PACKAGE INSERT

SCHEDULING STATUS: S4

PROPRIETARY NAME (AND DOSAGE FORM):

METAGYL TABLETS

METAGYL FORTE TABLETS

COMPOSITION:

METAGYL TABLETS

Each film coated tablet contains:

Metronidazole … 200 mg

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Each film coated tablet contains:

Metronidazole … 400 mg

Inactive ingredients include: microcrystalline cellulose, maize starch, povidone K30, crospovidone, colloidal anhydrous silica, magnesium stearate, hydroxypropylmethyl cellulose, macrogol-400, brilliant blue lake, titanium dioxide, talc purified.

Sugar free

PHARMACOLOGICAL CLASSIFICATION:

A 20.2 Antimicrobial (chemotherapeutic) agents other than antibiotics.

PHARMACOLOGICAL ACTION:

Antibacterial Activity

Metronidazole is active against protozoa including *Entamoeba histolytica. Giardia intestinalis (Giardia lamblia)*, and *Trichomonas vaginalis*. Most obligate anaerobic bacteria, including *Bacteroides* and *Clostridium spp.* are sensitive *in vitro* to metronidazole. Metronidazole is bactericidal. Metronidazole is active *in vitro* against most obligate anaerobes, but does not appear to have any clinical relevant activity against facultative anaerobes or obligate aerobes. Minimum inhibitory concentrations for susceptible anaerobic bacteria generally range from 0,1 to 8 mcg per ml. Resistance to metronidazole has been reported and cross-resistance to other nitroimidazoles, such as tinidazole demonstrated.

INDICATIONS:

a) In the oral treatment of:
   - urogenital trichomoniasis
   - nonspecific vaginitis
   - all forms of amoebiasis
   - giardiasis
   - acute ulcerative gingivitis (Vincent's)
   - acute pericoronitis

b) Treatment of infections in which anaerobic bacteria have been identified or are suspected as pathogens, particularly *Bacteroides fragilis* and other species of bacteroides and including other species for which metronidazole is bactericidal, such as fusobacteria, clostridia, eubacteria and anaerobic streptococci.

Metronidazole has been used successfully for anaerobic infections in the following conditions: pelvic inflammatory disease and postoperative wound infections. Combined therapy is often

indicated as there are usually mixed infections.

c) Prevention of postoperative infections due to anaerobic bacteria:

   i. Given before and after gynaecological surgery.

   ii. Given before and after appendicectomy.

   iii. Given before and after colonic surgery.

d) Treatment of *Helicobacter pylori*-associated gastritis and duodenal ulcer. Metronidazole is used in combination with bismuth subsalicylate or colloidal bismuth subcitrate and appropriate antibiotic therapy.

CONTRAINDICATIONS:

Hypersensitivity to metronidazole.

Active organic disease of central nervous system including epilepsy.

Blood dyscrasias or a history of blood dyscrasias.

Severe hepatic function impairment.

The safety in pregnancy and lactation has not been established.

Metronidazole is distributed into breast milk. The safety in lactation has not been established.

WARNINGS AND SPECIAL PRECUATIONS:

Patients should be advised not to take alcohol during metronidazole therapy and for at least one day afterwards because of the possibility of disulfiram-reaction.

Precautions

Metronidazole should be used with great care in patients with blood dyscrasias or with active disease of the central nervous system. All patients receiving metronidazole for more than 10 days should be monitored and treatment discontinued if signs of peripheral neuropathy or central nervous system toxicity develop. Dose should be reduced in patients with severe liver

disease.

Geriatrics

No information is available on the relationship of age to the effects of metronidazole in geriatric patients. However, elderly patients are more likely to have an age-related decrease in hepatic function, which may require an adjustment in dosage.

DOSAGE AND DIRECTIONS FOR USE:

The tablets should be taken with or after food.

Immature children and babies weighing less than 10 kg should receive proportionally smaller doses, as advised by the physician. Children over 10 years may be given a suitable proportion of the adult dosage according to body mass.

