### Acne Antibiotics

#### Prior Authorization Criteria

<table>
<thead>
<tr>
<th>Brand</th>
<th>Generic</th>
<th>Dosage Form</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Doxycycline products</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adoxa&lt;sup&gt;a&lt;/sup&gt;, Adoxa&lt;sup&gt;a&lt;/sup&gt; CK, Adoxa&lt;sup&gt;a&lt;/sup&gt; TT</td>
<td>doxycycline monohydrate</td>
<td>tablet, capsule, kit (capsule or tablet plus cleanser pads)</td>
</tr>
<tr>
<td>Alodox&lt;sup&gt;™&lt;/sup&gt;</td>
<td>doxycycline hyclate</td>
<td>kit (tablet plus cleanser)</td>
</tr>
<tr>
<td>Avidoxy&lt;sup&gt;™&lt;/sup&gt;, Avidoxy&lt;sup&gt;™&lt;/sup&gt; DK</td>
<td>doxycycline monohydrate</td>
<td>tablet, kit (tablet plus wash, sunscreen)</td>
</tr>
<tr>
<td>Doryx&lt;sup&gt;b&lt;/sup&gt;</td>
<td>doxycycline hyclate&lt;sup&gt;c&lt;/sup&gt;</td>
<td>delayed-release tablet</td>
</tr>
<tr>
<td>Doxycycline&lt;sup&gt;a&lt;/sup&gt;</td>
<td>doxycycline hyclate&lt;sup&gt;b&lt;/sup&gt;</td>
<td>delayed-release capsule</td>
</tr>
<tr>
<td>Monodox&lt;sup&gt;a&lt;/sup&gt;</td>
<td>doxycycline monohydrate&lt;sup&gt;b&lt;/sup&gt;</td>
<td>capsule</td>
</tr>
<tr>
<td>Oracea&lt;sup&gt;a&lt;/sup&gt;</td>
<td>doxycycline monohydrate</td>
<td>delayed-release capsule</td>
</tr>
<tr>
<td>Oraxyl&lt;sup&gt;a&lt;/sup&gt;</td>
<td>doxycycline hyclate</td>
<td>capsule</td>
</tr>
<tr>
<td>Periostat&lt;sup&gt;a&lt;/sup&gt;</td>
<td>doxycycline hyclate&lt;sup&gt;b&lt;/sup&gt;</td>
<td>tablet</td>
</tr>
<tr>
<td>Vibramycin&lt;sup&gt;a&lt;/sup&gt;</td>
<td>doxycycline hyclate&lt;sup&gt;b&lt;/sup&gt;</td>
<td>capsule</td>
</tr>
<tr>
<td>Vibra- Tabs&lt;sup&gt;a&lt;/sup&gt;</td>
<td>doxycycline hyclate&lt;sup&gt;b&lt;/sup&gt;</td>
<td>tablet</td>
</tr>
<tr>
<td><strong>Minocycline products</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cleeravue-M&lt;sup&gt;TM&lt;/sup&gt;</td>
<td>minocycline</td>
<td>kit (tablet plus cleanser foam)</td>
</tr>
<tr>
<td>Dynacin&lt;sup&gt;a&lt;/sup&gt;</td>
<td>minocycline&lt;sup&gt;b&lt;/sup&gt;</td>
<td>capsule, tablet</td>
</tr>
<tr>
<td>Minocin&lt;sup&gt;a&lt;/sup&gt;</td>
<td>minocycline&lt;sup&gt;b&lt;/sup&gt;</td>
<td>capsule</td>
</tr>
<tr>
<td>Minocin&lt;sup&gt;a&lt;/sup&gt; PAC</td>
<td>minocycline</td>
<td>capsule plus acne care products</td>
</tr>
<tr>
<td>Solodyn&lt;sup&gt;a&lt;/sup&gt;</td>
<td>minocycline&lt;sup&gt;b&lt;/sup&gt;</td>
<td>extended-release tablet</td>
</tr>
</tbody>
</table>

<sup>a</sup> - products not coded as generics in claims database will be targets in this program  
<sup>b</sup> - generic products are available, they are not included in this program  
<sup>c</sup> - generic product available, included as target in this program

#### PROGRAM OBJECTIVES

The intent of the prior authorization (PA) criteria for brand acne antibiotics (doxycycline and minocycline) products is to ensure appropriate selection of patients for treatment according to product labeling and/or clinical studies and/or guidelines, and to encourage use of first-line generic agents and topical acne products (where appropriate) before use of these brand products. Requests for these brand products will be reviewed through the manual review process. The manual process provides a member-specific review process where practitioner provided patient-specific parameters are taken into consideration.
PROGRAM FUNCTIONALITY

Electronic Edits

The overall process for a prior authorization will not allow the targeted drug(s) to adjudicate through the claims system. When a patient requests a targeted drug listed above, the system will reject the claim with the message indicating that prior authorization is necessary. The Prior Authorization (PA) Criteria for Approval would then be applied to requests submitted by the patient’s practitioner for evaluation.

