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**Month/Year of Review:** May 2013 **Date of Last Review:** March 2010
**PDL Classes:** Topical Antibiotics **Source Document:** Provider Synergies

**Current Status of PDL:**

- Preferred Agents: BACITRACIN, BACITRACIN ZINC, BACITRACIN/POLYMYXIN B SULFATE, GENTAMICIN SULFATE, MUPIROCIN, NEOMYCIN SULFATE/BACITRACIN ZINC/POLYMYXIN B SULFATE
- Non-Preferred Agents: ALTABAX RETAPAMULIN OINTMENT (ALTABAX®)

**Previous Recommendations:**

- Evidence does not support a difference in efficacy/effectiveness
- Evidence does not support a difference in harm/adverse events
- Recommend inclusion of at least mupirocin

**Methods:**

A Medline OVID search was conducted with the following search terms: bacitracin, polymyxin B, neomycin, gentamicin, mupirocin, retapamulin, MRSA, methicillin resistant staphylococcus aureus, MSSA, methicillin sensitive, staphylococcus aureous, staphylococcus epidermidis, staphylococcus saprophyticus, streptococcus pyogenes, streptococcus saprophyticus, positive haemophilus influenza, negative haemophilus influenza, pseudomonas aeruginosa, skin infection, soft tissue infections, impetigo, minor bacterial infection, minor cut, burn, scrape. The search was limited to English language articles of controlled trials conducted on humans published from 2010 to February week 2 2013.

The Cochrane Collection, Dynamed and Medline OVID were searched for high quality systematic reviews. The FDA website was searched for new drugs, indications, and safety alerts. Finally, a search for new or updated guidelines was conducted at the AHRQ National Guideline Clearinghouse (NGC), the Center for Disease Control (CDC) and Infectious Diseases Society of America (IDSA).

**FDA-Approved Microorganism Indications:**

| Drug | MRSA | MSSA | Staphylococcus Epidermidis | Staphylococcus saprophyticus | Streptococcus Pyogenes | Streptococcus sp. | Haemophilus. Influenza | Pseudomonas aeruginosa |
|---|---|---|---|---|---|---|---|---|
| Bacitracin/bacitracin zinc ointment | | X | | | | X | | |
| bacitracin zinc, neomycin, polymyxin B sulfate, hydrocortisone | | X | | | | X | X | X |
| Bacitracin zinc, neomycin, polymyxin B sulfate ointment | | X | | | | X | X | X |
| Bacitracin zinc, neomycin, polymyxin B sulfate, pramoxine | | X | | | | X | X | X |
| Bacitracin zinc, polymyxin B ointment | | X | | | | X | X | X |
| Gentamicin 0.1% cream/ointment | | X | X | | X | | X | X |
| Mupirocin 2% cream/ointment | X | X | X | X | X | | | |
| Neomycin, polymyxin B sulfate, hydrocortisone cream | | X | | | | X | X | X |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Retapamulin 1% ointment (altabax) | | X | | | X | | | |

**New Trials (Appendix 1):**
A total of 91 citations resulted from the initial MEDLINE search. Articles were excluded due to the wrong study design (observational), comparator (placebo), or outcome (non-clinical). After a review of titles and abstracts for inclusion, one relevant head-to-head clinical trial was identified.

McQuillan et al compared the efficacy of prophylactic topical mupirocin versus a triple antibiotic (bacitracin, polymyxin and gramicidin) ointment in preventing skin infection for patients undergoing peritoneal dialysis. [1] This was a small (n=201), low quality study with multiple opportunities for bias, including unclear blinding and allocation concealment. Seventy-five patients developed an infection during the study. There was no difference in incidence between groups: 36 patients in the mupirocin versus 39 in the triple antibiotic group (p=0.48). There was also no difference between groups in the time to first infection (p=0.41).

