**AUSTRALIAN PRODUCT INFORMATION**

# METROGYL®

*(Metronidazole) tablets*

## 1 NAME OF THE MEDICINE

Metronidazole

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each METROGYL 200 and METROGYL 400 contains the active ingredient metronidazole 200 mg and metronidazole 400 mg respectively.

Excipients with known effect: sulfites, galactose and sugars as lactose.

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS

## 3 PHARMACEUTICAL FORM

METROGYL 200 (Metronidazole) 200 mg: 11 mm, normal convex, white tablet debossed "MZ/200" on one side and "G" on the other side.METROGYL 400 (Metronidazole) 400 mg: 12.5 mm, normal convex, pale yellow tablet debossed "MZ/400" on one side and "G" on the other side

## 4 CLINICAL PARTICULARS

### 4.1 THERAPEUTIC INDICATIONS

Metronidazole is indicated in the oral treatment of:

1. Urogenital trichomoniasis in the female (trichomonal vaginitis) and in the male. The male consort of females suffering from urogenital trichomoniasis should be treated concurrently.
2. Bacterial vaginosis.
3. All forms of amoebiasis (intestinal and extra-intestinal disease).
4. Giardiasis.
5. Acute ulcerative gingivitis.
6. Anaerobic infections including: septicaemia, bacteraemia, brain abscess, necrotising pneumonia, osteomyelitis, puerperal sepsis, pelvic abscess, pelvic cellulitis and postoperative wound infections, in which the pathogens have been identified as Bacteroides fragilis and other species of bacteroides, and other species such as fusobacteria, eubacteria, clostridia and anaerobic streptococci.

Metronidazole may be used prophylactically to prevent infection by anaerobic organisms of the surgical site following appendicectomy, colonic surgery, vaginal hysterectomy, abdominal surgery in the presence of anaerobes in the peritoneal cavity and surgery performed in the presence of anaerobic septicaemia.

### 4.2 DOSE AND METHOD OF ADMINISTRATION

Summarised in **Table 1** below.

A maximum of 4 g should not be exceeded during 24 hour period.

**Oral**

The tablets should be swallowed, without chewing, with half a glass of water. Treatment for seven days should be satisfactory for most patients but, depending on clinical and bacteriological assessment, the clinician might decide to prolong treatment.

In patients with impaired liver function, dosage should be reduced or dosage intervals increased. Plasma metronidazole levels should be monitored (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

In elderly patients, the pharmacokinetics of metronidazole may be altered and therefore monitoring of serum levels may be necessary to adjust the metronidazole dosage accordingly. Plasma metronidazole levels should be monitored. (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

**Table 1: Dosage for different Indications**

| **Indication** | **Duration (days)** | **Adults and children over 12 years** | | **Children** | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | **7-12 years** | | **3-7 years** | | **1-3 years** | |
| | | **Dose** | **Doses per day** | **Dose** | **Doses per day** | **Dose** | **Doses per day** | **Dose** | **Doses per day** |
| Urogenital trichomoniasis (see notes in Section 4.2 DOSE AND METHOD OF ADMINISTRATION) | 7 | 200 mg | 3 | 100 mg | 3 | 100 mg | 2 | 50 mg | 3 |
| | 1 | 2 g | stat | | | | | | |
| Anaerobic infections | 7 | 400 mg | 3 | 200 mg | 3 | 100 mg | 4 | 100 mg | 3 |
| Bacterial vaginosis | 1 | 2 g | 1 | - | - | - | - | - | - |
| | 7 | 400 mg | 3 | - | - | - | - | - | - |
| Giardiasis | 3 | 2 g | daily | 1 g | 1 | 600 mg | 1 | 400 mg | 1 |
| Acute ulcerative gingivitis | 3 | 200 mg | 3 | 100 mg | 3 | 100 mg | 2 | 50 mg | 3 |
| Amoebiasis | | | | | | | | | |
| 1. Invasive intestinal disease in susceptible individuals | 5 | 800 mg | 3 | 400 mg | 3 | 200 mg | 4 | 200 mg | 3 |
| 2. Intestinal disease in less susceptible subjects and chronic amoebic hepatitis | 5-10 | 400 mg | 3 | 200 mg | 3 | 100 mg | 4 | 100 mg | 3 |
| 3. Amoebic liver abscess and other forms of extra-intestinal amoebiasis | 5 | 400 mg | 3 | 200 mg | 3 | 100 mg | 4 | 100 mg | 3 |
| 4. Symptomless cyst passers | 5-10 | 400 mg to 800 mg | 3 | 200 mg to 400 mg | 3 | 100 mg to 200 mg | 4 | 100 mg to 200 mg | 3 |
| Surgical prophylaxis - if oral ingestion is not | - | 400 mg | | 200 mg to 400 mg | | 100 mg to 200 mg | | | |
| | | Taken 1 to 2 hours before surgery and repeated 8 hourly for 24 hours | | | | | | | |

