HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use BACTROBAN Nasal Ointment safely and effectively. See full prescribing information for BACTROBAN Nasal Ointment.

BACTROBAN (mupirocin calcium) nasal ointment
Initial U.S. Approval: 1995

----------RECENT MAJOR CHANGES----------
Warnings and Precautions, *Clostridium difficile*-associated diarrhea (CDAD) (5.3) 09/2014

----------INDICATIONS AND USAGE----------
BACTROBAN nasal ointment is an antibacterial drug indicated for the eradication of nasal colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) in adult and pediatric patients (aged 12 years and older) and healthcare workers as part of a comprehensive infection control program to reduce the risk of infection among patients at high risk of MRSA infection during institutional outbreaks of infections with this microorganism. (1)

Limitations of Use (1)
- There are insufficient data at this time to establish that this product is safe and effective as part of an intervention program to prevent autoinfection of high-risk patients from their own nasal colonization with *Staphylococcus aureus (S. aureus)*.
- There are insufficient data at this time to recommend use of BACTROBAN nasal ointment for general prophylaxis of any infection in any patient population.

----------DOSAGE AND ADMINISTRATION----------
- For Intranasal Use Only. (2)
- Apply approximately one-half of the ointment from the single-use tube into 1 nostril and the other half into the other nostril twice daily (morning and evening) for 5 days. (2)
- After application, close the nostrils by pressing together and releasing the sides of the nose repetitively for approximately 1 minute to spread the ointment throughout the nares. (2)
- Discard tube after usage. Do not re-use. (2)
- Do not apply BACTROBAN nasal ointment concurrently with any other intranasal products. (2)

----------DOSAGE FORMS AND STRENGTHS----------
- Nasal ointment: 2.15% w/w mupirocin calcium (equivalent to 2% mupirocin free acid) in single-use 1-gram tubes. (3)

----------CONTRAINDICATIONS----------
- Known hypersensitivity to mupirocin or any of the excipients of BACTROBAN nasal ointment. (4)

----------WARNINGS AND PRECAUTIONS----------
- Severe Allergic Reactions: Including anaphylaxis, urticaria, angioedema, and generalized rash have been reported in patients treated with formulations of BACTROBAN. (5.1)
- Eye Irritation: Avoid contact with eyes. (5.2)
- Local Irritation: Discontinue in the event of sensitization or severe local irritation. (5.3)
- *Clostridium difficile*-associated Diarrhea (CDAD): If diarrhea occurs, evaluate patients for CDAD. (5.4)
- Potential for Microbial Overgrowth: Prolonged use may result in overgrowth of nonsusceptible microorganisms, including fungi. (5.5)

----------ADVERSE REACTIONS----------
- The most frequent adverse reactions (at least 1% in US trials) were headache, rhinitis, respiratory disorders, pharyngitis, taste perversion, burning/stinging, cough, and pruritus. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact GlaxoSmithKline at 1-888-825-5249 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 5/2015

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

BACTROBAN nasal ointment is indicated for the eradication of nasal colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) in adult and pediatric patients (aged 12 years and older) and healthcare workers as part of a comprehensive infection control program to reduce the risk of infection among patients at high risk of MRSA infection during institutional outbreaks of infections with this microorganism.

Limitations of Use

- There are insufficient data at this time to establish that this product is safe and effective as part of an intervention program to prevent autoinfection of high-risk patients from their own nasal colonization with *Staphylococcus aureus (S. aureus)*.
- There are insufficient data at this time to recommend use of BACTROBAN nasal ointment for general prophylaxis of any infection in any patient population.

2 DOSAGE AND ADMINISTRATION

- For Intranasal Use Only.
- Apply approximately one-half of the ointment from the single-use tube into 1 nostril and the other half into the other nostril twice daily (morning and evening) for 5 days.
- After application, close the nostrils by pressing together and releasing the sides of the nose repetitively for approximately 1 minute. This will spread the ointment throughout the nares.
- Do not apply BACTROBAN nasal ointment concurrently with any other intranasal products *[see Clinical Pharmacology (12.3)]*.
- The single-use 1-gram tube will deliver a total of approximately 0.5 grams of the ointment (approximately 0.25 grams per nostril).
- Discard the tube after usage. Do not re-use.

