

New Zealand Data Sheet

Arrow - Ornidazole

Ornidazole Tablets 500 mg

Antimicrobial agent for the treatment of infections due to trichomonads, amoebae, *Giardia lamblia* and anaerobic bacteria.

Composition

Active ingredient

Ornidazole: a-(chloromethyl)-2-methyl-5-nitroimidazole-1-ethanol. Each film-coated tablet contains 500 mg ornidazole.

Excipients

Tablets also contain maize starch, microcrystalline cellulose, hydroxypropylmethylcellulose, magnesium stearate, talc, titanium dioxide.

Appearance

White to slightly yellowish, cylindrical, biconvex film coated tablets.

Properties and Effects

ARROW-ORNIDAZOLE is effective against *Trichomonas vaginalis*, *Entamoeba histolytica* and *Giardia lamblia* (*Giardia intestinalis*), and also against certain anaerobic bacteria such as *Bacteroides* and *Clostridium* spp., *Fusobacterium* spp., and anaerobic cocci.

Pharmacokinetics

Absorption

Following oral administration ornidazole is rapidly absorbed. Mean absorption is 90%. Peak plasma concentrations are reached within three hours.

Distribution

The mean volume of distribution after i.v. administration is 1 litre per kg. Plasma protein binding of ornidazole is about 13%. The active ingredient of ARROW-ORNIDAZOLE penetrates the cerebrospinal fluid, the body fluids and the tissues very effectively.

Plasma concentrations are within the range considered to be optimal for the various indications (6 to 36 mg/l).

After repeated administration of 500 mg or 1000 mg every twelve hours to healthy volunteers, an accumulation factor of 1.5-2.5 was calculated.

Metabolism

Ornidazole is mainly metabolised to 2-hydroxymethyl and a-hydroxymethyl metabolites in the liver.

Both main metabolites are less active against *Trichomonas vaginalis* and anaerobic bacteria than the unchanged ornidazole.

Elimination

The half-life is about thirteen hours. 85% of a single dose is eliminated within the first five days, most of this being metabolised. 4% of the dose is excreted as unaltered substance in the urine.

Pharmacokinetics in Special Populations

Patients with hepatic impairment

In patients with liver cirrhosis the elimination half-life is longer (22 versus 14 hours) and clearance lower (35 versus 51 ml/min) than in healthy subjects. The dosing interval should be doubled in patients with severe hepatic impairment.

Patients with renal impairment

The pharmacokinetics of ornidazole are unaltered in renal impairment. Dose adjustment is therefore unnecessary in patients with impaired renal function. Ornidazole is removed by haemodialysis. An additional dose of 500 mg of ornidazole should be administered if the daily dose is 2 g/day, or an additional dose of 250 mg ornidazole if the daily dose is 1 g/day, should therefore be administered before the start of haemodialysis.

Neonates and children

The pharmacokinetics of ornidazole in neonates and young children are similar to those in adults.

Indications and Usage

1. Bacterial vaginosis (non-specific vaginitis).
2. Trichomoniasis. Genitourinary infections in women and men due to *Trichomonas vaginalis*.
3. Amoebiasis. All intestinal infections due to *Entamoeba histolytica*, including amoebic dysentery. All extraintestinal forms of amoebiasis, especially amoebic liver abscess.
4. Giardiasis (lambliaosis).
5. Infections due to anaerobic bacteria. Treatment of infections such as septicaemia, meningitis, peritonitis, postoperative wound infections, puerperal sepsis, septic abortion, and endometritis, with demonstrated or

suspected involvement of susceptible bacteria (see Properties and Effects).

6. Prophylaxis during surgical interventions, particularly those involving the colon, and in gynaecological operations.

Dosage and Administration

Standard Dosage

The tablets must always be taken after meals.

Trichomoniasis

There are two possible therapeutic regimens: Single-dose therapy (for acute trichomoniasis); five-day therapy (for chronic forms of trichomoniasis). The tablets should be taken after meals.

- (a) Single dose therapy
- (b) Five day therapy

Type of Treatment	Daily Dosage (500 mg tablets)
(a) Single dose	3 tablets in the evening
(b) Five-day therapy	2 tablets (1 tablet mornings and evenings)

In all cases, the *sexual partner* should also be treated using the same oral dosage so as to avoid reinfection.

The dosage for *children* is 25 mg per kg bodyweight per day, given in a single dose.

