MUPIROCIN OINTMENT

1 PRODUCT NAME

Medicianz Mupirocin Ointment
Mupirocin 2% w/w ointment.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Mupirocin 2% w/w equivalent to 20 mg/g
For the full list of excipients, see section *6.1 List of excipients*.

3 PHARMACEUTICAL FORM

Ointment.
Homogenous, off-white ointment.
Medicianz Mupirocin Ointment is a white, translucent, water-soluble, polyethylene glycol based, homogeneous off-white ointment, which is odourless or nearly odourless.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Medicianz Mupirocin Ointment is indicated for the topical treatment of the following primary and secondary skin infections due to susceptible pathogens: primary pyodermas such as impetigo, folliculitis, furunculosis, ecthyma; secondary infected dermatoses such as eczema, psoriasis, atopic dermatitis, herpes, epidermolysis bullosa, icthyosis, and infected traumatic lesions such as ulcers, minor burns, cuts, abrasions, lacerations, wounds, biopsy sites, surgical incisions and insect bites.

Prophylactically, Medicianz Mupirocin Ointment may be used to prevent bacterial contamination in minor burns, biopsy sites, incisions and other clean lesions. For abrasions, minor cuts and wounds the prophylatic use of mupirocin ointment may prevent the development of infection and permit wound healing.

4.2 Dose and method of administration

A small amount of Medicianz Mupirocin Ointment should be applied to the affected area three times daily for up to 10 days depending on response. The area treated may be covered with a gauze dressing if required.

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

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.

Special Populations
Renal impairment
For use in renal impairment, please refer to section *4.4 Special warnings and precautions for use.*

4.3 Contraindications

Medicianz Mupirocin Ointment should not be given to patients with a history of hypersensitivity to mupirocin or any components of the formulations.

4.4 Special warnings and precautions for use

In the rare event of a possible sensitisation reaction or severe local irritation occurring with the use of Medicianz Mupirocin Ointment, treatment should be discontinued, the product should be wiped off and appropriate alternative therapy for the infection instituted.

Medicianz Mupirocin Ointment is not suitable for ophthalmic use, intranasal use, use in conjunction with cannulae and at the site of central venous cannulation.

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

Polyethylene glycol can be absorbed from open wounds and damaged skin and is excreted by the kidneys. In common with other polyethylene glycol based ointments, Medicianz Mupirocin 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 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.

Paediatric population

Medicianz Mupirocin Ointment has not been studied in term and preterm newborn infants under 4 weeks of age and therefore it should not be used in these patients.

4.5 Interaction with other medicines and other forms of interaction

No drug interactions have been reported.

4.6 Fertility, pregnancy and lactation

Pregnancy

Category B1. Adequate human data on use during pregnancy are not available. Studies in animals do not indicate reproductive toxicity (see section *5.3 Preclinical Safety Data*).

Breast-feeding

Adequate human and animal data on use during lactation are not available. If a cracked nipple is being treated, the nipple should be thoroughly washed prior to breast feeding.

Fertility

There are no data on the effects of mupirocin on human fertility. Studies in rats showed no effects on fertility (see section *5.3 Preclinical Safety Data*).

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

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

Common and uncommon adverse reactions were determined from pooled safety data from a clinical trial population of 1573 treated patients encompassing 12 clinical studies. 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 have been reported with Medicianz Mupirocin ointment.

Skin and subcutaneous tissue disorders:
Common: Burning localised to the area of application.

Uncommon: Itching, erythema, stinging and dryness localised to the area of application. Cutaneous sensitisation reactions to mupirocin or the ointment base.

{Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/}

4.9 Overdose

There is currently limited experience with overdosage of Medicianz Mupirocin Ointment.

There is no specific treatment for an overdose of Medicianz Mupirocin 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.

{For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).}

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of action
Mupirocin is a novel antibiotic produced through fermentation of *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.

Following intravenous or oral administration, mupirocin is rapidly metabolised to the inactive monic acid.

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 Susceptibility Species:
Susceptible:

- *Staphylococcus aureus*[1,2]
- *Staphylococcus epidermidis*[1,2]
- Coagulase-negative *staphylococci*[1,2]
- *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

Cross-resistance:
Mupirocin does not demonstrate cross-resistance with any other known antimicrobial.

Resistance mechanisms:
Low-level resistance in staphylococci (MICs 8-256 mcg/ml) has been shown to be due to changes in the native isoleucyl tRNA synthetase enzyme. High-level resistance in staphylococci (MICs ≥ 512 mcg/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.

