Antibiotics, Topical
Therapeutic Class Review (TCR)

October 11, 2013

The literature review is current through March 11, 2020.

The materials contained herein represent the opinions of the collective authors and editors and should not be construed to be the official representation of any professional organization or group, any state Pharmacy and Therapeutics committee, any state Medicaid Agency, or any other clinical committee. This material is not intended to be relied upon as medical advice for specific medical cases and nothing contained herein should be relied upon by any patient, medical professional or layperson seeking information about a specific course of treatment for a specific medical condition. All readers of this material are responsible for independently obtaining medical advice and guidance from their own physician and/or other medical professional in regard to the best course of treatment for their specific medical condition. This publication, inclusive of all forms contained herein, is intended to be educational in nature and is intended to be used for informational purposes only. Send comments and suggestions to PSTCREditor@magellanhealth.com.

FDA-APPROVED INDICATIONS[1,2,3,4,5,6,7,8,9,10,11,12]

Drug	Manufacturer	Indication(s)
bacitracin ointment	generic	Prevention of skin and skin structure infections after a minor compromise in skin integrity such as minor burns or skin abrasion
bacitracin zinc ointment	generic	Prevention of skin and skin structure infections after a minor compromise in skin integrity such as minor burns or skin abrasion
bacitracin zinc, neomycin, polymyxin B sulfate ointment (Antibiotic, First Aid Antibiotic, Neosporin®, Triple Antibiotic)	generic	Prevention of skin and skin structure infections, including wound management for skin abrasion and minor burn wound infection
bacitracin zinc, neomycin, polymyxin B sulfate, pramoxine ointment (Antibiotic + Pain Relief, First Aid Antibiotic-Pain, Neosporin + Pain Relief Ointment, Triple Antibiotic- Pain, Triple Antibiotic Plus, Triple Antibiotic Xtra)	generic	Prevent infection and temporarily relief of pain or discomfort in minor cuts, scrapes, and/or burns
bacitracin zinc, polymyxin B ointment (Double Antibiotic Ointment, Polysporin® Ointment)	generic	Prevention of skin and skin structure infections, including wound management of skin abrasion and minor burn wound infection
gentamicin 0.1% cream	generic	Treatment of minor bacterial skin infection including ecthyma, folliculitis, furunculosis, impetigo, pyoderma gangrenosum, sycosis barbae, infectious eczematoid dermatitis, pustular acne, pustular psoriasis, infected seborrheic dermatitis, infected contact dermatitis, infected excoriations, and bacterial superinfections of fungal or viral infections
gentamicin 0.1% ointment	generic	Treatment of minor bacterial skin infection including ecthyma, folliculitis, furunculosis, impetigo, pyoderma gangrenosum, sycosis barbae, infectious eczematoid dermatitis, pustular acne, pustular psoriasis, infected seborrheic dermatitis, infected contact dermatitis, infected excoriations and bacterial superinfections of fungal or viral infections
mupirocin 2% cream	generic	Treatment of secondarily infected traumatic skin lesions (up to 10 cm in length or 100 cm^2 in area) due to susceptible strains of *Staphylococcus aureus* and *Streptococcus pyogenes*
mupirocin 2% ointment	generic	Treatment of impetigo due to *S. aureus* and *S. pyogenes*
mupirocin 2% ointment (Centany®, Centany AT Kit*)	Medimetriks	Treatment of impetigo due to *S. aureus* and *S. pyogenes*
neomycin, polymyxin B, pramoxine HCl cream (Antibiotic Plus, Antibiotic Plus Pain, Antibiotic-Pain, Double Antibiotic-Pain Relief, Neosporin + Pain Relief)	J&J Consumer product	Prevent infection and temporarily relief of pain or discomfort in minor cuts, scrapes, and burns

FDA-approved Indications (continued)

Drug	Manufacturer	Indication(s)
ozenoxacin 1% cream (Xepi™)	Cutanea	Treatment of impetigo due to *S. aureus* or *S. pyogenes*
retapamulin 1% ointment (Altabax®)	Almirall	Treatment of impetigo due to *S. aureus* (methicillin-susceptible isolates only) and *S. pyogenes*
tetracycline HCl 3% ointment (Viabecline®)	Accuria	Prevent skin infection in minor cuts, scrapes, and burns

* Products packaged as kits are discussed in the FDA Indications and Dosages sections, and components are addressed in the Pharmacology section. For other information regarding these products, please refer to the primary component throughout the text (e.g., mupirocin).

Mupirocin calcium 2% ointment (Bactroban® Nasal) by GlaxoSmithKline is a paraffin-based formulation for intranasal use and is indicated in the eradication of nasal colonization with methicillin-resistant *S. aureus* (MRSA) in adult patients and healthcare workers.[13]

FDA-Approved Microorganism Indications[14]

Drug	MRSA	MSSA	Staphylococcus epidermidis	Staphylococcus saprophyticus	Streptococcus pyogenes	Streptococcus sp.	Haemophilus. influenzae	Pseudomonas aeruginosa
bacitracin ointment, bacitracin zinc ointment		X				X		
bacitracin zinc, neomycin, polymyxin B sulfate ointment (Antibiotic, First Aid Antibiotic, Neosporin, Triple Antibiotic)		X				X	X	X
bacitracin zinc, neomycin, polymyxin B sulfate, pramoxine ointment (Antibiotic + Pain Relief, First Aid Antibiotic-Pain, Neosporin + Pain Relief Ointment, Triple Antibiotic- Pain, Triple Antibiotic Plus, Triple Antibiotic Xtra)		X				X	X	X
bacitracin zinc, polymyxin B ointment (Double Antibiotic Ointment, Polysporin Ointment)		X				X	X	X
gentamicin 0.1% cream, ointment		X	X		X		X	X
mupirocin 2% cream, ointment (generics, Centany, Centany AT Kit)	X	X	X	X	X			
ozenoxacin 1% cream (Xepi)	X	X			X			
retapamulin 1% ointment (Altabax)		X			X			

MRSA: methicillin-resistant *S. aureus*; MSSA: methicillin-sensitive *S. aureus*

Details on the spectrum of coverage for neomycin, polymyxin B, pramoxine HCl cream (Neosporin + Pain Relief Cream) or tetracycline HCl 3% ointment (Viabecline) are not contained in their respective labeling.

