Description:

Acticlate™ (doxycycline hyclate), Adoxa® (doxycycline monohydrate), Doryx® (doxycycline hyclate, delayed release), and Doryx MPC (doxycycline hyclate, delayed release) are broad-spectrum antibiotics synthetically derived from oxytetracycline, a tetracycline antibiotic. The antimicrobial mechanism of action of the tetracycline class of antibiotics is thought to be inhibition of protein synthesis resulting in bacteriostatic action against a wide variety of pathogens. The tetracyclines, including doxycycline, have similar antimicrobial spectrum of activity and safety profiles and are used for the treatment of a wide range of aerobic gram-positive, aerobic gram-negative, and anaerobic microorganisms, as well as other pathogens such as protozoans and spirochetes. To reduce the development of drug-resistant bacteria and maintain the effectiveness of Acticlate, Adoxa, Doryx, and Doryx MPC, they should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible microorganisms. Cross-resistance of these microorganisms to other tetracyclines is common.
ACTICLATE™ (doxycycline hyclate) oral tablet
DOXYCYCLINE HYCLATE oral tablet
ADOXA® (doxycycline monohydrate) oral capsule and tablet
DORYX® (doxycycline hyclate, delayed release) oral capsule and tablet
DORYX® MPC (doxycycline hyclate, delayed release) oral tablet (cont.)

All tetracyclines are readily absorbed. Doxycycline hyclate salts are very water soluble while the monohydrate form is only slightly water soluble, however doxycycline is virtually completely absorbed from all formulations after oral administration. Enteric coating delays the release of medication until the dosage form passes through the stomach to prevent the drug from being destroyed or inactivated by gastric juices.

Acticlate contains doxycycline hyclate in an immediate release oral formulation. Adoxa contains doxycycline monohydrate equivalent to doxycycline, mg to mg, for oral administration. Each Doryx product contains doxycycline hyclate in a delayed release (enteric coated) tablet or capsule that contains specially coated pellets of doxycycline hyclate for oral administration. Doryx MPC is a delayed release product that has pellets of doxycycline with a modified polymer enteric coat that has increased resistance to acid degradation to retard the release of doxycycline in the stomach. Doryx MPC tablets contain either 60 mg or 120 mg of doxycycline that is equivalent to doxycycline hyclate 69.4 mg and 138.8 mg respectively. It is not substitutable on a mg per mg basis with other oral doxycycline products.

Generic doxycycline as monohydrate or hyclate is available as capsules, tablets, and delayed release tabs in 20 mg, 50 mg, 75 mg, 100 mg, and 150 mg strengths depending on product selection. Doxycycline is also available in liquid form as a 25 mg/5 mL suspension and 50 mg/5 mL syrup.

Definitions:

Drug related events:
- Ineffective / failure
  Use of a drug employing optimal doses (FDA-recommended doses) for optimal duration; where the condition being treated has not improved or worsened

  A request for branded agent due to generic drug failure or ineffectiveness will be assessed for potential approval with documentation of use of optimal dose / duration of the generic product and meeting other criteria within the coverage guideline. When the drug in question is a combination product, there must be documentation of failure / ineffectiveness of concurrent use (each ingredient used at the same time) of individual generic components. When the drug in question is a low dose formulation, there must be documentation of failure / ineffectiveness of low dose generic formulation.

Adverse Drug Event: Allergic reaction / Hypersensitivity / Intolerance
  Use of a drug produced a significant reaction where continued use of the drug places the individual at risk for either lack of improvement or worsening of the condition being treated or at risk for harm and the concern is documented in medical record. A significant adverse drug event is when an individual's outcome is death, life-threatening, hospitalization (initial or prolonged), disability resulting in a significant, persistent, or permanent change, impairment, damage or disruption in the individuals' body function/structure, physical activities or quality of life, or requires intervention to prevent permanent impairment or damage.
Allergic reaction / hypersensitivity – may or may not involve the active ingredient. When the active ingredient is involved, use of same or a chemically similar agent places the individual at risk for harm when the same or chemically similar agent is used. The subsequent reaction may be the same as the original reaction or a more exaggerated response may be seen, potentially placing the individual at even greater risk for harm.