3 DOSAGE FORMS AND STRENGTHS

BACTROBAN nasal ointment is a white to off-white ointment that contains 2.15% w/w mupirocin calcium (equivalent to 2% mupirocin free acid) in a soft white ointment base supplied in single-use 1-gram tubes.

4 CONTRAINDICATIONS

BACTROBAN nasal ointment is contraindicated in patients with known hypersensitivity to mupirocin or any of the excipients of BACTROBAN nasal ointment.

5 WARNINGS AND PRECAUTIONS

5.1 Severe Allergic Reactions

Systemic allergic reactions, including anaphylaxis, urticaria, angioedema, and generalized rash have been reported in patients treated with formulations of BACTROBAN *[see Adverse Reactions (6.2)]*.

5.2 Eye Irritation

Avoid contact with the eyes. In case of accidental contact, rinse well with water. Application of BACTROBAN nasal ointment to the eye under testing conditions has caused severe symptoms

such as burning and tearing. These symptoms resolved within days to weeks after discontinuation of the ointment.

5.3 Local Irritation

In the event of a sensitization or severe local irritation from BACTROBAN nasal ointment, usage should be discontinued.

5.4 *Clostridium difficile*-associated Diarrhea

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

5.5 Potential for Microbial Overgrowth

As with other antibacterial products, prolonged use of BACTROBAN nasal ointment may result in overgrowth of nonsusceptible microorganisms, including fungi *[see Dosage and Administration (2)]*.

6 ADVERSE REACTIONS

The following adverse reactions are discussed in more detail in other sections of the labeling:

- Systemic allergic reactions *[see Warnings and Precautions (5.1)]*
- Eye irritation *[see Warnings and Precautions (5.2)]*
- Local irritation *[see Warnings and Precautions (5.3)]*
- *Clostridium difficile*-associated diarrhea *[see Warnings and Precautions (5.4)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In clinical trials, 210 domestic (US) and 2,130 foreign adult subjects received BACTROBAN nasal ointment. Less than 1% of domestic or foreign subjects in clinical trials were withdrawn due to adverse reactions.

The most frequently reported adverse reactions in foreign clinical trials were rhinitis (1%), taste perversion (0.8%), and pharyngitis (0.5%).

In domestic clinical trials, 17% (36 of 210) of adults treated with BACTROBAN nasal ointment reported adverse reactions thought to be at least possibly drug related. Table 1 shows the incidence of adverse reactions that were reported in at least 1% of adults enrolled in clinical trials conducted in the US.

Table 1. Adverse Reactions (≥1% Incidence) – Adults in US Trials

Adverse Reactions	% of Subjects Experiencing Reactions BACTROBAN Nasal Ointment (n = 210)
Headache	9%
Rhinitis	6%
Respiratory disorder, including upper respiratory tract congestion	5%
Pharyngitis	4%
Taste perversion	3%
Burning/stinging	2%
Cough	2%
Pruritus	1%

The following adverse reactions possibly drug related were reported in less than 1% of adults enrolled in domestic clinical trials: blepharitis, diarrhea, dry mouth, ear pain, epistaxis, nausea, and rash.

6.2 Postmarketing Experience

In addition to adverse reactions reported from clinical trials, the following reactions have been identified during postmarketing use of BACTROBAN nasal ointment. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. These reactions have been chosen for inclusion due to a combination of their seriousness, frequency of reporting, or potential causal relationship to BACTROBAN nasal ointment.

Immune System Disorders

Systemic allergic reactions, including anaphylaxis, urticaria, angioedema, and generalized rash *[see Warnings and Precautions (5.1)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category B.

There are no adequate and well-controlled studies of BACTROBAN nasal ointment (contains equivalent of 2% mupirocin free acid) 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.

