MUPINASE Ointment/ Cream (Mupirocin)

Composition

MUPINASE Ointment
Mupirocin, USP………………..2.0% w/w
Ointment base………………..q. s.

MUPINASE Cream
Mupirocin, USP………………..2.0% w/w

Dosage Forms

Ointment and cream

Pharmacology

Pharmacodynamics

Mupirocin is a novel antibacterial agent produced by fermentation using the organism, Pseudomonas fluorescens. Mupirocin inhibits bacterial protein synthesis by reversibly and specifically binding to bacterial isoleucyl transfer-RNA synthetase. Due to this unique mode of action, and its chemical structure, mupirocin demonstrates no in vitro cross-resistance with other classes of antimicrobial agents.

When mupirocin resistance does occur, it appears to result from the production of a modified isoleucyl-t RNA synthetase or the acquisition of, by genetic transfer, a plasmid mediating a new isoleucyl-t RNA synthetase. Low-level resistance in staphylococci is thought to result from point mutations within the usual staphylococcal chromosomal gene (ileS) for the target isoleucyl RNA synthetase enzyme. High-level resistance in staphylococci has been shown to be due to a distinct, plasmid encoded isoleucyl RNA synthetase enzyme. High-level plasmid mediated resistance (MIC >512mcg/mL) has been reported in some strains of Staphylococcus aureus (S. aureus) and with higher frequency in coagulase-negative staphylococci. Intrinsic resistance in Gram-negative organisms such as Enterobacteriaceae could be due to poor penetration of the outer membrane of the Gram-negative bacterial cell wall.

Mupirocin is bactericidal at concentrations achieved by topical administration. Mupirocin is highly protein-bound (>97%), and the effect of wound secretions on the MICs of mupirocin has not been determined.

Mupirocin has been shown to be active against strains of S. aureus and Streptococcus pyogenes (S. pyogenes), both in vitro and in clinical studies. Mupirocin is active against most strains of Staphylococcus epidermidis (S. epidermidis) and Staphylococcus saprophyticus (S. saprophyticus). Corynebacterium spp. and Micrococcus spp. are inherently resistant to mupirocin.

Pharmacokinetics

After topical application of mupirocin, it is only very minimally absorbed systemically and that which is absorbed is rapidly metabolized to the antimicrobially inactive metabolite, monic acid, which demonstrates no antibacterial activity.
Systemic absorption of mupirocin through intact human skin may occur because of broken/diseased skin. Mupirocin is rapidly eliminated from the body by metabolism to its inactive metabolite, monic acid, which is rapidly excreted by the kidneys. Penetration of mupirocin into the deeper epidermal and dermal layers of the skin is enhanced in traumatized skin and under occlusive dressings.

Application of $^{14}$C-labelled mupirocin ointment to the lower arm of normal male subjects followed by occlusion for 24 hours showed no measurable systemic absorption (<1.1 nano gramm mupirocin per millilitre of whole blood). Measurable radioactivity was present in the stratum corneum of these subjects 72 hours after application. In a study conducted in 7 healthy adult male subjects, the elimination half-life after intravenous administration of mupirocin was 20 to 40 minutes for mupirocin and 30 to 80 minutes for monic acid.

The systemic absorption of mupirocin was studied following application of mupirocin cream 3 times daily for 5 days to various skin lesions (>10 cm in length or 100 cm$^2$ in area) in 16 adults (aged 29 to 60 years) and 10 children (aged 3 to 12 years). Some systemic absorption was observed as evidenced by the detection of the metabolite, monic acid, in urine. Data from this trial indicated more frequent occurrence of percutaneous absorption in children (90% of subjects) compared with adults (44% of subjects); however, the observed urinary concentrations in children (0.07 to 1.3 mcg/mL) are within the observed range (0.08 to 10.03 mcg/mL) in the adult population. In general, the degree of percutaneous absorption following multiple dosing appears to be minimal in adults and children.

The pharmacokinetics of mupirocin has not been studied in individuals with renal impairment.

