Tinidazole Tablets I.P.
FASIGYN® 500 mg
FASIGYN® DS 1000 mg

1. GENERIC NAME

Tinidazole Tablets I.P.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains: Tinidazole I.P. 500 mg
Each film coated tablet contains: Tinidazole I.P. 1000 mg

List of Excipients

Fasigyn 500/Fasigyn DS tablets contain the following inert ingredients: maize starch, microcrystalline cellulose, alginic acid, magnesium stearate, sodium lauryl sulfate, hydroxy propyl methyl cellulose, propylene glycol, titanium dioxide.

All strengths/presentations mentioned in this document might not be available in the market.

3. DOSAGE FORM AND STRENGTH

500 mg & 1000 mg film coated tablets

4. CLINICAL PARTICULARS

4.1 Therapeutic indication

Prophylaxis:

a) Prevention of post-operative infections caused by anaerobic bacteria, especially those associated with colonic, gastrointestinal and gynecological surgery.

Treatment of the following infections:

b) Anaerobic infections such as:

Intraperitoneal infections: peritonitis, abscess

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Gynecological infections: endometritis, endomyometritis, tubo-ovarian abscess
Bacterial septicemia
Post-operative wound infections
Skin and soft tissue infections
Upper and lower respiratory tract infections: pneumonia, empyema, lung abscess

c) Non-specific vaginitis

d) Acute ulcerative gingivitis

e) Urogenital trichomoniasis in both male and female patients

f) Giardiasis

g) Intestinal amebiasis

h) Amebic involvement of the liver

4.2 Posology and method of administration

Prophylaxis

a) Prevention of post-operative infections

Use in Adults:

Oral: A single dose of 2 g approximately 12 hours before surgery.

Use in Children less than 12 years:

There is no data available to permit dosage recommendations for prophylaxis of anaerobic infections in children below the age of 12 years.

Treatment

b) Anaerobic infections

Use in Adults:

Oral: An initial dose of 2 g the first day followed by 1 g daily, given as a single dose or as 500 mg twice daily.

Treatment for 5 to 6 days will generally be adequate, but clinical judgment must be used in determining the duration of therapy, particularly when eradication of infection from certain sites may be difficult.

Routine clinical and laboratory observation is recommended if it is considered necessary to continue therapy for more than 7 days.

Use in Children Less Than 12 Years:

There is no data available to permit dosage recommendations for treatment of anaerobic infections in children below the age of 12 years.

c) Non-specific vaginitis

Use in Adults:

Non-specific vaginitis has been successfully treated with a single oral dose of 2 g. Higher cure rates have been achieved with 2 g single daily doses for two consecutive days (total dosage 4 g).

d) Acute ulcerative gingivitis

Use in Adults:

A single oral dose of 2 g.

e) Urogenital trichomoniasis

When infection with *Trichomonas vaginalis* is confirmed, simultaneous treatment of the consort is recommended.

Use in Adults:

Preferred Regimen:

A single oral dose of 2 g.

Use in Children:

A single dose of 50 to 75 mg/kg of body weight. It may be necessary to repeat this dose once in some cases.

f) Giardiasis

Use in Adults:

A single oral dose of 2 g.

Use in Children:

A single dose of 50 to 75 mg/kg of body weight. It may be necessary to repeat this dose once in some cases.

g) Intestinal amebiasis

Use in Adults:

A single oral daily dose of 2 g for 2 to 3 days. Occasionally, when a three-day single daily dose is ineffective, treatment may be continued for up to six days. When a five-day, twice daily course is ineffective, treatment may be continued for up to 10 days.

Use in Children:

A single dose of 50 to 60 mg/kg of body weight/ day for three successive days.

h) Amebic involvement of the liver

For amebic involvement of the liver, the aspiration of pus may be required in addition to therapy with tinidazole.

Use in Adults:

Oral: Total dosage varies from 4.5 to 12 g, depending on the virulence of *Entamoeba histolytica*.

Initiate treatment with 1.5 to 2 g orally as a single daily dose for 3 days. Occasionally, when a three-day course is ineffective, treatment may be continued for up to 6 days.

Use in Children:

A single oral dose of 50 to 60 mg/kg of body weight/ day for five successive days.

Use in 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.

Oral Administration

It is recommended that oral tinidazole be taken during or after a meal.