If the reaction occurred from the active/main generic ingredient; request for branded agent with same active ingredient will not be considered unless it is proven (documented) that active ingredient did not cause reaction and the request meets other criteria within the coverage guideline

Intolerance – these events represent circumstance(s) where use of a drug produced a significant reaction and continued use may result in non-adherence to proposed therapy and this concern is documented in medical record

Contraindication
Use of a drug that is not recommended by the manufacturer or FDA labelling
Use of any drug in the face of a contraindication is outside of the FDA and manufacturer’s labelled recommendation and is considered investigational or experimental

Non-adherence
Individual does not follow prescribe regimen that places the individual at risk for lack of improvement or worsening of the condition being treated and this concern is documented in medical record

Precertification:

Precertification (Prior Authorization) is required for members with a Blue Cross Blue Shield of Arizona (BCBSAZ) pharmacy benefit for medication(s) or product(s) indicated in this guideline.

This Pharmacy Coverage Guideline does not apply to FEP or other states’ Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.
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Criteria:
See “Resources” section for FDA-approved dosage.

- Precertification for Acticlate, doxycycline hyclate, Adoxa, Doryx, or Doryx MPC requires completion of the specific request form in its entirety. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. Incomplete forms will be returned.

- FDA-approved product labeling (indication, age, dosage, testing, contraindications, exclusions, etc.) of Acticlate, doxycycline hyclate, Adoxa, Doryx (except 200 mg, see below), Doryx MPC is considered medically necessary when ALL of the following criteria are met:

  1. Individual is 8 years of age or older

  2. Individual has medical record documentation of a confirmed diagnosis of ONE of the following conditions:
     - Adjunctive therapy for severe acne
     - Treatment of infection known or strongly suspected to be caused by susceptible microorganism
     - Prevention of infection known or strongly suspected to be caused by susceptible microorganism
     - Adjunctive therapy for acute intestinal amebiasis
     - Prophylaxis of malaria

  3. Individual is unable to use generic Doxycycline due to ONE of the following:
     - Experienced a significant intolerant reaction to generic Doxycycline, medical record documentation of the reaction must be submitted with the request
     - Experienced an allergic or hypersensitivity reaction that was due to an excipient in generic Doxycycline that has been identified
     - Has a contraindication to an excipient in generic Doxycycline that has been identified

  4. Absence of ALL of the following contraindications:
     - Hypersensitivity or contraindication to any tetracycline

  5. Absence of ALL of the following exclusions:
     - Woman of child bearing potential who is pregnant or not currently using effective contraception
     - Woman who is breast feeding an infant or child

- FDA-approved product labeling (indication, age, dosage, testing, contraindications, exclusions, etc.) of Doryx 200 mg is considered medically necessary when ALL of the following criteria are met:

  1. Individual is 8 years of age or older

  2. Individual has medical record documentation of a confirmed diagnosis of ONE of the following conditions:
     - Chlamydia trachomatis infection ( uncomplicated) involving the urethra
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DORYX® MPC (doxycycline hyclate, delayed release) oral tablet (cont.)

- Chlamydia trachomatis infection (uncomplicated) involving the endocervix
- Chlamydia trachomatis infection (uncomplicated) involving the rectum

3. Individual is unable to use generic Doxycycline due to ONE of the following:
   - Unable to use generic Doxycycline 100 mg twice daily or use two 100 mg once daily, medical record documentation must be submitted with the request
   - Experienced a significant intolerant reaction to generic Doxycycline, medical record documentation of the reaction must be submitted with the request
   - Experienced an allergic or hypersensitivity reaction that was due to an excipient in generic Doxycycline that has been identified
   - Has a contraindication to an excipient in generic Doxycycline that has been identified

4. Absence of ALL of the following contraindications:
   - Hypersensitivity or contraindication to any tetracycline

5. Absence of ALL of the following exclusions:
   - Woman of child bearing potential who is pregnant or not currently using effective contraception
   - Woman who is breast feeding an infant or child

- Acticlate, doxycycline hyclate, Adoxa, Doryx, or Doryx MPC for all other indications not previously listed or if above criteria not met is considered experimental or investigational based upon:
  - Lack of final approval from the Food and Drug Administration, and
  - Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  - Insufficient evidence to support improvement of the net health outcome, and
  - Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
  - Insufficient evidence to support improvement outside the investigational setting.