**Indications**

MUPINASE Ointment is a topical antibacterial agent, active against those organisms responsible for the majority of skin infections (impetigo, folliculitis, furunculosis, etc.), e.g. *S. aureus*, other *Staphylococci* and *Streptococci* (e.g. *S. pyogenes*). It is also active against Gram-negative organisms such as *Escherichia coli* and *Haemophilus influenzae*.

MUPINASE Cream is indicated for the topical treatment of secondarily infected traumatic skin lesions such as small lacerations, sutured wounds or abrasions (up to 10 cm in length or 100 cm$^2$ in area) due to susceptible strains of *S. aureus* and *S. pyogenes*.

**Dosage And Administration**

MUPINASE Ointment or Mupinase Cream is applied topically.

A small amount of MUPINASE Ointment or MUPINASE Cream should be applied to the affected area up to three times a day for up to 10 days, depending on the response.

A small quantity of MUPINASE Ointment/ thin layer of MUPINASE 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. The area may be covered with a gauze dressing or occluded if desired.

Patients not showing a clinical response within 3 to 5 days should be re-evaluated.

- **Renal Impairment**
  No dosage adjustment is necessary.

- **Hepatic Impairment**
  No dosage adjustment is necessary.

Do not mix with other preparations as there is a risk of dilution, resulting in a reduction of the antibacterial activity and potential loss of stability of the mupirocin in the ointment/cream. Any product remaining at the end of treatment should be discarded.
Contraindications

This drug is contraindicated in individuals with a history of sensitivity reactions/known hypersensitivity to mupirocin and any of its components.

Warnings And Precautions

General

In the event of sensitization reaction or severe local irritation should occur with the use of mupirocin ointment/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 nonsusceptible organisms, including fungi.

Pseudo membranous colitis and Clostridium difficile-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including mupirocin, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C. difficile.

If CDAD is suspected or confirmed, ongoing antibacterial drug use not directed against C. difficile may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibacterial treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated.

It is important to consider diagnosis of pseudomembranous colitis in patients who develop diarrhea during or after antibiotic use. Although this is less likely to occur with topically applied mupirocin, if prolonged or significant diarrhea occurs or the patient experiences abdominal cramps, treatment should be discontinued immediately and the patient investigated further.

Mupirocin ointment/cream is not formulated for use on mucosal surfaces. Mupirocin ointment is not suitable for ophthalmic use, intranasal use, use in conjunction with cannulae, and at the site of central venous cannulation because of the potential to promote fungal infections and antimicrobial resistance. Intranasal use has been associated with isolated reports of stinging and drying.

Avoid contact with the eyes. In case of accidental contact, the eyes should be thoroughly irrigated with water until the ointment/cream residue has 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, 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.

Mupirocin cream contains cetyl alcohol and stearyl alcohol. These inactive ingredients may cause local skin reactions (e.g., contact dermatitis).

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

Information for Patients

Use this medication only as directed by the healthcare provider. It is for external use only. Avoid contact with the eyes. If mupirocin gets in or near the eyes, rinse thoroughly with water. If no improvement is seen in 3 to 5 days, contact the healthcare provider. The treated area may be covered by gauze dressing if desired.

Report to the healthcare provider any signs of local adverse reactions. The medication should be stopped and the healthcare provider contacted if irritation, severe itching, or rash occurs.

Drug Interactions

The effect of the concurrent application of mupirocin ointment or cream and other drug/topical products has not been...
Renal Impairment
No dosage adjustment is necessary.

Hepatic Impairment
No dosage adjustment is necessary.

Pregnancy
Pregnancy Category B
Since there are no adequate and well-controlled studies in pregnant women, mupirocin should be used during pregnancy only if clearly needed.

Lactation
It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when mupirocin ointment or cream is administered to a lactating woman. If a cracked nipple is to be treated, it should be thoroughly washed prior to breastfeeding.