4.3 Contraindications

Use of tinidazole is contraindicated during the first trimester of pregnancy, in nursing mothers (See section 4.6 Use in special populations), in patients with organic neurological disorders and in patients with known hypersensitivity to tinidazole, other 5-nitroimidazole derivatives,

or any of the components of this product. As with other drugs of similar structure, tinidazole is also contraindicated in patients having, or with a history of blood dyscrasias, although no persistent hematologic abnormalities have been noted in clinical or animal studies.

4.4 Special warnings and precautions for use

As with related compounds, alcoholic beverages should be avoided during and for at least 72 hours following completion of tinidazole therapy because of the possibility of a disulfiram-like reaction (flushing, abdominal cramps, vomiting, tachycardia).

Drugs of similar chemical structure, including tinidazole, have been associated with various neurological disturbances such as dizziness, vertigo, ataxia, peripheral neuropathy and rarely, convulsions. If any abnormal neurological signs develop during tinidazole therapy, the drug should be discontinued.

Carcinogenicity has been seen in mice and rats treated chronically with metronidazole, another nitroimidazole agent. Although carcinogenicity data is not available for tinidazole, the two drugs are structurally related and therefore there is a potential for similar biologic effects.

Mutagenicity results with tinidazole were mixed (positive and negative) (See section 6.1). The use of tinidazole for longer treatment than usually required should be carefully considered.

4.5 Drugs interactions

Alcohol: Concurrent use of tinidazole and alcohol may produce a disulfiram-like reaction and should be avoided (See section 4.4).

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.

4.6 Use in special populations

Pregnancy:

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 the possible hazards to the mother or fetus (See section 6.1).

Lactation:

Tinidazole is distributed into breast milk. Tinidazole may be present in breast milk for more than 72 hours after administration. Women should not nurse during and for at least three days after having discontinued taking tinidazole.

4.7 Effects on ability to drive and use machines

The effect of tinidazole on the ability to drive or use machinery has not been studied. There is no evidence to suggest that tinidazole may affect these abilities.

4.8 Undesirable effects

All ADRs listed in the CDS are presented by MedDRA SOC. Within each frequency category, the ADRs are presented in the order of clinical importance.

Adverse Reactions Table

System Organ Class	**Common ≥1/100 to <1/10**	**Frequency Not Known (cannot be estimated from available data)**
Blood and the Lymphatic System Disorders		Leukopenia
Immune System Disorders		Drug hypersensitivity
Metabolism and Nutrition Disorders	Decreased appetite	
Nervous System Disorders	Headache	Convulsions Neuropathy peripheral Paraesthesia Hypoaesthesia Sensory disturbances Ataxia Dizziness Dysgeusia
Ear and Labyrinth Disorders	Vertigo	
Vascular Disorders		Thrombophlebitis‡ Flushing
Gastrointestinal Disorders	Vomiting Diarrhoea Nausea Abdominal pain	Glossitis Stomatitis Tongue discolouration
Skin and Subcutaneous Tissue Disorders	Dermatitis allergic Pruritus Skin Hyperpigmentation	Angioedema Urticaria
Renal and Urinary Disorders		Chromaturia
General Disorders and Administration Site Conditions		Pyrexia Fatigue

CIOMS III categories: Common ≥1/100 to <1/10 (≥% and <10%), Not known: frequency cannot be estimated from available data

‡ Thrombophlebitis has occasionally been observed at the infusion site with the intravenous dosage form.

4.9 Overdose

Signs and Symptoms of Overdose

Reports of overdoses in humans with tinidazole are anecdotal and do not provide consistent data regarding the signs and symptoms of overdose.

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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of Action

Tinidazole is a 5-nitroimidazole derivative of the substituted imidazole compounds and possesses antimicrobial activity against anaerobic bacteria and protozoa. The mode of action of tinidazole against anaerobic bacteria and protozoa is believed to involve the penetration of the drug into the cell of the microorganism and subsequent damage of DNA strands or inhibition of their synthesis.

5.2 Pharmacodynamic properties

Tinidazole is active against both protozoa and obligate anaerobic bacteria. The activity against protozoa includes *Trichomonas vaginalis*, *Entamoeba histolytica* and *Giardia lamblia*.