**New drugs:**
None

**New Formulations/Indications:**
None

**New FDA safety alerts:**
None

**New Systematic Reviews (appendix 2):**
A 2012 updated Cochrane systematic review evaluated the treatments for impetigo.[2] Sixty-eight trials were included with a total of 5578 participants; 50 treatments were examined including topical antibiotics (neomycin, bacitracin, polymyxin B, gentamycin, fusidic acid, mupirocin, or retapamulin). Trials were mostly low quality: risk of bias was high with only 15 trials reporting information about blinding. Only one study showed one topical antibiotic as superior over another: gentamycin over neomycin (RR 1.43, 95% CI 1.03 to 1.98). In another single study, the difference between retapamulin over fusidic acid was not statistically significant (RR 1.05, 95% CI 1.00 to 1.11). There were four studies which compared mupirocin with fusidic acid (RR 1.03, 95% CI 0.95 to 1.11) but the difference was not significant. Topical antibiotics were also found to be superior to placebo (RR 2.24, 95% CI 1.61 to 3.13), disinfecting agents (RR 1.15, 95% CI 1.01 to 1.32), and oral erythromycin (RR 1.07, 95% CI 1.01 to 1.13).

**Guidelines:**
The IDSA 2011 guidelines for the diagnosis and management of skin and soft-tissue infections recommended mupirocin ointment as the topical antibacterial drug of choice in the treatment of impetigo in infants two months and older and in adults.[3]

The 2012 updated version for diabetic foot infection treatment was reviewed. [4] No changes regarding the use of topical antibiotics were found.

**Conclusions and Recommendations:**
- No further research or review needed at this time.
- Evaluate comparative costs in executive session.

## References:

1. McQuillan RF, Chiu E, Nessim S, et al. A Randomized Controlled Trial Comparing Mupirocin and Polysporin Triple Ointments in Peritoneal Dialysis Patients: The MP3 Study. *Clinical Journal of the American Society of Nephrology*. 2011;7(2):297–303. doi:10.2215/CJN.07970811.

2. Koning S, van der Sande R, Verhagen AP, et al. Interventions for impetigo. *Cochrane Database Syst Rev*. 2012;1:CD003261. doi:10.1002/14651858.CD003261.pub3.

3. 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: executive summary. *Clin. Infect. Dis.* 2011;52(3):285–292. doi:10.1093/cid/cir034.

4. Lipsky BA, Berendt AR, Cornia PB, et al. 2012 Infectious Diseases Society of America Clinical Practice Guideline for the Diagnosis and Treatment of Diabetic Foot Infections. *Clinical Infectious Diseases*. 2012;54(12):e132–e173. doi:10.1093/cid/cis346.

**Appendix 1 : Abstracts of Randomized Control Trials**

**McQuillan RF, Chiu E, Nessim S, et al. A Randomized Controlled Trial Comparing Mupirocin and Polysporin Triple Ointments in Peritoneal Dialysis Patients: The MP3 Study. *Clinical Journal of the American Society of Nephrology*. 2011;7(2):297–303.**

Background and objectives: Infectious complications remain a significant cause of peritoneal dialysis (PD) technique failure. Topical ointments seem to reduce peritonitis; however, concerns over resistance have led to a quest for alternative agents. This study examined the effectiveness of applying topical Polysporin Triple ointment (P3) against mupirocin in a multi-centered, double-blind, randomized controlled trial.

Design, setting, participants, & measurements: PD patients routinely applied either P3 or mupirocin ointment to their exit site. Patients were followed for 18 months or until death or catheter removal. The primary study outcome was a composite endpoint of exit-site infection (ESI), tunnel infection, or peritonitis.

Results: Seventy-five of 201 randomized patients experienced a primary outcome event (51 peritonitis episodes, 24 ESIs). No difference was seen in the time to first event for P3 (13.2 months; 95% confidence interval, 11.9–14.5) and mupirocin (14.0 months; 95% confidence interval, 12.7–15.4) (P=0.41). Twice as many patients reported redness at the exit site in the P3 group (14 versus 6, P=0.10).Over the complete study period, a higher rate per year of fungal ESIs was seen in patients using P3 (0.07 versus 0.01; P=0.02) with a corresponding increase in fungal peritonitis (0.04 versus 0.00, respectively; P, 0.05).

