Mupirocin

Bactroban® 2%

20 mg/g Cream

PRODUCT DESCRIPTION

Mupirocin *(Bactroban®)* 2% Cream is a white cream for topical administration in a multi-use tube.
Each gram contains 20 mg Mupirocin free acid (2% w/w) as Mupirocin calcium in mineral oil cream base.

PHARMACOLOGIC PROPERTIES

Pharmacodynamics

Pharmacodynamic properties

Mechanism of Action

Mupirocin is a novel antibiotic produced through fermentation by *Pseudomonas fluorescens*. Mupirocin inhibits isoleucyl transfer-RNA synthetase, thereby arresting bacterial protein synthesis. Due to this particular mode of action and its unique chemical structure, mupirocin does not show any cross-resistance with other clinically available antibiotics.
Mupirocin has bacteriostatic properties at minimum inhibitory concentrations and bactericidal properties at the higher concentrations reached when applied locally.

Pharmacodynamic Effects

Mupirocin is a topical antibacterial agent showing *in vivo* activity against *Staphylococcus aureus* (including methicillin-resistant strains), *S. epidermidis* and beta-haemolytic *Streptococcus* species.
The *in vitro* spectrum of activity includes the following bacteria:
Commonly Susceptible Species:
Staphylococcus aureus[1,2]
Staphylococcus epidermidis[1,2]
Coagulase-negative staphylococci[1,2]
Streptococcus species[1]
Haemophilus influenzae
Neisseria gonorrhoeae
Neisseria meningitides
Moraxella catarrhalis
Pasteurella multocida.

[1]Clinical efficacy has been demonstrated for susceptible isolates in approved clinical indications.
[2]Including beta-lactamase producing strains and methicillin-resistant strains

Resistant Species:
Corynebacterium species
Enterobacteriaceae
Gram negative non-fermenting rods
Micrococcus species
Anaerobes.

Mupirocin susceptibility (MIC) breakpoints for *Staphylococcus spp*.
Susceptible: less than or equal to 1 microgram/ml
Intermediate: 2 to 256 micrograms/ml
Resistant: greater than 256 micrograms/ml

Resistance mechanisms:
Low-level resistance in staphylococci (MICs 8 to 256 micrograms/ml) has been shown to be due to changes in the native isoleucyl tRNA synthetase enzyme. High-level resistance in staphylococci (MICs greater than or equal to 512 micrograms/ml) has been shown to be due to a distinct, plasmid encoded isoleucyl tRNA synthetase enzyme. Intrinsic resistance in Gram-negative organisms such as the Enterobacteriaceae could be due to poor penetration into the bacterial cell.

Pharmacokinetics

Absorption

Systemic absorption of mupirocin through intact human skin is low although it may occur through broken/diseased skin. However, clinical trials have shown that when given systemically, it is metabolised to the microbiologically inactive metabolite monic acid and rapidly excreted.

Elimination

Mupirocin is rapidly eliminated from the body by metabolism to its inactive metabolite monic acid which is rapidly excreted by the kidney.

Pre-Clinical Safety Data

Carcinogenesis/mutagenesis

Carcinogenesis

Carcinogenicity studies with mupirocin have not been conducted.

Genotoxicity

Mupirocin was not mutagenic in *Salmonella typhimurium* or *Escherichia coli* (Ames assay). In a Yahagi assay, small increases in *Salmonella typhimurium* TA98 were observed at highly cytotoxic concentrations. In an *in vitro* mammalian gene mutation assay (MLA), no increase in mutation frequency was observed in the absence of metabolic activation. In the presence of metabolic activation, small increases in mutation frequency were observed at highly cytotoxic concentrations. However, no effects were observed in, yeast cell assays for gene conversion/mutation, an *in vitro* human lymphocyte assay or in an *in vitro* unscheduled DNA synthesis (UDS) assay. Furthermore, an *in vivo* mouse micronucleus assay (chromosome damage) and a rat Comet assay (DNA strand breakage) were negative, indicating the small increases observed at highly cytotoxic concentrations *in vitro* do not translate to the *in vivo* situation.

Reproductive Toxicology

Fertility

Mupirocin administered subcutaneously to male rats 10 weeks prior to mating and to female rats 15 days prior to mating until 20 days post coitum at doses up to 100 mg/kg/day had no effect on fertility.