Table 1: Details of Acne Antibiotics Prior Authorization

<table>
<thead>
<tr>
<th>Targeted Agents</th>
<th>GPI</th>
<th>Multisource Code</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ANY ONE of:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adoxa, Adoxa CK, Adoxa TT, Alodox,</td>
<td>0400002000****,</td>
<td>M, N, or O</td>
</tr>
<tr>
<td>Avidoxy, Avidoxy DK, doxycycline,</td>
<td>040000201001**,</td>
<td></td>
</tr>
<tr>
<td>Monodox, Oracea, Oraxyl, Periostat,</td>
<td>040000201003**,</td>
<td></td>
</tr>
<tr>
<td>Vibramycin, Vibra-Tabs</td>
<td>040000201067**,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>040000206064**,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>040000207064**,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>04990003156430,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>90060025006520</td>
<td></td>
</tr>
<tr>
<td>OR</td>
<td>040000201006**</td>
<td>M, N, O, or Y</td>
</tr>
<tr>
<td>Doryx, doxycycline hyclate delayed-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>release</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ANY ONE of:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cleeravue-M, Dynacin, Minocin, Minocin</td>
<td>040000406064**,</td>
<td>M, N, or O</td>
</tr>
<tr>
<td>PAC, Solodyn</td>
<td>040000401001**,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>040000401003**</td>
<td></td>
</tr>
<tr>
<td></td>
<td>040000405064**</td>
<td></td>
</tr>
<tr>
<td></td>
<td>040000401075**</td>
<td></td>
</tr>
</tbody>
</table>

Prior Authorization Criteria for Approval

Initial and Renewal Evaluation

1. Is the patient 8 years of age or older?
   If yes, continue to 2. If no, deny.

2. Does the patient have a diagnosis of moderate to severe acne vulgaris?
   If yes, continue to 3. If no, continue to 5.

3. Has the patient previously tried and failed therapy with a prescription topical acne treatment?
   If yes, continue to 5. If no, continue to 4.

4. Does the patient have an allergy, contraindication, or intolerance to prescription topical acne treatment?
   If yes, continue to 5. If no, deny.

5. Has the patient previously tried and failed therapy with an oral prerequisite generic minocycline product or generic doxycycline product?
   If yes, approve for 12 weeks. If no, continue to 6.
   (Note: PA approvals will be limited to one approval per 12 months.)

6. Does the patient have an allergy, contraindication, or intolerance to an oral prerequisite generic minocycline product or generic doxycycline product?
   If yes, approve for 12 weeks. If no, deny.
   (Note: PA approvals will be limited to one approval per 12 months.)
CLINICAL RATIONALE
The 2007 guidelines from the American Academy of Dermatology on treatment of acne vulgaris\(^\text{16}\) include the following recommendations:

1. Topical therapy is a standard of care in acne treatment
   - Topical retinoids, benzoyl peroxide, and antibiotics are strongly recommended.
   - Topical antibiotics used alone can be associated with the development of bacterial resistance.
   - Azelaic acid is effective but some experts consider its efficacy limited.
   - Employing multiple topical agents that affect different aspects of acne pathogenesis can be useful.

2. Systemic antibiotics are a standard of care in moderate and severe acne and treatment-resistant forms of inflammatory acne
   - Doxycycline and minocycline are more effective than tetracycline, and there is evidence that minocycline is superior to doxycycline in reducing \(P.\ acnes\).
   - Although erythromycin is effective, use should be limited to those who cannot use the tetracyclines
   - Trimethoprim-sulfamethoxazole and trimethoprim alone are also effective in instances where other antibiotics cannot be used.

