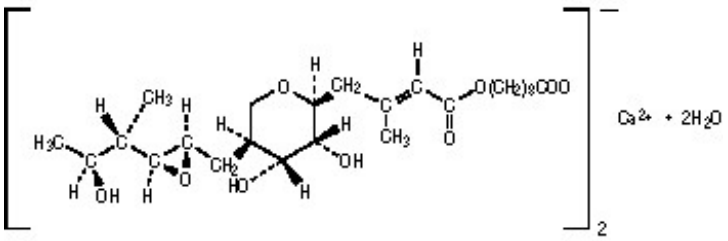
BACTROBAN- mupirocin calcium cream
GlaxoSmithKline LLC

BACTROBAN® Cream
(mupirocin calcium cream, 2%)
For Dermatologic Use

DESCRIPTION

BACTROBAN Cream (mupirocin calcium cream, 2%) contains the dihydrate crystalline calcium hemi-salt of the antibiotic mupirocin. Chemically, it is (α*E*,2*S*,3*R*,4*R*,5*S*)-5-[(2*S*,3*S*,4*S*,5*S*)-2,3-Epoxy-5-hydroxy-4-methylhexyl]tetrahydro-3,4-dihydroxy-β-methyl-2*H*-pyran-2-crotonic acid, ester with 9-hydroxynonanoic acid, calcium salt (2:1), dihydrate.

The molecular formula of mupirocin calcium is $(C_{26}H_{43}O_9)_2Ca \cdot 2H_2O$, and the molecular weight is 1075.3. The molecular weight of mupirocin free acid is 500.6. The structural formula of mupirocin calcium is:



BACTROBAN Cream is a white cream that contains 2.15% w/w mupirocin calcium (equivalent to 2.0% mupirocin free acid) in an oil and water-based emulsion. The inactive ingredients are benzyl alcohol, cetomacrogol 1000, cetyl alcohol, mineral oil, phenoxyethanol, purified water, stearyl alcohol, and xanthan gum.

CLINICAL PHARMACOLOGY

Pharmacokinetics

Systemic absorption of mupirocin through intact human skin is minimal. The systemic absorption of mupirocin was studied following application of BACTROBAN 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 [1 pediatric subject had no detectable level]) are within the observed range (0.08 to 10.03 mcg/mL [9 adults had no detectable level]) in the adult population. In general, the degree of percutaneous absorption following multiple dosing appears to be minimal in adults and children. Any mupirocin reaching the systemic circulation is rapidly metabolized, predominantly to inactive monic acid, which is eliminated by renal excretion.

Microbiology

Mupirocin is an antibacterial agent produced by fermentation using the organism *Pseudomonas fluorescens*. It is active against a wide range of gram-positive bacteria including methicillin-resistant *Staphylococcus aureus* (MRSA). It is also active against certain gram-negative bacteria. Mupirocin

inhibits bacterial protein synthesis by reversibly and specifically binding to bacterial isoleucyl transfer-RNA synthetase. Due to this unique mode of action, mupirocin demonstrates no in vitro cross-resistance with other classes of antimicrobial agents.

Resistance occurs rarely; however, when mupirocin resistance does occur, it appears to result from the production of a modified isoleucyl-tRNA synthetase. High-level plasmid-mediated resistance (MIC >1,024 mcg/mL) has been reported in some strains of *Staphylococcus aureus* and coagulase-negative staphylococci.

Mupirocin is bactericidal at concentrations achieved by topical application. The minimum bactericidal concentration (MBC) against relevant pathogens is generally 8-fold to 30-fold higher than the minimum inhibitory concentration (MIC). In addition, 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 most strains of *S. aureus* and *Streptococcus pyogenes*, both in vitro and in clinical trials (see INDICATIONS AND USAGE). The following in vitro data are available, BUT THEIR CLINICAL SIGNIFICANCE IS UNKNOWN. Mupirocin is active against most strains of *Staphylococcus epidermidis* and *Staphylococcus saprophyticus*.

INDICATIONS AND USAGE

BACTROBAN Cream is indicated for the treatment of secondarily infected traumatic skin lesions (up to 10 cm in length or 100 cm^2 in area) due to susceptible strains of *S. aureus* and *S. pyogenes*.

CONTRAINDICATIONS

BACTROBAN Cream is contraindicated in patients with known hypersensitivity to any of the constituents of the product.

WARNINGS

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

In the event of a sensitization or severe local irritation from BACTROBAN Cream, usage should be discontinued, and appropriate alternative therapy for the infection instituted.

Clostridium difficile-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including BACTROBAN, 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*.

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin-producing isolates of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibacterial drug use. Careful medical history is necessary since CDAD has been reported to occur over 2 months after the administration of antibacterial agents.

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.

PRECAUTIONS

General

As with other antibacterial products, prolonged use may result in overgrowth of nonsusceptible microorganisms, including fungi (see DOSAGE AND ADMINISTRATION).