OVERVIEW

Skin and soft tissue bacterial infections are some of the most common issues with ambulatory care visits.[15] Most infections can be treated outpatient although physicians should be on alert for signs and symptoms of more severe infections. Therefore, clinical assessment of the severity of the infection, diagnosis, and knowledge of pathogen-specific antibiotic resistance is important.[16]

Skin and soft tissue infections can be caused by many different bacteria. Most infections are due to gram-positive microbes such as *Staphylococcus aureus, Streptococcus viridans*, *Enterococcus faecalis*, and group A (*S. pyogenes*) and B streptococci. Though not as common, gram-negative skin and soft tissue infections can occur due to *Haemophilus influenza, Pasteurella multocida*, *Aeromonas* species, *Clostridium* species, *Vibrio* species, *Mycobacterium* species, *Capnocytophaga* species*, Pseudomonas* species, *Proteus* species, and other anaerobes.[17] The most common skin infections are caused by *S. aureus, S. pyogenes*, or the normal skin flora.[18] However, *S. aureus* and *S. pyogenes* also happen to show the most antibacterial resistance.[19,20]

Patients who have compromised epidermis, poor hygiene, live in crowded conditions, have comorbidities, and have close contact with people having skin and soft tissue infections are at high risk of acquiring a skin and soft tissue infection themselves.[21, 22] Trauma to the epidermis exposes deeper tissue and allows for bacteria to enter the integumentary system. Other comorbidities which place patients at higher risk include eczema, psoriasis, superficial fungal infections, venous stasis, and lymphedema.[23] A CDC study demonstrated that invasive, life-threatening, methicillin-resistant *S. aureus* (MRSA) infections that began in hospitals declined 54% between 2005 and 2011, with 30,800 fewer severe methicillin-resistant staphylococcal infections. The study also showed 9,000 fewer deaths in hospital patients in 2005 versus 2011.[24]

Family physicians often treat patients with common skin infections such as impetigo.[25] The Infectious Diseases Society of America (IDSA) 2014 practice guidelines update for the diagnosis and management of skin and soft-tissue infections (SSTIs) recommend mupirocin ointment 3 times daily or retapamulin (Altabax) twice daily for 5 days as the topical antibacterials of choice in the treatment of impetigo, but oral therapy is recommended in patients with numerous lesions or during outbreaks.[26] Mupirocin ointment has activity against *S. pyogenes* and both methicillin-sensitive *S. aureus* (MSSA) and methicillin-resistant *S. aureus* (MRSA), but some resistance has been reported.[27] Topical tetracycline (Viabecline) and ozenoxacin (Xepi) are not included in these guidelines. Other topical agents, such as bacitracin and neomycin, are considerably less effective topical treatments when compared to mupirocin ointment. Topical therapy with mupirocin ointment is equivalent to oral systemic antimicrobials. IDSA guidelines for the treatment and prevention of MRSA recommend topical mupirocin ointment for children with minor skin infections (e.g., impetigo) and secondarily infected skin lesions (e.g., eczema, ulcers, lacerations).[28] Twice daily mupirocin for 5 to 10 days may be used for MRSA nasal decolonization in patients with recurrent MRSA SSTIs. Mupirocin may also be used for mild, localized neonatal pustulosis in full-term neonates and infants.

PHARMACOLOGY[29,30,31,32,33,34,35,36]

Bacitracin is a bacteriostatic against gram-positive and some gram negative bacteria and may also possess some bactericidal activity at certain concentrations. Bacitracin works by interfering with the mucopeptide transferring process and therefore prevents bacteria cell wall development.

Neomycin and gentamicin are aminoglycoside antibiotics with gram-positive and gram-negative bactericidal activity. Neomycin and gentamicin work by establishing irreversible binding to receptors present on the 30S ribosomal subunit of bacteria. The binding prevents the initiation complex between the bacterial messenger RNA and the ribosomal subunit which results in the misreading of the bacterial DNA and formation of nonfunctional proteins. As a result, bacteria containing these non-functional proteins die. Neomycin also inhibits DNA polymerase.

Mupirocin is a topical antibiotic that reversibly and specifically binds to bacterial isoleucyl transfer-RNA synthetase resulting in the inhibition of protein synthesis. Mupirocin is bactericidal at concentrations achieved by topical administration; however, the minimum bactericidal concentration (MBC) against relevant pathogens is generally 8-fold to 30-fold higher than the minimum inhibitory concentration (MIC).

Ozenoxacin (Xepi) is quinolone antibiotic that inhibits the bacterial DNA replication enzymes DNA gyrase A and topoisomerase IV. Ozenoxacin is bacteriocidal against *S. aureus*, including methicillin resistant strains, and *S. pyogenes*.

Polymyxin B is a bactericidal agent which binds to the cell membranes of gram-negative bacteria. Once bound, polymyxin destroys the bacterial cell membrane which results in cell membrane permeability and loss of metabolites. Pramoxine is a local anesthetic agent which blocks both the initiation and conduction of nerve impulses by decreasing the permeability of the neuronal membrane to sodium ions. This reversibly stabilizes the membrane and inhibits depolarization, resulting in the failure of a propagated action potential and subsequent conduction blockade.

Retapamulin (Altabax) is the first in a new class of antibacterial agents, the pleuromutilins, which inhibit normal bacterial protein biosynthesis by binding at the unique site (L3) on the ribosomal 50S subunit. This prevents the formation of active 50S ribosomal subunits by inhibiting peptidyl transfer and blocking P-site interactions at this site. Retapamulin is bacteriostatic against *S. aureus* and *S. pyogenes* at the retapamulin *in vitro* minimum inhibitory concentration (MIC) for these organisms. At concentrations 1,000 times the *in vitro* MIC, retapamulin is bactericidal against these same organisms.

A study that included 400 *S. pyogenes* isolates, including multidrug-resistant isolates, evaluated the in vitro activity of retapamulin compared to that of 16 other antimicrobial agents for topical and systemic use to treat acute bacterial skin infections. The isolates were divided into those obtained from skin lesions (n=144), blood (n=17), and other body sites such as the pharynx or ear fluid (n=239). Retapamulin showed potent in vitro activity against all clinical S. pyogenes isolates independently of the source of the sample and the resistance phenotype, including macrolide-, tetracycline-, fusidic acid-, quinolone-, and bacitracin-resistant isolates. The range of retapamulin susceptibility was between 0.015 and 0.12 g/mL, showing the highest intrinsic activity of the antimicrobial drugs often used topically. Based on MIC90 values, retapamulin was at least 4-fold, 533-fold, 133-fold, and 1,066-fold more active than the most frequently used topical drugs, mupirocin, bacitracin, fusidic acid, and neomycin, respectively.

Tetracycline is bacteriostatic against most organisms, but can be bactericidal at high concentrations. Bacteriostatic action appears to be due to reversible binding to the 30S ribosomal subunit thereby preventing binding of tRNA to the mRNA-ribosome complex and interfering with protein synthesis in multiplying organisms. In general, tetracycline is more effective against gram positive than gram negative organisms.

