

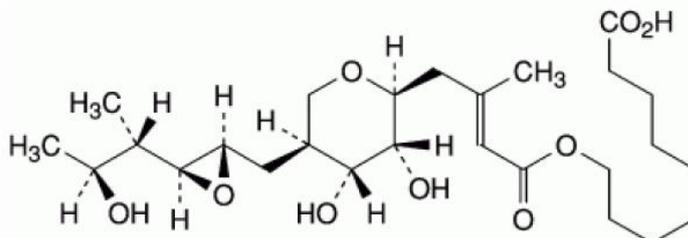
APO-MUPIROCIN

NAME OF THE MEDICINE

Mupirocin

Chemical Name: 9-[[[(2E)-4-[(2S,3R,4R,5S)-3,4-Dihydroxy-5-[[[(2S,3S)-3-[(1S,2S)-2-hydroxyl-1-methylpropyl]oxiranyl]methyl]tetrahydro-2H-pyran-2-yl]-3-methylbut-2-enoyl]oxy]nonanoic acid

Structural Formula:



Molecular Formula: C₂₆H₄₄O₉

Molecular Weight: 500.622 g/mol

CAS Registry Number: 12650-69-0

DESCRIPTION

Mupirocin is a naturally occurring antibiotic, produced by fermentation of the organism *Pseudomonas fluorescens*.

Mupirocin is slightly soluble in water and freely soluble in acetone, methylene chloride, chloroform and methanol.

Mupirocin ointment is a white, semi-transparent, homogeneous ointment. Each gram of mupirocin ointment contains 20 mg of mupirocin (2% w/w) as the active ingredient. In addition, the ointment also contains the following inactive ingredients: macrogol 400 and macrogol 3350.

PHARMACOLOGY

Microbiology

Mupirocin inhibits bacterial protein synthesis by reversibly and specifically binding to bacterial isoleucyl transfer RNA (tRNA) synthetase. It shows no cross resistance with other commonly used and clinically important antibiotics.

In vitro mupirocin is active mainly against Gram positive aerobes including *Staphylococcus aureus* (including methicillin resistant *Staph. aureus* (MRSA) positive strains), *Staph. saprophyticus*, *Staph. epidermidis*, *Streptococcus pyogenes*, *Strep. viridans*, *Strep. agalactiae* and *Strep. pneumoniae*.

Group D Streptococci (including *Strep. faecalis* and *Strep. faecium*) are much less sensitive to mupirocin. Most Gram negative organisms (except for *Haemophilus influenzae*, *Neisseria* and *Branhamella*) and anaerobes (including *Propionibacterium acnes*) are not sensitive to mupirocin.

When mupirocin resistance does occur, it appears to result from the production of a modified isoleucyl tRNA synthetase. High level plasmid mediated resistance (MIC > 1024 microgram/mL) has been reported in some strains of *Staph. aureus* and coagulase negative staphylococci.

Pharmacokinetics

Absorption and Distribution

Mupirocin is poorly absorbed through intact human skin; less than 0.24% of a 0.5 g dose being available systemically following the topical application of mupirocin in the ointment base. Application of ¹⁴C-labelled mupirocin ointment to the lower arm of normal male subjects followed by occlusion for 24 hours showed no measurable systemic absorption. Measurable radioactivity was present in the stratum corneum of these subjects 72 hours after application.

Metabolism

If mupirocin is absorbed through broken skin or is given systemically, it is metabolised to the inactive metabolite, monic acid. The mean plasma half-lives of mupirocin and monic acid are 19 and 77 minutes, respectively.

Excretion

The major elimination pathway is via the kidney (90%).

INDICATIONS

APO-Mupirocin is indicated for the topical treatment of mild impetigo.

CONTRAINDICATIONS

APO-Mupirocin is contraindicated in patients who have demonstrated hypersensitivity to mupirocin, mupirocin calcium, or any components of the formulation.

PRECAUTIONS

If a reaction suggesting sensitivity or chemical irritation should occur with the use of APO-Mupirocin, treatment should be discontinued, the product should be wiped off and appropriate alternative therapy for the infection instituted.

APO-Mupirocin is not suitable for ophthalmic use, intranasal use or application to other mucosal surfaces.

Avoid contact with eyes. If contaminated, the eyes should be thoroughly irrigated with water until the residues have been removed.

APO-Mupirocin is not suitable for application to the site of cannulation or for use in conjunction with cannulae.

