FASIGYN
500mg Tablets

QUALITATIVE AND QUANTITATIVE COMPOSITION
FASIGYN tablets contain 500 mg of tinidazole as the active component.

PHARMACEUTICAL FORM
Film coated tablets 500 mg.

CLINICAL PARTICULARS

THERAPEUTIC INDICATIONS

For the oral treatment of Trichomonas Vaginalis infections of the genitourinary tract in both female and male. For the prevention of anaerobic infections after gynecological operations and stomach operations.

POSOLOGY AND METHOD OF ADMINISTRATION

It is recommended that FASIGYN be taken during or after a meal

Prevention of postoperative infections:

Adult

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

Children less than 12 years

Data are not available to permit dosage recommendations for prophylaxis of anaerobic infections in children below the age of 12 years.

Urogenital trichomoniasis:

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

Adult Preferred Regimen

A single oral dose of 2 g.

Adult Alternative Regimen

One 150 mg tablet orally three times daily for 5 days, or one 150 mg tablet orally twice daily for 7 days.

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.

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.

CONTRAINDICATIONS

Use of FASIGYN is contraindicated during the first trimester of pregnancy, in nursing mothers (See section– **Fertility, Pregnancy and Lactation**), in patients with organic neurological disorders and in patients with known hypersensitivity to tinidazole, other 5-nitroimidazole derivatives, or any of the components of FASIGYN. As with other drugs of similar structure, FASIGYN 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.

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 FASIGYN therapy because of the possibility of a disulfiram-like reaction (flushing, abdominal cramps, vomiting, tachycardia).

Drugs of similar chemical structure, including FASIGYN, have been associated with various neurological disturbances such as dizziness, vertigo, ataxia, peripheral neuropathy and rarely, convulsions. If any abnormal neurological signs develop during FASIGYN 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 – **Preclinical safety data**). The use of tinidazole for longer treatment than usually required should be carefully considered.

INTERACTION WITH OTHER MEDICAMENTS AND OTHER FORMS OF INTERACTION

Alcohol: concurrent use of tinidazole and alcohol may produce a disulfiram-like reaction and should be avoided (see **Special warnings and precautions for use**).
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.

FERTILITY, PREGNANCY AND LACTATION

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 FASIGYN 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– Preclinical safety data).

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 FASIGYN.

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.

UNDESIRABLE EFFECTS

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

Vascular disorders: Flushing
General disorders and administration site conditions: Pyrexia, Fatigue
Nervous system disorders: Ataxia, Convulsions (rarely), Dizziness, Headache, Hypoaesthesia, Paresthesia, Neuropathy peripheral, Sensory disturbances, Dysgeusia
Ear and labyrinth disorders: Vertigo
Gastrointestinal disorders: Abdominal pain, Diarrhea, tongue discolouration, Glossitis, Nausea, Stomatitis, Vomiting
Metabolism and nutrition disorders: Decreased appetite
Blood and lymphatic system disorders: Leukopenia.
Skin and subcutaneous tissue disorders: Dermatitis allergic, Pruritus, Urticaria, and Angioedema
Immune system disorders: Drug hypersensitivity
Renal and urinary disorders: Chromaturia

OVERDOSE

Signs and Symptoms of Overdose
Reports of overdoses in humans with FASIGYN 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.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties

FASIGYN brand of tinidazole is a 5-nitroimidazole derivative of the substituted imidazole compounds and possesses anti microbial activity against anaerobic bacteria and protozoa. The mode of action of FASIGYN 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.

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.

Pharmacokinetic Properties

Absorption: Tinidazole is rapidly and completely absorbed following oral administration. When compared with oral dosing, systemic absorption from vaginal dosage forms is minimal at 10%.

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.

Healthy volunteers who received 800 mg and 1.6 g tinidazole intravenously over 10-15 minutes achieved peak plasma concentrations that ranged from 14 to 21 mcg/ml for the 800 mg dose and averaged 32 mcg/ml for the 1.6 g dose. At 24 hours post infusion, plasma levels of tinidazole decreased to 4-5 mcg/ml and 8.6 mcg/ml, respectively, justifying once daily dosing.

Plasma levels decline slowly and tinidazole can be detected in plasma at concentrations of 0.5 mcg/ml at 72 hours post infusion and up to 1 mcg/ml at 72 hours following oral administration. The plasma elimination half-life for tinidazole is between 12-14 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 **Posology and method of administration**).

Preclinical Safety Data

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.

PHARMACEUTICALS PARTICULARS

List of excipients: Maize starch (dried), Microcrystalline cellulose PH 102, Alginic acid, Vegetable Magnesium stearate, Sodium lauryl sulfate, Hydroxypropyl methylcellulose 2910, Propylene glycol, Titanium dioxide E171.

Special precautions for storage: Store in **Room Tempertaure below 25°C, in a dry place, protect from light.**
Nature and contents of container: Blister packs of 4 tablets

Manufacturer: Pfizer PGM, France

License Holder: Pfizer Pharmaceuticals Israel Ltd.
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