| | | |
|---|---|---|
| prohibited prior to surgery | | |

### Urogenital trichomoniasis

The usual oral dosage is shown in the Table. To prevent reinfection, the partner should receive a similar course of treatment concurrently.

If treated during the second or third trimester, the one day course of therapy should not be used as it results in higher serum levels which reach the foetal circulation (see Section 4.6 FERTILITY, PREGNANCY AND LACTATION).

When repeat courses of the drug are required, it is recommended that an interval of four to six weeks elapse between courses and the presence of the trichomonad be reconfirmed by appropriate laboratory measures. Total and differential leucocyte counts should be made before and after retreatment.

### Surgical prophylaxis

**Note:** Prevention of infection at the surgical site requires that adequate tissue concentration of the drug should have been achieved at the time of surgery. The doses and route of administration should be selected in this case to achieve this objective.

As an oral ingestion is often prohibited 12 hours or longer before surgery, and it may not be practical for a variable period following surgery, tablets are not considered to be an appropriate formulation for prophylactic use. However, if oral intake is not contraindicated and is feasible following surgery, 400 mg may be taken one to two hours before surgery and repeated every eight hours for 24 hours.

## 4.3 CONTRAINDICATIONS

1. Patients with active organic disease of the central nervous system.
2. Patients with evidence of, or history of blood dyscrasias should not receive the drug since upon occasion a mild leucopenia has been observed during its administration. However, no persistent haematological abnormalities have been observed in animals or clinical studies.
3. Hypersensitivity to metronidazole and other imidazoles.

## 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

### Alcohol

Alcoholic beverages and drugs containing alcohol, should not be consumed by patients being treated with metronidazole, or for at least 24 hours afterwards, as nausea, vomiting, abdominal cramps, headaches, tachycardia and flushing may occur. There is the possibility of a disulfiram-like (Antabuse) effect reaction.

### Candidiasis

*Candida* overgrowth in the gastrointestinal or genital tract may occur during metronidazole therapy and require treatment with a candidacidal drug.

### Cockayne Syndrome

Cases of severe hepatotoxicity/acute hepatic failure, including cases with a fatal outcome with a very rapid onset after treatment initiation, have been reported in patients with Cockayne syndrome, with products containing metronidazole for systemic use. In this population, metronidazole should therefore be used, after careful risk-benefit assessment, with caution in these patients, and only if there is no alternative treatment available.

Liver function tests must be performed just prior to the start of therapy, throughout and after end of treatment under liver function is within normal ranges, or until the baseline values are reached. If the liver function 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, (such as sustained new-onset abdominal pain, anorexia, nausea, vomiting, fever, malaise, fatigue, jaundice, dark urine or itching), to their physician and stop taking metronidazole.