PHARMACOKINETICS[37,38,39,40,41,42]

Bacitracin, neomycin, and polymyxin B have negligible systemic absorption after topical administration except when applied to large areas or long periods of time. Polymyxin B has little absorption even when applied to open wounds. However, systemic absorption has been reported when bacitracin, neomycin, or gentamicin has been applied to damaged epithelium. Gentamicin absorption across denuded skin had a rate of 5% but was not associated with systemic toxicity.

Absorption of topically applied mupirocin is low. Data indicate more frequent occurrence of percutaneous absorption in children (90% of patients) than adults (44% of patients); however, mupirocin systemically absorbed is rapidly metabolized to the inactive metabolite, monic acid, which is renally excreted.

Ozenoxacin (Xepi) has no systemic absorption in most subjects and negligible absorption in a small percentage. Ozenoxacin (Xepi) exhibits 85% to 90% protein binding. It is minimally metabolized by human hepatocytes and *in vivo* excretion has not been studied due to negligible absorption.

Systemic absorption following topical application of retapamulin to intact and abraded skin is low. Retapamulin (Altabax) is 94% protein bound. Retapamulin (Altabax) is metabolized by cytochrome (CYP) 3A4 hepatic enzymes by mono-oxygenation and di-oxygenation to multiple metabolites.

CONTRAINDICATIONS/WARNINGS[43,44,45,46,47]

Hypersensitivity to these agents or their components is considered a contraindication. These agents are for topical use only. They should not be used via the ophthalmic, intranasal, oral, or intra-vaginally routes. They should be discontinued should sensitization or severe local irritation occur, and super-infection occur.

Retapamulin (Altabax) should not be used in the absence of proven or strongly suspected bacterial infection as it may increase the risk of the development of drug resistance bacteria. Epistaxis has been reported with retapamulin (Altabax) in the nasal mucosa.

Mupirocin ointment contains polyethylene glycol (PEG) and should be avoided in conditions where absorption of large quantities of PEG is possible, especially if there is evidence of moderate to severe renal impairment; mupirocin cream and mupirocin (Centany) ointment do not contain PEG base.

Like all antibiotics, use of ozenoxacin (Xepi) may result in overgrowth of nonsusceptible organisms.

Bacitracin and neomycin should be used with caution in patients with damaged epithelium, high risk for altered epithelium (e.g., elderly, children < 2 years old, infants, and neonates), renal impairment, or renal failure due to increased systemic exposure and risk for adverse effects, such as nephrotoxicity and irreversible ototoxicity. Bacitracin should not be used for serious burns, puncture wounds, deep wounds, or animal bites unless directed by a physician. When absorbed systemically, neomycin has been reported to cause ototoxicity; therefore, application to damaged epithelium is cautioned.

Prolonged use of bacitracin, neomycin, and polymyxin B may result in secondary infections; therefore, treatment greater than 7 days is not recommended.

DRUG INTERACTIONS[48,49,50,51,52]

The effect of concurrent application of mupirocin ointment or cream and other drugs has not been studied.

Oral ketoconazole was shown to increase AUC and Cmax of retapamulin by 81% after topical application to abraded skin. Systemic absorption of retapamulin is low; therefore, interactions with other CYP 450 substrates are not expected. The effect of concurrent application of retapamulin and other topical agents to the same area of skin has not been studied.

Antagonism of ozenoxacin (Xepi) with ciprofloxacin were observed against *S. aureus*.

If absorbed systemically, bacitracin, gentamicin, neomycin, and polymyxin B may cause nephrotoxicity and neurotoxicity. Caution should be used in patients taking additional medications with nephrotoxic or neurotoxic adverse effects.

There are no reported drug interactions reported between pramoxine and other medications.

ADVERSE EFFECTS[53,54,55,56,57,58,59,60,61]

Drug	Application Site Irritation	Rash	Pruritus	Headache	Diarrhea	Nausea
bacitracin ointment	reported	reported	reported	nr	nr	nr
bacitracin zinc ointment	reported	reported	reported	nr	nr	nr
bacitracin zinc, neomycin, polymyxin B sulfate ointment (Antibiotic, First Aid Antibiotic, Neosporin, Triple Antibiotic)	reported	reported	reported	nr	nr	nr
bacitracin zinc, neomycin, polymyxin B sulfate, pramoxine ointment (Antibiotic + Pain Relief, First Aid Antibiotic-Pain, Neosporin + Pain Relief Ointment, Triple Antibiotic- Pain, Triple Antibiotic Plus, Triple Antibiotic Xtra)	reported	reported	reported	nr	nr	nr
bacitracin zinc, polymyxin B ointment (Double Antibiotic Ointment, Polysporin Ointment)	reported	reported	reported	nr	nr	nr

Adverse effects are reported as a percentage. Adverse effects data are obtained from package inserts and are not meant to be comparative or all inclusive. nd = no data; nr = not reported.

Adverse Effects (continued)

Drug	Application Site Irritation	Rash	Pruritus	Headache	Diarrhea	Nausea
gentamicin 0.1% cream, ointment	reported	reported	reported	nr	nr	nr
mupirocin 2% cream	< 1-3.6	1.1	2.4	1.7-3.6	nr	1.1-4.9
mupirocin 2% ointment	1-1.5	< 1	1	nr	nr	< 1
mupirocin 2% ointment (Centany)	1	0.3	1	nr	nr	nr
neomycin, polymyxin B, pramoxine HCl cream (Antibiotic Plus, Antibiotic Plus Pain, Antibiotic-Pain, Double Antibiotic-Pain Relief, Neosporin + Pain Relief)	reported	reported	reported	nr	nr	nr
ozenoxacin 1% cream (Xepi)	nr	nr	nr	nr	nr	nr
retapamulin 1% ointment (Altabax)	1.6-1.9	nr	1.5	1.2-2	1.4-1.7	1.2
tetracycline HCl 3% ointment (Viabecline)	nd	nd	nd	nd	nd	nd

Adverse effects are reported as a percentage. Adverse effects data are obtained from package inserts and are not meant to be comparative or all inclusive. nd = no data; nr = not reported.

SPECIAL POPULATIONS[62,63,64,65,66,67]

Pediatrics

Safety and effectiveness of mupirocin ointment and ozenoxacin (Xepi) cream have been established in patients aged ≥ 2 months, and retapamulin (Altabax) ointment in patients ≥ 9 months. Mupirocin cream has been FDA-approved in patients aged ≥ 3 months. Bacitracin, neomycin, and polymyxin B ointment have been FDA-approved in patients ≥ 2 years old. Gentamicin cream and ointment have been FDA-approved for children ≥ 1 year.