3. Other Therapies
   - Estrogen-containing oral contraceptives can be useful in treatment of acne in some women.
   - Spironolactone and cyproterone can be useful, but the strength of recommendation is less
   - Oral isotretinoin is useful for severe recalcitrant nodular acne and also lesser degrees of acne that are treatment-resistant of for acne that is scarring
   - Intralesional corticosteroid injections are effective in the treatment of individual acne nodules\(^\text{16}\)

The safety and efficacy of Solodyn in the treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris was assessed in two 12-week, multi-center, randomized, double-blind, placebo-controlled, studies in subjects \(\geq\) 12 years. The mean age of subjects was 20 years and subjects were from the following racial groups: white (73%), Hispanic (13%), black (11%), Asian/Pacific islander (2%), and other (2%). In the two efficacy and safety trials, a total of 924 subjects with non-nodular moderate to severe acne vulgaris received 1 mg/kg of Solodyn or placebo for a total of 12 weeks. The two primary efficacy endpoints were:

1. Mean percent change in inflammatory lesion counts from baseline to 12 weeks
2. Percentage of subjects with an Evaluator’s Global Severity Assessment (EGSA) of clear or almost clear at 12 weeks.

Patients on Solodyn had a greater mean percent improvement in inflammatory lesions (43.1% and 45.8% in studies one and two respectively) compared to placebo (31.7% and 30.8%) (\(p<0.05\)). Solodyn did not demonstrate any effect on non-inflammatory lesions.\(^\text{14}\)

There are no clinical studies comparing extended-release minocycline with older immediate-release formulations. Reviews of tetracycline products used in the treatment of acne\(^\text{17,18}\) have found tetracycline, minocycline, and doxycycline all to be effective in the treatment of acne, particularly during the inflammatory stage. One review of seven randomized trials which were set up to compare the efficacy of tetracyclines found no evidence of superiority of one tetracycline over another in reducing acne lesion counts.\(^\text{17}\)

A Medical Letter review of Solodyn\(^\text{19}\) concluded “Solodyn is an expensive new formulation of minocycline labeled for once-daily use. Whether Solodyn is as effective as immediate-release minocycline and less likely to cause vertigo remains to be established.”\(^\text{18}\)

In the treatment of periodontitis, it is thought that doxycycline works by inhibiting collagenase. Collagenase breaks down connective tissue which leads to the separation of the gum from the tooth. Products (e.g., Periostat, Oraxyl) used for treatment of periodontitis contain lower amounts of doxycycline. Doxycycline concentrations produced by these products are too low to exert a direct antibacterial effect. Clinical studies of patients receiving Periostat for 9-18 months show that it has no effect on total anaerobic and facultative bacteria in plaque samples. These lower dose doxycycline products should not be used as an antibiotic in the treatment of periodontitis.\(^\text{9}\)
To receive an AB rating by the Food and Drug Administration (FDA) generic agents must be pharmaceutical equivalents to the innovator brand drug (contain the same active ingredients, are the same dosage form, the same route of administration, and are identical in strength or concentration) and the agent can be expected to have the same clinical effect and safety profile when administered to patients under the conditions specified in the innovator drug labeling. Generic may differ in shape, scoring, configuration, release mechanisms, packaging, excipients (including colors, flavors, preservatives), expiration time, and, within certain limits, labeling. AB-rated agents have had actual or potential bioequivalence problems resolved with adequate in vivo and/or in vitro evidence supporting bioequivalence. Doxycycline in oral capsules, oral tablets, and oral suspension and minocycline in oral capsules, oral tablets, and extended-release tablets are available as AB-rated generics.

FDA APPROVED INDICATIONS

The following information is taken from individual drug prescribing information and is provided here as background information only. Not all FDA-approved indications may be considered medically necessary. All criteria are found in the section “Prior Authorization (PA) Criteria for Approval.”

Adoxa, Avidoxy, Doxycycline, Doryx, Monodox, Vibramycin, Vibra-Tabs:
To reduce the development of drug-resistant bacteria and maintain effectiveness of doxycycline and other antibacterial drugs, doxycycline should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Doxycycline is indicated for the treatment of the following infections:
- Rocky mountain spotted fever, typhus fever and the typhus group, Q fever, rickettsialpox, and tick fevers caused by Rickettsiae.
- Respiratory tract infections caused by Mycoplasma pneumoniae.
- Lymphohgranuloma venereum caused by Chlamydia trachomatis.
- Psittacosis (ornithosis) caused by Chlamydia psittaci.
- Trachoma caused by Chlamydia trachomatis, although the infectious agent is not always eliminated as judged by immunofluorescence.
- Inclusion conjunctivitis caused by Chlamydia trachomatis.
- Uncomplicated urethral, endocervical or rectal infections in adults caused by Chlamydia trachomatis.
- Nongonococcal urethritis caused by Ureaplasma urealyticum.
- Relapsing fever due to Borrelia recurrentis.

