Metronidazole Injection USP (0.5% w/v) 100 ml

Metris™

QUALITATIVE AND QUANTITATIVE COMPOSITION
The active component of this injection is Metronidazole USP 0.5% w/v.

PHARMACEUTICAL FORM
A clean, bright, pale yellow sterile isotonic solution for intravenous infusion.

CLINICAL PARTICULARS
Therapeutic indications : Metronidazole is indicated in the prophylaxis and treatment of infections in which anaerobic bacteria have been identified or are suspected to be the cause. Metronidazole is active against a wide range of pathogenic micro-organisms notably species of *Bacteroides, Fusobacteria, Clostridia, Eubacteria, anaerobic cocci* and *Gardnerella vaginalis*. It is indicated in:
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.

Posology and method of administration : Metronidazole injection should be infused intravenously at an approximate rate of 5 ml/min. Oral medication should be substituted as soon as feasible.
ANAEROBIC INFECTIONS: Treatment for seven days should be satisfactory for most patients but, depending upon clinical and bacteriological assessments, the physician might decide to prolong treatment e.g. for the eradication of infection from sites which cannot be drained or are liable to endogenous recontamination by anaerobic pathogens from the gut, oropharynx or genital tract.
PROPHYLAXIS AGAINST ANAEROBIC INFECTION: Chiefly in the context of abdominal (especially colorectal) and gynaecological surgery. Adults : 500mg shortly before operation, repeated 8 hourly. Oral doses of 200 mg or 400 mg 8 hourly to be started as soon as feasible Children : 7.5 mg/kg (1.5 ml/kg) 8 hourly.
TREATMENT OF ESTABLISHED ANAEROBIC INFECTIONS : Intravenous route is to be used initially if patient's symptoms preclude oral therapy.
ADULTS : 500 mg 8 hourly.
CHILDREN : 7.5 mg/kg 8 hourly.
ELDERLY : Caution is advised in the elderly. Particularly at high doses although there is limited information available on modification of dosage.

Contraindications : Known hypersensitivity to Metronidazole.

Special warnings and special precautions for use : Metronidazole has no direct activity against aerobic or facultative anaerobic bacteria.
Regular clinical and laboratory monitoring are advised if administration of Metronidazole 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. Therefore the dosage of Metronidazole 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 efficiently removed during an eight-hour period of dialysis. Metronidazole should therefore be re-administered immediately after haemodialysis.
No routine adjustment in the dosage of Metronidazole need be made in patients with renal failure undergoing intermittent peritoneal dialysis (IDP) 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. Metronidazole 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 daily.
Aspartate amino transferase assays may give spuriously low values in patients being treated with metronidzole depending on the method used. Metronidazole should be used with caution in patients with active disease of the CNS.
Cefuroxime is physically and chemically compatible with Metronidazole. The following drugs have been shown to be physically compatible in terms of pH and appearance with Metronidazole injection over the normal period of administration, although there is no evidence of chemical stability: amikacin sulphate, ampicillin sodium, carbenicillin sodium, cephazolin sodium, cefotaxime sodium, cephalothin sodium, chloramphenicol sodium succinate, clindamycin phosphate, gentamicin sulphate, hydrocortisone sodium succinate, latamoxef disodium, netilmicin sulphate and tobramycin sulphate. In patients maintained on intravenous fluids, Metronidazole injection may be diluted with appropriate volumes of normal saline, dextrose-saline, dextrose 5% w/v or potassium chloride infusions (20 and 40 mmol/litre). Apart from the above, Metronidazole should on no account be mixed with any other substance.

Interaction with other medicaments and other forms of Interaction : 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 effect) reaction.
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 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 concentrations of lithium, creatinine and electrolytes should be monitored in patients under treatment with lithium while they receive metronidazole.
Patients receiving phenobarbitone metabolise metronidazole at a much greater rate than normally, reducing the half-life to approximately 3 hours.

Metronidazole reduces the clearance of 5 fluorouracil and can therefore result in increased toxicity of 5 fluorouracil.
Patients receiving cyclosporin are at risk of elevated cyclosporin serum levels. Serum cyclosporin and serum creatinine should be closely monitored when coadministration is necessary.

Pregnancy and lactation : There is inadequate evidence of the safety of metronidazole in pregnancy. Metronidazole should not therefore be given during pregnancy or during lactation unless the physician considers it essential; in these circumstances the short, high-dosage regimens are not recommended.

Effects on ability to drive and use machines : Patients should be warned about the potential for drowsiness, dizziness, confusion, hallucinations, convulsions or transient visual disorders, and advised not to drive or operate machinery if these symptoms occur.

Undesirable effects : During intensive and/or prolonged metronidazole therapy, a few instances of peripheral neuropathy or transient epileptiform seizures have been reported. In most cases neuropathy disappeared after treatment was stopped or when dosage was reduced. A moderate leucopenia has been reported in some patients but the white cell count has always returned to normal before or after treatment has been completed.
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.
Serious adverse reactions occur rarely with standard recommended regimens. Taste disorders, oral mucositis, furred tongue, nausea, vomiting, gastro-intestinal disturbances, anorexia, urticaria and angioedema occur occasionally. Anaphylaxis may occur rarely. Erythema multiforme may occur, which may be reversed on drug withdrawal.
Abnormal liver function tests, cholestatic hepatitis, jaundice and pancreatitis, reversible on drug withdrawal, have been reported very rarely.
Agranulocytosis, neutropenia, thrombocytopenia and pancytopenia, often reversible on drug withdrawal, have very rarely been reported, although fatalities have occurred.
Drowsiness, dizziness, headaches, ataxia, skin rashes, pustular eruptions, pruritus, inco-ordination of movement, darkening of urine (due to metronidazole metabolite) myalgia arthralgia and transient visual disorders such as diplopia and myopia have been reported but very rarely.
Psychotic disorders, including confusion and hallucinations, have been reported very rarely.

Overdose : There is no specific treatment for gross overdosage of Metronidazole.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties : 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.

Pharmacodynamic properties : Metronidazole is widely distributed in body tissues after injection. At least half the dose is excreted in the urine as metronidazole and its metabolites, including an acid oxidation product, a hydroxy derivative and glucuronide. Metronidazole diffuses across the placenta, and is found in breast milk of nursing mothers in concentrations equivalent to those in serum.
10% of the dose is bound in plasma.
Clearance: 1.3 ± 0.3 ml/min/kg.
Volume of distribution: 1.1 ± 0.4 litres/kg.
Half-life: 8.5 ± 2.9 hours.
Effective concentration: 3-6 micrograms/ml.

PHARMACEUTICAL PARTICULARS

List of excipients : Metronidazole injection also contains the following excipients: sodium chloride, citric acid monohydrate, disodium hydrogen phosphate, sodium hydroxide, hydrochloric acid.

Incompatibilities : Metronidazole injection should not be mixed with cefamandole nafate, cefoxitin sodium, dextrose 10% w/v, compound sodium lactate injection, penicillin G potassium.

Shelf life : 36 months from the date of manufacture.

Special precautions for storage : 100 ml bottle, store below 30°C, protect from light.

Nature and contents of container : Metronidazole injection 0.5% w/v (100 ml) is available in 100 ml Plastic Bottle.

Instructions for use and handling : The containers are for single use only. Discard any unused portion. Do not reconnect partially used containers.

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THIS IS A MEDICAMENT

Medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you. Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.

- The doctor and the pharmacist are experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription, without consulting your Doctor.
- Keep all medicaments out of the reach of children.

Council of Arab Health Ministers, Union of Arab Pharmacists.

Manufactured by :
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