Pregnancy

Mupirocin and retapamulin are Pregnancy Category B; bacitracin, neomycin, polymyxin B, and pramoxine are Pregnancy Category C. Gentamicin is categorized by the manufacturer as Pregnancy Category D but Briggs' *Drugs in Pregnancy and Lactation* categorizes it as Pregnancy Category C. There are no human or animal data regarding ozenoxacin use during pregnancy.

DOSAGES[68,69,70,71,72,73,74,75,76,77,78,79,80]

Drug	Adult	Pediatrics	Availability
bacitracin ointment	Apply thin film 1 to 3 times daily (max 5 times daily)	Apply thin film 2 to 3 times daily (max 5 times daily)	500 U/1 gm ointment in tubes: 14 gm, 28 gm, 30 gm; 500 U/1 gm ointment in packets: 0.9 gm (OTC)
bacitracin zinc ointment	Apply thin film 1 to 3 times daily (max 5 times daily)	Apply thin film 2 to 3 times daily (max 5 times daily)	500 U/1 gm ointment in tubes: 14 gm, 15 gm, 28 gm; 500 U/1 gm ointment in packets: 0.9 gm; 500 U/1 gm ointment in jars: 425 gm, 454 gm (OTC)
bacitracin zinc, neomycin, polymyxin B sulfate ointment (Antibiotic, First Aid Antibiotic, Neosporin, Triple Antibiotic)	Apply thin film 1 to 3 times daily	Apply thin film 1 to 3 times daily for patients 2 years and older	bacitracin 400 U/ neomycin 3.5 mg/ polymyxin B 5000 U/1 gm ointment: 9 gm, 14 gm, 15 gm, 28 gm, 30 gm, 56 gm, 60 gm in tubes; 1 gm ointment in packets (OTC)
bacitracin zinc, neomycin, polymyxin B sulfate, pramoxine ointment (Antibiotic + Pain Relief, First Aid Antibiotic-Pain; Neosporin + Pain Relief Ointment, Triple Antibiotic- Pain, Triple Antibiotic Plus, Triple Antibiotic Xtra)	Apply thin film 1 to 3 times daily	Apply thin film 1 to 3 times daily for patients 2 years and older	bacitracin 500 U/ neomycin 3.5 mg/ polymyxin B 10,000 U/ pramoxine 10 mg/1 gm ointment in tubes: 14 gm, 15 gm, 28 gm, 30 gm (OTC)
bacitracin zinc, polymyxin B ointment (Double Antibiotic Ointment, Polysporin Ointment)	Apply thin film 1 to 3 times daily	Apply thin film 1 to 3 times daily	bacitracin 500 U/ polymyxin B 10,000 U/ 1 gm ointment in tubes: 14 gm, 28 gm; bacitracin 500 U/ polymyxin B 10,000 U/ 1 gm ointment in packets: 0.9 gm (OTC)

Dosages (continued)

Drug	Adult	Pediatrics	Availability
gentamicin 0.1%	Apply 3 to 4 times daily	Apply 3 to 4 times daily for patients over 1 year old	0.1% cream in tubes: 15 gm, 30 gm 0.1% ointment in tubes: 15 gm, 30 gm (Rx)
mupirocin 2% cream	Apply 3 times daily for 10 days; re-evaluate after 3 to 5 days if no clinical response	Apply 3 times daily for 10 days; re-evaluate after 3 to 5 days if no clinical response	2% cream in tubes: 15 gm, 30 gm (Rx)
mupirocin 2% ointment	Apply 3 times daily; re-evaluate after 3 to 5 days if no clinical response	Apply 3 times daily for patients 2 months to 16 years old; re-evaluate after 3 to 5 days if no clinical response	2% ointment in tubes: 1 gm, 15 gm, 22 gm (Rx)
mupirocin 2% ointment (Centany, Centany AT Kit)	Apply 3 times daily; re-evaluate after 3 to 5 days if no clinical response	Apply 3 times daily for patients 2 months to 16 years old; re-evaluate after 3 to 5 days if no clinical response.	2% ointment in tubes: 30 gm Kit: 30 gm ointment in tube with cloth tape and gauze pad (Rx)
neomycin, polymyxin B, pramoxine HCl cream (Antibiotic Plus, Antibiotic Plus Pain, Antibiotic-Pain, Double Antibiotic-Pain Relief, Neosporin + Pain Relief)	Apply small amount 1 to 3 times daily	Children 2 years and above: Apply small amount 1 to 3 times daily	neomycin 3.5 mg polymyxin B 10,000 U/ pramoxine HCl 10 mg ointment in tubes: 14 gm, 28 gm (OTC)
ozenoxacin 1% cream (Xepi)	Apply a thin layer over not more than 100 cm^2 twice daily for 5 days	Children 2- 11 years apply twice daily for 5 days over not more than 2% of the total body surface area not to exceed 100 cm^2	ozenoxacin 10 mg/gm cream in tubes: 30 gm (Rx)
retapamulin 1% ointment (Altabax)	Apply twice daily for 5 days; total treatment area should not exceed 100 cm^2	For patients 9 months to 17 years old: apply twice daily for 5 days; total treatment area should not exceed 2% body surface area	1% ointment in tubes: 15 gm, 30 gm (Rx)
tetracycline HCl 3% ointment (Viabecline)	Apply small amount 1 to 3 times daily	--	3% ointment in bottles: 5 mL, 15 mL (OTC)

OTC = over-the-counter; Rx = prescription only

CLINICAL TRIALS

Search Strategies

Studies were identified through searches performed on PubMed and review of information sent by manufacturers. Search strategy included the FDA-approved use of all drugs in this class. Randomized, controlled trials studying agents within this class for the approved indications are considered the most relevant in this category. Studies included for analysis in the review were published in English, performed with human participants and randomly allocated participants to comparison groups. In

addition, studies must contain clearly stated, predetermined outcome measure(s) of known or probable clinical importance, use data analysis techniques consistent with the study question and include follow-up (endpoint assessment) of at least 80% of participants entering the investigation. Despite some inherent bias found in all studies including those sponsored and/or funded by pharmaceutical manufacturers, the studies in this therapeutic class review were determined to have results or conclusions that do not suggest systematic error in their experimental study design. While the potential influence of manufacturer sponsorship/funding must be considered, the studies in this review have also been evaluated for validity and importance.

The literature review of significant trials comparing agents within this therapeutic class is complete as of March 11, 2020.