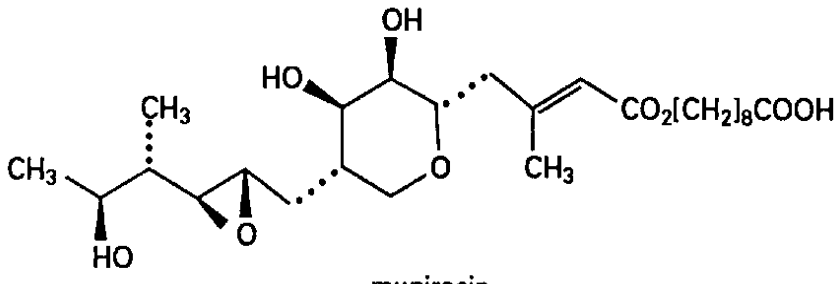
Clinical safety and efficacy
Comparability of Medicianz Mupirocin Ointment and Bactroban® Ointment

The efficacy and safety of Medicianz Mupirocin Ointment for the treatment of impetigo were assessed in a multicentre, randomised, double-blind clinical trial with the originator (Bactroban® 2% Ointment) as the active comparator. Both ointments were administered topically three times a day for 7 days. Patients of either gender, aged 28 days to 15 years, were eligible for study participation, if their SIRS (Skin Infection Rating Scale) score was 4 or higher and at least 3 SIRS categories were present. A baseline swab from the affected skin area had to be positive for *Staphylococcus aureus* and/or *Streptococcus pyogenes*. Clinical cure was assessed as the primary efficacy parameter on day 14 ± 4, i.e. 7 days after the end of treatment.

A total of 120 patients with a positive baseline bacteriological finding were treated in this study (57 with Medicianz Mupirocin Ointment, 63 with Bactroban® 2% Ointment). The mITT (modified intention-to-treat) population consisted of 119 patients (56/63), the per-protocol population consisted of 115 patients (55/60). The clinical cure rates in the per-protocol population were 100.0 % for Medicianz Mupirocin Ointment and 95.0 % for the comparator. The treatment difference was 0.050 with a 90% CI of -0.01 to +0.11 which was entirely within the predefined equivalence margin of -0.20 to +0.20, indicating a statistical equivalence of both medications. This was confirmed in a corresponding analysis in the mITT population. The microbiological cure rates at day 14 (absence of *Staphylococcus aureus* and *Streptococcus pyogenes*) were 100.0 % for Medicianz Mupirocin Ointment and 98.3 % for the comparator in the PP population and 100.0 % versus 98.4 % in the mITT population.

Active Ingredient
Medicianz Mupirocin Ointment contains mupirocin 2% w/w equivalent to 20 mg/g mupirocin as the active ingredient.

The chemical name is: 9-[4-[5S-[2S,3S-epoxy-5S-hydroxy-4S-methylhexyl]-3R,4R-dihydroxytetrahydropyran-2S-yl]-3-methylbut-2-(E)-enoyloxy]nonanoic acid. The chemical structure of mupirocin is shown below:



mupirocin

Molecular Formula: $C_{26}H_{44}O_9$

Molecular Mass: 500.63

The CAS number for mupirocin is 12650-69-0.

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

5.2 Pharmacokinetic properties

Absorption
Mupirocin is poorly absorbed through intact human skin. However, if it is absorbed (e.g. through broken/diseased skin) or it is 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 excreted mainly by the kidney (90%).

Special Populations

Elderly patients: No restrictions unless the condition being treated could lead to absorption of polyethylene glycol and there is evidence of moderate or severe renal impairment (see section *4.4 Special warning and precautions for use*).

5.3 Preclinical 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.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Polyethylene glycol (macrogol) 400

Polyethylene glycol (macrogol) 3350.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store below 25°C.

After first opening of the tube, the contents can be used for up to 10 days.

6.5 Nature and contents of container

Medicianz Mupirocin Ointment is supplied in aluminium tube with polypropylene cap in the following presentations.

Presentation	Pack size
5 g	Single
15 g	Single

Not all pack sizes may be distributed in New Zealand.

6.6 Special precautions for disposal

No special requirements for disposal.

7 MEDICINE SCHEDULE

Prescription Medicine

8 SPONSOR

Medicianz Healthcare Limited
PO Box 331054
Takapuna
Auckland 0622
Email: info@medicianz.com.au

Marketed and distributed by Medsurge Healthcare Pty Ltd.

9 DATE OF FIRST APPROVAL

28 June 2018

10 DATE OF REVISION OF THE TEXT

Not Applicable.

SUMMARY TABLE OF CHANGES

New datasheet