Amoebiasis

- (a) Three-day treatment of patients with amoebic dysentery
- (b) Five-to-ten-day treatment for all forms of amoebiasis

Duration of Treatment	Daily Dosage	
	Adults and children over 35 kg	Children up to 35 kg
a) Three days	3 tablets in one evening dose <u>Over 60 kg bodyweight:</u> 4 tablets (2 tablets mornings and evenings)	125 mg (¼ tablet) per 3 kg body weight in one dose (equivalent to 40 mg per kg)
b) Five to ten days	2 tablets (1 tablet mornings and evenings)	125 mg (¼ tablet) per 5 kg body weight in one dose (equivalent to 25 mg per kg)

Giardiasis (lambliaosis)

Duration of Treatment	Daily Dosage	
	Adults and children over 35 kg	Children up to 35 kg
One to two days	3 tablets in the evening in one dose	125 mg (¼ tablet) per 3 kg body weight in one dose (equivalent to 40 mg per kg)

Anaerobic Infections

Prophylaxis: 1500 mg orally, 12 hours before surgery the 500 mg 12-hourly for 3 to 5 days postoperatively.

Contraindications

ARROW-ORNIDAZOLE is contraindicated in patients with known hypersensitivity to the medicine or to other nitroimidazole derivatives.

Precautions

Ornidazole must be used with caution in patients with diseases of the CNS (e.g., epilepsy or multiple sclerosis) and liver disease.

The effect of other medicines can be intensified or impaired.

Effects on Ability to Drive and Use Machines

Somnolence, dizziness, tremor, rigidity, poor coordination, seizures, vertigo or temporary loss of consciousness may occur in patients receiving ARROW-ORNIDAZOLE. If they occur, such effects may affect tasks requiring alertness including the patient's ability to drive and operate machinery.

Pregnancy, Nursing Mothers

There is no clinical data available for ornidazole exposure in pregnancy. Studies conducted on animals do not demonstrate direct or indirect harmful effects on pregnancy/embryonic/foetal development/birth or post-natal development. The effect of ornidazole on women of childbearing potential or birth control methods is unknown.

Extensive studies in various species have revealed no sign of any teratogenic or foetotoxic action of ornidazole. However, no controlled studies have been carried out in pregnant women. As a matter of principle, ARROW-ORNIDAZOLE should not be prescribed in early pregnancy or to nursing mothers except when absolutely necessary.

It is not known whether ornidazole is excreted in human milk. The excretion of ornidazole via milk in animals has not been researched. In making the decision whether or not to discontinue breastfeeding or whether or not ornidazole treatment should be discontinued/avoided, the benefit of

breastfeeding to the infant and the benefit of ornidazole treatment for the nursing mother must be considered.

Reproduction/Fertility

When ornidazole is administered at a high dosage of 400mg/kg/day, it produces infertility in male rats by inhibiting epididymal sperm motility in terms of decreased sperm velocity.

No data has been obtained from research involving humans.

Undesirable Effects

Very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1,000$ to $< 1/100$), rare ($\geq 1/10,000$ to $< 1/1,000$), very rare ($< 1/10,000$), not known (cannot be estimated from the available data).

Diseases of the vascular and lymph system

Rare: Leukopenia

Nervous system disorders

Very rare: Somnolence, headache, dizziness, tremor, rigidity, coordination impairments, seizures, fatigue, vertigo, temporary loss of consciousness and sensory or mixed peripheral neuropathy.

Gastrointestinal disorders

Uncommon: Nausea, vomiting, diarrhoea, epigastric discomfort, dry mouth, loss of appetite.

Rare: Impairment of the sense of taste

Hepatobiliary diseases

Unknown: Jaundice, abnormal liver function tests

Skin and subcutaneous tissue diseases

Rare: Pruritus and skin reactions

Interactions

Alcohol must not be ingested when taking ornidazole or for at least 3 days after discontinuing the medicine.

Ornidazole potentiates the effect of coumarin type oral anticoagulants. The dosage of the anticoagulant has to be adjusted accordingly.

Caution must be exercised when taking ARROW-ORNIDAZOLE together with lithium, cimetidine and antiepileptic medicines such as phenytoin and phenobarbital. Ornidazole prolongs the muscle relaxant effect of vecuronium bromide.

Overdosage

In the event of overdose, the symptoms referred to under Undesirable Effects occur with greater severity.

There is no specific antidote to ornidazole. In the event of cramps occurring, it is recommended that diazepam be given.

Further Information

Stability

This medicine should not be used after the expiry date shown on the pack.

Medicine Classification

Prescription medicine

Package Quantities

Tablets 500 mg, 10's.

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Date of Preparation

22 March 2017