There are no published head to head trials comparing mupirocin, ozenoxacin (Xepi), and retapamulin (Altabax) in the treatment of impetigo. Due to the lack of studies, placebo-controlled trials have been included.

bacitracin ointment and white petrolatum

Bacitracin was compared to white petrolatum to evaluate the incidence of wound infection, allergic contact dermatitis, and overall healing characteristics.[81] The study was a double-blinded, randomized study conducted in an outpatient dermatology and tertiary referral advanced surgical clinic. A total of 922 patients entered the study with 884 patients (440 white petrolatum patients and 444 bacitracin patients) completing the 4 week study. Thirty-four patients with 38 wounds (20 white petrolatum patients with 22 wounds and 14 bacitracin patients with 16 wounds) developed pus, erythema, or tenderness at the wound. Cultures were performed on the 38 wounds and 18 cultures produced no growth, 6 cultures produced coagulase-negative *Staphylococcus* species, and 14 produced pathogenic bacteria. The 14 cultures were from 13 patients with 9 (2%; 95% CI, 0.9% to 3.8%) patients being from the white petrolatum group and 4 patients (0.9%; 95% CI, 0.2% to 2.3%) being from the bacitracin group (95% for CI difference, -0.4% to 2.7%; p=0.37). Eight of the infections from the white petrolatum and zero from the bacitracin group were due to *Staphylococcus aureus* (p=0.004). No patients in the white petrolatum group developed allergic contact dermatitis versus 4 patients using bacitracin (p=0.12). The study found that patients using white petrolatum did not experience a significant difference in infection incidence compared to the bacitracin group. There was a higher rate of *S. aureus* infection in the white petrolatum group compared to the bacitracin group although this is to be expected since this is the most common bacterial to infect the skin, and bacitracin will eliminate it. Overall, the study concluded bacitracin and white petrolatum have an equally low infection rate, and there were no clinically significant differences in healing between the white petrolatum and bacitracin groups on day 1 (p=0.98), day 7 (p=0.86), or day 28 (p=0.28) after the procedure.

bacitracin zinc ointment, bacitracin zinc/neomycin/polymyxin B ointment, sulfadiazine cream, and petrolatum ointment

A randomized, double-blind, placebo-controlled study was performed on 465 patients who presented to a military community hospital emergency department with a traumatic wound less than 12 hours old.[82] Thirty-nine patients were excluded from the study due to study protocol violations. There were more males in the study (n=300) compared to females (n=126), but the male-to-female ratios were similar between treatment groups. Patients were instructed to change the wound dressing and apply a blinded ointment to the wound every 8 hours until the return visit to the emergency department for

removal of stitches. The wound depths and locations were also not statistically significant, p=0.66 and p=0.89, respectively. Wound scrubbing (p=0.69) and wound debridement (p=0.67) were also not statistically different. The study concluded the wound infection rates for bacitracin zinc ointment (5.5%), bacitracin zinc/neomycin/polymyxin B ointment (4.5%), sulfadiazine cream (12.1%) were lower than petrolatum ointment (17.6%, p=0.0034), and bacitracin zinc ointment and bacitracin zinc/neomycin/polymyxin B ointment had the lowest rate of wound infection.

mupirocin cream and gentamicin cream

A multicenter, randomized, double-blind study was conducted to compare the effectiveness of daily gentamicin and mupirocin cream in the prevention of peritoneal dialysis (PD) site infections.[83] Mupirocin treats *S. aureus* PD infections but does not decrease *Pseudomonas aeruginosa* or other Gram-negative infections which often result in morbidity and even death in PD patients. The study included 133 patients; 67 patients received gentamicin cream, and 66 patients received mupirocin cream. The study found the time to first catheter infection was longer in patients using gentamicin compared to mupirocin (p=0.03). Likewise, the incident and prevalent patients had lower catheter infection rates with gentamicin compared to mupirocin and controlling for center and incident/prevalent status, only gentamicin had a lower catheter infection rate predictor (RR, 0.41; 95% CI, 0.22 to 0.78; p<0.007). Gentamicin also showed a lower incidence of Gram-negative (p=0.03) and Gram-positive (p<0.02) infections. The frequency of peritonitis was lower in patients using gentamicin (0.34/year) compared to mupirocin (0.52/year; p=0.03). Gentamicin use was also associated with a significant predictor of lower peritonitis rates when controlling for center and incident/prevalent patients (RR, 0.52; 95% CI, 0.29 to 0.93; p<0.03). Similarly gentamicin users also had a lower gram-negative peritonitis rate (p<0.05) when controlling for center and incident/prevalent status. In conclusion, researchers determined gentamicin cream was as effective as mupirocin in preventing *S. aureus* infections, and gentamicin reduced *P. aeruginosa* and gram-negative catheter exit site infections and decreased the rate peritonitis by 35%.

mupirocin ointment and placebo

The efficacy of mupirocin ointment in impetigo was assessed in a randomized, double-blind trial of adults and children aged 2 months and older.[84] Of the patients studied, 91% were between the ages of 2 months and 15 years. Patients received either mupirocin 2% ointment 3 times daily or placebo for 8 to 12 days. Clinical efficacy rates at the end of therapy in the population were 71% for mupirocin (n=49) and 35% for placebo (n=51). Pathogen eradication rates were 94% and 62%, in the mupirocin and placebo groups, respectively. There were no adverse events reported for the mupirocin group.

mupirocin ointment and oral erythromycin

Mupirocin ointment 3 times daily for 8 days was compared to oral erythromycin 40 mg/kg/day in a randomized open-label trial of patients 5 months to 13 years old with impetigo.[85] Patients were seen on days 4 to 5 of therapy, at end of therapy, and 7 days after therapy had ended. At the first visit, 24 of 30 children in the mupirocin and 14 of 32 children in the erythromycin group were cured or had at least a 75% reduction in size of lesions. At the completion of the study, all 29 patients in the mupirocin group and 27 of the 29 patients in the erythromycin group were cured. Mild diarrhea developed in the erythromycin group. The study concluded that mupirocin appears to be safe and effective in the treatment of impetigo in children.

A prospective double-blind, randomized trial, compared topical mupirocin with oral erythromycin to determine the prevalence of erythromycin-resistant *S. aureus* strains in impetigo and whether an increased rate of failure of erythromycin was associated with such resistance.[86] A total of 102 patients between 3 months and 15.5 years old were enrolled and received erythromycin 50 mg/kg/day or mupirocin 2% ointment, plus respective placebos for 7 days. *S. aureus* was cultured from 88% of patients of which 28% were erythromycin-resistant. In all cases *S. aureus* was sensitive to mupirocin. Only patients with erythromycin-resistant *S. aureus* strains had unfavorable courses compared with mupirocin (failure rate 47% versus 2%, respectively). Patients with erythromycin-susceptible *S. aureus* strains who received erythromycin had a failure rate of 8%. In 4 patients, *S. aureus* strains initially susceptible to erythromycin became resistant during treatment. The study concluded that erythromycin-resistant *S. aureus* strains were commonly isolated from impetigo lesions in the study region.

mupirocin cream and oral cephalexin

A randomized, double-blind, double-dummy, multicenter trial of 159 patients with secondarily infected eczema and a total skin infection rating scale score of 8 or greater compared mupirocin 2% cream 3 times daily to oral cephalexin 250 mg 4 times daily for 10 days.[87] Per protocol clinical success, defined partly as a patient with a response of improvement in the skin infection rating scale, was similar in both arms: 89% and 82%, in the mupirocin and cephalexin groups, respectively (95% CI, -8.4 to 22.5; p=0.29). Bacteriological success defined as eradication, improvement, or colonization of bacteria at end of therapy, was higher in the mupirocin group versus cephalexin, 50% versus 28%, respectively (p=0.005). Both drugs were well tolerated. Diarrhea and nausea were common adverse effects.

