Protoxil

(Metronidazole) B.P

TABLETS

INFUSION

COMPOSITION
PROTOXIL 200mg Tablet:
Each film coated tablet contains: Metronidazole (B.P).....200mg
PROTOXIL 400mg Tablet:
Each film coated tablet contains: Metronidazole (B.P).....400mg
PROTOXIL Infusion:
Each 100ml contains: Metronidazole (B.P).....500mg

PHARMACO-THERAPEUTIC CLASS
Anti-amoebic, Anti-infective.

THERAPEUTIC INDICATIONS
INTRAVENOUS INFUSION: PROTOXIL is indicated in the prophylaxis and treatment of infections in which anaerobic bacteria have been identified or are suspected to be the cause.
PROTOXIL 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: The prevention of postoperative infections due to anaerobic bacteria, particularly species of Bacteroides and anaerobic Streptococci. 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.

ORAL ROUTE OF ADMINISTRATION
PROTOXIL is indicated in the prophylaxis and treatment of infections in which anaerobic bacteria have been identified or are suspected to be the cause. PROTOXIL is active against a wide range of pathogenic micro-organisms notably species of Bacteroides, Fusobacteria, Clostridia, Eubacteria, anaerobic cocci and Gardnerella vaginalis. It is also active against Trichomonas, Entamoeba histolytica, Giardia lamblia and Balantidium coli.

IT IS INDICATED IN
1. The prevention of post-operative 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 (e.g. acute pericoronitis and acute apical infections).

DOSAGE AND ADMINISTRATION
INTRAVENOUS INFUSION
PROTOXIL injection should be infused intravenously at an approximate rate of 5ml/min. Oral medication should be substituted as soon as feasible.

1- 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.

2- PROPHYLAXIS AGAINST ANAEROBIC INFECTION: Intravenous route is to be used initially if patient's symptoms preclude oral therapy. 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.

3- TREATMENT OF ESTABLISHED ANAEROBIC INFECTIONS
ADULTS: 500 mg 8 hourly.
CHILDREN: 7.5mg/kg 8 hourly.
- Initial loading dose 15 mg/kg IV infused over 60 minutes,
- Term infants, maintenance, 7.5 mg/kg IV every 24 hrs, starting 48 hrs after initial dose
- Term infants, (1-4 weeks of age) maintenance, 7.5 mg/kg IV every 12 hrs starting 24 hrs after the initial dose
- Infants and children maintenance, 30 mg/kg/day IV divided every 6 hr; maximum 4 g/day

ELDERLY: Caution is advised in the elderly. Particularly at high doses although there is limited information available on modification of dosage.

ORAL ROUTE OF ADMINISTRATION
PROTOXIL tablets should be swallowed with water (not chewed). It is recommended that the tablets be taken during or after a meal.
1- ANAEROBIC INFECTIONS: The duration of a course of PROTOXIL treatment is about 7 days but it will depend upon the seriousness of the patient's conditions assessed clinically and bacteriologically.
2- PROPHYLAXIS AGAINST ANAEROBIC INFECTION: Chiefly in the context of abdominal (especially colorectal) and gynecological surgery.
ADULTS: 400 mg 8 hourly intervals during 24 hours immediately preceding operation followed by postoperative intravenous or rectal administration until the patient is able to take tablets.
CHILDREN: 7.5 mg/ kg - 8 hourly.
3- TREATMENT OF ESTABLISHED ANAEROBIC INFECTION
ADULTS: 800 mg followed by 400 mg 8 hourly.
CHILDREN: 7.5 mg/kg 8 hourly
4- PROTOZOAL AND OTHER INFECTIONS
Dosage is given in terms of metronidazole or metronidazole equivalent

	Duration of Dosage in Days	Adults and Children Over 10 Years
Urogenital trichomoniasis	7 or	200 mg three times daily or 400 mg twice daily
Where re-infection is likely, in adults the consort should receive a similar course of treatment concurrently	2 or	800 mg in the morning and 1,200 mg in the evening
		2.0 g as a single dose
Bacterial Vaginosis	7 or	400 mg twice daily
	1	2.0g as a single dose
Amoebiasis **a)** Invasive intestinal disease in susceptible subjects	5	800 mg three times daily
b) Intestinal disease in less susceptible subjects and chronic amoebic hepatitis	5-10	400 mg three times daily
c) Amoebic liver abscess also other forms of extra-intestinal amoebiasis	5	400 mg three times daily —
d) Symptomless cyst passers	5-10	400-800 mg three times daily
Giardiasis	3	2.0 g once daily
Acute ulcerative gingivitis	3	200 mg three times daily
Acute dental infections	3-7	200 mg three times daily
Leg ulcers and pressure sores	7	400 mg three times daily

CONTRAINDICATIONS: Hypersensitivity to imidazoles.

WARNINGS: Metronidazole should be used with caution in patients with active or chronic severe peripheral and central nervous system diseases due to the risk of neurological aggravation.
Patients should be advised not to take alcohol during metronidazole therapy and for at least one day afterwards because of the possibility of a disulfiram-like (Antabuse effect) reaction.

PRECAUTIONS
The use of PROTOXIL for prolonged treatment duration should be carefully weighed.
If for compelling reasons, metronidazole must be administered longer than the usually recommended duration, it is recommended that hematological tests, especially leukocytes count should be carried out regularly and that patients should be monitored for adverse reactions such as peripheral or central neuropathy (such as paresthesia, ataxia, dizziness, convulsive seizures).
PROTOXIL should be administered with caution to patients with hepatic encephalopathy. Patients should be warned that metronidazole may darken urine (due to metronidazole metabolite).

