APPROVED PACKAGE INSERT:

SCHEDULING STATUS

S4

PROPRIETARY NAME (AND DOSAGE FORM):

ANAEROBYL 200 (TABLETS)

ANAEROBYL 400 (TABLETS)

COMPOSITION:

Anaerobyl 200 tablets contain metronidazole 200 mg.

Anaerobyl 400 tablets contain metronidazole 400 mg.

Other ingredients: Microcrystalline cellulose (avicel pH 200), stearic acid.

Sugar free.

PHARMACOLOGICAL CLASSIFICATION:

A 20.2.6 Medicines against protozoa.

PHARMACOLOGICAL ACTION:

Metronidazole possesses trichomonacidal and amoebicidal activity against T. Vaginalis and E Histolytica. Metronidazole is active in-vitro against most obligate anaerobes, but does not appear to have any clinically relevant activity against facultative anaerobes or obligate aerobes.

Metronidazole has been shown to have in-vitro activity against the following:

Anaerobic gram-negative bacilli including bacteroides species (including the B. Fragilis group) and the Fusobacterium species.

Anaerobic gram-positive bacilli including Clostridium species and the susceptible strains of Eubacterium.

Anaerobic gram-positive cocci including Peptococcus species and Peptostreptococcus species.

If possible, when treating anaerobic infections susceptibility tests should be performed prior to initiation of therapy.

INDICATIONS:

Metronidazole is indicated for treatment of symptomatic and asymptomatic trichomoniasis in females and males. The asymptomatic consort of patients should also be treated.

Vaginitis caused by gardnerella vaginalis.

Acute intestinal amoebiasis and amoebic liver abscess.

Symptomless cyst passers.

Giardiasis.

Acute ulcerative gingivitis and dental infections due to anaerobic bacteria.

Acute pericoronitis.

Prevention of post-operative infections due to anaerobic bacteria:

Given before and after gynaecological surgery.

Given before and after appendectomy.

Given before and after colonic surgery.

CONTRAINDICATIONS:

Metronidazole is contra-indicated in patients with a prior history of hypersensitivity to metronidazole or other nitroimidazole derivatives. It is contra-indicated in patients with history or evidence of blood dyscrasia.

Safety in pregnancy has not been established.

Metronidazole appears in breast milk in concentrations similar to those found in plasma. If use of metronidazole in a nursing woman is deemed essential, institution of alternative methods of infant feeding is recommended.

WARNINGS AND SPECIAL PRECAUTIONS:

Convulsive seizures and peripheral neuropathy, the latter characterised by numbness or parasthesia of an extremity, have been reported in patients treated with metronidazole.

The appearance of abnormal neurologic signs requires immediate assessment of the benefits of continued treatment weighed against the potential risks. Metronidazole should be administered with caution to patients with central nervous system diseases.

Metronidazole has been shown to be carcinogenic in mice and rats. Currently there is no evidence available associating metronidazole with tumours in man.

Special precautions:

Indicated surgical procedures should be performed in conjunction with metronidazole treatment, such as incision and draining of an abscess. In a mixed aerobic and anaerobic infection, antibiotics appropriate for the treatment of the aerobic infection should be used in addition to metronidazole.

The drug is not effective against aerobic or facultative anaerobic organisms.

Metronidazole has been reported to potentiate the activity of warfarin and other oral coumarin anticoagulants. There is no interaction with heparin.

Patients receiving concurrent therapy of drugs inducing microsomal enzymes, such as phenytoin and phenobarbitone, may metabolize metronidazole at a much greater rate than normally, resulting in reduced plasma levels.

Alcoholic beverages should not be consumed during metronidazole therapy because abdominal cramps, nausea, vomiting, headaches and flushing may occur as a result of the blockade of acetaldehyde metabolism.

Metronidazole may interfere with certain chemical analyses for aspartate aminotransferase (AST, SGOT), alanine aminotransferase (ALT, SGPT) triglycerides and glucose using the hexokinase method resulting in decreased values.

DOSAGE AND DIRECTIONS FOR USE:

Do not exceed 4,0 grams in 24 hours. The tablets should be taken at or after meals.