Two identical randomized, double-blind studies of 706 patients with secondarily infected wounds (small lacerations, abrasions, or sutured wounds) compared mupirocin 2% cream topically 3 times daily to oral cephalexin 4 times daily for 10 days.[88] Clinical success at follow-up was the same in the 2 groups, 95.1% versus 95.3% in the mupirocin cream and the cephalexin groups, respectively (95% CI, -4% to 3.6%; p=0.89). The intention-to-treat success rate was 83% in both groups. Bacteriologic success at follow-up was similar in the 2 groups: 96.9% in the mupirocin cream versus 98.9% in the cephalexin groups (95% CI, -6% to 2%; p=0.22). Adverse event profile was similar; however, more diarrhea in the cephalexin group was reported.

Mupirocin cream was compared to oral cephalexin in 2 randomized, double-blind, double-dummy studies of secondarily infected skin lesion studies.[89] In the studies, 93 pediatric patients aged 2 weeks to 16 years old were randomized to mupirocin 2% cream 3 times daily or oral cephalexin 250 mg 4 times daily for patients > 40 kg or 25 mg/kg/day oral suspension in 4 divided doses for patients ≤ 40 kg for 10 days. At follow-up (7 to 12 days after therapy), clinical efficacy was achieved in 97.7% and 93.9%, in mupirocin and cephalexin, respectively.

ozenoxacin cream (Xepi) and placebo

The safety and efficacy of ozenoxacin cream for the treatment of impetigo was evaluated in 2 multicenter, randomized, double-blind placebo controlled clinical trials.[90] A total of 723 subjects ≥ 2 months of age with an affected body surface area (BSA) of up to 100 cm^2 (up to 2% BSA for subjects aged 2 months to 11 years) were randomized to ozenoxacin or placebo twice daily for 5 days. Clinical success was defined as no need for additional antimicrobial therapy of the baseline affected area(s) and absence or reduction in clinical signs and symptoms at the end of therapy (Day 6 to 7). Respective

clinical success rates for ozenoxacin and placebo were 34.8% versus 19.2% (p=0.002) in trial 1, and 54.4% versus 37.9% (p=0.001) in trial 2.

retapamulin (Altabax) and placebo

The safety and efficacy of retapamulin were evaluated in a randomized, double-blind, placebo-controlled, multicenter study enrolling 213 patients.[91, 92] A total of 210 adults and children aged 9 months and older with impetigo (up to 100 cm^2 in total area- up to 10 lesions - or a total body surface area not exceeding 2%) were randomized to retapamulin 1% ointment or placebo applied twice daily for 5 days. Patients with underlying skin disease or skin trauma with evidence of secondary infections were excluded from the study. Most of the patients (78%) were less than 13 years old. Clinical success rates, defined as response of impetigo at 7 days where no further antimicrobial treatment was required, were higher in the retapamulin group versus placebo, 85.6% versus 52.1% for the intent to treat population, respectively (95% CI, 20.5 to 46.5; p<0.0001). Pruritus at the application site was reported by 6% and 1% of the retapamulin and placebo groups, respectively.

META-ANALYSES

A meta-analysis of 57 randomized controlled trials including 3,533 patients, studied comparisons of 20 oral and 18 topical treatments for impetigo.[93] Topical antibiotics had better cure rates than placebo (pooled OR, 6.49; 95% CI, 3.93 to 10.73). There was no significant difference between topical mupirocin and topical fusidic acid (pooled OR of mupirocin versus fusidic acid, 1.76; 95% CI, 0.69 to 2.16). Fusidic acid is not commercially available in the United States. Topical mupirocin had better cure rates compared to oral erythromycin (OR; 1.22; 95% CI, 1.05 to 2.97). There were no significant differences in cure rates among other topical and oral antibiotics studied.

Another meta-analysis of 16 randomized controlled trials, including double-blinded and observer-blinded trials, indicated that topical antibiotics were more effective than placebo (OR, 2.69; 95% CI, 1.49 to 4.86) for the treatment of impetigo.[94] There was weak evidence favoring topical antibiotics over some oral antibiotics such as erythromycin (OR, 0.48; 95% CI, 0.23 to 1). There was no significant difference between the topical therapies, mupirocin and fusidic acid. (OR, 1.76; 95% CI, 0.77 to 4.03).

SUMMARY

Skin and soft tissue bacterial infections are a common problem seen in many clinical practices. Most skin and soft tissue infections can be managed on an outpatient basis and are easily treatable; however, physicians should observe for any signs or symptoms of severe infection. Several bacterial microorganisms can infect the skin and soft tissue, but the most common agents are *S. aureus* and group A (*S. pyogenes*) streptococci. In general, the selection of topical antibiotic agent will be dependent on the probable microorganism causing the infection.

Mupirocin cream is FDA approved for the treatment of secondary infected traumatic skin lesions due to susceptible strains of *S. aureus* and *S. pyogenes*. It is not indicated for impetigo; however, mupirocin ointment is FDA approved for the treatment of impetigo due to *S. aureus* and *S. pyogenes*. Mupirocin cream is not in a polyethylene glycol (PEG) base like mupirocin ointment. PEG can be absorbed from open wounds and damaged skin therefore should be avoided in patients with moderate to severe renal impairment. Direct comparative trials of the cream and ointment formulations are lacking, and they are not considered interchangeable.

Mupirocin ointment, ozenoxacin (Xepi), and retapamulin (Altabax) have not been studied in head to head trials in the treatment of impetigo. Retapamulin (Altabax) is not FDA-approved for use in infections caused by MRSA, but ozenoxacin (Xepi) and retapamulin (Altabax) has an advantage in that their dosage regimen is twice daily versus that of mupirocin, which is 3 times daily. Impetigo is usually a self-limiting skin infection, but resistance patterns should be taken into account in the choice of therapy.

The Infectious Diseases Society of America (IDSA) 2014 practice guidelines update for the diagnosis and management of skin and soft-tissue infections recommend mupirocin ointment or retapamulin (Altabax) as the topical antibacterials of choice in the treatment of impetigo, but oral therapy is recommended in patients with numerous lesions or during outbreaks. Topical tetracycline (Viabecline) and ozenoxacin (Xepi) are not addressed in these guidelines.