BACTROBAN Cream is not formulated for use on mucosal surfaces.

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 BACTROBAN Cream gets in or near the eyes, rinse thoroughly with water.

•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.

•If no improvement is seen in 3 to 5 days, contact the healthcare provider.

Drug Interactions

The effect of the concurrent application of topical mupirocin calcium cream and other topical products has not been studied.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals to evaluate carcinogenic potential of mupirocin calcium have not been conducted.

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

Fertility studies were performed in rats with mupirocin administered subcutaneously at doses up to 49 times a human topical dose of 1 gram/day (approximately 20 mg mupirocin per day) on a mg/m^2 basis and revealed no evidence of impaired fertility from mupirocin sodium.

Pregnancy

Teratogenic Effects: Pregnancy Category B. Teratology studies have been performed in rats and rabbits with mupirocin administered subcutaneously at doses up to 78 and 154 times, respectively, a human topical dose of 1 gram/day (approximately 20 mg mupirocin per day) on a mg/m^2 basis and revealed no evidence of harm to the fetus due to mupirocin. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers

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 BACTROBAN Cream is administered to a nursing woman.

Pediatric Use

The safety and effectiveness of BACTROBAN Cream have been established in the age groups 3 months to 16 years. Use of BACTROBAN Cream in these age groups is supported by evidence from adequate and well-controlled trials of BACTROBAN Cream in adults with additional data from 93 pediatric subjects studied as part of the pivotal trials in adults (see CLINICAL STUDIES).

Geriatric Use

In 2 well-controlled trials, 30 subjects older than 65 years were treated with BACTROBAN Cream. No overall difference in the efficacy or safety of BACTROBAN Cream was observed in this patient population when compared with that observed in younger patients.

ADVERSE REACTIONS

In 2 randomized, double-blind, double-dummy trials, 339 subjects were treated with topical BACTROBAN Cream plus oral placebo. Adverse events thought to be possibly or probably drug-related occurred in 28 (8.3%) subjects. The incidence of those events that were reported in at least 1% of subjects enrolled in these trials were: 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 subjects were: abdominal pain, burning at application site, cellulitis, dermatitis, dizziness, pruritus, secondary wound infection, and ulcerative stomatitis.

In a supportive trial in the treatment of secondarily infected eczema, 82 subjects were treated with BACTROBAN 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 1 report each of abdominal pain, bleeding secondary to eczema, pain secondary to eczema, hives, dry skin, and rash.

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

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. There is no information regarding overdose of BACTROBAN Cream.

DOSAGE AND ADMINISTRATION

A small amount of BACTROBAN Cream should be applied to the affected area 3 times daily for 10 days. The area treated may be covered with gauze dressing if desired. Patients not showing a clinical response within 3 to 5 days should be re-evaluated.

CLINICAL STUDIES

The efficacy of topical BACTROBAN Cream for the treatment of secondarily infected traumatic skin lesions (e.g., lacerations, sutured wounds, and abrasions not more than 10 cm in length or 100 cm^2 in total area) was compared with that of oral cephalexin in 2 randomized, double-blind, double-dummy clinical trials. Clinical efficacy rates at follow-up in the per-protocol populations (adults and pediatric subjects included) were 96.1% for BACTROBAN Cream (n = 231) and 93.1% for oral cephalexin (n = 219). Pathogen eradication rates at follow-up in the per-protocol populations were 100% for both BACTROBAN Cream and oral cephalexin.

Pediatrics: There were 93 pediatric subjects aged 2 weeks to 16 years enrolled per protocol in the secondarily infected skin lesion trials, although only 3 were less than 2 years of age in the population treated with BACTROBAN Cream. Subjects were randomized to either 10 days of topical BACTROBAN Cream 3 times daily or 10 days of oral cephalexin (250 mg 4 times daily for subjects >40 kg or 25 mg/kg/day oral suspension in 4 divided doses for subjects ≤40 kg). Clinical efficacy at follow-up (7 to 12 days post-therapy) in the per protocol populations was 97.7% (43/44) for BACTROBAN Cream and 93.9% (46/49) for cephalexin. Only 1 adverse event (headache) was thought to be possibly or probably related to drug therapy with BACTROBAN Cream in the intent-to-treat pediatric population of 70 children (1.4%).

HOW SUPPLIED

BACTROBAN Cream is supplied in 15-gram and 30-gram tubes.

NDC 0029-1527-22 (15-gram tube)

NDC 0029-1527-25 (30-gram tube)

Store at or below 25°C (77°F). Do not freeze.

GlaxoSmithKline

Research Triangle Park, NC 27709

September 2014

BBC:1PI

Principal Display Panel

NDC 0029-1527-22

BACTROBAN CREAM®

MUPIROCIN CALCIUM CREAM 2%

15 grams (Net Wt.)