Indications	**Duration of dosage in days**	**Adults**	**Children**		
			7 -10 years	**3 – 7 years**	**1 -3 years**
Urogenital trichomoniasis	1	2 g as a single dose			
where re-infection is likely, the	7	200 mg 3 times a day	100 mg 3 times daily	100 mg 2 times daily	50 mg 3 times daily
consort should receive a similar treatment concurrently.	5		400 mg morning and night		
Non -specific vaginitis	7	400 mg twice daily			
	1	2 g as a single dose			
Amoebiasis a) Invasive intestinal	5	800 mg 3 times daily	400 mg 3 times daily	200 mg 4 times daily	200 mg 3 times daily

disease in susceptible patients	3	2 g once daily			
b) Intestinal disease in less susceptible subjects and chronic amoebic hepatitis	5 - 10	400 mg 3 times daily	200 mg 3 times daily	100 mg 4 times daily	100 mg 3 times daily
	2	2 g once daily			
c) Amoebic liver abscess, also other forms of extra intestinal amoebiasis	5	400 mg 3 times daily	200 mg 3 times daily	100 mg 4 times daily	100 mg 3 times daily
	2	2 g once daily			
d) Symptomless cyst passers	5-10	400-800 mg 3 times daily	200-400 mg 3 times daily	100 -200 mg 4 times daily	100 - 200 mg 3 times daily
Giardiasis : A second course of treatment may be necessary for some patients two	3	2 g once daily	1 g once daily	600 – 800 mg once daily	500 mg once daily

weeks after the end of the first course					
Acute Ulcerative Gingivitis	3	400 mg morning and night	100 mg 3 times daily	100 mg 2 times daily	50 mg 3 times daily
Acute Pericoronitis	3 – 5	400 mg night and morning	200 mg 2 times daily	100 mg 2 times daily	30 mg 3 times daily
Prevention of post operative infections		400 mg every 8 hours 24 hours prior to surgery then post-operatively by IV/rectal administration until oral therapy is possible at 400 mg every 8 hours			

SIDE EFFECTS:

The following side-effects have been reported:

Gastrointestinal symptoms such as nausea, vomiting, abdominal discomfort and unpleasant metallic taste; reversible neutropenia; erythematous rash and pruritus; central nervous system effects such as headache, dizziness, and syncope; fever; darkened urine, which appears to have no clinical significance; dysuria, cystitis or polyuria; flattening of the T-wave in electrocardiographic tracings.

Slow metabolism in patients with hepatic disease results in increased plasma levels of metronidazole and its metabolites.

Candida overgrowth may occur during therapy with metronidazole and should be treated with a candicidal agent.

A mild leucopenia has been observed during administration of metronidazole; however, no persistent haematologic abnormalities attributable to metronidazole have been observed. Total and differential leucocyte counts are recommended before and after therapy.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Single oral doses of metronidazole, up to 15 g, have been reported in overdoses. Symptoms reported include nausea, vomiting and ataxia.

Oral metronidazole has been studied as a radiation sensitizer in the treatment of malignant tumours. Neurotoxic effects, including seizures and peripheral neuropathy, have been reported after 5 to 7 days of doses of 6 to 1 0,4 g every other day.

Treatment:

There is no specific antidote for metronidazole overdose; therefore, management of the patient should consist of symptomatic and supportive therapy.

IDENTIFICATION:

ANAEROBYL 200 tablets:

White to off-white round biconvex tablets 9,5 mm in diameter with breakline on one face.

ANAEROBYL 400 tablets:

White to off-white, round shape tablets with breakline on one side.

PRESENTATION:

ANAEROBYL 200 tablets:

Rectangular or round amber glass bottles containing 21 or 500 tablets.

Securitainers containing 21 or 500 tablets, and HDPE containers containing 1 000 tablets.

White Low Density Polyethylene plastic Patient Ready Packs containing different pack sizes.

ANAEROBYL 400 tablets:

Rectangular or round amber glass bottles containing 1 0 or 500 tablets.

Securitainers containing 10 or 500 tablets, and HDPE containers containing 1 000 tablets.

White Low Density Polyethylene plastic Patient Ready Packs containing different pack sizes.

STORAGE INSTRUCTIONS:

Store in a dry place at or below 25 ºC.

Protect from light.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

ANAEROBYL 200 tablets: R/20.2.6/300

ANAEROBYL 400 tablets: R/20.2.6/301

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

SHANUR HEALTHCARE (PTY) LTD,

Loch House, Unit 003,

3A Eton Road, Parktown

Johannesburg, Gauteng, 2193

South Africa.

DATE OF PUBLICATION OF THE PACKAGE INSERT:

To be allocated