

BACTROBAN 2% CREAM OR OINTMENT

PRODUCT INFORMATION

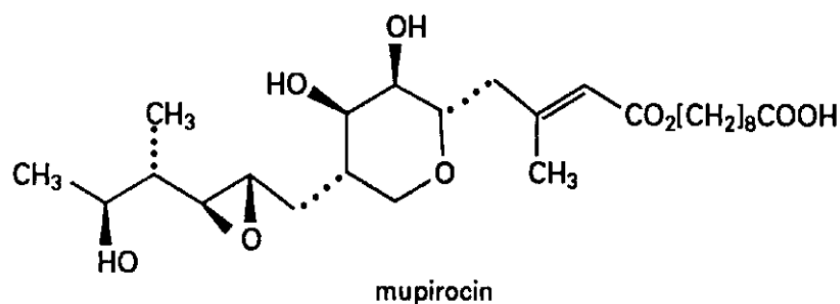
For Dermatologic Use

NAME OF THE MEDICINE

BACTROBAN Cream and BACTROBAN Ointment contain mupirocin calcium 2% w/w equivalent to 20 mg mupirocin as the active ingredient.

DESCRIPTION

Mupirocin is a naturally occurring antibiotic, produced by fermentation of the organism *Pseudomonas fluorescens*. The chemical name is: 9-[4-[5S-[2S,3S-epoxy-5S-hydroxy-4S-methylhexyl]-3R,4R-dihydroxytetrahydropyran-2S-y1]-3-methylbut-2-(E)-enoyloxy]nonanoic acid. The chemical structure of mupirocin is shown below:



The CAS number for mupirocin is 12550-69-0.

Each gram of BACTROBAN 2% Cream contains mupirocin calcium, equivalent to 20 mg of mupirocin. BACTROBAN Cream also contains xanthan gum, liquid paraffin, cetomacrogol 1000, stearyl alcohol, cetyl alcohol, phenoxyethanol, benzyl alcohol and purified water.

Each gram of BACTROBAN 2% Ointment contains 20 mg of mupirocin. BACTROBAN Ointment also contains macrogol 400 and macrogol 3350.

PHARMACOLOGY

Microbiology

Mupirocin inhibits bacterial protein synthesis by reversibly and specifically binding to bacterial isoleucyl transfer - RNA 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 MRSA positive strains), *Staphylococcus*

saprophyticus, *Staphylococcus epidermidis*, *Streptococcus pyogenes*, *Streptococcus viridans*, *Streptococcus agalactiae*, and *Streptococcus pneumoniae*.

Group D Streptococci (including *S. faecalis* and *S. faecium*), are much less sensitive to mupirocin. Most Gram negative organisms (except for *H. 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 mcg/mL) has been reported in some strains of *S. aureus* and coagulase-negative staphylococci.

Pharmacokinetics

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.

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 minutes and 77 minutes, respectively. The major elimination pathway is via the kidney (90%).

Special Patient Populations

Elderly patients: No restrictions unless there is evidence of moderate or severe renal impairment (see PRECAUTIONS).

CLINICAL TRIALS

The efficacy of topical BACTROBAN Cream for the treatment of secondarily infected traumatic skin lesions (e.g. small lacerations, sutured wounds, and abrasions) was compared to that of oral cephalexin in two randomized, double-blind, double-dummy clinical trials. BACTROBAN Cream was administered topically three times a day for 10 days; Cephalexin 250 mg was given orally four times a day for 10 days. Patients weighing less than 40 kg were given 25 mg/kg/day oral Cephalexin in four divided doses. Patients of either gender of any age were eligible for the study. Lacerations or sutured wounds were up to 10 cm in length and erythema surrounding abrasions did not exceed 2 cm from the edge of the abrasion.

In a combined analysis of the two pivotal clinical trials, the clinical and bacteriological efficacy rates of mupirocin at follow-up (7-12 days post therapy) were shown to be equivalent to those of oral Cephalexin. A total of 245 patients treated with BACTROBAN Cream and 233 patients treated with oral Cephalexin were evaluable for per-protocol clinical efficacy at follow-up. The per-protocol clinical efficacy rate was 95.1% for BACTROBAN Cream and 95.3% for oral Cephalexin (95% Confidence Interval for difference between treatment groups -4.04, 3.64). Ninety eight patients given BACTROBAN Cream and 92 patients given Cephalexin were evaluable for per-protocol bacteriological efficacy at follow-up. The per-

protocol bacteriological success rate was 96.9% for BACTROBAN Cream and 98.9% for oral Cephalexin (95% Confidence Interval -6.04, 2.04).