	DURATION OF DOSAGE IN DAYS	ADULTS	CHILDREN		
			7 TO 10 YEARS	3 TO 7 YEARS	1 TO 3 YEARS
UROGENITAL TRICHOMONIASIS Where re-infection is likely, in adults the consort should receive a similar course of treatment concurrently.	1	2 g as a single dose.			
	7	200 mg three times daily or 400 mg twice daily.	100 mg three times daily.	100 mg twice daily.	50 mg three times daily.
	2	800 mg in the morning and 1.2 g in the evening.			
NON-SPECIFIC VAGINITIS	7	400 mg twice daily.			
	OR 1	2 g as a single dose.			
AMOEBIASIS a) Invasive intestinal disease	5	800 mg three times	400 mg three times	200 mg four times	200 mg three times

susceptible subjects.		daily.	daily.	daily	daily.
AMOEBIASIS b) Intestinal disease in less susceptible subjects and "chronic amoebic hepatitis".	5 to 10	400 mg three times daily.	200 mg three times daily.	100 mg four times daily	100 mg three times daily
AMOEBIASIS c) Amoebic liver abscess, other forms of extra-intestinal amoebiasis.	5	400 mg three times daily	200 mg three times daily	100 mg four times daily	100 mg three times daily
AMOEBIASIS d) Symptomless cyst passers.	5 to 10	400 to 800 mg three times daily	200 to 400 mg three times daily	100 to 200 mg four times daily	100 to 200 mg three times daily
GIARDIASIS A second course of treatment may be necessary for some patients two weeks after the end of the first course.	3	2 g once daily.	1 g once daily.	600 to 800 mg once daily	500 mg once daily
ACUTE ULCERATIVE GINGIVITIS	3	200 mg three times daily	100 mg three times daily	100 mg twice daily	50 mg three times daily
ACUTE PERICORONITIS	3 to 7	200 mg three times daily.			

Anaerobic Infection

a) Treatment:

METAGYL tablets may be given alone or concurrently with other bacteriologically appropriate antibacterial agents. They should be given for 7 days or longer depending on clinical and bacteriological assessments of the patient's condition.

Adults: Initially, 800 mg followed by 400 mg by mouth every 8 hours.

Children: 7,5 mg/kg bodymass by mouth every 8 hours.

b) Prevention:

Adults: Administered in doses similar to those used for the treatment of established infection. 400 mg may be given every 8 hours in the 24 hours before surgery followed postoperatively by intravenous or rectal administration until oral therapy is possible.

Children: as for treatment (a)

Treatment of *Helicobacter polori*-associated gastritis and duodenal ulcer.

Heliobacter pylori-associated gastritis or duodenal ulcer (treatment adjunct)	-	500 mg three times a day in conjunction with other medicines used for treatment (ie., bismuth subsalicylate, colloidal bismuth subcitrate, ampicillin or amoxicillin) for one to two weeks.

SIDE-EFFECTS:

Following side-effects with metronidazole have been reported:-

Gastrointestinal system	-	Dryness of mouth, unpleasant metallic taste, diarrhoea, loss of appetite, nausea or vomiting, stomach pain or cramps, pancreatitis, pseudomembranous colitis.
Central nervous system	-	Ataxia, encephalopathy, headache, dizziness or light headedness, seizures, peripheral neuropathy, insomnia, changes in mood or mental state such as depression or confusion have been reported.
Hypersensitivity	-	Skin rash, hives, redness or itching.

		Anaphylaxis has been reported less frequently.
Hematological	-	Leukopenia, bone marrow aplasia, reduced erythropoiesis and granulopoiesis, aplastic anaemia.
Renal	-	Dark urine, dysuria, cystitis, sense of pelvic pressure.

Raised liver enzyme values have been reported.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

See side effects: Treatment is symptomatic and supportive.

IDENTIFICATION:

METAGYL TABLETS

Sky blue, round, biconvex film coated tablets.

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Sky blue, round, biconvex film coated tablets.

PRESENTATION:

METAGYL TABLETS: Blisters and patient ready packs of 21's, 28's or 250's

HDPE Bottle of 1000's.

METAGYL FORTE TABLETS: Blisters and patient ready packs of 5's, 14's, 21's or 100's

HDPE Bottle of 500's.

STORAGE INSTRUCTIONS:

Keep well closed in light-resistant containers, below 25°C.

Keep out of reach of children.

REGISTRATION NUMBER

METAGYL TABLETS: 32/20.2/0218

METAGYL FORTE TABLETS: 32/20.2/0219

NAME AND BUSINESS ADDRESS OF APPLICANT:

OETHMAAN BIOSIMS (PTY) LTD.

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