Doxycycline is also indicated for the treatment of infections caused by the following gram-negative microorganisms:
- Chancroid caused by Haemophilus ducreyi.
- Plague due to Yersinia pestis (formerly Pasteurella pestis).
- Tularemia due to Francisella tularensis (formerly Pasteurella tularensis).
- Cholera caused by Vibrio cholerae (formerly Vibrio comma).
- Campylobacter fetus infections caused by Campylobacter fetus (formerly Vibrio fetus).
- Brucellosis due to Brucella species (in conjunction with streptomycin).
- Bartonellosis due to Bartonella bacilliformis.
- Granuloma inguinale caused by Klebsiella granulomatis.

Because many strains of the following groups of microorganisms have been shown to be resistant to doxycycline, culture and susceptibility testing are recommended. Doxycycline is indicated for treatment of infections caused by the following gram-negative microorganisms, when bacteriologic testing indicates appropriate susceptibility to the drug:
- Escherichia coli
• *Enterobacter aerogenes* (formerly *Aerobacter aerogenes*)
• *Shigella* species
• *Acinetobacter species* (formerly *Mima* species and *Herellea* species)
• Respiratory tract infections caused by *Haemophilus influenzae*.
• Respiratory tract and urinary tract infections caused by *Klebsiella species*.

Doxycycline is indicated for treatment of infections caused by the following gram-positive microorganisms when bacteriologic testing indicates appropriate susceptibility to the drug:

• Upper respiratory infections caused by *Streptococcus pneumoniae* (formerly *Diplococcus pneumoniae*).
• Skin and skin structure infections caused by *Staphylococcus aureus*.
• Anthrax due to *Bacillus anthracis*, including inhalational anthrax (post-exposure): to reduce the incidence or progression of disease following exposure to aerosolized *Bacillus anthracis*.

Doxycycline is not the drug of choice in the treatment of any type of staphylococcal infections.

When penicillin is contraindicated, doxycycline is an alternative drug in the treatment of the following infections:

• Uncomplicated gonorrhea caused by *Neisseria gonorrhoeae*.
• Syphilis caused by *Treponema pallidum*.
• Yaws caused by *Treponema pertenue*.
• Listeriosis due to *Listeria monocytogenes*.
• Vincent’s infection caused by *Fusobacterium fusiforme*.
• Actinomycosis caused by *Actinomyces israelii*.
• Infections caused by *Clostridium species*.

In acute intestinal amebiasis, doxycycline may be a useful adjunct to amebicides.

In severe acne, doxycycline may be useful adjunctive therapy.

Doxycycline is indicated for the prophylaxis of malaria due to *Plasmodium falciparum* in short-term travelers (<4 months) to areas with chloroquine and/or pyrimethamine-sulfadoxine resistant strains.

**Adoxa CK, Adoxa TT, and Avidoxy DK**
Adoxa CK, Adoxa TT, and Avidoxy DK are kits intended for treatment of acne which include additional topical products such as skin cleansers or sunscreens.

**Alodox, Oraxyl, Periostat**
Alodox, Oraxyl and Periostat are indicated for use as an adjunct to scaling and root planning to promote attachment level gain and to reduce pocket depth in patients with adult periodontitis.

**Oracea**
Oracea is indicated for the treatment of only inflammatory lesions (papules and pustules) of rosacea in adult patients. No meaningful effect was demonstrated for generalized erythema (redness) of rosacea. Oracea has not been evaluated for the treatment of the erythematous, telangiectatic, or ocular components of rosacea. Efficacy of Oracea beyond 16 weeks and safety beyond 9 months have not been established. This formulation of doxycycline has not been evaluated in the treatment or prevention of infections. Oracea should not be used for treating bacterial infections, providing antibacterial prophylaxis, or reducing the numbers or eliminating microorganisms associated with any bacterial disease. To reduce the development of drug-resistant bacteria as well as to maintain the effectiveness of other antibacterial drugs, Oracea should be used only as indicated.