REFERENCES

1 Available at: http://www.clinicalpharmacology.com/. Accessed February 15, 2018.
2 Bactroban Ointment [package insert]. Research Triangle Park, NC; GlaxoSmithKline; October 2012.
3 Bactroban Cream [package insert]. Research Triangle Park, NC; GlaxoSmithKline; October 2012.
4 Altabax [package insert]. Research Triangle Park, NC; GlaxoSmithKline; July 2013.
5 Gentamicin Ointment [package insert]. Melville, NY; Fougera; March 2010.
6 Gentamicin Cream [package insert]. Melville, NY; Fougera; March 2010.
7 Triple Antibiotic Plus Ointment. Available at: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=0c8b4476-03f7-45b1-abae-b6f5a298523e. Accessed February 12, 2019.
8 Neosporin Plus Pain Relief Ointment. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=27db5da1-9616-4b11-bba9-d30f701d52ec. Accessed February 12, 2019.
9 Neosporin Plus Pain Relief Cream. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=8398f0d1-cb06-4b69-ba16-b8073faed8e4. Accessed February 20, 2018.
10 Centany AT Kit. [package insert]. Fairfield, NJ. Medimetriks; February 2016. Available at: http://www.medimetriks.com/sites/default/files/pi-files/Centany_PI_website.pdf. Accessed February 21, 2018.
11 Xepi [package insert]. Wayne, PA; Cutanea: February 2019.
12 Viabecline Ointment. Available at : https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=9fd7041a-6c23-4332-90fe-759bb4aea2ae. Accessed February 12, 2019.
13 Bactroban Nasal Ointment [package insert]. Research Triangle Park, NC; GlaxoSmithKline; July 2011.
14 Available at: http://www.clinicalpharmacology.com/. Accessed February 12, 2019.
15 McCaig LF, McDonald LC, Mandal S, et al. Staphylococcus aureus associated skin and soft tissue infections in ambulatory care. Emerg Infect Dis. 2006; 12:1715–23.
16 Stevens DL, Bisno AL, Chambers HF, et al. Infectious Diseases Society of America (IDSA). Practice guidelines for the diagnosis and management of skin and soft-tissue infections: 2014 update by the Infectious Diseases Society of America. Clin Infect Dis. 2014; 59(2):e10-52. DOI: 10.1093/cid/ciu444. Available at: http://cid.oxfordjournals.org/content/early/2014/06/14/cid.ciu296.full.pdf+html. Accessed February 12, 2019.
17 Stevens DL, Bisno AL, Chambers HF, et al. Infectious Diseases Society of America (IDSA). Practice guidelines for the diagnosis and management of skin and soft-tissue infections. Clin Infect Dis. 2005; 41(10):1373-1406.
18 Hirschmann JV. Antimicrobial therapy for skin infections. Cutis. 2007; 79(6S):26-36.
19 Stevens DL, Bisno AL, Chambers HF, et al. Infectious Diseases Society of America (IDSA). Practice guidelines for the diagnosis and management of skin and soft-tissue infections. Clin Infect Dis. 2005; 41(10):1373-1406.
20 Sabitha R. Skin and soft-tissue infections: Classifying and treating a spectrum. Cleveland Clinic Journal of Medicine. 2012; 79 (1): 57-66.
21 Stevens DL, Bisno AL, Chambers HF, et al. Infectious Diseases Society of America (IDSA). Practice guidelines for the diagnosis and management of skin and soft-tissue infections. Clin Infect Dis. 2005; 41(10):1373-1406.
22 Bisno AL, Stevens DL. Streptococcal infections of skin and soft tissues. N Engl J Med. 1996;334:240–5.
23 Templer SJ, Brito MO. Bacterial Skin and Soft Tissue Infections. Hospital Physician. 2009; 45(3): 9-16, 26.
24 Dantes R, Mu Y, Belflower R, et al.. National Burden of Invasive Methicillin-Resistant Staphylococcus aureus Infections, United States, 2011. JAMA Internal Medicine. 2013; published on line.
25 Stulberg, DL, Penrod, MA, and Blatny RA. Common Bacterial Skin Infections. American Academy of Family Physicians. 2002; 66(1): 119-124.
26 Stevens DL, Bisno AL, Chambers HF, et al. Infectious Diseases Society of America (IDSA). Practice guidelines for the diagnosis and management of skin and soft-tissue infections: 2014 update by the Infectious Diseases Society of America. Clin Infect Dis. 2014; 59(2):e10-52. DOI: 10.1093/cid/ciu444. Available at: http://cid.oxfordjournals.org/content/early/2014/06/14/cid.ciu296.full.pdf+html. Accessed February 12, 2019.
27 Yun HJ, Lee SW, Yoon GM, et al. Prevalence and mechanisms of low and high-level mupirocin resistance in staphylococci isolated from a Korean hospital. J Antimicrob Chemother. 2003; 51(3):619–623.
28 Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant staphylococcus aureus infections in adults and children. Clinical Infectious Diseases 2011;e18-e55. Available at: http://www.idsociety.org/Organ_System/. Accessed February 12, 2019.
29 Bactroban Ointment [package insert]. Research Triangle Park, NC; GlaxoSmithKline; October 2012.

