium Starch Glycolate (TYPE-A)	BP	12.000	Disintegrant
6.	Purified Talc	BP	6.000	Glidant
7.	Colloidal Anhydrous silica (Aerosil)	BP	7.000	Glidant
8.	Sodium Lauryl sulphate	BP	4.000	surfactant
9.	Microcrystalline Cellulose (PH 101)	BP	66.000	Diluent
10.	Magnesium Stearate	BP	5.000	Lubricant
11.	Colour White SC-SP 3180 (Spraycel)	In-House	20.000	Colouring Agent

12.	Purified Water	BP	Q.S.	Vehicle

1.6.1.3 Pharmaceutical Form

Oral Tablet

White coloured, capsule shaped, film coated tablets, plain both side.

1.6.1.4 Clinical Particulars

1.6.1.4.1 Therapeutic Indications

Tinidazole is indicated for the treatment of trichomoniasis caused by Trichomonas vaginalis; giardiasis caused by Giardia duodenalis (G. lamblia); intestinal amebiasis and amebic liver abscess caused by Entamoeba histolytica; and bacterial vaginosis caused by Bacteroides spp, Gardnerella vaginalis, and Prevotella spp in non pregnant females.

1.6.1.4.2 Posology and Method of Administration

Adults:

Trichomoniasis: 2 g as a single dose; sexual partners should be treated at the same time.

Giardiasis: 2 g as a single dose.

Amebiasis, intestinal: 2 g/day for 3 days.

Amebiasis, liver abscess: 2 g/day for 3-5 days.

Bacterial vaginosis: 2 g/day for 2 days or 1 g/day for 5 days.

Pediatrics (Children >3 years):

Amebiasis, intestinal: 50 mg/kg/day for 3 days (maximum dose: 2 g/day)

Amebiasis, liver abscess: 50 mg/kg/day for 3-5 days (maximum dose: 2 g/day)

Giardiasis: 50 mg/kg as a single dose (maximum dose: 2 g)

Elderly:

Refer to adult dosing.

1.6.1.4.3 Contraindications

Tinidazole is contraindicated in patients with a previous history of Hypersensitivity to Tinidazole or other 5-nitroimidazole derivatives.

1.6.1.4.4 Special Warnings and Special Precautions for Use

Convulsive seizures and peripheral neuropathy, the latter characterized mainly by numbness or paresthesia of an extremity, have been reported in patients treated with Tinidazole. The appearance of abnormal neurologic signs demands the prompt discontinuation of Tinidazole therapy.

Tinidazole should be used with caution in patients with evidence of or history of blood dyscrasia.

Prolonged use may result in fungal or bacterial superinfection, including C. difficile-associated diarrhea (CDAD), pseudomembranous colitis, and/or vaginal candidiasis. CDAD has been observed >2 months postantibiotic treatment.

Pregnancy: Pregnancy Category C

Tinidazole crosses the placental barrier. Since the effects of compounds of this class on fetal development are unknown, the use of Tinidazole during the first trimester is contraindicated.

There is no evidence that Tinidazole is harmful during the latter stages of pregnancy, but its use during the second and third trimesters requires that the potential benefits be weighed against possible hazards to mother or fetus.

Lactation: Tinidazole is excreted in breast milk in concentrations similar to those seen in serum. Tinidazole can be detected in breast milk for up to 72 hours after administration. Interruption of breast-feeding is recommended during Tinidazole therapy and for 3 days following the last dose.

Pediatrics: Other than for use in the treatment of giardiasis and amebiasis in pediatric patients older than three years of age, safety and effectiveness of tinidazole in pediatric patients have not been established.

Patients with renal impairment: Dosage adjustments in patients with impaired renal function are generally not necessary. However because Tinidazole is easily removed by haemodialysis, patients may require additional doses of Tinidazole to compensate.

Patients with hepatic impairment: Use with caution in patients with current or a history of hepatic impairment.

Effects on Ability to Drive and Use Machines: None.

1.6.1.4.5 Interaction with other medicinal products and other forms of interaction

Alcohol: concurrent use of tinidazole and alcohol may produce a disulfiram-like reaction and should be avoided.

Anticoagulants: Drugs of similar chemical structure have been shown to potentiate the effects of oral anticoagulants. Prothrombin times should be closely monitored and adjustments to the dose of the anticoagulant should be made as necessary.

Conivaptan: May increase the serum concentration of CYP3A4 Substrates.

Tocilizumab: May decrease the serum concentration of CYP3A4 Substrates.

1.6.1.4.6 Fertility, Pregnancy and Lactation

Pregnancy: Pregnancy Category C

Tinidazole crosses the placental barrier. Since the effects of compounds of this class on fetal development are unknown, the use of Tinidazole during the first trimester is contraindicated. There is no evidence that Tinidazole is harmful during the latter stages of pregnancy, but its use during the second and third trimesters requires that the potential benefits be weighed against possible hazards to mother or fetus.

Lactation: Tinidazole is excreted in breast milk in concentrations similar to those seen in serum. Tinidazole can be detected in breast milk for up to 72 hours after administration. Interruption of breast-feeding is recommended during Tinidazole therapy and for 3 days following the last dose.