Developmental toxicity studies have been performed with mupirocin administered subcutaneously to rats and rabbits at doses up to 65 and 130 times, respectively, the human intranasal dose (approximately 20 mg mupirocin per day) based on body surface area. There was no evidence of fetal harm due to mupirocin.

8.3 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 nasal ointment is administered to a nursing woman.

8.4 Pediatric Use

Safety and efficacy in children younger than 12 years have not been established *[see Clinical Pharmacology (12.3)]*.

Pharmacokinetic data in neonates and premature infants indicate that, unlike in adults, significant systemic absorption occurred following intranasal administration of BACTROBAN nasal ointment in this population.

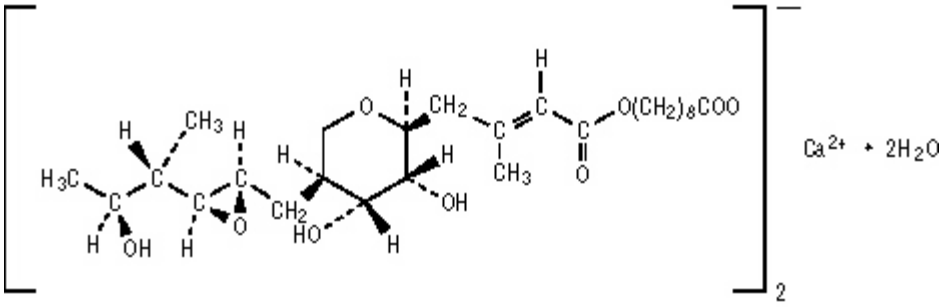
10 OVERDOSAGE

Following single or repeated intranasal applications of BACTROBAN nasal ointment to adults, no evidence for systemic absorption of mupirocin was obtained. There is no information regarding local overdose of BACTROBAN nasal ointment or regarding oral ingestion of the nasal ointment formulation.

11 DESCRIPTION

BACTROBAN (mupirocin calcium) nasal ointment, 2% contains the dihydrate crystalline calcium hemi-salt of the antibacterial drug, 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 nasal ointment is a white to off-white ointment that contains 2.15% w/w mupirocin calcium (equivalent to 2% mupirocin free acid) in a soft white ointment base. The inactive ingredients are paraffin and a mixture of glycerin esters (SOFTISAN® 649).

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Mupirocin is an antibacterial drug *[see Clinical Pharmacology (12.4)]*.

12.3 Pharmacokinetics

Absorption

Following single or repeated intranasal applications of 0.2 grams of BACTROBAN nasal ointment 3 times daily for 3 days to 5 healthy adult male subjects, no evidence of systemic absorption of mupirocin was demonstrated. The dosage regimen used in this trial was for pharmacokinetic characterization only; *see Dosage and Administration (2)* for proper clinical dosing information.

In this trial, the concentrations of mupirocin in urine and of monic acid in urine and serum were below the limit of determination of the assay for up to 72 hours after the applications. The lowest levels of determination of the assay used were 50 ng/mL of mupirocin in urine, 75 ng/mL of monic acid in urine, and 10 ng/mL of monic acid in serum. Based on the detectable limit of the urine assay for monic acid, one can extrapolate that a mean of 3.3% (range: 1.2% to 5.1%) of the applied dose could be systemically absorbed from the nasal mucosa of adults.

The effect of concurrent application of BACTROBAN nasal ointment with other intranasal products has not been studied *[see Dosage and Administration (2)]*.

Elimination

In a trial 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.

Metabolism: Following intravenous or oral administration, mupirocin is rapidly metabolized. The principal metabolite, monic acid, demonstrates no antibacterial activity.

Excretion: Monic acid is predominantly eliminated by renal excretion.

Special Populations

Pediatrics: The pharmacokinetic properties of mupirocin following intranasal application of BACTROBAN nasal ointment have not been adequately characterized in neonates or other children younger than 12 years, and in addition, the safety and efficacy of the product in children younger than 12 years have not been established.

Renal Impairment: The pharmacokinetics of mupirocin have not been studied in individuals with renal insufficiency.

12.4 Microbiology

Mupirocin is an antibacterial agent produced by fermentation using the organism *Pseudomonas fluorescens*.

