

TRICHOZOLE

Metronidazole

Presentation

TRICHOZOLE 200mg Tablets: White biconvex tablets, 7/16" diameter, imprinted "M" breakline "200" on one side. Each tablet contains 200mg metronidazole.

TRICHOZOLE 400mg Tablets: Yellow biconvex tablets, 1/2" diameter, imprinted "M" over "400" on one side. Each tablet contains 400mg metronidazole.

Uses

Actions

Pharmacotherapeutic group: Antibacterials for systemic use, ATC code: J01X D01

Metronidazole has antiprotozoal and antibacterial actions and is effective against *Trichomonas vaginalis* and other protozoa including, *Entamoeba histolytica* and *Giardia lamblia* and against anaerobic bacteria..

Pharmacokinetics

Metronidazole is rapidly and almost completely absorbed on administration; peak plasma concentrations occur after 20 minutes to 3 hours.

The half-life of metronidazole is 8.5 ± 2.9 hours. Metronidazole can be used in chronic renal failure; it is rapidly removed from the plasma by dialysis. Metronidazole is excreted in breast milk but the intake of a suckling infant of a mother receiving normal dosage would be considerably less than the therapeutic dosage for infants.

Indications

1. The prevention of postoperative infections due to anaerobic bacteria, particularly species of bacteroides and anaerobic streptococci.
2. The treatment of septicaemia, bacteraemia, peritonitis, brain abscess, necrotising pneumonia, osteomyelitis, puerperal sepsis, pelvic abscess, pelvic cellulitis, and post operative wound infections from which pathogenic anaerobes have been isolated.
3. Urogenital trichomoniasis in the female (trichomonal vaginitis) and in the male.
4. Bacterial vaginosis (also known as non-specific vaginitis, anaerobic vaginosis or *Gardnerella vaginitis*).
5. All forms of amoebiasis (intestinal and extra-intestinal disease and that of symptomless cyst passers).
6. Giardiasis.
7. Acute ulcerative gingivitis.
8. Anaerobically infected leg ulcers and pressure sores.
9. Acute dental infections due to anaerobic organisms (eg. acute pericoronitis and acute apical infections).

Dosage and Administration

TRICHOZOLE tablets should be swallowed with water (not chewed). It is recommended that the tablets be taken during or after a meal.

The 200 mg tablet may be halved to provide a 100mg dose.

This product is not able to deliver all approved dose regimens.

Anaerobic Infections

The duration of a course of TRICHOZOLE treatment is about 7 days but it will depend upon the seriousness of the patient's condition as assessed clinically and bacteriologically.

Prophylaxis (against anaerobic infection):

Chiefly in the context of abdominal (especially colo-rectal) and gynaecological surgery.

400mg at 8-hourly intervals during the 24 hours preceding operation, followed by postoperative intravenous or rectal administration until the patient is able to take tablets.

Children: 7.5mg/kg 8-hourly.

Treatment of established anaerobic infection:

800 mg followed by 400 mg 8 hourly.

Children: 7.5 mg/kg 8-hourly.

Treatment of Protozoal and other infections

See table.	Duration of dosage in days	Adults* and children over 10 years	Children+		
			7 to 10 years	3 to 7 years	1 to 3 years
Urogenital trichomoniasis (Where re-infection is likely, the consort should receive a similar course of treatment concurrently.)	7	200 mg three times daily or 400mg twice daily	100 mg three times daily	100 mg twice daily	50 mg three times daily
	or 2	800 mg in the morning and 1,200 mg in the evening	-	-	-
	or 1	2.0 g as a single dose	-	-	-
Non-specific vaginitis	7	400 mg twice daily	-	-	-
	1	2.0 g as a single	-	-	-

		dose			
Amoebiasis					
(a) Invasive intestinal disease in susceptible subjects.	5	800 mg three times daily	400 mg three times daily	200 mg four times daily	200 mg three times daily
(b) Intestinal disease in susceptible subjects and chronic amoebic hepatitis	5 – 10	400 mg three times daily	200 mg three times daily	100 mg four times daily	100 mg three times daily
(c) Amoebic liver abscess, also 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
(d) Symptomless cyst passers	5 – 10	400 – 800 mg three times daily	200 – 400 mg three times daily	100 – 200 mg four times daily	100 – 200 mg three times daily
Giardiasis	3	2.0 g once daily	1.0 g once daily	600 – 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 dental infections	3-7	400 mg three times daily	-	-	-
Leg ulcers and pressure sores	7	400 mg three times daily	-	-	-
Anaerobic infections (general)	See data sheet text				
+Children and infants weighing less than 10 kg should receive proportionately smaller dosages.					
*Elderly: Metronidazole is well tolerated by the elderly, but a pharmacokinetic study suggests cautious use of high dosage regimens in this age group.					

Contraindications

Known hypersensitivity to metronidazole or any of the excipients. Known hypersensitivity to imidazoles.

Warnings and Precautions

Regular clinical and laboratory monitoring are advised if administration of TRICHOZOLE for more than 10 days is considered to be necessary.

There is a possibility that after *Trichomonas vaginalis* has been eliminated a gonococcal infection might persist.

The elimination half-life of metronidazole remains unchanged in the presence of renal failure. The dosage of metronidazole therefore needs no reduction. Such patients however retain the metabolites of metronidazole. The clinical significance of this is not known at present.