Polyethylene glycol (macrogol) can be absorbed from open wounds and damaged skin and is excreted by the kidneys. In common with other polyethylene glycol based ointments, APO-Mupirocin should not be used in conditions where absorption of large quantities of polyethylene glycol is possible, especially if there is evidence of moderate or severe renal impairment.

As with other antibacterial products, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

Pseudomembranous colitis has been reported with the use of antibiotics and may range in severity from mild to life threatening. Therefore, it is important to consider its diagnosis in patients who develop diarrhoea during or after antibiotic use. Although this is less likely to occur with topically applied mupirocin, if prolonged or significant diarrhoea occurs or the patient experiences abdominal cramps, treatment should be discontinued immediately and the patient investigated further.

Effects on Fertility

Fertility of male and female rats was not affected by mupirocin at subcutaneous doses up to 100 mg/kg/day.

Use in Pregnancy (Category B1)

Reproduction studies have been performed in rats and rabbits at systemic doses up to 160 mg/kg and have revealed no evidence of harm to the foetus due to mupirocin.

There are, however, no adequate and well controlled studies in pregnant women. Because animal studies are not always predictive of human response, mupirocin ointment should be used during pregnancy only if clearly needed.

Use in Lactation

Adequate human and animal data on use during lactation are not available.

Caution should be exercised when mupirocin ointment is administered to a nursing woman. If a cracked nipple is being treated, the nipple should be thoroughly washed prior to breastfeeding.

Paediatric Use

The safety and efficacy of mupirocin ointment has not been established in children less than two years of age.

Use in Elderly

No restrictions unless there is evidence of moderate or severe renal impairment.

Carcinogenicity

The carcinogenic potential of mupirocin has not been assessed in long-term animal studies.

Genotoxicity

Results of the following studies performed with mupirocin calcium or mupirocin sodium *in vitro* and *in vivo* did not indicate a potential for mutagenicity: rat primary hepatocyte unscheduled DNA synthesis, sediment analysis for DNA strand breaks, metaphase analysis of human lymphocytes, mouse lymphoma assay and bone marrow micronuclei assay in mice.

INTERACTIONS WITH OTHER MEDICINES

No drug interactions have been studied with mupirocin.

APO-Mupirocin should not be combined with other topical preparations as there is a risk of dilution, resulting in a reduction in the antibacterial activity and potential loss of stability of the mupirocin.

ADVERSE EFFECTS

Systemic allergic reactions such as generalised rash, urticaria and angioedema have been reported with mupirocin ointment.

Local Reactions

Common (approximately 2%): itching, burning, erythema, stinging, pain/ swelling at site of application and dryness. Less than 1% of patients discontinued therapy because of these local reactions.

Uncommon: cutaneous sensitisation reactions to mupirocin or the ointment base.

Gastrointestinal

One case of nausea has been reported in studies of mupirocin ointment so far.

Mupirocin ointment did not demonstrate any delayed hypersensitivity, cutaneous sensitisation, phototoxicity or photo-contact sensitisation in studies on normal subjects.

Cutaneous sensitisation has been reported rarely in postmarketing surveillance of mupirocin ointment.

DOSAGE AND ADMINISTRATION

A small amount of mupirocin ointment should be applied to the affected area three times daily. The area treated may be covered with gauze dressing if desired. Usually treatment should not continue for more than 10 days.

Any product remaining at the end of treatment should be discarded.

Renal Impairment

Use in renal impairment (see **PRECAUTIONS**).

OVERDOSAGE

There is currently limited experience with overdosage of mupirocin ointment. There is no specific treatment for an overdose of mupirocin. In the event of overdose, the patient should be treated supportively with appropriate monitoring as necessary.

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

PRESENTATION AND STORAGE CONDITIONS

APO-Mupirocin is intended for topical application only.

Each tube contains 20 mg/g (2% w/w) of mupirocin, as the active ingredient.

APO-Mupirocin is a white semi-transparent homogeneous preparation.
Aluminium tube with polyethylene cap containing 15 g of ointment (AUST R 276520).

Storage

Store below 25°C.

NAME AND ADDRESS OF THE SPONSOR

Southern Cross Pharma Pty Ltd
Suite 5/118 Church Street
Hawthorn, VIC 3122

NAME AND ADDRESS OF THE DISTRIBUTOR

Apotex Pty Ltd
16 Giffnock Avenue
Macquarie Park NSW 2113

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POISON SCHEDULE OF THE MEDICINE

S4 – Prescription Only Medicine.

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (THE ARTG):

12 April 2017