NEW ZEALAND DATA SHEET

1. PRODUCT NAME
Arrow – Ornidazole, 500 mg, film coated tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet contains 500 mg of ornidazole.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
White to slightly yellowish, cylindrical, biconvex film coated tablets.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
ARROW-ORNIDAZOLE is an antimicrobial agent for the treatment of infections due to trichomonads, amoebae, Giardia lamblia and anaerobic bacteria.

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 (lambliasis).
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 section 5.1 Pharmacodynamic properties).
6. Prophylaxis during surgical interventions, particularly those involving the colon, and in gynaecological operations.

4.2 Dose and method of administration
Dose

Trichomoniasis

Adults

There are two possible therapeutic regimens:

(a) Single-dose therapy (for acute trichomoniasis)
(b) Five-day therapy (for chronic forms of trichomoniasis)

Type of Treatment	Daily Dosage (500 mg tablets)
(a) Single dose therapy	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.

Children

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 Over 60 kg bodyweight: 4 tablets (2 tablets mornings and evenings)	125 mg 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 per 5 kg body weight in one dose (equivalent to 25 mg per kg)

Giardiasis (lambliasis)

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 per 3 kg body weight in one dose (equivalent to 40 mg per kg)

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

Patients with hepatic impairment
In patients with liver cirrhosis the elimination half-life is longer and clearance lower 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.

Method of administration
The tablets must always be taken after meals. Arrow – Ornidazole does not have the strengths or dose forms available to deliver the smaller doses required for some paediatric patients therefore other pharmaceutical forms/strengths may be more appropriate for administration to this population.

4.3 Contraindications
ARROW-ORNIDAZOLE is contraindicated in patients with known hypersensitivity to ornidazole, other nitroimidazole derivatives, or any of the excipients listed in section 6.1 List of excipients.

4.4 Special warnings and precautions for use
Discontinue treatment if ataxia, dizziness or confusion occur.

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

In severe hepatic impairment or during haemodialysis the dosage should be adjusted (see sections 4.2 Dose and method of administration and 5.2 Pharmacokinetic properties).

Regular blood counts are recommended if there is a history of haematological disorders, or with high dose treatment and/or prolonged treatment.

4.5 Interaction with other medicines and other forms of interaction

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

Ornidazole may potentiate the effect of coumarin type oral anticoagulants. More frequent monitoring of INR may be necessary.

Caution should be exercised when co-administering ornidazole with lithium, cimetidine, phenytoin, phenobarbital and 5-fluorouracil.

Plasma levels of lithium may be increased by ornidazole. More frequent monitoring of lithium levels may be warranted.

Ornidazole may reduce the clearance of fluorouracil, leading to toxicity.

Ornidazole prolongs the muscle relaxant effect of vecuronium bromide.

Cimetidine may prolong the half-life and decrease plasma clearance of ornidazole.

Phenobarbital or phenytoin may reduce the half-life of ornidazole.

4.6 Fertility, pregnancy and lactation

Use in pregnancy

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.

Use in lactation

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.

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.

4.7 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.

4.8 Undesirable effects

Very common (≥1/10)
Common (≥1/100 to <1/10)

Uncommon	(≥1/1,000 to <1/100)
Rare	(≥1/10,000 to <1/1,000)
Very rare	(<1/10,000)
Not known	(cannot be estimated from the available data)

Infections and infestations
Unknown frequency: vulvovaginal candidiasis due to overgrowth of *Candida albicans*

Blood and lymphatic system disorders
Rare: Leukopenia

Psychiatric disorders

Unknown frequency: confusion, dysphoria, euphoria, disorientation, feeling abnormal

Immune system disorders

Unknown frequency: hypersensitivity reactions, anaphylaxis, angioedema

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 disorders
Unknown: Jaundice, abnormal liver function tests, hepatitis

Musculoskeletal and connective tissue disorders

Unknown frequency: Arthralgia

Skin and subcutaneous tissue disorders
Rare: Pruritus and skin reactions

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/.

4.9 Overdose
In the event of overdose, the symptoms referred to under section 4.8 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.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Antiprotozoals, Nitroimidazole derivatives; ATC code: P01AB03

Chemical name: a-(chloromethyl)-2-methyl-5-nitroimidazole-1-ethanol

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.

5.2 Pharmacokinetic properties

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.

Special Populations

Patients with hepatic impairment

In patients with liver cirrhosis the elimination half-life is longer and clearance lower 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 or ornidazole in neonates and young children are similar to those in adults.

5.3 Preclinical safety data

No conventional safety pharmacology studies have been reported.

Oral administration of ornidazole in repeated dose toxicity studies showed ataxia in dogs at 100 mg/kg.

A reversible reduction in fertility was observed in male rats at an oral dose of 400 mg/kg/day (corresponding to 3 times the maximum recommended dose for humans expressed in mg/m^2).

Limited studies have not demonstrated any teratogenic effect up to oral doses of 400 mg/kg/day in mice and rats, and 100 mg/kg/day in rabbits (corresponding to 1-3 times the maximum recommended dose for humans expressed in mg/m^2).

A peri- and post-natal toxicity study carried out in rats showed an increase in post-natal mortality and a reduction in the weight gain of the young at an oral dose of 400 mg/kg/day (corresponding to 3 times the maximum recommended dose for humans expressed in mg/m^2).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize starch, microcrystalline cellulose, hydroxypropylmethylcellulose, magnesium stearate, talc, titanium dioxide.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

60 months

6.4 Special precautions for storage

Store at or below 30°C. Protect from light.

6.5 Nature and contents of container

PVC/Aluminium foil blister packs. Pack size of 10 tablets.

Not all pack types or pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.

7. MEDICINE SCHEDULE

Prescription Medicine

8. SPONSOR

Teva Pharma (New Zealand) Limited
PO Box 128 244
Remuera
Auckland 1541
Telephone: 0800 800 097

9. DATE OF FIRST APPROVAL

17 March 2011

10. DATE OF REVISION OF THE TEXT

18 June 2024

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
4.2	Add dose adjustment information for patients with hepatic and renal impairments from section 5.2.
4.3	List hypersensitivy to excipients as contraindications
4.4	Include: severe hepatic impairment or during haemodialysis the dosage should be adjusted, discontinue treatment if ataxia, dizziness or confusion occurs. Include peripheral neuropathy.

4.5	Add fluoraouracil interaction and inclusion of more frequent monitoring of INR may be necessary
4.8	Add infections and infestations; update SOC names for blood and lymphatic system disorders, skin and subcutaneous tissue disorders, add psychiatric disorders, immune system disorders, add hepatitis to hepatobiliary disorders, add musculoskeletal and connective tissue disorders. ADR URL updated.
5.3	Update section.