BACTROBAN NASAL

Mupirocin calcium as free acid

QUALITATIVE AND QUANTITATIVE COMPOSITION

Mupirocin calcium equivalent to 2% w/w mupirocin free acid in a white soft paraffin based ointment.

PHARMACEUTICAL FORM

Nasal ointment.

CLINICAL PARTICULARS

Indications

Elimination of nasal carriage of staphylococci, including methicillin-resistant *Staphylococcus aureus* (MRSA).

For the treatment of bacterial skin infections *BACTROBAN* ointment should be used. See package leaflet for this *BACTROBAN* formulation or contact the manufacturer for details.

Dosage and Administration

Populations

Adults and Children: BACTROBAN nasal ointment should be applied to the anterior nostrils 2 to 3 times a day, as follows:

A small amount of ointment, about the size of a match head is squeezed on the little finger or a cotton-tipped applicator, if available.

The ointment is applied to the inside of one nostril.

This is repeated for the other nostril.

The nostrils are closed by pressing the sides of the nose together. This spreads the ointment throughout the nostrils.

Nasal carriage should normally clear within 3 to 5 days of commencing treatment.

Dosage should not exceed 10 days.

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 ointment.

Contraindications

BACTROBAN nasal ointment should not be given to patients with a history of hypersensitivity to mupirocin or any of the constituents of the preparations.

Warnings and Precautions

In the rare event of a possible sensitisation reaction or severe local irritation occurring with the use of the product, treatment should be discontinued, the product should be wiped 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.

BACTROBAN nasal ointment is not suitable for ophthalmic use.

As with all topical preparations care should be taken to avoid contact with the eyes. If contaminated, the eyes should be thoroughly irrigated with water until the ointment residues have been removed.

Interactions

None reported.

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*).

Lactation

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

Effects on Ability to Drive and Use Machines

No adverse effects on the ability to drive or use machinery have been observed.

Adverse Reactions

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.

Respiratory, thoracic and mediastinal disorders:

Uncommon:	Nasal mucosa reactions.

Immune system disorders:

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

Overdose

Symptoms and Signs

There is currently limited experience with overdosage of *BACTROBAN* nasal ointment.

Treatment

There is no specific treatment for an overdose of *BACTROBAN* nasal ointment. 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 poisons centre, where available.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamics

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

Activity

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*[2]
Streptococcus species
Haemophilus influenzae
Neisseria gonorrhoeae
Neisseria meningitidis
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.

PRE-CLINICAL INFORMATION

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.

PHARMACEUTICAL PARTICULARS

List of Excipients

White soft paraffin

Softisan

Incompatibilities

None reported.

Shelf-Life

The expiry date is indicated on the packaging.

Special Precautions for Storage

Store below 25^{o}C.

Nature and Contents of Container

As registered locally.

Instructions for Use/Handling

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

Wash your hands after application.

Manufactured by:
Glaxo Operations UK Limited*, Barnard Castle, UK
*Member of the GSK group of companies

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