1.6.1.4.7 Effects on ability To Drive and use Machines

None.

1.6.1.4.8 Undesirable Effects

Reported side effects have generally been infrequent, mild and self-limiting.

Nervous System: convulsions (rarely), dizziness, headache, peripheral neuropathy, sensory disturbances, vertigo, flushing.

Gastrointestinal disorders: abdominal pain, anorexia, diarrhea, nausea, vomiting

Skin and subcutaneous tissue disorders: hypersensitivity reactions, occasionally severe, may occur in rare cases in the form of skin rash, puritus, urticaria and angioneurotic edema

Renal and Urinary disorders: dark urine

Blood and lymphatic system disorders: transient leukopenia

1.6.1.4.9 Overdose

There are no reported overdoses with tinidazole in humans.

Treatment of Overdose: There is no specific antidote for the treatment of overdosage with tinidazole. Treatment is symptomatic and supportive. Gastric lavage may be useful. Tinidazole is easily dialyzable

1.6.1.5 Pharmacological Properties

1.6.1.5.1 Pharmacodynamics Properties

Tinidazole is an antiprotozoal, antibacterial agent. The nitro- group of tinidazole is reduced by cell extracts of Trichomonas. The free nitro- radical generated as a result of this reduction may be responsible for the antiprotozoal activity. Chemically reduced tinidazole was shown to release nitrites and cause damage to purified bacterial DNA in vitro. Additionally, the drug caused DNA base changes in bacterial cells and DNA strand breakage in mammalian cells. The mechanism by which tinidazole exhibits activity against Gisardia and Entamoeba species is not known.

1.6.1.5.2 Pharmacokinetic Properties

Absorption: Estimated oral bioavailability >90%. Tinidazole absorbed rapidly following oral administration; peak plasma concentrations usually attained within about 2 hours.

Distribution: Distributed into virtually all body tissues and body fluids. It crosses blood-brain barrier, placenta and distributed in milk. Plasma protein binding of tinidazole is 12%. The apparent volume of distribution is about 50 liters.

Metabolism: Extensively metabolized prior to elimination. Partially it is metabolized via oxidation, hydroxylation, and conjugation. It is metabolized principally by CYP3A4. Present in plasma principally as unchanged drug with small amounts of the 2-hydroxymethyl metabolite.

Elimination: Eliminated by the liver and kidneys. Excreted in urine as unchanged drug (20–25%) and in feces (12%).

Half-life: Approximately 12–14 hours.

1.6.1.5.3 Preclinical Safety Data

Tinidazole has been shown to be mutagenic in some bacterial strains tested in vitro (with and without metabolic activation). Tinidazole was negative for mutagenicity in a mammalian cell culture system utilising Chinese hamster lung V79 cells (HGPRT test system) and negative for genotoxicity in the Chinese hamster ovary (CHO) sister chromatid exchange assay. Tinidazole was positive for in vivo genotoxicity in the mouse micronucleus assay.

1.6.1.6 Pharmaceutical Particulars

1.6.1.6.1 List of Excipients

Lactose (Lactose Monohydrate)
Povidone (P.V.P K-30)
Maize starch
Sodium Starch Glycolate
(TYPE-A)
Purified Talc
Colloidal Anhydrous silica (Aerosil)
Sodium Lauryl sulphate
Microcrystalline Cellulose (PH 101)
Magnesium Stearate
Colour White SC-SP 3180 (Spraycel)
Purified Water

1.6.1.6.2 Incompatibilities

Not applicable.

1.6.1.6.3 Shelf Life

36 months

1.6.1.6.4 Special Precautions for Storage

Store below 30°C. Protect from light.

1.6.1.6.5 Nature and Contents of Container

10 Tablets packed in Blister Such a 10 Tablets Packed in Printed Carton With Package Insert.

1.6.1.6.6 Special precaution for disposal and other handling

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

1.6.1.7 Marketing Authorization Holder And Manufacturing Site Addresses

1.6.1.7.1 Name and Address of Marketing Authorization Holder

Lincoln Pharmaceuticals Limited
Trimul Estate, Khatraj, Taluka: Kalol,
District: Gandhinagar Gujarat, India.
Telephone no.: +91-02764-665000
Fax: +91-02764-281809
Email: info@lincolnpharma.com
Website: www.lincolnpharma.com

1.6.1.7.2 Name and Address of manufacturing site(s)

Lincoln Pharmaceuticals Limited
Trimul Estate, Khatraj, Taluka: Kalol,
District: Gandhinagar Gujarat, India.
Telephone no.: +91-02764-665000
Fax: +91-02764-281809
Email: info@lincolnpharma.com
Website: www.lincolnpharma.com

1.6.1.8 Marketing Authorization Number

To be included after obtaining first registration.

1.6.1.9 Date of First <Registration> / Renewal of The <Registration>

It will be applicable after registration of this product.

1.6.1.10 **Date of Revision of the Text**

1.6.1.11 Dosimetry (If Applicable)

Not Applicable

1.6.1.12 Instructions for preparation of radiopharmaceuticals (if Applicable)

Not Applicable