In patients undergoing haemodialysis metronidazole and metabolites are removed during an eight-hour period of dialysis. Metronidazole should therefore be administered immediately after haemodialysis.

No routine adjustment in the dosage of TRICHOZOLE need be made in patients with renal failure undergoing intermittent peritoneal dialysis (IPD) or continuous ambulatory peritoneal dialysis (CAPD).

Metronidazole is mainly metabolised by hepatic oxidation. Substantial impairment of metronidazole clearance may occur in the presence of advanced hepatic insufficiency. Significant cumulation may occur in patients with hepatic encephalopathy and the resulting high plasma concentrations of metronidazole may contribute to the symptoms of the encephalopathy. TRICHOZOLE should, therefore, be administered with caution to patients with hepatic encephalopathy. The daily dosage should be reduced to one-third and may be administered once a day.

Effects on ability to drive and use machines

Patients should be warned about the potential for confusion, dizziness, hallucinations, or convulsions, and advised not to drive or operate machinery if these symptoms occur.

Pregnancy and lactation

There is inadequate evidence of the safety of metronidazole in pregnancy, but it has been in wide use for many years without apparent ill consequence. Nevertheless TRICHOZOLE, like other medicines, should not be given during pregnancy or during lactation unless the physician considers it essential; in these circumstances the short, high-dose regimens are not recommended.

Adverse Effects

The frequency of adverse events listed below is defined using the following convention:

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).

Serious adverse reactions occur very rarely with standard recommended regimens. Clinicians who contemplate continuous therapy for the relief of chronic conditions, for periods longer than those recommended, are advised to consider the possible therapeutic benefit against the risk of peripheral neuropathy.

Blood and lymphatic system disorders:

Very rare: agranulocytosis, neutropenia, thrombocytopenia, pancytopenia

Not known: leucopenia

Immune system disorders

Rare: anaphylaxis

Not known: angiodema, urticaria

Metabolism and nutrition disorders

Not known: anorexia

Psychiatric disorders

Very rare: psychotic disorders, including hallucinations.

Nervous system disorders

Very rare: encephalopathy (eg. Confusion, fever, headache, hallucinations, paralysis, light sensitivity, disturbances in sight and movement, stiff neck) and subacute cerebellar syndrome (e.g ataxia, dysathria, gait impairment, nystagmus and tremor) which may resolve on discontinuation of the drug.

Very rare: drowsiness, dizziness, convulsions, headaches.

Not known: during intensive and/or prolonged metronidazole therapy, peripheral sensory neuropathy or transient epileptiform seizures have been reported. In most cases neuropathy disappeared after treatment was stopped or when dosage was reduced.

Eye disorders

Very rare: diplopia, myopia

Gastrointestinal

Not known: taste disorders oral mucositis, furred tongue, nausea, vomiting, gastrointestinal disturbances.

Hepatobiliary disorders

Very rare: abnormal liver function tests, cholestatic hepatitis, jaundice and pancreatitis which is reversible on drug withdrawal.

Skin and subcutaneous tissue disorders

Very rare: skin rashes, pustular eruptions, purities

Not known: erythema multiforme.

Musculoskeletal, connective tissue and bone disorders

Very rare: myalgia, arthralgia.

Renal and urinary tract disorders

Very rare: darkening of urine (due to metronidazole metabolite)

Interactions

Some potentiation of anticoagulant therapy has been reported when metronidazole has been used with the warfarin type oral anticoagulants. Dosage of the latter may require reducing. Prothrombin times should be more frequently monitored. There is no interaction with heparin.

Lithium retention accompanied by evidence of possible renal damage has been reported in patients treated simultaneously with lithium and metronidazole. Lithium treatment should be tapered or withdrawn before administering metronidazole. Plasma concentration of lithium, creatinine and electrolytes should be monitored in patients under treatment with lithium while they receive metronidazole.

Patients receiving phenobarbital metabolise metronidazole at a much greater rate than normally, reducing the half life to approximately 3 hours.

Patients should be advised not to take alcohol during metronidazole therapy and for at least 48 hours afterwards, because of the possibility of a disulfiram-like (Antabuse) reaction

Patients receiving cyclosporine are at risk of elevated cyclosporine serum levels. Cyclosporin and serum creatinine should be closely monitored when co-administration is necessary.

Metronidazole reduces the clearance of 5-fluorouracil and can therefore result in increased toxicity of 5-fluorouracil.

Plasma levels of busulfan may be increased by metronidazole which may lead to severe busulfan toxicity.

Overdosage

There is no specific treatment for gross overdosage of TRICHOZOLE tablets.

Pharmaceutical Precautions

Store below 25°C. Protect from light.

Medicine Classification

Prescription Medicine.

Package Quantities

TRICHOZOLE 200: 100 tablets.

TRICHOZOLE 400: 100 tablets.

Further Information

Metronidazole has no useful direct activity against aerobic and facultatively anaerobic bacteria.

TRICHOZOLE 200 mg tablets also contain lactose, maize starch, microcrystalline cellulose, Povidone and magnesium stearate.

TRICHOZOLE 400 mg tablets also contain lactose, maize starch, microcrystalline cellulose, Povidone, magnesium stearate, sodium starch glycollate and Quinoline Yellow Aluminium Lake (E104).

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