### Severe bullous skin reactions

Cases of severe bullous skin reactions such as Stevens Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) or acute generalised exanthematous pustulosis (AGEP) have been reported with metronidazole (see Section 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)). If symptoms or signs of SJS, TEN or AGEP are present, metronidazole treatment must be immediately discontinued.

### Long-term therapy

If metronidazole is to be administered for more than 10 days, it is recommended that haematological tests, especially total and differential leucocyte counts, be carried out regularly and that patients be monitored for adverse reactions such as peripheral neuropathy or central neuropathy (such as paresthesia, ataxia, dizziness, vertigo, convulsive seizures). If leucopenia or abnormal neurological signs occur, the drug should be discontinued immediately.

### Surgical drainage

Use of metronidazole does not obviate the need for aspiration of pus whenever indicated.

### Nervous System

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 damage.

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

### Suicidal ideation

Cases of suicidal ideation with or without depression have been reported during treatment with metronidazole. Patients should be advised to discontinue treatment and contact their healthcare provider immediately if they experience psychiatric symptoms during treatment.

### Use in Hepatic Impairment

No information available. As metronidazole is partly metabolised in the liver, caution should be exercised in patients with impaired liver function or hepatic encephalopathy.

Metronidazole may interfere with certain chemical analysis of serum aspartate transaminase (AST), alanine transaminase (ALT), lactate dehydrogenase (LDH), triglycerides and hexokinase glucose to give abnormally low values.

Dosage should be reduced or dosage intervals increased (see Section 4.2 DOSE AND METHOD OF ADMINISTRATION).

### Use in Renal Impairment

In patients on twice weekly haemodialysis, metronidazole and its major active metabolite are rapidly removed during an 8 hour period of dialysis, resulting in plasma concentration falling below the therapeutic range. Hence a further dose of metronidazole would be needed after dialysis to restore an adequate plasma concentration. In patients with renal failure, the half-life of metronidazole is unchanged but those of its major metabolites are prolonged 4-fold or greater. The accumulation of the hydroxy metabolite could be associated with side effects

and measurement of its plasma concentrations by high pressure liquid chromatography (HPLC) has been recommended.

### Use in the Elderly

The pharmacokinetics of metronidazole may be altered and therefore monitoring of serum levels may be necessary to adjust the metronidazole dosage accordingly (see Section 4.2 DOSE AND METHOD OF ADMINISTRATION).

### Paediatric Use

No data available.

### Effects on Laboratory Tests

Metronidazole may interfere with certain types of blood test determinations in blood (aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), triglycerides, glucose), which may lead to false negative or an abnormally low result. These analytical determinations are based on a decrease in ultraviolet absorbance, a fact that occurs when nicotinamide adenine dinucleotide hydrogen (NADH) is oxidized to nicotinamide adenine dinucleotide (NAD). The interference is due to the similarity in the absorption peaks of NADH (340 nm) and metronidazole (322 nm) at pH 7.

## 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

### Warfarin

Metronidazole enhances the activity of warfarin, therefore if METROGYL is to be given to patients receiving this or other anticoagulants, the dosages of anticoagulants should be recalibrated. There is an increased haemorrhagic risk caused by decreased hepatic metabolism. Prothrombin times and anticoagulant activity should be monitored.

### Alcohol

Alcoholic beverages and drugs containing alcohol should not be consumed during metronidazole therapy and for at least one day afterwards because the possibility of a disulfiram-like (antabuse effect) reaction (vomiting, tachycardia, and flushing)

### Carmustine (BCNU) or cyclophosphamide

Metronidazole should be used with caution in patients receiving these drugs.

### Lithium

In patients stabilised on relatively high doses of lithium, short-term metronidazole therapy has been associated with elevation of serum lithium and, in a few cases, signs of lithium toxicity. Serum lithium and serum creatinine levels and electrolytes should be obtained several days after beginning metronidazole to detect any increase that may precede clinical symptoms of lithium intoxication.

### Disulfiram

Psychotic reactions have been reported in patients who were using metronidazole and disulfiram concurrently. Metronidazole should not be given to patients who have taken disulfiram within the last two weeks.