The safety and efficacy of BACTROBAN Cream has not been established in the topical treatment of burns.

INDICATIONS

BACTROBAN (mupirocin) Cream is indicated for the topical treatment of secondarily infected traumatic skin lesions such as small lacerations, sutured wounds or abrasions.

BACTROBAN (mupirocin) Ointment is indicated for the topical treatment of mild impetigo.

CONTRAINDICATIONS

BACTROBAN Cream and BACTROBAN Ointment are contraindicated in patients who have demonstrated hypersensitivity to mupirocin calcium or any components of the formulations.

PRECAUTIONS

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

BACTROBAN 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.

BACTROBAN 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, BACTROBAN Ointment 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.

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 160mg/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, this drug 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 BACTROBAN is administered to a nursing woman. If a cracked nipple is being treated, the nipple should be thoroughly washed prior to breast feeding.

Paediatric use

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

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.

Carcinogenicity

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

OVERDOSAGE

There is currently limited experience with overdosage of BACTROBAN.

There is no specific treatment for an overdose of BACTROBAN. In the event of overdose, the patient should be treated supportively with appropriate monitoring as necessary. Further management should be as clinically indicated or as recommended by the Poison Information Centre on 131126 (Australia).

INTERACTIONS WITH OTHER MEDICINES

No drug interactions have been studied with mupirocin.

BACTROBAN Cream or Ointment 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 including anaphylaxis, generalised rash, urticaria and angioedema have been reported with BACTROBAN Cream or Ointment.

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 BACTROBAN Ointment so far.

BACTROBAN Ointment did not demonstrate any delayed hypersensitivity, cutaneous sensitization, phototoxicity or photo-contact sensitisation in studies on normal subjects. Cutaneous sensitisation has been reported rarely in post marketing surveillance of BACTROBAN Ointment.

Cream

Skin and subcutaneous tissue disorders:

Common: Cutaneous hypersensitivity reactions

Generally, BACTROBAN Cream was well tolerated. Adverse events from the two pivotal clinical trials, thought to be at least possibly drug-related, are listed below.

Related/Possibly Related Adverse Events Occurring in >1% (common) of BACTROBAN Cream-treated Patients

Event	BACTROBAN Cream N=357 %	Cephalexin* N=349 %
Headache	2.0	1.1
Diarrhoea	1.1	2.3
Nausea	1.1	1.1

*250 mg q.i.d. for patients > 40 kg or 25 mg/kg/day oral suspension in four divided doses for patients ≤ 40 kg.

In the two pivotal clinical trials, application site reactions were reported in 0.8% patients treated with either BACTROBAN Cream or placebo. In a supportive safety study, where BACTROBAN Cream was used in the treatment of secondarily infected eczema, application site reactions were reported in 2.4% of patients.

DOSAGE AND ADMINISTRATION

A small amount of BACTROBAN should be applied to the affected area three times daily. The area treated may be covered with a 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 (BACTROBAN Ointment)

For use in renal impairment, please refer to **PRECAUTIONS**.

PRESENTATION AND STORAGE CONDITIONS

Presentations

BACTROBAN Ointment 2% is supplied in 1 g, 2 g, 5 g, 15 g and 30 g tubes.

BACTROBAN Cream 2% is supplied in 15 g tubes.

Not all pack sizes may be distributed in Australia.

Storage Conditions

Store below 25°C. Do not freeze.

NAME AND ADDRESS OF THE SPONSOR

GlaxoSmithKline Australia Pty Ltd
Level 4
436 Johnston Street
Abbotsford Victoria 3067

POISON SCHEDULE OF THE MEDICINE

Schedule 4 – Prescription Only Medicine

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS

3 April 1998

DATE OF MOST RECENT AMENDMENT

23 April 2015

Bactroban[®] is a registered trade mark of the GlaxoSmithKline group of companies.

Version 4.0