1.3.1.1 PROFESSIONAL INFORMATION

SCHEDULING STATUS S4

PROPRIETARY NAME AND DOSAGE FORM

ADCO METRONIDAZOLE 500 mg/100 ml

Infusion (Parenteral)

COMPOSITION

Each 100 ml sterile non-pyrogenic solution contains 500 mg metronidazole.

List of excipients: Citric acid monohydrate BP or citric acid anhydrous BP, sodium phosphate BP (dodecahydrate), sodium chloride BP, 10 % citric acid, sodium phosphate dodecahydrate 10 % solution, water for injection.

Sugar free

CATEGORY AND CLASS

A 20.2.6. Antimicrobial agents; Medicines against protozoa

PHARMACOLOGICAL ACTION

Metronidazole has antiprotozoal activity against *Trichomonas vaginalis* and other protozoa, including *Entamoeba histolytica* and *Giardia lamblia.* It does not affect the acidophilic flora of the vagina and it has no effect on candida species. Metronidazole displays antibacterial activity against all anaerobic cocci and both anaerobic Gram-negative bacilli, including bacteroides species and anaerobic spore-forming Gram-positive bacilli.

Nonsporulating Gram-positive bacilli are often resistant, as are aerobic and facultatively anaerobic bacteria.

The liver is the main site of metabolism, and this accounts for over 50 % of the systemic clearance of metronidazole. Both the two principal metabolites, resulting from oxidation of side chains, have antitrichomonal activity. The unchanged metronidazole and several metabolites are excreted in various proportions in the urine.

The half-life of metronidazole in plasma is about 8 hours and its volume of distribution is approximately that of total body water. The half-life of metronidazole is reported to be longer in neonates and in patients with severe liver disease. About 10 % of the metronidazole is bound to plasma proteins. Metronidazole penetrates well into body tissues and fluids, including vaginal secretions, seminal fluid, saliva, breast milk, cerebrospinal fluid, bile, urine, amniotic fluid and in abscess cavities.

The mechanism of action of metronidazole is reflected in a selective toxicity to anaerobic or microaerophilic micro-organisms and for anoxic or hypoxic cells. The parent compound penetrates the cell membrane unchanged, but once inside the cell the nitro group is reduced in the redox conditions prevalent in the anaerobic cell. The reduced product is known to damage DNA causing eventual death of the organism.

INDICATIONS

Intravenous administration should be restricted to emergency pre-operative loading, in patients who are unable to receive oral or rectal administration.

a) For the treatment of infections in which anaerobic bacteria have been identified or are suspected as pathogens, particularly *Bacteroides fragilis* and other species of bacteroides, for which metronidazole is bactericidal, such as *fusobacteria, eubacteria, clostridia* and anaerobic streptococci. Metronidazole may also be used along with appropriate antimicrobial agents for concomitant infections with aerobic micro-organisms.

b) For the treatment of all symptomatic forms of amebiasis.

c) Metronidazole has shown to be effective in treating giardiasis.

d) For the prevention of post-operative infections due to anaerobic bacteria, particularly species of bacteroides and anaerobic streptococci:

- given before and after gynaecological surgery;
- given before and after appendectomy;
- given before and after colonic surgery.

e) ADCO METRONIDAZOLE 500 mg/100 ml has also been used successfully in the following conditions from which one or more of these anaerobes have been isolated:

- Pelvic abscess
- post operative wound infections

CONTRAINDICATIONS

Contraindicated in patients sensitive to metronidazole. Should not be given to patients with blood dyscrasias or with active diseases of the central nervous system. Contraindicated in pregnancy and lactation.

WARNINGS AND SPECIAL PRECAUTIONS

It is recommended that other medicine not be added to ADCO METRONIDAZOLE 500 mg/100 ml as additives may be incompatible. Do not use unless the solution is clear.

The dosage should be reduced in patients with severe obstructive hepatic disease, alcohol cirrhosis or severe renal dysfunction.

Precautions: Prolonged courses of treatment should be avoided as studies have indicated that metronidazole is carcinogenic in some animals and mutagenic in bacteria.

Renal failure: The dose interval should be prolonged from 8 to 12 hours in the presence of glomerular filtration rate below 10 ml per minute.

Do not remove unit from over pouch until ready for use. After removing overwrap, check bag for minute leaks by squeezing firmly. If leaks are found, discard solution as sterility may be impaired.

