# SUMMARY OF PRODUCT CHARACTERISTICS

## 1 NAME OF THE MEDICINAL PRODUCT

Metrolyl* (Metronidazole) Tablets BP 400mg

Metronidazole 400mg Tablets

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 400mg tablet contains metronidazole BP 400mg.

## 3. PHARMACEUTICAL FORM

Tablet.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Metrolyl* is indicated in adults and children for the following indications:

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 eg: Fusobacteria, Eubacteria, Clostridia and anaerobic cocci.

Metrolyl* can be used in septicaemia, bacteraemia, brain abscess, necrotising pneumonia, osteomyelitis, puerperal sepsis, pelvic abscess, peritonitis and post-operative wound infection from which one or more of these anaerobes have been isolated.

Prevention of post-operative infections due to anaerobic bacteria.

Use in treatment of acute ulcerative gingivitis and acute dental, pericoronitis and apical infections.

Trichomonas infections.

Amoebiasis.

Giardiasis.

Anaerobically infected leg ulcers and pressure sores.

Bacterial vaginosis.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

## 4.2 Posology and method of administration

Seven days' treatment should be satisfactory for most patients. Prolonged treatment can be used if the physician considers it to be necessary.
Recommended doses are given as a guideline based on experience. If therapy is to continue for longer than 10 days, clinical and laboratory monitoring is advised.

Metrolyl* Tablets should be swallowed with water during or after a meal.

**TREATMENT OF ANAEROBIC INFECTIONS**

Metronidazole tablets may be given alone or in association with other appropriate bactericidal agents.

Adults:

400mg, 3 times daily.

Children:

Children > 8 weeks to 12 years of age: The usual daily dose is 20-30 mg/kg/day as a single dose or divided into 7.5 mg/kg every 8 hours. The daily dose may be increased to 40 mg/kg, depending on the severity of the infection. Duration of treatment is usually 7 days.

Children < 8 weeks of age: 15 mg/kg as a single dose daily or divided into 7.5 mg/kg every 12 hours. In newborns with a gestation age <40 weeks, accumulation of metronidazole can occur during the first week of life, why the concentrations of metronidazole in serum should preferable be monitored after a few days therapy.

**PROPHYLAXIS AGAINST POSTOPERATIVE INFECTIONS CAUSED BY ANAEROBIC BACTERIA**

**Gynaecological Surgery**

Adults:

1 gram orally as a single dose followed by 200mg orally, 3 times daily until pre-operative withholding of solids and liquids by mouth becomes necessary. Oral

medication with 200mg, 3 times daily should be resumed after the operation and for up to 7 days.

Children:

Children < 12 years: 20-30 mg/kg as a single dose given 1-2 hours before surgery.
Newborns with a gestation age <40 weeks: 10 mg/kg body weight as a single dose before
operation.

**Pre-operative Medication for Elective Colonic Surgery**

Adults:

(i) 200mg orally, 6 hourly co-administered with an aminoglycoside antibiotic for 3 days before surgery.

(ii) 400mg orally, 8 hourly with phthalylsulphathiazole (2.5g, 6 hourly) for 4 days before surgery.

Children:

Children < 12 years: 20-30 mg/kg as a single dose given 1-2 hours before surgery.
Newborns with a gestation age <40 weeks: 10 mg/kg body weight as a single dose before operation.

