

Pharmacoce Reading Direction

2045

220 mm

170 mm

SCHEDULING STATUS: S4

PROPRIETARY NAME (AND DOSAGE FORM):

METAGYL TABLETS

METAGYL FORTE TABLETS

COMPOSITION:

METAGYL TABLETS

Each film coated tablet contains:

Metronidazole 200 mg

METAGYL FORTE TABLETS

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:

A20.2 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 µg 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 appendectomy.
 - 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 PRECAUTIONS:

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 bodymass.

	DURATION OF DOSAGE IN DAYS	ADULTS			
		ADULTS	CHILDREN		
		7 TO 10 YEARS	3 TO 7 YEARS	1 TO 3 YEARS	
UROGENITAL TRICHO MONIASIS 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.
NON-SPECIFIC VAGINITIS	2	800 mg in the morning and 1.2 g in the evening.			
	7	400 mg twice daily.			
	OR 1	2 g as a single dose.			

AMOEBIASIS a) Invasive intestinal disease susceptible subjects.	5	800 mg three times daily.	400 mg three times daily.	200 mg four times daily.	200 mg three times 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 pylori*-associated gastritis and duodenal ulcer.

Helicobacter 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.

METAGYL FORTE TABLETS

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 in well closed in light-resistant containers, at or 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.
207A Sherwood House
Greenacres Office Park
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Victory Park
Johannesburg
2195

DATE OF PUBLICATION OF THIS PACKAGE INSERT

29 July 1998

1148001

SKEDULERINGSSTATUS: S4

HANDELSNAAM (EN DOSEERVORM)
METAGYL TABLETTE
METAGYL FORTE TABLETTE

SAMESTELLING

METAGYL TABLETTE

Elke filmbedekte tablet bevat:

Metronidasool 200 mg

METAGYL FORTE TABLETTE

Elke filmbedekte tablet bevat:

Metronidasool 400 mg

Onaktiewe bestanddele: mikrokristallyne sellulose, melielysiel, povidoon K30, kruispovidoon, anhidiese kolloidale silica, magnesiumstearaat, hidrokispropielmeielysellulose, makrogol-400, briliantblou lake, titanium dioksied, gesuiwerde talk.

Sulkerary

FARMAKOLOGIESE KLASSIFIKASIE

A. 20.2 Antimikrobiële middels (chemoterapeuties) anders as antibiotika

FARMAKOLOGIESE WERKING

Antibakteriese aktiwiteit

Metronidasool is aktief teen protosoë waaronder *Entamoeba histolytica*, *Giardia intestinalis* (*Giardia lamblia*), en *Trichomonas vaginalis*. Die meeste obligate anaëroëse bakterieë, waaronder *Bacteroides* en *Clostridium* spp. is *in vitro* sensitief vir metronidasool. Metronidasool is bakteriedodend. Metronidasool is *in vitro* aktief teen die meeste obligate anaëroëse, maar het blykbaar nie enige kiniese relevante aktiwiteit teen fakultatiewe anaëroëse of obligate aëroëse nie. Die minimum inhibisiekonsentrasies vir vatbare

anaëroëse bakterieë wissel gewoonlik tussen 0,1 en 8 µg per ml. Weerstand teen metronidasool is aangemeld en kruisweerstand teen ander nitro-imidasole, soos tinidasool, is aangetoon.

INDIKASIES

- a) Vir die mondelike behandeling van:
- urogenitale trichomoniasis
 - nie-spesifieke vaginitis
 - alle vorme van amoëbiëse
 - giardiëse
 - akute ulseratiewe gingivitis (Vincent se gingivitis)
 - akute perikoronitis
- b) Behandeling van infeksies waarin anaëroëse bakterieë as die patogeen geïdentifiseer is of vermoed word, veral *Bacteroides fragilis* en ander spesies van *Bacteroides* waarvoor metronidasool bakterisidies is, soos anaëroëse streptokokke, fusobakterieë, klostridia, eubakterieë en anaëroëse stafielokokke.
- Metronidasool is suksesvol gebruik vir anaëroëse infeksies onder die volgende toestande: pelviese inflammatoriese siekte en postoperatiewe wondinfeksies. Gekombineerde behandeling is dikwels aangedui aangesien daar gewoonlik gemengde infeksies is.
- c) Voorkoming van postoperatiewe infeksies as gevolg van anaëroëse bakterieë:
- i. gegee voor en na 'n ginekologiese operasie.
 - ii. gegee voor en na appendektomie.
 - iii. gegee voor en na 'n dikdarmoperasie.
- d) Behandeling van gastritis en duodenale ulkus vanweë *Helicobacter pylori*. Metronidasool word gebruik in kombinasie met bismutsubsalisilaat of kolloidale bismutsubstraat en toepaslike antibiotiese behandeling.

