MUPIROCIN

MUPICIN®

20 mg/g(2%) Ointment
Topical Antibacterial

FORMULATION
Each gram ointment contains:
Mupirocin..... 20 mg (2%)

PRODUCT DESCRIPTION
Mupirocin (Mupicin®) 20mg/g (2%) Ointment is a colorless, viscous ointment with faint characteristic odor.

PHARMACODYNAMICS
Mupirocin is a naturally occurring antibiotic produced by fermentation using the microorganism *Pseudomonas fluorescens*. It inhibits bacterial protein synthesis by reversibly and specifically binding to bacterial isoleucyl transfer-RNA synthetase. Due to its unique mode of action, mupirocin shows no cross resistance with other classes of antibiotics including erythromycin, fusidic acid, gentamicin, lincomycin, methicillin, neomycin, novobiocin, penicillin, streptomycin, chloramphenicol, or tetracycline.

Mupirocin is bactericidal at concentrations achieved with topical application. The minimum bactericidal concentration (MBC) of the drug against *Staphylococcus aureus* is usually 8 to 32 times higher than the minimum inhibitory concentration (MIC) of the drug. The effect of wound secretions on the MICs of mupirocin has not been determined.

Based on *in vitro* studies, mupirocin's antibacterial activity is enhanced at a slightly acidic pH than at neutral or alkaline pH. It is inactivated at pH less than 4 or greater than 9. The normal skin pH (approximately 5.5) presumably contributes to the activity of mupirocin when applied topically to the skin.

ANTIMICROBIAL SPECTRUM OF ACTIVITY
Mupirocin is active against most strains of *Staphylococcus aureus* [including methicillin-resistant *Staphylococcus aureus* (MRSA)] and *Streptococcus pyogenes*, both *in vitro* and in clinical infection.

Mupirocin has demonstrated *in vitro* activity against most strains of the following microorganisms; however, clinical significance is unknown:

Aerobic Gram-positive Microorganisms	Aerobic Gram-negative Microorganisms
Staphylococcus epidermidis	*Haemophilus influenzae*
Staphylococcus saprophyticus	*Neisseria gonorrheae*
Other coagulase-negative *staphylococci* (including methicillin-resistant strains)	*Neisseria meningitidis*
	Branhamella catarrhalis
Streptococcus pneumoniae	*Bordetella pertussis*
Group B streptococci (*Streptococcus agalactiae*)	*Pasteurella multocida*
	Proteus mirabilis
Groups C and G *streptococci*	*Proteus vulgaris*
Viridans streptococci	*Enterobacter cloacae*
Listeria monocytogenes	*Enterobacter aerogenes*
Erysipelothrix rhusiopathiae	

Resistance:
• High-level plasmid-mediated resistance (MIC ≥ 512 μg/mL) has been reported in some strains of *Staphylococcus aureus* and coagulase-negative staphylococci (including *Staphylococcus epidermidis*).
• Low-level resistance in staphylococci (MIC 8-256 μg/mL) has been shown to be due to changes in native isoleucyl tRNA synthetase enzyme.
• *Pseudomonas fluorescens*, the organism that produces mupirocin, is resistant to the drug.
• *Propionibacterium acnes, Bacteroides fragilis, Clostridium difficile, Pseudomonas aeruginosa, Peptococcus, Peptostreptococcus, Trichophyton mentagrophytes, Malassezia ovalis, Candida albicans, Aspergillus fumigatus* and enterococci, including *Enterococcus faecalis* are resistant to mupirocin. Intrinsic resistance in Gram-negative microorganisms such as Enterobacteriaceae could be due to poor penetration into the bacterial cell wall.

PHARMACOKINETICS
Mupirocin does not appear to be appreciably absorbed into the systemic circulation after topical application to intact skin. When radiolabeled mupirocin was applied topically to intact skin under an occlusive dressing, less than 0.3% of a topical dose of the drug was absorbed systemically after 24 hours. The drug was not detected in urine or feces collected for 5 days after the dose. About 2 to 4% of the radioactivity was present in the stratum corneum after 24 hours and was still detectable for at least 72 hours.

When the drug is applied to broken or diseased skin, the drug may be absorbed into deeper epidermis and possibly into the systemic circulation.

About 95% to 97% of mupirocin is highly bound to serum proteins *in vitro*.

Any systemically absorbed mupirocin is eliminated from the body by de-esterification of the drug to its inactive metabolite, monic acid, which is rapidly excreted in the urine.

INDICATIONS
For the topical treatment of primary and secondary bacterial skin infections due to susceptible organisms:

• **Primary skin infections:** Impetigo, folliculitis, furunculosis, and ecthyma
• **Secondary skin infections:** Infected dermatoses, such as infected abrasions and insect bites, minor wounds, and minor burns

Prophylaxis:
Mupirocin may be used to prevent bacterial contamination of small cuts and wounds, abrasions, incisions, and other clean lesions.