### Hepatic enzyme inducers

The simultaneous administration of drugs that induce microsomal hepatic enzymes, such as phenytoin or (phenobarbital) phenobarbitone, may accelerate the elimination of METROGYL resulting in reduced plasma levels; impaired clearance of phenytoin has also been reported.

### Hepatic enzyme inhibitors
The simultaneous administration of drugs that decrease microsomal hepatic enzyme activity, such as cimetidine, may prolong the half-life and decrease plasma clearance of metronidazole.

### Ciclosporin
There is a risk of ciclosporin serum levels increasing when it is used in combination with metronidazole. Serum ciclosporin and serum creatinine should be closely monitored when coadministration is necessary.

### 5-fluorouracil
Metronidazole used in combination with 5-fluorouracil may lead to reduced clearance of 5 fluorouracil, resulting in increased toxicity.

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

### QT interval
QT prolongation has been reported, particularly when metronidazole was administered with drugs with the potential for prolonging the QT interval.

## 4.6 FERTILITY, PREGNANCY AND LACTATION

### Effects on Fertility
No data available.

### Use in Pregnancy
Pregnancy Category: B2

Metronidazole should not be given in the first trimester of pregnancy as it crosses the placenta and enters fetal circulation rapidly. As its effects on human fetal organogenesis are not known, its use in pregnancy should be carefully evaluated. Although it has not been shown to be teratogenic in either human or animal studies, such a possibility cannot be excluded.

Use of metronidazole for trichomoniasis in the second and third trimesters should be restricted to those in whom local palliative treatment has been inadequate to control symptoms.

If a patient is treated during the 2nd or 3rd trimesters of pregnancy for urogenital trichomoniasis, the 2 g stat dose therapy should not be used as it results in higher serum levels which reach the fetal circulation.

### Use in Lactation
Metronidazole is secreted in breast milk (see Section 5.2 PHARMACOKINETIC PROPERTIES). In view of its tumorigenic and mutagenic potential, breastfeeding is not recommended (see Section 5.3 PRECLINICAL SAFETY DATA).

## 4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Patients should be warned about the potential for confusion, dizziness, vertigo, hallucinations or convulsions or transient visual disorders and advised not to drive or use machinery if these symptoms occur. See Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE and Section 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS).

## 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

### Gastrointestinal

Metronidazole when given orally is well tolerated. Common adverse reactions refer to the gastrointestinal tract, particularly nausea, sometimes accompanied by headache, anorexia and occasionally vomiting, diarrhoea, epigastric pain or distress and abdominal cramping; constipation, oral mucositis and taste disorders have also been reported. A metallic, sharp, unpleasant taste is not unusual. Cases of pancreatitis which abated on withdrawal of the drug, have been reported. Patients with Crohn's disease are known to have an increased incidence of gastrointestinal and certain extraintestinal cancers. If patients receiving metronidazole drink alcoholic beverages, they may experience abdominal distress, nausea, vomiting, flushing or headache. A modification of the taste of alcoholic beverages has also been reported.

Furry tongue, tongue discolouration, glossitis and stomatitis have occurred; these may be associated with a sudden overgrowth of Candida which may occur during effective therapy.

### Body as a whole

Hypersensitivity reactions include rash, pruritus, flushing, urticaria, fever, angioedema and anaphylactic shocks. Nasal congestion and dryness of the mouth have been reported. Mild erythematous eruptions have been experienced, as have fleeting joint pains sometimes resembling serum sickness. Pustular eruptions and acute generalised exanthematous pustulosis have been reported. Fixed drug eruption has been reported. Stevens-Johnson syndrome and toxic epidermal necrolysis have also been reported.

### Liver

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 requiring liver transplant have been reported in patients treated with metronidazole in combination with other antibiotic drugs; all spiramycin except one case of tetracycline.