KONTRA-INDIKASIES

Hipersensitiewe vir metronidasool.

Aktiewe organiese siekte van die sentrale sensustelsel waaronder epilepsie.

Bloeddiskrasie of 'n geskiedenis van bloeddiskrasie.

Erge swak lewerfunksie.

Veiligheid en effektiwiteit tydens swangerskap en borsvoeding is nie bepaal nie.

Metronidasool word in borsmelk uitgeskei. Die veiligheid tydens borsvoeding is nie bepaal nie.

WAARSKUWINGS EN SPESIALE VOORSORGMATREËLS

Pasiënte moet aangeraai word om tydens behandeling met metronidasool en ten minste een dag daarna as gevolg van die moontlikheid van disulfraamreaksie nie alkohol te gebruik nie.

Voorsorgmaatreëls

Metronidasool moet baie versigtig gebruik word deur pasiënte met bloeddiskrasie of met aktiewe siekte van die sentrale sensustelsel. Alle pasiënte wat metronidasool vir meer as 10 dae kry, moet gemonitor word en die behandeling moet gestaak word indien tekens van perifere neuropatie of toksisiteit op die sentrale sensustelsel ontwikkel. Dosisse moet verlaag word vir pasiënte met erge lewersiekte.

Bejaardes

Geen inligting is beskikbaar oor die effek van ouderdom op die werking van metronidasool in bejaarde pasiënte nie. Ouer pasiënte is egter geneig om verwagte ouderdom 'n afname in lewerfunksie te hê, waarvoor 'n aanpassing in die dosis nodig kan wees.

DOSIS EN GEBRUIKSAANWYSINGS

Die tablette moet tydens etes of net daarna gedrink word.

Onvolwasse kinders en babas wat minder as 10 kg weeg, moet proporsioneel kleiner dosisse ontvang, soos deur die dokter aangeraai. Kinders ouer as 10 jaar mag 'n geskikte deel van die volwasse dosis volgens die liggaamsmassa kry.

	DUUR VAN DOSIS IN DAE	VOLWASSENES	KINDERS		
			7 tot 10 jaar	3 tot 7 jaar	1 tot 3 jaar
UROGENITALE TRICHOMONIASIE	1	2 g as enkelvoudige			
	7	200 mg drie keer per dag of 400 mg twee keer per dag	100 mg drie keer per dag	100 mg twee keer per dag	50 mg drie keer per dag
Waar herinfeksie waarskynlik is, moet volwassenes in die konsortium gelyktydig dieselfde behandeling kry.	2	800 mg in die oggend en 1,2 g in die aand			
NIE-SPE-SIFIEKE VAGINITIS	7	400 mg twee keer per dag			
	OF 1	2 g as enkelvoudige			
AMEBIASIE	5	800 mg drie keer per dag	400 mg drie keer per dag	200 mg vier keer per dag	200 mg drie keer per dag
a) Persone vatbaar vir invalende intestinale siekte.					