Conclusions: This study shows that P3 is not superior to mupirocin in the prophylaxis of PD-related infections. Colonization of the exit site with fungal organisms is of concern and warrants further study. As such, the use of P3 over mupirocin is not advocated in the prophylaxis of PD-related infections.

**Appendix 2 : Abstracts of Systematic Reviews**

**Koning S, Van der Sande R, Verhagen AP, et al. Interventions for impetigo. In: The Cochrane Collaboration, van der Wouden JC, eds. *Cochrane Database of Systematic Reviews*. Chichester, UK: John Wiley & Sons, Ltd; 2012. Available at: http://doi.wiley.com/10.1002/14651858.CD003261.pub3.**

Background Impetigo is a common, superficial bacterial skin infection, which is most frequently encountered in children. There is no generally agreed standard therapy, and guidelines for treatment differ widely.Treatment options includemany different oral and topical antibiotics as well as disinfectants. This is an updated version of the original review published in 2003.

Objectives To assess the effects of treatments for impetigo, including non-pharmacological interventions and 'waiting for natural resolution'.

Search methods We updated our searches of the following databases to July 2010: the Cochrane Skin Group Specialised Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (from 2005), EMBASE (from 2007), and LILACS (from 1982). We also searched online trials registries for ongoing trials, and we handsearched the reference lists of new studies found in the updated search.

Selection criteria Randomised controlled trials of treatments for non-bullous, bullous, primary, and secondary impetigo.

Data collection and analysis Two independent authors undertook all steps in data collection. We performed quality assessments and data collection in two separate stages.

Main results We included 57 trials in the first version of this review. For this update 1 of those trials was excluded and 12 new trials were added. The total number of included trials was, thus, 68, with 5578 participants, reporting on 50 different treatments, including placebo. Most trials were in primary impetigo or did not specify this. For many of the items that were assessed for risk of bias, most studies did not provide enough information. Fifteen studies reported blinding of participants and outcome assessors. Topical antibiotic treatment showed better cure rates than placebo (pooled risk ratio (RR) 2. 24, 95% confidence interval (CI) 1.61 to 3.13) in 6 studies with 575 participants. In 4 studies with 440 participants, there was no clear evidence that either of the most commonly studied topical antibiotics (mupirocin and fusidic acid) was more effective than the other (RR 1.03, 95% CI 0.95 to 1.11). In 10 studies with 581 participants, topical mupirocin was shown to be slightly superior to oral erythromycin (pooled RR 1.07, 95% CI 1.01 to 1.13). There were no significant differences in cure rates from treatment with topical versus other oral antibiotics. There were, however, differences in the outcome from treatment with different oral antibiotics: penicillin was inferior to erythromycin, in 2 studies with 79 participants (pooled RR 1.29, 95% CI 1.07 to 1.56), and cloxacillin, in 2 studies with 166 participants (pooled RR 1.59, 95% CI 1.21 to 2.08). There was a lack of evidence for the benefit of using disinfectant solutions. When 2 studies with 292 participants were pooled, topical antibiotics were significantly better than is infecting treatments (RR 1.15, 95% CI 1.01 to 1.32). The reported number of side-effects was low, and most of these were mild. Side-effects were more common for oral antibiotic treatment compared to topical treatment. Gastrointestinal effects accounted for most of the difference. Worldwide, bacteria causing impetigo show growing resistance rates for commonly used antibiotics. For a newly developed topical treatment, retapamulin, no resistance has yet been reported.

Authors' conclusions There is good evidence that topical mupirocin and topical fusidic acid are equally, or more, effective than oral treatment. Due to the lack of studies in people with extensive impetigo, it is unclear if oral antibiotics are superior to topical antibiotics in this group. Fusidic acid and mupirocin are of similar efficacy. Penicillin was not as effective as most other antibiotics. There is a lack of evidence to support disinfection measures to manage impetigo.