### Haematology

A moderate leucopenia may be observed occasionally. If this occurs, the total leucocyte count may be expected to return to normal after the course of medication is completed. One case of bone marrow depression has been reported. If profound bone marrow suppression occurs, use of metronidazole should be ceased and appropriate supportive therapy instituted. Cases of agranulocytosis, neutropenia or thrombocytopenia have been reported.

### Psychiatric/central nervous system disorders

Dizziness, vertigo, incoordination, headache and convulsive seizures have been reported. Psychotic disorders such as confusion and hallucinations have been reported. Depression, depressed mood, insomnia, irritability, weakness have been experienced, as has peripheral neuropathy, characterised mainly by numbness or paraesthesia of an extremity. There have been reports of encephalopathy (e.g. confusion, vertigo) and subacute cerebellar syndrome (e.g. ataxia, dysarthria, gait impairment, nystagmus and tremor), which may resolve with the discontinuation of the drug. Since persistent peripheral neuropathy has been reported in some patients receiving prolonged administration of metronidazole, such subjects should be specifically warned about these reports and should be told to stop the drug and report immediately if any neurological symptoms occur. Aseptic meningitis has been reported.

Frequency not known: vertigo

### Eye Disorders

Optic neuropathy/neuritis and transient vision disorders such as diplopia, myopia, blurred vision, decreased visual acuity and changes in colour vision have been reported.

### Ear and Labyrinth Disorders
Impaired hearing/hearing loss (including sensorineural) and tinnitus have been reported.

### Genitourinary tract
Proliferation of *Candida* also may occur in the vagina. Dryness of the vagina or vulva, pruritus, dysuria, cystitis and a sense of pelvic pressure have been reported. Very rarely dyspareunia, fever, polyuria, incontinence, decrease of libido, proctitis and pyuria have occurred in patients receiving the drug.

Instances of a darkened urine have been reported and this manifestation has been the subject of special investigation. Although the pigment which is probably responsible for this phenomenon has not been positively identified, it is almost certainly a metabolite of metronidazole. It seems certain that it is of no clinical significance and may be encountered only when metronidazole is administered in higher than recommended doses.

### Cardiovascular
Flattening of the T wave may be seen in ECG tracings.

Frequency not known: QT prolongation has been reported, particularly when metronidazole was administered with drugs with the potential for prolonging the QT interval.

### Reporting Suspected Adverse Effects
Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

## 4.9 OVERDOSE

### Symptoms
Overdosage with metronidazole appears to be associated with very few abnormal signs or symptoms. Disorientation, ataxia and vomiting may occur, especially after ingestion of large amounts. In case of suspected massive overdosages, a symptomatic and supportive treatment should be instituted.

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

### Treatment
There is no specific antidote for metronidazole overdosage. In cases of suspected overdosage, a symptomatic and supportive treatment should be instituted.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

# 5 PHARMACOLOGICAL PROPERTIES

## 5.1 PHARMACODYNAMIC PROPERTIES

### Mechanism of Action
No data available.

### Clinical Trials
No data available.

## 5.2 PHARMACOKINETIC PROPERTIES

### Pharmacokinetic

Metronidazole is readily absorbed, peak serum concentration is reached approximately 1 to 2 hour after an oral dose. Food does not significantly affect absorption and the bioavailability of the dose approaches 100% when compared with intravenous administration. Traces of metronidazole are detectable after 24 hours. The biological half-life of oral metronidazole has been determined as 6 to 7 and 7.3 hours respectively.

Metronidazole is widely distributed in body tissues and fluids. It crosses the blood-brain barrier and the placenta. The concentration in breast milk of nursing mothers is similar to those in serum. The serum half-life of unchanged metronidazole is about 8 to 10 hours. Metronidazole is excreted in the urine as unchanged drug and its metabolites including acid oxidation products and glucuronides. Metronidazole is not protein bound to any significant degree. Most of the dose is excreted in the urine as metronidazole and its metabolites, including acid oxidation products and glucuronides.