DOSAGE AND ADMINISTRATION
Wash hands before and after each application unless mupirocin ointment is used to treat a hand condition.
• Clean the affected and adjacent area with mild soap and water.
• Rinse thoroughly and pat dry.
• Apply a small amount of mupirocin ointment on the affected area three times daily for up to 10 days, or as prescribed by a physician. The treated area may be covered with gauze dressing if needed.
• Re-assess patients not showing a clinical response within 3 to 5 days.
• Do not apply concurrently with other topical medications **[see Interactions with Other Medicaments]**

CONTRAINDICATIONS
• Known hypersensitivity to mupirocin or any component of the product.
• Not for ophthalmic or intranasal use.

WARNINGS AND PRECAUTIONS
• For external use on the skin only.
• Avoid contact with the eyes. If the ointment comes in contact with the eyes, rinse out promptly and thoroughly with water.
• Do not use at the site of central venous cannulation.
• As with other polyethylene glycol-based ointments, do not use mupirocin ointment in conditions where large amount of polyethylene glycol may be absorbed (e.g., in open wounds, extensive burns, broken skin), particularly in patients with moderate or severe renal impairment.
• In cases of sensitivity or severe local irritation, discontinue mupirocin treatment and consult a physician.
• As with other antibacterial products, long term use may result in overgrowth of non-susceptible organisms, including fungi.

Carcinogenesis, Mutagenesis, Impairment of Fertility:
The carcinogenic potential of mupirocin has not been evaluated in long-term animal studies.

The mutagenic potential of the drug has been investigated *in vitro* and *in vivo* using rat primary hepatocyte unscheduled DNA synthesis, sediment analysis for DNA strand breaks, the Ames test, *Escherichia coli* mutation assay, metaphase analysis of human lymphocytes, mouse lymphoma assay, and bone marrow micronuclei assay in mice. Results of these studies did not indicate a potential for genotoxicity.

Studies in male and female rats have shown that subcutaneous doses up to 14 times the human topical dose (about 60 mg/day) on a mg/m^2 basis were found to have no evidence of impairment on fertility and reproductive performance attributable to mupirocin.

INTERACTIONS WITH OTHER MEDICAMENTS
In general, mupirocin ointment should not be mixed with other topical medications which may lead to reduction of antibacterial activity and probably loss of stability of mupirocin.

• Hydrocortisone, phenol, sulfur, or triamcinolone acetonide is compatible with mupirocin 2% ointment for at least 28 days at room temperature when extemporaneously admixed with the ointment to provide concentrations of these drugs of 1, 3, 2, or 0.1%, respectively. However, the stability of admixtures of mupirocin ointment and *commercially available* topical formulations of these drugs has not been established.
• Mupirocin 2% ointment is incompatible with salicylic acid 2%.
• Mupirocin should not be admixed with water-containing vehicles or formulations such as Aquaphor® or coal tar solution.

STATEMENT ON USAGE FOR HIGH RISK GROUPS
• ***Pregnancy:*** *(Pregnancy Category B).* Animal studies have demonstrated no evidence of impaired fertility or harmful effects to the fetus. There are no adequate and well-controlled clinical studies in pregnant women. Since animal studies are not always predictive of human response, use this drug during pregnancy only if clearly needed.

• ***Lactation:*** It is not known whether mupirocin is excreted in human milk. Since many drugs are distributed into human milk, use with caution when breastfeeding. If a cracked nipple is to be treated with mupirocin, lactation from the affected breast should be maintained by manual expression until the end of treatment. During this time, milk from the affected breast should be discarded.
• ***Use in Children:*** The safety and efficacy of mupirocin ointment have been established in children 2 months to 16 years old.
• ***Use in Elderly Patients:*** The safety and efficacy of mupirocin in elderly patients more than 65 years old are comparable to those in younger adults.

UNDESIRABLE EFFECTS
In general, mupirocin is well tolerated after topical application. Most adverse effects of mupirocin are mild and transient. The following local adverse effects have been reported rarely in patients using mupirocin ointment: application site reactions, burning, stinging, pain, pruritus, rash, dryness, erythema, tenderness, cellulitis, pain or bleeding secondary to eczema, secondary wound infection, urticaria, swelling, contact dermatitis, furunculosis, exfoliative dermatitis, increased exudates, and cutaneous sensitization reactions to mupirocin or the ointment base.

The following systemic effects have occurred very rarely in patients receiving topical mupirocin: systemic allergic reactions, nausea, headache, dizziness, abdominal pain, and ulcerative stomatitis.

OVERDOSAGE AND TREATMENT
The toxicity of mupirocin is very low. In case of overdosage, symptomatic treatment is recommended. In case of accidental swallowing, seek medical help immediately.

STORAGE CONDITIONS
• Keep container tightly closed.
• Keep the product out of sight and reach of children.
• Store in a dry place at temperatures not exceeding 25°C.

CAUTION
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

AVAILABILITY
Mupirocin (Mupicin®) 20mg/g (2%) Ointment in aluminum collapsible tube of 5g and 3g (Physician's sample).

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Manufactured by
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