R_x only

Store at or below 25ºC (77ºF). Do not freeze.

Each gram contains 21.5 mg mupirocin calcium in a mineral oil cream base.

Dosage: For dermatologic use only. Apply a small amount of cream to the affected area three times daily for 10 days. Patients not showing clinical response within 3 to 5 days should be re-evaluated. See accompanying prescribing information.

GlaxoSmithKline

Research Triangle Park, NC 27709

Made in England

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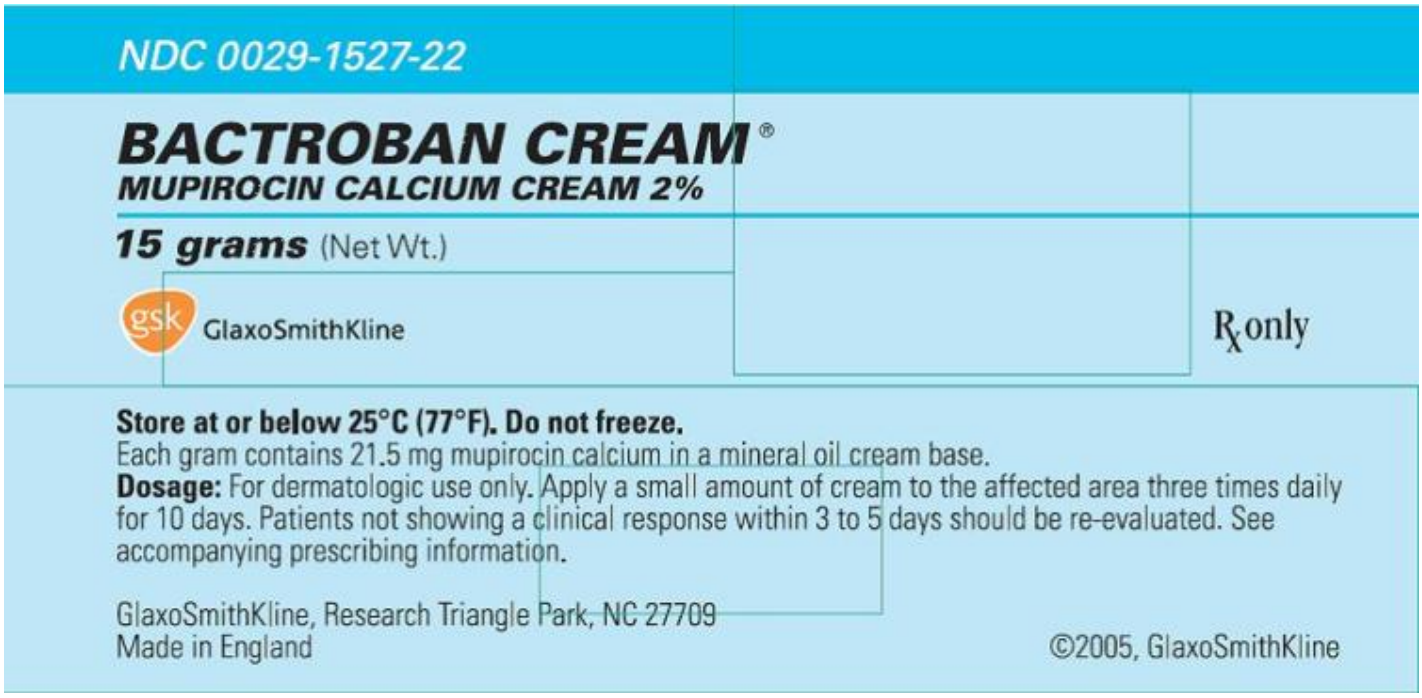

BACTROBAN

mupirocin calcium cream

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG LABEL	**Item Code (Source)**	NDC:0029-1527
Route of Administration	TOPICAL	**DEA Schedule**	

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
MUPIROCIN CALCIUM (MUPIROCIN)	MUPIROCIN	20 mg in 1 g

Inactive Ingredients	
Ingredient Name	**Strength**
BENZYL ALCOHOL	
CETETH-20	
CETYL ALCOHOL	
MINERAL OIL	
PHENOXYETHANOL	
WATER	
STEARYL ALCOHOL	
XANTHAN GUM	

Product Characteristics			
Color	WHITE	**Score**	
Shape		**Size**	

Flavor		**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0029-1527-22	1 in 1 CARTON	01/23/1998	
1		15 g in 1 TUBE; Combination Product Type = C112160		
2	NDC:0029-1527-25	1 in 1 CARTON	01/23/1998	
2		30 g in 1 TUBE; Combination Product Type = C112160		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA050746	01/23/1998	

Labeler - GlaxoSmithKline LLC (167380711)

Revised: 9/2014 GlaxoSmithKline LLC