### Microbiology

Metronidazole is active against a wide range of pathogenic microorganisms, notably Trichomonas vaginalis and other trichomonads, Entamoeba. histolytica, Giardia lamblia, Balantidium coli and the causative organisms of acute ulcerative gingivitis. Metronidazole also displays antibacterial activity in vitro against several species of anaerobic bacteria including Bacteroides fragilis and other species of Bacteroi, and other species such as Fusobacteria, Eubacteria, Clostridia and anaerobic Streptococci. The minimum inhibitory concentration (MIC) for most susceptible anaerobes is < 6.2 microgram/mL.

Metronidazole is inactive against aerobic and facultative anaerobic bacteria.

## 5.3 PRECLINICAL SAFETY DATA

### Genotoxicity

In studies on the mutagenic potential of metronidazole, the Ames test was positive, while several nonbacterial tests in animals were negative. In patients with Crohn's disease, metronidazole increased the chromosome abnormalities in circulating lymphocytes. The use of metronidazole for longer treatment than usually required should be carefully weighed (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE) and the benefit/risk ratio should therefore be carefully assessed in each case particularly in relation to the severity of the disease and the age of the patient.

### Carcinogenicity

Metronidazole has been shown to be tumorigenic and carcinogenic in rodents.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 LIST OF EXCIPIENTS

METROGYL 200 and METROGYL 400 contain the following excipients:

- lactose monohydrate
- disodium edetate
- ethylcellulose
- sodium starch glycollate
- colloidal anhydrous silica
- guar gum
- magnesium stearate

- quinoline yellow aluminium lake (METROGYL 400 only)

## 6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

## 6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

## 6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30°C. Protect from light.

## 6.5 NATURE AND CONTENTS OF CONTAINER

### METROGYL 200

Container type: HDPE bottle

Pack sizes: 21 or 250 tablets

### METROGYL 400

Container type: HDPE bottle

Pack sizes: 21 tablets

Some pack sizes may not be marketed.

### Australian Register of Therapeutic Goods (ARTG)

AUST R 17654 – METROGYL 200 metronidazole 200mg tablet bottle

AUST R 17655 – METROGYL 400 metronidazole 400mg tablet bottle

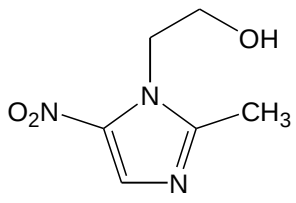
## 6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking it to your local pharmacy.

## 6.7 PHYSICOCHEMICAL PROPERTIES

### Chemical Structure

Structural formula :




Metronidazole is a 1-(2-hydroxyethyl)-2-methyl-5-nitroimidazole.

### CAS Number

443-48-1

Metronidazole crystals are white to brownish in colour.

Metronidazole has a melting point of 159-162°C. A saturated solution of aqueous metronidazole has a pH of between 6 and 7.5. Solubility (g/100 mL) of metronidazole at 20 C: 1 in water; 0.5 in ethanol; 0.4 in chloroform; slightly soluble in ether; soluble in dilute acids.

# 7 MEDICINE SCHEDULE (POISONS STANDARD)

S4 (Prescription Only Medicine)

# 8 SPONSOR

**Alphapharm Pty Ltd trading as Viatris**

Level 1, 30 The Bond

30 – 34 Hickson Road

Millers Point NSW 2000

www.viatris.com.au

Phone: 1800 274 276

# 9 DATE OF FIRST APPROVAL

20/09/1991

# 10 DATE OF REVISION

27/03/2023

**Summary Table of Changes**

| Section Changed | Summary of New Information |
|---|---|
| **3** | Update of product description for 200 mg and 400 mg tablets |
| **6.1** | Update of excipient quinoline yellow aluminium lake (400mg only) |

METROGYL® is a Viatris company trade mark

**METROGYL_pi\Mar23/01**