Resources:
Doryx MPC package insert. Revised by the manufacturer on May 2016, reviewed on August 31, 2016
Acticlate® package insert (revised by manufacturer on July 2013) reviewed on January 20, 2015.
Doryx® package insert (revised by manufacturer on April 2013) reviewed on May 16, 2013.
Adoxa® package insert (revised by manufacturer on March 2008) reviewed on February 17, 2011.
Doryx® package insert (revised by manufacturer on August 2009) reviewed on February 17, 2011.
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Refer to package insert for complete dosing information. 
FDA-approved indication and dosage:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
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<tr>
<td>Acticlate (doxycycline hyclate), Adoxa (doxycycline monohydrate), and Doryx (doxycycline hyclate, delayed release).</td>
<td>Adult: usual dose is 200 mg on the first day of treatment (administered 100 mg every 12 hours), followed by a maintenance dose of 100 mg daily. The maintenance dose may be administered as a single dose or as 50 mg every 12 hours. In the management of more severe infections (particularly chronic infections of the urinary tract), 100 mg every 12 hours is recommended. Pediatric patients above eight years of age: The recommended dosage schedule for children weighing 45 kg or less is 4.4 mg/kg of body weight divided into two doses on the first day of treatment, followed by 2.2 mg/kg of body weight given as a single daily dose or divided into two doses on subsequent days. For more severe infections up to 4.4 mg/kg of body weight may be used. For children over 45 kg, the usual adult dose should be used. Uncomplicated urethral, endocervical, or rectal infection caused by <em>Chlamydia trachomatis</em>: 100 mg by mouth twice a day for 7 days. As an alternate dosing regimen for uncomplicated urethral or endocervical infection caused by <em>Chlamydia trachomatis</em>, administer 200 mg by mouth once-a-day for 7 days. Uncomplicated gonococcal infections in adults (except anorectal infections in men): 100 mg, by mouth, twice-a-day for 7 days. As an alternate single visit dose, administer 300 mg stat followed in one hour by a second 300 mg dose.</td>
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<td>Doxycycline is indicated to treat or prevent infections that are proven or strongly suspected to be caused by bacteria in the following:</td>
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<td>• Rickettsial infections</td>
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<td>• Sexually transmitted infections</td>
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<td>• Anthrax, including inhalational anthrax (post-exposure)</td>
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<tr>
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</tbody>
</table>
| Doryx MPC is indicated to treat or prevent infections that are proven or strongly suspected to be caused by bacteria in the following: | Dosage in Adults
| • Rickettsial infections                                                 | The usual dosage of Doryx MPC is 240 mg on the first day of treatment (administered 120 mg every 12 hours) followed by a maintenance dose of 120 mg daily. |
| • Sexually transmitted infections                                      | In the management of more severe infections (particularly chronic infections of the urinary tract), 120 mg every 12 hours is recommended. |
| • Respiratory tract infections                                         |                                                                  |
| • Specific bacterial infections                                        |                                                                  |
| • Ophthalmic infections                                                |                                                                  |
| • Anthrax, including inhalational anthrax (post-exposure)              |                                                                  |
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- Alternative treatment for selected infections when penicillin is contraindicated
- Adjunctive therapy in acute intestinal amebiasis
- Adjunctive therapy in severe acne
- Prophylaxis of malaria

Doryx MPC is not substitutable on a mg per mg basis with other oral doxycycline products.

Dosage in Pediatric Patients
For all pediatric patients weighing less than 45 kg with severe or life threatening infections (e.g., anthrax, Rocky Mountain spotted fever), the recommended dosage of Doryx MPC is 2.6 mg per kg of body weight administered every 12 hours. Pediatric patients weighing 45 kg or more should receive the adult dose.

For pediatric patients with less severe disease (greater than 8 years of age and weighing less than 45 kg), the recommended dosage schedule of Doryx MPC is 5.3 mg per kg of body weight divided into two doses on the first day of treatment, followed by a maintenance dose of 2.6 mg per kg of body weight (given as a single daily dose or divided into twice daily doses). For pediatric patients weighing over 45 kg, the usual adult dose should be used.