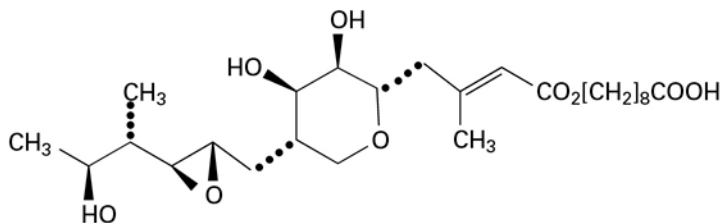


PRESCRIBING INFORMATION

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3 **BACTROBAN[®] Ointment**
4 **(mupirocin ointment, 2%)**
5 **For Dermatologic Use**

6 **DESCRIPTION**

7 Each gram of BACTROBAN Ointment (mupirocin ointment, 2%) contains 20 mg mupirocin
8 in a bland water miscible ointment base (polyethylene glycol ointment, N.F.) consisting of
9 polyethylene glycol 400 and polyethylene glycol 3350. Mupirocin is a naturally occurring
10 antibiotic. The chemical name is (*E*)-(2*S*,3*R*,4*R*,5*S*)-5-[(2*S*,3*S*,4*S*,5*S*)-2,3-Epoxy-5-hydroxy-4-
11 methylhexyl]tetrahydro-3,4-dihydroxy-β-methyl-2*H*-pyran-2-crotonic acid, ester with
12 9-hydroxynonanoic acid. The molecular formula of mupirocin is C₂₆H₄₄O₉, and the molecular
13 weight is 500.63. The chemical structure is:
14



15
16 **CLINICAL PHARMACOLOGY**

17 Application of ¹⁴C-labeled mupirocin ointment to the lower arm of normal male subjects
18 followed by occlusion for 24 hours showed no measurable systemic absorption (<1.1 nanogram
19 mupirocin per milliliter of whole blood). Measurable radioactivity was present in the stratum
20 corneum of these subjects 72 hours after application.

21 Following intravenous or oral administration, mupirocin is rapidly metabolized. The principal
22 metabolite, monic acid, is eliminated by renal excretion, and demonstrates no antibacterial
23 activity. In a trial conducted in 7 healthy adult male subjects, the elimination half-life after
24 intravenous administration of mupirocin was 20 to 40 minutes for mupirocin and 30 to
25 80 minutes for monic acid. The pharmacokinetics of mupirocin has not been studied in
26 individuals with renal insufficiency.

27 **Microbiology:** Mupirocin is an antibacterial agent produced by fermentation using the
28 organism *Pseudomonas fluorescens*. Mupirocin inhibits bacterial protein synthesis by reversibly
29 and specifically binding to bacterial isoleucyl transfer-RNA (tRNA) synthetase. Due to this
30 unique mode of action, mupirocin does not demonstrate cross-resistance with other classes of
31 antimicrobial agents.

32 When mupirocin resistance occurs, it results from the production of a modified
33 isoleucyl-tRNA synthetase, or the acquisition of, by genetic transfer, a plasmid mediating a new

34 isoleucyl-tRNA synthetase. High-level plasmid-mediated resistance (MIC >512 mcg/mL) has
35 been reported in increasing numbers of isolates of *Staphylococcus aureus* and with higher
36 frequency in coagulase-negative staphylococci. Mupirocin resistance occurs with greater
37 frequency in methicillin-resistant than methicillin-susceptible staphylococci. Because of the
38 occurrence of mupirocin resistance in methicillin-resistant *Staphylococcus aureus* (MRSA), it is
39 appropriate to test MRSA populations for mupirocin susceptibility prior to the use of mupirocin
40 using a standardized method.^{1,2,3}

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

44 Mupirocin has been shown to be active against susceptible strains of *S. aureus* and
45 *Streptococcus pyogenes*, both in vitro and in clinical trials (see INDICATIONS AND USAGE).
46 The following in vitro data are available, **but their clinical significance is unknown**. Mupirocin
47 is active against most isolates of *Staphylococcus epidermidis*.

48 INDICATIONS AND USAGE

49 BACTROBAN Ointment is indicated for the topical treatment of impetigo due to: *S. aureus*
50 and *S. pyogenes*.

51 CONTRAINDICATIONS

52 This drug is contraindicated in patients with known hypersensitivity to any of the constituents
53 of the product.

54 WARNINGS

55 Avoid contact with the eyes. In case of accidental contact, rinse well with water.

56 In the event of sensitization or severe local irritation from BACTROBAN Ointment, usage
57 should be discontinued.

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

62 *C. difficile* produces toxins A and B which contribute to the development of CDAD.
63 Hypertoxin-producing isolates of *C. difficile* cause increased morbidity and mortality, as these
64 infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be
65 considered in all patients who present with diarrhea following antibacterial drug use. Careful
66 medical history is necessary since CDAD has been reported to occur over two months after the
67 administration of antibacterial agents.

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

72 **PRECAUTIONS**

73 As with other antibacterial products, prolonged use may result in overgrowth of
74 nonsusceptible organisms, including fungi.

75 BACTROBAN Ointment is not formulated for use on mucosal surfaces. Intranasal use has
76 been associated with isolated reports of stinging and drying. A paraffin-based formulation —
77 BACTROBAN[®] Nasal (mupirocin calcium ointment) — is available for intranasal use.

78 Polyethylene glycol can be absorbed from open wounds and damaged skin and is excreted by
79 the kidneys. In common with other polyethylene glycol-based ointments, BACTROBAN
80 Ointment should not be used in conditions where absorption of large quantities of polyethylene
81 glycol is possible, especially if there is evidence of moderate or severe renal impairment.