**Cleeravue-M, Dynacin, Minocin/Minocin PAC, Minocycline USP**
Cleeravue-M, Dynacin, Minocin/Minocin PAC, minocycline USP are indicated in the treatment of the following infections due to susceptible strains of the designated microorganisms:

• Rocky Mountain spotted fever, typhus fever and the typhus group, Q fever, rickettsialpox and tick fevers caused by rickettsiae.
• Respiratory tract infections caused by *Mycoplasma pneumoniae*.
• Lymphogranuloma venereum caused by *Chlamydia trachomatis*.
• Psittacosis (Ornithosis) due to *Chlamydia psittaci*.
• Trachoma caused by *Chlamydia trachomatis*, although the infectious agent is not always eliminated, as judged by immunofluorescence.
• Inclusion conjunctivitis caused by *Chlamydia trachomatis*.
• Nongonococcal urethritis, endocervical, or rectal infections in adults caused by *Ureaplasma urealyticum* or *Chlamydia trachomatis*.
• Relapsing fever due to *Borrelia recurrentis*.
• Chancroid caused by *Haemophilus ducreyi*.
• Plague due to *Yersinia pestis*.
• Tularemia due to *Francisella tularensis*.
• Cholera caused by *Vibrio cholerae*.
• Campylobacter fetus infections caused by *Campylobacter fetus*.
• Brucellosis due to *Brucella* species (in conjunction with streptomycin).
• Bartonellosis due to *Bartonella bacilliformis*.
• Granuloma inguinale caused by *Calymmatobacterium granulomatis*.

Minocycline is indicated for treatment of infections caused by the following gram-negative microorganisms, when bacteriologic testing indicates appropriate susceptibility to the drug:

- Respiratory tract infections caused by *Haemophilus influenzae*.
- Respiratory tract and urinary tract infections caused by *Klebsiella* species.

Minocycline is indicated for the treatment of infections caused by the following gram-positive microorganisms when bacteriologic testing indicates appropriate susceptibility to the drug:

- Upper respiratory tract infections caused by *Streptococcus pneumoniae*.
- Skin and skin structure infections caused by *Staphylococcus aureus*. (Note: Minocycline is not the drug of choice in the treatment of any type of staphylococcal infection).

When penicillin is contraindicated, minocycline is an alternative drug in the treatment of the following infections:

- Uncomplicated urethritis in men due to *Neisseria gonorrhoeae* and for the treatment of other gonococcal infections.
- Infections in women caused by *Neisseria gonorrhoeae*.
- Syphilis caused by *Treponema pallidum* subspecies *pallidum*.
- Yaws caused by *Treponema pallidum* subspecies *pertenue*.
- Listeriosus due to *Listeria monocytogenes*.
- Anthrax due to *Bacillus anthracis*.
- Vincent’s infection caused by *Fusobacterium fusiforme*.
- Actinomycosis caused by *Actinomyces israelii*.
- Infections caused by *Clostridium* species.

In *acute intestinal amebiasis*, minocycline may be a useful adjunct to amebicides.

In *severe acne*, minocycline may be useful adjunctive therapy.

Oral minocycline is indicated in the treatment of asymptomatic carriers of *Neisseria meningitidis* to eliminate meningococci from the nasopharynx. In order to preserve the usefulness of minocycline in the treatment of asymptomatic meningococcal carriers, diagnostic laboratory procedures, including serotyping and susceptibility testing, should be performed to establish the carrier state and the correct treatment. It is recommended that the prophylactic use of minocycline be reserved for situations in which the risk of meningococcal meningitis is high.
Oral minocycline is not indicated for the treatment of meningococcal infection.

Although no controlled clinical efficacy studies have been conducted, limited clinical data show that oral minocycline hydrochloride has been used successfully in the treatment of infections caused by *Mycobacterium marinum*.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of minocycline and other antibacterial drugs, minocycline should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

**Solodyn, minocycline ER tablets**

Solodyn (minocycline extended-release) is indicated to treat only inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients 12 years of age and older. Solodyn did not demonstrate any effect on non-inflammatory lesions. Safety of Solodyn has not been established beyond 12 weeks of use.

This formulation of minocycline has not been evaluated in the treatment of infections.

To reduce the development of drug-resistant bacteria as well as to maintain the effectiveness of other antibacterial drugs, Solodyn should be used only as indicated.

**REFERENCES**

Original Client Specific criteria, approved by HCSC Corporate Clinical Committee 07/2010
Client specific Mid-year Review (clarification that generics are not targets; update of generic products) 11/2010
Administrative Addition (addition of generic for Doryx as target) 01/2011
Administrative Action (revision of name to Acne Antibiotics PA) 02/2011