Paediatric Use
The safety and effectiveness of mupirocin ointment have been established in the age range of 2 months to 16 years. Use of mupirocin ointment in these age groups is supported by evidence from adequate and well-controlled studies of mupirocin ointment in impetigo in paediatric patients studied as a part of the pivotal clinical trials. The safety and effectiveness of mupirocin cream have been established in the age groups 3 months to 16 years. Use of mupirocin cream in these age groups is supported by evidence from adequate and well-controlled studies of mupirocin cream in adults, with additional data from 93 paediatric patients studied as part of the pivotal trials in adults.

Geriatric Use
In two well-controlled studies, 30 patients older than 65 years were treated with mupirocin cream. No overall difference in the efficacy or safety of mupirocin cream was observed in this patient population when compared with that observed in younger patients. No restrictions in use of mupirocin ointment, in elderly patients unless the condition being treated could lead to absorption of polyethylene glycol and there is evidence of moderate or severe renal impairment.

Undesirable Effects

Mupirocin Ointment
Adverse reactions are listed below by system organ class and frequency. Frequencies are defined as follows: very common (≥1/10), common (≥1/100 and <1/10), uncommon (≥1/1,000 and <1/100), rare (≥1/10,000 and <1/1,000), and very rare (<1/10,000), including isolated reports. Very rare adverse reactions were primarily determined from postmarketing experience data and, therefore, refer to the reporting rate rather than true frequency.

Immune System Disorders
Very rare: Systemic allergic reactions have been reported.

Skin and Subcutaneous Tissue Disorders
Common: Burning localized to the area of application.
Uncommon: Itching, erythema, stinging and dryness localized to the area of application.
Uncommon: Cutaneous sensitization reactions to mupirocin or the ointment base.
Pain was seen in 1.5% of patients; rash, nausea, tenderness, swelling, contact dermatitis, and increased exudate in less than 1% of patients have also been observed. Systemic allergic reactions, including anaphylaxis, urticaria, angioedema, and generalized rash have been reported in patients treated with formulations of mupirocin.

Data from clinical trials was used to determine the frequency of very common to rare undesirable effects. The following convention has been used for the classification of frequency: very common (>1/10), common (>1/100 and <1/10), uncommon (>1/1,000 and <1/100), rare (>1/10,000 and <1/1,000), and very rare (<1/10,000).

**Immune system disorders**

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

**Skin and Subcutaneous Tissue Disorders**

*Common:* Application site hypersensitivity reactions, including urticaria, pruritus, erythema, burning sensation, contact dermatitis, rash.

Skin dryness and erythema have been reported in irritancy studies in volunteers.

In two randomized, double-blind, double-dummy trials, 339 patients were treated with topical mupirocin cream plus oral placebo. Adverse events thought to be possibly or probably drug-related occurred in 28 (8.3%) patients. The incidence of those events that were reported in at least 1% of patients enrolled in these trials was as follows: headache (1.7%), rash, and nausea (1.1% each).

Other adverse events thought to be possibly or probably drug-related, which occurred in less than 1% of patients were as follows: abdominal pain, burning at application site, cellulitis, dermatitis, dizziness, pruritus, secondary wound infection, and ulcerative stomatitis.

In a supportive study in the treatment of secondarily infected eczema, 82 patients were treated with mupirocin cream. The incidence of adverse events thought to be possibly or probably drug-related was as follows: nausea (4.9%), headache, and burning at application site (3.6% each), pruritus (2.4%) and one report each of abdominal pain, bleeding secondary to eczema, pain secondary to eczema, hives, dry skin, and rash.

**Overdosage**

Intravenous infusions of 252 mg, as well as single oral doses of 500 mg of mupirocin, have been well tolerated in healthy adult subjects. The toxicity of mupirocin is very low. In the event of accidental ingestion, symptomatic treatment should be given. If mupirocin topical gets in your eyes or mouth, rinse with water.

In case of erroneous oral intake of large quantities of the ointment, renal function should be closely monitored in patients with renal impairment because of the possible side effects of polyethylene glycol.

**Storage And Handling Instructions**

Store at a controlled room temperature of 20° to 25°C (68° to 77°F).

**Packaging Information**

MUPINASE Ointment ................................................................. Tube of 5 g
MUPINASE Cream ................................................................. Tube of 7.5 g

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