30 Altabax [package insert]. Research Triangle Park, NC; GlaxoSmithKline; July 2013.
31 DRUGDEX® System [Internet database]. Greenwood, CO: Thompson Micromedex. Updated periodically.
32 Bactroban Cream [package insert]. Research Triangle Park, NC; GlaxoSmithKline; October 2012.
33 Xepi [package insert]. Wayne PA; Cutanea; February 2019.
34 Available at: http://www.clinicalpharmacology.com/. Accessed February 12, 2019.
35 Pérez-Trallero E, Tamayo E, Montes M, et al. *In vitro* activities of retapamulin and 16 other antimicrobial agents against recently obtained *Streptococcus pyogenes* isolates. Antimicrob Agents Chemother. 2011;55(5):2406-8.
36 Available at: http://www.clinicalpharmacology.com/. Accessed February 12, 2019.
37 Bactroban Ointment [package insert]. Research Triangle Park, NC; GlaxoSmithKline; October 2012.
38 Altabax [package insert]. Research Triangle Park, NC; GlaxoSmithKline; July 2013.
39 Xepi [package insert]. Wayne PA; Cutanea; February 2019.
40 Bactroban Cream [package insert]. Research Triangle Park, NC; GlaxoSmithKline; October 2012.
41 Available at: http://www.clinicalpharmacology.com/. Accessed February 12, 2019.
42 Available at http://www.thomsonhc.com. Accessed March 9, 2017.
43 Bactroban Ointment [package insert]. Research Triangle Park, NC; GlaxoSmithKline; October 2012.
44 Altabax [package insert]. Research Triangle Park, NC; GlaxoSmithKline; July 2013.
45 Bactroban Cream [package insert]. Research Triangle Park, NC; GlaxoSmithKline; October 2012.
46 Available at: http://www.clinicalpharmacology.com/. Accessed February 12, 2019.
47 Centany Ointment [package insert]. Fairfield, NJ; Perrigo; July 2011.
48 Bactroban Ointment [package insert]. Research Triangle Park, NC; GlaxoSmithKline; October 2012.
49 Altabax [package insert]. Research Triangle Park, NC; GlaxoSmithKline; July 2013.
50 Xepi [package insert]. Wayne PA; Cutanea; February 2019.
51 Bactroban Cream [package insert]. Research Triangle Park, NC; GlaxoSmithKline; October 2012.
52 Available at: http://www.clinicalpharmacology.com/. Accessed February 12, 2019.
53 Available at: http:// online.factsandcomparisons.com. Accessed March 9, 2017.
54 Bactroban Ointment [package insert]. Research Triangle Park, NC; GlaxoSmithKline; October 2012.
55 Bactroban Cream [package insert]. Research Triangle Park, NC; GlaxoSmithKline; October 2012.
56 Altabax [package insert]. Research Triangle Park, NC; GlaxoSmithKline; July 2013.
57 Gentamicin Ointment [package insert]. Melville, NY; Fougera; March 2010.
58 Gentamicin Cream [package insert]. Melville, NY; Fougera; March 2010.
59 Available at http://www.thomsonhc.com. Accessed March 9, 2017.
60 Centany Ointment [package insert]. Fairfield, NJ; Perrigo; December 2008.
61 Xepi [package insert]. Wayne PA; Cutanea; February 2019.
62 Bactroban Ointment [package insert]. Research Triangle Park, NC; GlaxoSmithKline; October 2012.
63 Xepi [package insert]. Wayne PA; Cutanea; February 2019.
64 Altabax [package insert]. Research Triangle Park, NC; GlaxoSmithKline; July 2013.
65 Bactroban Cream [package insert]. Research Triangle Park, NC; GlaxoSmithKline; October 2012.
66 Available at: http://www.clinicalpharmacology.com/. Accessed February 12, 2019.
67 Available at http:// online.factsandcomparisons.com. Accessed March 9, 2017.
68 Available at: http://www.clinicalpharmacology.com/. Accessed February 12, 2019.
69 Bactroban Ointment [package insert]. Research Triangle Park, NC; GlaxoSmithKline; October 2012.
70 Bactroban Cream [package insert]. Research Triangle Park, NC; GlaxoSmithKline; October 2012.
71 Altabax [package insert]. Research Triangle Park, NC; GlaxoSmithKline; July 2013.
72 Gentamicin Ointment [package insert]. Melville, NY; Fougera; March 2010.
73 Gentamicin Cream [package insert]. Melville, NY; Fougera; March 2010.
74 Available at http://www.thomsonhc.com. Accessed March 9, 2017.
75 Centany Ointment [package insert]. Fairfield, NJ; Perrigo; July 2011.
76 Neosporin Plus Pain Relief Ointment. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=27db5da1-9616-4b11-bba9-d30f701d52ec. Accessed February 12, 2019.
77 Neosporin Plus Pain Relief Cream. Available a : https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=8398f0d1-cb06-4b69-ba16-b8073faed8e4. Accessed February 20, 2018.
78 Centany Kit. [package insert]. Farifield, NJ. Medimetriks; February 2016. Available at: http://www.medimetriks.com/sites/default/files/pi-files/Centany_PI_website.pdf. Accessed February 21, 2018.
79 Viabecline Ointment. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=9fd7041a-6c23-4332-90fe-759bb4aea2ae. Accessed February 12, 2019.
80 Xepi [package insert]. Wayne PA; Cutanea; February 2019.
81 Smack DP, Harrington AC, Dunn c, et al. Infection and Allergy Incidence in Ambulatory Surgery Patients Using White Petrolatum vs. Bacitracin Ointment. JAMA. 1996; 276(12): 972-977.
82 Dire DJ, Coppola M, Dwyer DA, et al. Prospective Evaluation of Topical Antibiotics for Preventing Infections in Uncomplicated Soft-tissue Wounds Repaired in the ED. Acad. Emerg. Med. 1995; 2(4): 4-10.
83 Bernardini J, Bender F, Florio T, et al. Randomized, Double-Blind Trial of Antibiotic Exit Site Cream for Prevention of Exit Site Infection in Peritoneal Dialysis Patients. J Am Soc Nephrol. 2005; 16: 539-545.
84 Bactroban Ointment [package insert]. Research Triangle Park, NC; GlaxoSmithKline; October 2012.
85 Goldfarb J, Crenshaw D, O'Horo J, et al. Randomized clinical trial of topical mupirocin versus oral erythromycin for impetigo. Antimicrob Agents Chemother. 1988; 32(12):1780-1783.
86 Dagan R, Bar-David Y. Double-blind study comparing erythromycin and mupirocin for treatment of impetigo in children: implications of a high prevalence of erythromycin-resistant Staphylococcus aureus strains. Antimicrob Agents Chemother. 1992; 36(2):287-290.

87 Rist T, Parish LC, Capin LR, et al. A comparison of the efficacy and safety of mupirocin cream and cephalexin in the treatment of secondarily infected eczema. Clin Exp Dermatol. 2002; 27(1):14-20.
88 Kraus SJ, Eron LJ, Bottenfield GW, et al. Mupirocin cream is as effective as oral cephalexin in the treatment of secondarily infected wounds. J Fam Pract .1998; 47(6):429-433.
89 Bactroban Cream [package insert]. Research Triangle Park, NC; GlaxoSmithKline; October 2012.
90 Xepi [package insert]. Wayne PA; Cutanea; February 2019.
91 Altabax [package insert]. Research Triangle Park, NC; GlaxoSmithKline; July 2013.
92 Koning S, van der Wouden JC, Chosidow O, et al. Efficacy and safety of retapamulin ointment as treatment of impetigo: randomized double-blind multicentre placebo-controlled trial. Br J Dermatol. 2008; 158(5):1077-82.
93 Koning S, Verhagen AP, van Suijlekom-Smit LW, et al. Interventions for impetigo. Cochrane Database Sys Rev. 2004; (2):CD003261.
94 George A, Rubin G. A systematic review and meta-analysis of treatments for impetigo. Br J Gen Pract. 2003; 53(491):480-487.