82 BACTROBAN Ointment should not be used with intravenous cannulae or at central
83 intravenous sites because of the potential to promote fungal infections and antimicrobial
84 resistance.

85 **Information for Patients:** Use this medication only as directed by the healthcare provider. It
86 is for external use only. Avoid contact with the eyes. If BACTROBAN Ointment gets in or near
87 the eyes, rinse thoroughly with water. The medication should be stopped and the healthcare
88 provider contacted if irritation, severe itching, or rash occurs.

89 If impetigo has not improved in 3 to 5 days, contact the healthcare provider.

90 **Drug Interactions:** The effect of the concurrent application of BACTROBAN Ointment and
91 other drug products has not been studied.

92 **Carcinogenesis, Mutagenesis, Impairment of Fertility:** Long-term studies in animals to
93 evaluate carcinogenic potential of mupirocin have not been conducted.

94 Results of the following studies performed with mupirocin calcium or mupirocin sodium in
95 vitro and in vivo did not indicate a potential for genotoxicity: Rat primary hepatocyte
96 unscheduled DNA synthesis, sediment analysis for DNA strand breaks, *Salmonella* reversion test
97 (Ames), *Escherichia coli* mutation assay, metaphase analysis of human lymphocytes, mouse
98 lymphoma assay, and bone marrow micronuclei assay in mice.

99 Reproduction studies were performed in male and female rats with mupirocin administered
100 subcutaneously at doses up to 14 times a human topical dose (approximately 60 mg mupirocin
101 per day) on a mg/m² basis and revealed no evidence of impaired fertility and reproductive
102 performance from mupirocin.

103 **Pregnancy: Teratogenic Effects:** Pregnancy Category B. Reproduction studies have been
104 performed in rats and rabbits with mupirocin administered subcutaneously at doses up to 22 and
105 43 times, respectively, the human topical dose (approximately 60 mg mupirocin per day) on a
106 mg/m² basis and revealed no evidence of harm to the fetus due to mupirocin. There are, however,
107 no adequate and well-controlled studies in pregnant women. Because animal studies are not
108 always predictive of human response, this drug should be used during pregnancy only if clearly
109 needed.

110 **Nursing Mothers:** It is not known whether this drug is excreted in human milk. Because many
111 drugs are excreted in human milk, caution should be exercised when BACTROBAN Ointment is
112 administered to a nursing woman.

113 **Pediatric Use:** The safety and effectiveness of BACTROBAN Ointment have been established
114 in the age range of 2 months to 16 years. Use of BACTROBAN Ointment in these age groups is
115 supported by evidence from adequate and well-controlled trials of BACTROBAN Ointment in
116 impetigo in pediatric subjects studied as a part of the pivotal clinical trials (see CLINICAL
117 STUDIES).

118 **ADVERSE REACTIONS**

119 The following local adverse reactions have been reported in connection with the use of
120 BACTROBAN Ointment: burning, stinging, or pain in 1.5% of subjects; itching in 1% of
121 subjects; rash, nausea, erythema, dry skin, tenderness, swelling, contact dermatitis, and increased
122 exudate in less than 1% of subjects.

123 Systemic allergic reactions, including anaphylaxis, urticaria, angioedema, and generalized
124 rash have been reported in patients treated with formulations of BACTROBAN.

125 **DOSAGE AND ADMINISTRATION**

126 A small amount of BACTROBAN Ointment should be applied to the affected area 3 times
127 daily. The area treated may be covered with a gauze dressing if desired. Patients not showing a
128 clinical response within 3 to 5 days should be re-evaluated.

129 **CLINICAL STUDIES**

130 The efficacy of topical BACTROBAN Ointment in impetigo was tested in 2 trials. In the first,
131 subjects with impetigo were randomized to receive either BACTROBAN Ointment or vehicle
132 placebo 3 times daily for 8 to 12 days. Clinical efficacy rates at end of therapy in the evaluable
133 populations (adults and pediatric subjects included) were 71% for BACTROBAN Ointment
134 (n = 49) and 35% for vehicle placebo (n = 51). Pathogen eradication rates in the evaluable
135 populations were 94% for BACTROBAN Ointment and 62% for vehicle placebo. There were no
136 side effects reported in the group receiving BACTROBAN Ointment.

137 In the second trial, subjects with impetigo were randomized to receive either BACTROBAN
138 Ointment 3 times daily or 30 to 40 mg/kg oral erythromycin ethylsuccinate per day (this was an
139 unblinded trial) for 8 days. There was a follow-up visit 1 week after treatment ended. Clinical
140 efficacy rates at the follow-up visit in the evaluable populations (adults and pediatric subjects
141 included) were 93% for BACTROBAN Ointment (n = 29) and 78.5% for erythromycin (n = 28).
142 Pathogen eradication rates in the evaluable populations were 100% for both test groups. There
143 were no side effects reported in the group receiving BACTROBAN Ointment.

144 **Pediatrics:** There were 91 pediatric subjects aged 2 months to 15 years in the first trial
145 described above. Clinical efficacy rates at end of therapy in the evaluable populations were 78%
146 for BACTROBAN Ointment (n = 42) and 36% for vehicle placebo (n = 49). In the second trial
147 described above, all subjects were pediatric except 2 adults in the group receiving

148 BACTROBAN Ointment. The age range of the pediatric subjects was 7 months to 13 years. The
149 clinical efficacy rate for BACTROBAN Ointment (n = 27) was 96%, and for erythromycin it was
150 unchanged (78.5%).

151 **HOW SUPPLIED**

152 BACTROBAN Ointment is supplied in 22-gram tubes.

153 NDC 0029-1525-44 (22-gram tube)

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

155 **REFERENCES**

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171 GlaxoSmithKline

172 Research Triangle Park, NC 27709

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179 March/2015

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