Mechanism of Action

Mupirocin inhibits bacterial protein synthesis by reversibly and specifically binding to bacterial isoleucyl-transfer RNA (tRNA) synthetase.

Mupirocin is bactericidal at concentrations achieved by topical intranasal administration. Mupirocin is highly protein bound (>97%), and the effect of nasal secretions on the minimum inhibitory concentrations (MICs) of intranasally applied mupirocin has not been determined.

Mechanism of Resistance

When mupirocin resistance occurs, it results from the production of a modified isoleucyl-tRNA synthetase, or the acquisition of, by genetic transfer, a plasmid mediating a new isoleucyl-tRNA synthetase. High-level plasmid-mediated resistance (MIC ≥512 mcg/mL) has been reported in increasing numbers of isolates of *S. aureus* and with higher frequency in coagulase-negative staphylococci. Mupirocin resistance occurs with greater frequency in methicillin-resistant than methicillin-susceptible staphylococci.

Cross Resistance

Due to its mode of action, mupirocin does not demonstrate cross resistance with other classes of antimicrobial agents.

Susceptibility Testing

High-level mupirocin resistance (≥512 mcg/mL) may be determined using standard disk diffusion or broth microdilution tests[1,2]. The significance of these results, with regard to decolonization regimens, should be evaluated at each medical facility, in conjunction with laboratory, medical, and infection control staff.

Correlation of BACTROBAN nasal ointment in vitro activity and MRSA nasal decolonization has been demonstrated in clinical trials *[see Clinical Studies (14)]*.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals to evaluate carcinogenic potential of mupirocin 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 genotoxicity: 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.

Reproduction studies were performed with mupirocin administered subcutaneously to male and female rats at doses up to 40 times the human intranasal dose (approximately 20 mg mupirocin per day) based on body surface area. Neither evidence of impaired fertility nor impaired reproductive performance attributable to mupirocin was observed.

14 CLINICAL STUDIES

All adequate and well-controlled trials of this product were vehicle-controlled; therefore, no data from direct, head-to-head comparisons with other products are available. The safety and effectiveness of applications of this medication for greater than 5 days have not been established. There are no human clinical or pre-clinical animal data to support the use of this product in a chronic manner or in manners other than those described in this prescribing information.

In clinical trials, 210 domestic (US) and 2,130 foreign adult subjects received BACTROBAN nasal ointment. Greater than 90% of subjects in clinical trials had eradication of nasal colonization 2 to 4 days after therapy was completed. Approximately 30% recolonization was reported in 1 domestic trial within 4 weeks after completion of therapy. These eradication rates were clinically and statistically superior to those reported in subjects in the vehicle-treated arms of the adequate and well-controlled trials. Those treated with vehicle had eradication rates of 5% to 30% at 2 to 4 days post-therapy with 85% to 100% recolonization within 4 weeks.

15 REFERENCES

1. Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing; 25th Informational Supplement. CLSI document M100-S22. CLSI, 950 West Valley Rd., Suite 2500, Wayne, PA 19087, 2015.
2. Patel J, Gorwitz RJ, et al. Mupirocin Resistance. *Clinical Infectious Diseases.* 2009; 49(6); 935-41.

16 HOW SUPPLIED/STORAGE AND HANDLING

BACTROBAN nasal ointment, 2% is supplied in single-use 1-gram tubes.

BACTROBAN nasal ointment is a white to off-white ointment that contains mupirocin calcium (equivalent to 2% mupirocin free acid).

NDC 0029-1526-03 Single-use 1-gram tube in Package of 10: NDC 0029-1526-11.

Store between 20°C and 25°C (68°F and 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F). Do not refrigerate.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Advise the patient to administer BACTROBAN nasal ointment as follows:

- Apply approximately one-half of the ointment from the single-use tube directly into 1 nostril and the other half into the other nostril.
- Press the sides of the nose together and gently massage after application to spread the ointment throughout the inside of the nostrils.
- Avoid contact of the medication with the eyes; if BACTROBAN nasal ointment gets in or near the eyes, rinse thoroughly with water.
- Discard the tube after using. Do not re-use.
- Discontinue usage of the medication and call the healthcare practitioner if sensitization or severe local irritation occurs.
- It is important that you take the full course of BACTROBAN nasal ointment. Do not stop early because the amount of bacteria in your nose may not be reduced.