Tinidazole is active against *Gardnerella vaginalis* and most anaerobic bacteria including: *Bacteroides fragilis*, *Bacteroides melaninogenicus*, *Bacteroides* spp., *Clostridium* spp., *Eubacterium* spp., *Fusobacterium* spp., *Peptococcus* spp., *Peptostreptococcus* spp., and *Veillonella* spp.

5.3 Pharmacokinetic properties

Absorption: Tinidazole is rapidly and completely absorbed following oral administration.

In studies with healthy volunteers receiving 2 g tinidazole orally, peak serum levels of 40-51 mcg/ml were achieved within two hours and decreased to between 11-19 mcg/ml at 24 hours.

Distribution: Tinidazole is widely distributed in all body tissues and also crosses the blood brain barrier, obtaining clinically effective concentrations in all tissues. The apparent volume of distribution is about 50 liters. About 12% of plasma tinidazole is bound to plasma proteins.

Elimination: Tinidazole is excreted by the liver and kidneys. Studies in healthy patients have shown that over 5 days, 60%-65% of an administered dose is excreted by the kidneys with 20%-25% of the administered dose excreted as unchanged tinidazole. Up to 5% of the administered dose is excreted in the feces.

Studies in patients with renal failure (creatinine clearance <22 ml/min) indicate that there is no statistically significant change in tinidazole pharmacokinetic parameters in these patients (See section 4.2).

6 NONCLINICAL PROPERTIES

6.1 Animal Toxicology or Pharmacology

Fertility studies in rats receiving 100 mg or 300 mg tinidazole/kg had no effect on fertility, adult and pup weights, gestation, viability or lactation. There was a slight, not significant, increase in resorption rate at the 300 mg/kg dose. In the study with 60 days duration, NOAEL related with testicular adverse effects and spermatogenesis was 100 mg/kg.

In acute animal studies with mice and rats, the LD_{50} for mice was >3600 mg/kg and >2300 mg/kg for oral and intraperitoneal administration, respectively. For rats, the LD_{50} was >2000 mg/kg for both oral and intraperitoneal administration.

Tinidazole was mutagenic in TA 100, *S. typhimurium* tester strain both with and without the metabolic activation system and was negative for mutagenicity in the TA 98 strain.

Mutagenicity results were mixed (positive and negative) in the TA 1535, 1537, and 1538 strains. Tinidazole was also mutagenic in a tester strain of *Klebsiella pneumonia*. Tinidazole was negative for mutagenicity in a mammalian cell culture system utilizing 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.

7. DESCRIPTION

Fasigyn 500 mg: Smooth, well formed, round, biconvex, white speckled film coated tablet.

Fasigyn DS 1000 mg: Smooth, well formed, white to off-white, speckled film coated oblong shaped tablet.

8. PHARMACEUTICAL PARTICULARS

8.1 Incompatibilities

None reported.

8.2 Shelf-life

Fasigyn 500/Fasigyn DS should be used within 3 years from the date of manufacture.

8.3 Packaging information

Each carton of Fasigyn 500 contains 25 aluminum foil strips. Each strip holds 4 tablets.

Each carton of Fasigyn DS contains 25 aluminum foil strips. Each strip holds 2 tablets.

8.4 Storage and handling instructions

Storage condition - Store below 30°C. Protect from light and moisture.

Instructions for Use/Handling

No special instructions applicable.

9. PATIENT COUNSELLING INFORMATION

It is recommended that oral tinidazole be taken during or after a meal. Use of tinidazole is contraindicated during the first trimester of pregnancy, in nursing mothers, in patients with organic neurological disorders and in patients with known hypersensitivity to tinidazole, other 5-nitroimidazole derivatives, or any of the components of this product. If any abnormal neurological signs develop during tinidazole therapy, the drug should be discontinued. Tinidazole is also contraindicated in patients having, or with a history of blood dyscrasias, although no persistent hematologic abnormalities have been noted in clinical or animal studies. Alcoholic beverages should be avoided during and for at least 72 hours following completion of tinidazole therapy. The use of tinidazole for longer treatment than usually required should be carefully considered. Store below 30°C. Protect from light and moisture.

10. DETAILS OF MANUFACTURER

Manufactured by: Pfizer Limited, Plot No. L-137, Phase III A, Verna Industrial Estate, Verna, Salcete-Goa, India

11. DETAILS OF PERMISSION OR LICENSE NUMBER WITH DATE

Permission no. 544 dated 01-Dec-2014

12. DATE OF REVISION

July 2021