**Oral Dosage Regime for Metrolyl***

| | Adults/Children over 10 years | Children 7-10 years | Children 3-7 years | Children 1-3 years |
|---|---|---|---|---|
| Urogenital trichomoniasis (treat sexual partners concurrently) | 200mg tds x 7d **or** 400mg bds x 5-7d **or** 2g once | Children < 10 years: 40 mg/kg orally as a single dose or 15 – 30 mg/kg/day divided in 2-3 doses for 7 days; not to exceed 2000 mg/dose. | | |
| Bacterial vaginosis | 400mg bds x 5-7d **or** 2g once | | | |
| Amoebiasis:<br>a) invasive intestinal disease in susceptible subjects | 800mg tds x 5d | 400mg tds x 5d | 200mg qds x 5d | 200mg tds x 5d |

| | | | | |
|---|---|---|---|---|
| b) intestinal disease in less susceptible subjects and chronic amoebic hepatitis | 400mg tds x 5-10d | 200mg tds x 5-10d | 100mg qds x 5-10d | 100mg tds x 5-10d |
| c) amoebic liver abscess and other forms of extra-intestinal amoebiasis | 400mg tds x 5d | 200mg tds x 5d | 100mg qds x 5d | 100mg tds x 5d |
| d) symptomless cyst passers | 400mg-800mg tds x 5-10d | 200mg-400mg tds x 5-10d | 100mg-200mg qds x 5-10d | 100mg-200mg tds x 5-10d |
| | Alternatively, doses may be expressed by body weight 35 to 50 mg/kg daily in 3 divided doses for 5 to 10 days, not to exceed 2400 mg/day. | | | |
| Giardiasis: | 2,000mg od x 3d **or** 400mg tds x 5d **or** 500mg bds x 7-10d | 1,000mg od x 3d | 600mg-800mg od x 3d | 500mg od x 3d |
| | Alternatively, as expressed in mg per kg of body weight: 15-40 mg/kg/day divided in 2-3 doses. | | | |
| Acute ulcerative gingivitis: | 200mg tds x 3d | 100mg tds x 3d | 100mg bd x 3d | 50mg tds x 3d |
| Acute dental infections: | 200mg tds x 3-7d | | | |
| Leg ulcers and pressure sores: | 400mg tds x 7d | | | |

Proportionately smaller dosages should be given to children and babies weighing less than 10kg.

Eradication of Helicobacter pylori in paediatric patients:

As a part of a combination therapy, 20 mg/kg/day not to exceed 500 mg twice daily for 7-14 days.

Official guidelines should be consulted before initiating therapy

Method of administration: oral. Metrolyl* Tablets should be swallowed with water during or after a meal.

## 4.3. Contra-Indications

There are no known absolute contraindications for the use of Metrolyl*, however, known sensitivity to metronidazole is an absolute contraindication.

## 4.4 Special warnings and precautions for use

Hepatotoxicity in patients with Cockayne Syndrome:

Cases of severe hepatotoxicity/acute hepatic failure, including cases with a fatal outcome with very rapid onset after treatment initiation in patients with Cockayne syndrome have been reported with products containing metronidazole for systemic use. In this population, metronidazole should not be used unless the benefit is considered to outweigh the risk and if no alternative treatment is available. Liver function tests must be performed just prior to the start of therapy, throughout and after end of treatment until liver function is within normal ranges, or until the baseline values are reached. If the liver function tests become markedly elevated during treatment, the drug should be discontinued.

Patients with Cockayne syndrome should be advised to immediately report any symptoms of potential liver injury to their physician and stop taking metronidazole (see section 4.8).

Clinicians considering continuous therapy for relief of chronic conditions are advised to consider the therapeutic benefit against risk of peripheral neuropathy.

Underlying gonococcal infection may persist after elimination of *Trichomonas vaginalis*.

No dose modification is needed in renal failure since the elimination half-life of metronidazole is unchanged in this condition. The clinical significance of retained metabolites is not known; their efficient removal occurs during dialysis so that metronidazole should be re-administered after haemodialysis. No dosage adjustment is needed for patients undergoing intermittent or continuous ambulatory peritoneal dialysis.

Impairment of metronidazole clearance may occur in patients with advanced hepatic insufficiency since the drug is mainly metabolised by hepatic oxidation. High concentrations of metronidazole may contribute to the symptoms of hepatic encephalopathy - a condition in which significant cumulation may occur. Dose reduction to one-third once daily may be needed.