DRIVING A VEHICLE OR PERFORMING OTHER HAZARDOUS TASKS
Patients should be warned about the potential for confusion, dizziness, hallucinations, convulsions or eye disorders, and advised not to drive or operate machinery if these symptoms occur.

INTERACTIONS
DISULFIRAM: psychotic reactions have been reported in patients who were using metronidazole and disulfiram concurrently.
ALCOHOL: alcoholic beverages and drugs containing alcohol should not be consumed during therapy and for atleast one day afterwards because of the possibility of a disulfiram-like (antabuse effect) reaction (flushing, vomiting and tachycardia)
ORAL ANTICOAGULANT THERAPY (WARFARIN TYPE): Potentiation of the anticoagulant effect and increased hemorrhagic risk caused by decreased hepatic catabolism. In case of coadministration, prothrombin time should be more frequently monitored and anticoagulant therapy adjusted during treatment with metronidazole.
LITHIUM: Plasma levels of lithium may be increased by metronidazole. Plasma concentration of lithium, creatinine and electrolytes should be monitored in patients under treatment with lithium while they receive metronidazole.
CYCLOSPORIN: Risk of elevation of cyclosporin serum levels. Serum cyclosporin and serum creatinine should be closely monitored when coadministration is necessary.
PHENYTOIN OR PHENOBARBITAL: Increased elimination of metronidazole resulting in reduced plasma levels.
5 FLUOROURACIL: Reduced clearance of 5 fluorouracil resulting in increased toxicity of 5 fluorouracil.
BUSULFAN: Plasma levels of busulfan may be increased by metronidazole, which may lead to severe busulfan toxicity.
PREGNANCY: As metronidazole crosses the placental barrier and as its effects on human fetal organogenesis are not known, its use in pregnancy should be carefully evaluated.
LACTATION: As metronidazole is excreted in human milk, unnecessary exposure to the drug should be avoided.

ADVERSE REACTIONS
The following CIOMS frequency rating is used, when applicable:-
Very common ≥ 10%; Common ≥ 1 and <10%; Uncommon ≥ 0.1 and < 1%; Rare ≥ 0.01 and < 0.1%; Very rare < 0.01%, Unknown (cannot be estimated from available data).
GASTROINTESTINAL DISORDERS
- Epigastric pain, nausea, vomiting, diarrhea.
- Oral mucositis, taste disorders, anorexia.
- Reversible cases of pancreatitis.

IMMUNE SYSTEM DISORDERS
- Angioedema, anaphylactic shock.

NERVOUS SYSTEM DISORDERS
- Peripheral sensory neuropathy.
- Headache, convulsions, dizziness.
- Reports of encephalopathy (e.g. confusion) and subacute cerebellar syndrome (e.g. ataxia, dysarthria, gait impairment, nystagmus, and tremor), which may resolve with discontinuation of the drug.
- Aseptic meningitis.

PSYCHIATRIC DISORDERS
- Psychotic disorders including confusion, hallucinations
- Depressed mood
- Eye disorders
- Transient vision disorders such as diplopia, myopia, blurred vision, decreased visual acuity, changes in color vision.
- Optic neuropathy/ neuritis.

BLOOD AND LYMPHATIC SYSTEM DISORDERS
Cases of agranulocytosis, neutropenia and thrombocytopenia have been reported.
HEPATOBILIARY DISORDERS
- Increase in liver enzymes (AST, ALT, alkaline phosphatase), cholestatic or mixed hepatitis and hepatocellular liver injury, sometimes with jaundice, have been reported.
- Cases of liver failure requirement liver transplant have been reported in patients treated with metronidazole in combination with other antibiotic drugs.

SKIN AND SUBCUTANEOUS TISSUE DISORDERS
- Rash, pruritus, flushing, urticaria.
- Pustular eruptions.

GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS
- Fever

OVERDOSE
Single oral doses of metronidazole, up to 12 g have been reported in suicide attempts and accidental overdoses.

SIGNS AND SYMPTOMS
Symptoms were limited to vomiting, ataxia and slight disorientation.

MANAGEMENT
There is no specific Antidote for metronidazole overdosages. In case of suspected massive overdosages, a symptomatic and supportive treatment should be instituted.

INSTRUCTIONS
PROTOXIL TABLETS AND INFUSION: Store below 30°C.
INTRAVENOUS INFUSION: Do not use if bottle is leaking, solution is cloudy or contains foreign matter.
Protect from light & heat. Keep all medicines out of the reach of children.
To be sold on the prescription of a registered medical practitioner only.

PRESENTATION
PROTOXIL 200mg Tablet: Pack of 10x10 Tablets
PROTOXIL 400mg Tablet: Pack of 10x10 Tablets
PROTOXIL IV Infusion: 1 x 100ml Bottle

پروٹوکسل ٹیبلیٹس/ اِنفیوژن

(میٹرو نیڈازول) بی پی

خون کی نالی میں لگانے کے لیے

انفیوژن کے ایک ہونے، دھندلا ہونے یا اس میں کوئی غیر حل پذیر شے نظر آنے کی صورت میں ہرگز استعمال نہ کریں۔

ہدایات: دوا کو **30°** سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ روشنی اور حرارت سے بچائیں۔ تمام دوائیں بچوں کی پہنچ سے دُور رکھیں۔ صرف مستند ڈاکٹر کے نسخے پر فروخت کریں۔

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