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GlaxoSmithKline
Research Triangle Park, NC 27709

BBN:XPI

PHARMACIST-DETACH HERE AND GIVE INSTRUCTIONS TO PATIENT

PATIENT INFORMATION
BACTROBAN® (BACK-troh-ban)
(mupirocin calcium) nasal ointment
For intranasal use only

Read this Patient Information Leaflet before you start using BACTROBAN nasal ointment and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

What is BACTROBAN nasal ointment?

BACTROBAN nasal ointment is an antibiotic. It is used to reduce the amount of bacteria in your nose.

Who should not use BACTROBAN nasal ointment?

Do not use BACTROBAN nasal ointment if:

- you are allergic to mupirocin or any of the ingredients in BACTROBAN nasal ointment.

Before using BACTROBAN nasal ointment, tell your healthcare provider about your medical conditions and medicines you take including, if you:

- are pregnant or plan to become pregnant. It is not known if BACTROBAN nasal ointment will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if BACTROBAN nasal ointment passes into your breast milk.
- are taking any prescription or over-the-counter medicines, vitamins, or herbal supplements. Do not mix BACTROBAN nasal ointment with other intranasal products.

How should I use BACTROBAN nasal ointment?

- Always use BACTROBAN nasal ointment exactly as your healthcare provider tells you to use it.
- It is important that you take the full course of BACTROBAN nasal ointment. Do not stop early because the amount of bacteria in your nose may not be reduced.
- Wash your hands before and after applying BACTROBAN nasal ointment.
- Apply approximately one-half of the ointment from a single-use tube to the inside surface at the front of each nostril 2 times a day for 5 days.
- Press the sides of your nose together and gently rub between your finger and thumb for about 1 minute. This spreads the ointment around the nose.
- Keep BACTROBAN nasal ointment away from your eyes. If the ointment gets in your eyes accidentally, wash them thoroughly with water.

What are the possible side effects of BACTROBAN nasal ointment?

BACTROBAN nasal ointment may cause serious side effects, including:

- **allergic reactions.** Stop using BACTROBAN nasal ointment and get medical help right away if you have any symptoms of an allergic reaction, including a raised and itchy rash, or swelling, sometimes of the face or mouth, causing difficulty breathing.
- **inflammation of the colon (colitis)**. Stop using BACTROBAN nasal ointment and call your healthcare provider right away if you have severe watery diarrhea or bloody diarrhea.

- **skin irritation.** If you get a skin reaction, stop using BACTROBAN nasal ointment. Remove any ointment and tell your doctor as soon as possible.

Common side effects of BACTROBAN nasal ointment may include headache, runny nose, congestion, sore throat, distorted sense of taste, burning and/or stinging, cough, and itching.

These are not all the possible side effects of BACTROBAN nasal ointment. Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store BACTROBAN nasal ointment?

- Store BACTROBAN nasal ointment at room temperature up to 25ºC (77ºF). Do not refrigerate.

General information about the safe and effective use of BACTROBAN nasal ointment.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information Leaflet. You can ask your pharmacist or healthcare provider for information about BACTROBAN nasal ointment that is written for health professionals. Do not use BACTROBAN nasal ointment for a condition for which it was not prescribed. Do not give BACTROBAN nasal ointment to other people, even if they have the same symptoms that you have. It may harm them.

What are the ingredients in BACTROBAN nasal ointment?

Active Ingredient: mupirocin calcium

Inactive Ingredients: paraffin and SOFTISAN® 649

For more information call 1-888-825-5429.

This Patient Information has been approved by the U.S. Food and Drug Administration.

BACTROBAN is a registered trademark of the GSK group of companies.

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Manufactured by

GlaxoSmithKline
Research Triangle Park, NC 27709

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