Metronidazole has no activity against aerobic or facultative anaerobic bacteria.

## 4.5. Interactions with other Medicaments and other forms of Interaction

The consumption of alcohol during metronidazole therapy should be avoided since there could be a disulfiram-like reaction.

The half-life of metronidazole is reduced from 7-8 hours to about 3 hours in patients receiving phenobarbitone.

In patients taking metronidazole, the assay of aspartate amino transferase may give spuriously low values: this depends on the method used.

Potentiation of warfarin-type (but not heparin) anticoagulant therapy has been reported so that dose adjustment of the anticoagulant may be needed.

Lithium retention with evidence of possible renal damage has been reported where this compound and metronidazole have been used concurrently. Preferably, apart from monitoring lithium, creatinine and electrolyte concentrations, lithium therapy should be tapered and/or withdrawn before use of metronidazole.

## 4.6. Pregnancy and Lactation

The safety of use of metronidazole in pregnancy has not been established and its use should be avoided; if essential, short high-dose regimes should not be used. Metronidazole is excreted in milk and no adverse effects in the new-born have been reported; the intake by the suckling infant of a mother receiving normal dosage is less than a therapeutic dose for infants.

## 4.7. Effects on Ability to Drive and Use Machines

Patients should be warned not to drive or operate machinery if they become dizzy or drowsy.

## 4.8 Undesirable effects

Serious reactions are rare.

An unpleasant taste in the mouth, oral mucositis, furred tongue, nausea, vomiting or other gastro-intestinal disturbance have been reported.

There is evidence that metronidazole has been associated with abnormal liver function tests, cholestatic hepatitis and jaundice which may be reversed upon drug withdrawal. Urticaria, skin rash, pruritus, angioedema and rarely anaphylaxis have occurred.

Erythema multiforme has been reported but this resolved on drug withdrawal.

Drowsiness, dizziness, headache, confusion, hallucinations, ataxia and darkening of the urine (due to metabolites) have been reported rarely.

Peripheral neuropathy and/or transient epileptiform seizures have occurred during prolonged or intensive treatment but in most cases neuropathy disappears on cessation of therapy.

There have been reports of bone marrow depression disorders such as agranulocytosis, leucopenia, neutropenia, thrombocytopenia and pancytopenia which may be reversed on drug withdrawal, although fatalities have been reported.

Other side affects reported include myalgia and arthralgia.

Frequency, type and severity of adverse reactions in children are the same as in adults

Cases of severe irreversible hepatotoxicity/acute liver failure, including cases with fatal outcomes with very rapid onset after initiation of systemic use of metronidazole, have been reported in patients with Cockayne Syndrome (see section 4.4).

### 4.9. Overdose

There is no specific treatment and uneventful recovery has followed ingestion of up to 12g.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 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.

### 5.2. Pharmacokinetic Properties

Absorption following administration of Metrolyl* Tablets is very rapid. Peak serum concentrations were reached in 45 to 60 minutes.

### 5.3. Preclinical Safety Data

Not required.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Lactose, microcrystalline cellulose, maize starch, povidone and magnesium stearate.

### 6.2. Incompatibilities

Not known.

### 6.3. Shelf Life

36 months.

### 6.4. Special Precautions for Storage

Do not store above 25°C. Store in the original container.

### 6.5. Nature and Contents of Container

Securitainers. Pack size: 100.

And

PVC/PE/PVDC and Alu foil blister pack.
Pack sizes of 14 and 21

### 6.6. Instruction for Use/Handling

Not relevant.

## 7 MARKETING AUTHORISATION HOLDER

Sandoz Limited

200 Frimley Business Park

Frimley

Camberley

GU16 7SR

United Kingdom

## 8. MARKETING AUTHORISATION NUMBER(S)

PL 4416/0061

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

12/03/2009

## 10 DATE OF REVISION OF THE TEXT

24/07/2023