Pregnancy

In embryo-foetal development studies in rats there was no evidence of developmental toxicity at subcutaneous doses up to 375 mg/kg/day.

In an embryo-foetal development study in rabbits at subcutaneous doses up to 160 mg/kg/day, maternal toxicity (impaired weight gain and severe injection site irritation) at the high dose resulted in abortion or poor litter performance. However, there was no evidence of developmental toxicity in foetuses of rabbits maintaining pregnancy to term.

INDICATIONS

Mupirocin *(Bactroban®)* 2% Cream is indicated for the topical treatment of secondarily infected traumatic lesions such as small lacerations, sutured wounds or abrasions.

DOSAGE AND ADMINISTRATION

Populations

Dosage

Adults/children/elderly

3 times a day for up to 10 days, depending on the response.

Hepatic impairment: No dosage adjustment is necessary.

Renal impairment: No dosage adjustment is necessary.

Method of administration

A small quantity of cream should be applied to the affected area with a piece of clean cotton wool or gauze swab.

The treated area may be covered by a dressing.

Do not mix with other preparations as there is a risk of dilution, resulting in a reduction in the antibacterial activity and potential loss of stability of the mupirocin in the cream.

CONTRAINDICATIONS

Mupirocin *(Bactroban®)* 2% Cream should not be given to patients with a history of hypersensitivity to any of its constituents.

WARNINGS AND PRECAUTIONS

In the rare event of a possible sensitisation reaction or severe local irritation occurring with the use of Mupirocin *(Bactroban®)* 2% Cream, treatment should be discontinued, the product should be washed off and appropriate alternative therapy for the infection instituted.

As with other antibacterial products, prolonged use may result in overgrowth of non-susceptible organisms.

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.

Mupirocin *(Bactroban®)* 2% Cream is not suitable for ophthalmic use and intranasal use.

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

Effects on Ability to Drive and Use Machines

No adverse effects on the ability to drive or operate machinery have been identified.

DRUG INTERACTIONS

No drug interactions have been identified.

PREGNANCY AND LACTATION

Fertility

There are no data on the effects of mupirocin on human fertility. Studies in rats showed no effects on fertility (see *Pre-Clinical Information*).

Pregnancy

Adequate human data on use during pregnancy are not available. Studies in animals do not indicate reproductive toxicity (see *Pre-Clinical Information*).

Mupirocin should only be used in pregnancy when the potential benefits outweigh the potential risks associated with treatment.

Lactation

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

If a cracked nipple is to be treated, it should be thoroughly washed prior to breast-feeding.

ADVERSE EFFECTS

Adverse reactions are listed below by system organ class and frequency. Frequencies are defined as: very common (greater than or equal to 1/10), common (greater than or equal to 1/100, less than 1/10), uncommon (greater than or equal to 1/1000, less than 1/100), rare (greater than or equal to 1/10,000, less than 1/1000), very rare (less than 1/10,000), including isolated reports.

Data from clinical trials was used to determine the frequency of very common to rare undesirable effects.

Very rare adverse reactions were primarily determined from post-marketing experience data and therefore refer to reporting rate rather than true frequency.

Immune system disorders:

Very rare: Systemic allergic reactions including anaphylaxis, generalised rash, urticaria and angioedema

Skin and subcutaneous tissue disorders:

Common: Cutaneous hypersensitivity reactions

OVERDOSAGE

Symptoms and Signs

There is currently limited experience with overdosage of Mupirocin *(Bactroban®)* 2% Cream.

Treatment

There is no specific treatment for an overdose of Mupirocin *(Bactroban®)* 2% Cream. 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 national poison center, where available.

STORAGE CONDITIONS

Store at temperatures not exceeding 25^{o}C. Do not freeze.

INCOMPATIBILITIES
None identified.

INSTRUCTIONS FOR USE/HANDLING
No special instructions.
Any product remaining at the end of treatment should be discarded.
Wash your hands after application.

AVAILABILITY
Mupirocin *(Bactroban®)* 2% Cream: packaging of 5g and 15g aluminum tubes with a screw cap (Box of 1's).

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Version number: GDS16/IPI05 Revision Date: 01 October 2015

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