INTERACTIONS

Alcohol should be avoided during treatment with **ADCO METRONIDAZOLE 500 mg/100 ml**, because of the possibility of a disulfiram-like reaction. Slight and transient falls in blood pressure have been reported with the parent substance; it may therefore be advisable to lower the dosage of any anti-hypertensive medicine which may be given concurrently with **ADCO METRONIDAZOLE 500 mg/100 ml.**

Metronidazole enhances the effect of warfarin and if ADCO METRONIDAZOLE 500 mg/100 ml is to be given to patients receiving this or other oral anticoagulants, the dosage of the latter should be recalibrated. There is no interaction with heparin.

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

HUMAN REPRODUCTION

Safety in pregnancy and lactation has not been established

DOSAGE AND DIRECTIONS FOR USE

a) Treatment - adults and children over 12 years:

The recommended intravenous dosage regimen for anaerobic

infections include a loading dose (15 mg/kg) followed 6 hours

later by a maintenance dose of 7,5 mg/kg every six hours, usually

for 7 to 10 days.

When the 100 ml intravenous infusion is given eight-hourly, the injection rate should be 5 ml per minute.

It may be administered alone or concurrently (but separately) with other bacteriologically appropriate antibacterial agents in parenteral dosage forms. Oral medication should be substituted as soon as this becomes feasible. Treatment for seven days should be satisfactory for most patients but, depending upon clinical and bacteriological assessments, the doctor might decide to prolong the treatment, e.g. for the eradication of infection from sites which cannot be drained or are liable to endogenous re-contamination by anaerobic pathogens from the gut, oropharynx or genital tract.

Children under 12 years:

As for adults, but a single intravenous dose is based on 1,5 ml

(7,5 mg metronidazole)/kg body mass and the oral dose on 7

mg/kg body mass.

b) *Prevention - adults and children over 12 years:*

100 ml by intravenous infusion immediately before, during or after operation, followed by the same dose eight-hourly until oral medication can be given to complete a seven-day course.

Children under 12 years:

As for adults, but the single intravenous dose is based on 1,5 ml (7,5 mg metronidazole)/kg body mass.

In infants and other patients maintained on intravenous fluids, ADCO METRONIDAZOLE 500 mg/100 ml may be diluted with appropriate volumes of normal saline, dextrose-saline, dextrose 5 % m/v or potassium chloride injections (20 mmol and 40 mmol/L).

ADCO METRONIDAZOLE 500 mg/100 ml is compatible with the following injections:

Sodium Chloride Injection 0,9 % m/v

Dextrose 5 % m/v Injection

Potassium Chloride injection 20 mmol/L.

Potassium Chloride injection 40 mmol/L.

SIDE EFFECTS

The adverse effects of metronidazole are generally dose related. The most common are gastrointestinal disturbances; especially nausea (sometimes accompanied by headache); an unpleasant metallic taste, anorexia and vomiting. Diarrhoea, abdominal cramps, epigastric comfort, dry mouth and vagina, a furred tongue, glossitis and stomatitis may also occur.

Metronidazole may cause peripheral neuropathy, especially at high doses or prolonged treatment. Weakness, dizziness, ataxia, drowsiness, insomnia and changes in mood or mental state such as depression or confusion have also been reported. Patients receiving ADCO METRONIDAZOLE 500 mg/100 ml for more than ten days should be closely monitored for signs of peripheral neuropathy or central nervous system toxicity. The use of ADCO METRONIDAZOLE 500 mg/100 ml should be discontinued if neurological side effects are noted.

Temporary moderate leucopenia, raised liver enzyme values, skin rashes, pruritus, urticaria and cystitis may occur. Anaphylaxis has been reported. Other side effects include urethral discomfort and darkening of the urine. Thrombophlebitis may follow intravenous administration of metronidazole.

KNOWN SYMPTOMS OF OVER-DOSAGE AND PARTICULARS OF ITS TREATMENT

See "**SIDE EFFECTS".** There is no specific treatment for gross overdosage of metronidazole.

Treatment is symptomatic and supportive.

IDENTIFICATION

A clear, bright, pale yellow solution.

PRESENTATION

ADCO METRONIDAZOLE 500 mg/100 ml is supplied in a 100 ml Viaflex® plastic container.

STORAGE INSTRUCTIONS

Store at or below 25 °C. Protect from direct sunlight.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS

27/20.2.6/0562

NA: NS2 17/20.2.6/0086

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

Adcock Ingram Critical Care (Pty) Ltd

1 Sabax Road,

Aeroton,

Johannesburg, 2013

www.adcock.co.za

DATE OF PUBLICATION OF THIS PROFESSIONAL INFORMATION

Date of Registration: 24 September 1993

Date amended: 31/01/2018

Viaflex® is a registered trademark of BAXTER INTERNATIONAL INC.

Under license from BAXTER INTERNATIONAL INC.