AMEBIASIE	5 tot 10	400 mg drie keer per dag	200 mg drie keer per dag	100 mg vier keer per dag	100 mg drie keer per dag
b) Intestinale siekte in minder vatbare persone en "chroniese amoëbiëse hepatitis".					
AMEBIASIE	5	400 mg drie keer per dag	200 mg drie keer per dag	100 mg vier keer per dag	100 mg drie keer per dag
c) Amoëbiëse lewerabsess, ander vorme van ekstra-intestinale amoëbiëse.					
AMEBIASIE	5 tot 10	400 tot 800 mg drie keer per dag	200 tot 400 mg drie keer per dag	100 tot 200 mg vier keer per dag	100 tot 200 mg drie keer per dag
d) Simptoomlose sist-uitskeiers.					
GIARDIASIE	3	2 g een keer per dag	1 g een keer per dag	600 tot 800 mg een keer per dag	500 mg een keer per dag
'n Tweede kursus behandeling twee weke na die einde van die eerste kursus kan vir sommige pasiënte nodig wees.					
AKUTE ULSERATIEWE GINGIVITIS	3	200 mg drie keer per dag	100 mg drie keer per dag	100 mg twee keer per dag	50 mg drie keer per dag
AKUTE PERIKORONITIS	3 tot 7	200 mg drie keer per dag			

Anaëroëse Infeksie

Behandeling

METAGYL tablette kan alleen of saam met ander bakteriologies toepaslike antibakteriese middels gegee word. Hulle moet vir 7 dae of langer gegee word afhankende van kiniese en bakteriologiese assesserings van die pasiënt se toestand.

Volwassenes: Aanvanklik 800 mg gevolg deur 400 mg per mond elke 8 uur.

Kinders: 7,5 mg/kg liggaamsmassa per mond elke 8 uur.

Voorkoming

Volwassenes: Gegee in dosisse soortgelyk aan dié wat vir die behandeling van gevestigde infeksie gebruik word. 400 mg kan elke 8 uur in die 24 uur voor die operasie postoperatief gegee word, gevolg deur intraveneuse of rektale toediening tot dat mondelike terapie moontlik is.

Kinders: soos vir behandeling (a)

Behandeling van gastritis en duodenale ulkus vanweë *Helicobacter*

pylori.

Gastritis en duodenale ulkus - 500 mg drie keer per dag in kombinasie met ander medisyne wat vir behandeling gebruik word (bv. bismutsubsalisilaat, kolloidale bismutsubstraat, ampisillien of amoksisillien) vir een tot twee weke.

NEWE-EFFEKTE

Die volgende newe-effekte van metronidasool is aangemeld:

- Gastro-intestinale stelsel - Droogheid van die mond, onaangename metaalmaak, diarree, verties aan eetlus, naarheid of braking, maagpyn of -krampe, pankreatitis, psudomembranokolitis.
- Sentrale sensustelsel - Ataksie, enkefalopatie, hoofpyn, duiseligheid of lighoofdigheid, aanvalle, perifere neuropatie, slaapproëse, veranderinge in gemoed of geestelike toestand, soos depressie of verwardheid, is aangemeld.
- Hipersensitiewe - Veluitslag, galbule, rooiheid of jeuk.
- Hematologies - Anafylaksie is minder dikwels aangemeld.
- Renaal - Leukopenie, beenmurgplasie, laer entropoëse en granulopoëse, aplasiese anemie.
- Houa - Donker urien, disurie, blaasontsteking, gevoel van druk in die bekken.
- Hoë vlakke van lewerensiemie is aangemeld.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VIR DIE BEHANDELING

DAARVAN

Kyk newe-effekte. Behandeling is simptomaties en ondersteunend.

IDENTIFIKASIE

METAGYL TABLETTE

Helmeblou, ronde, bikonvekse, filmbedekte tablette.

METAGYL FORTE TABLETTE

Helmeblou, ronde, bikonvekse, filmbedekte tablette.

AANBIEDING

METAGYL TABLETTE:

Sluipakke en pasiëntregpakke met 21, 28 of 250 tablette

HDPE-bottel met 1000 tablette

METAGYL FORTE TABLETTE:

Sluipakke en pasiëntregpakke met 5, 14, 21 of 100 tablette

HDPE-bottel met 500 tablette

BEWARINGSINSTRUKSIES

Hou dig geslote in ligbestande houers, teen of benede 25 °C.

HOU BUITE BEREIK VAN KINDERS.

REGISTRASIONOMMER

METAGYL TABLETTE: 32/20.2/0218

METAGYL FORTE TABLETTE: 32/20.2/0219

NAAM EN BESIGHEIDSADRES VAN APPLIKANT

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DATUM VAN PUBLIKASIE VAN HIERDIE VOUJLJET

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