Clinical Policy: Doxycline (Doryx, Oracea)

Reference Number: PA.CP.PMN.79
Effective Date: 01/18
Last Review Date: 04/18

Coding Implications
Revision Log

Description
Doxycycline (Acticlate, Doryx®, Doryx® MPC, Oracea®) is a tetracycline-class drug.

FDA approved indication
Doryx/Doryx MPC is indicated for

- Rickettsial infections
- Sexually transmitted infections
- Respiratory tract infections
- Specific bacterial infections
- Ophthalmic infections
- Anthrax, including inhalational anthrax (post-exposure)
- Alternative treatment for selected infections when penicillin is contraindicated
- Adjunctive therapy in acute intestinal amebiasis and severe acne
- Prophylaxis of malaria

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.

Limitations of Use: 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. Efficacy of Oracea beyond 16 weeks and safety beyond 9 months have not been established. Oracea has not been evaluated for the treatment of the erythematous, telangiectatic, or ocular components of rosacea.

Policy/Criteria
Provider must submit documentation (including office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of Pennsylvania Health and Wellness® that Acticlate, Doryx, Doryx MPC, or Oracea is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Rosacea (must meet all):

1. Diagnosis of rosacea with inflammatory lesions (papules and pustules);
2. Request is for Oracea;
3. Age ≥18 years;

4. Member experienced clinically significant adverse effects to immediate-release doxycycline or has contraindication(s) to the excipients in immediate-release doxycycline;
5. Failure of ≥ 4 week trial of one additional PDL oral tetracycline antibiotic, unless clinically significant adverse effects are experienced;
6. Dose does not exceed 40 mg/day (1 capsule/day).

Approval duration: 16 weeks

B. Acne Vulgaris (must meet all)**:**

1. Diagnosis of acne vulgaris;
2. Request is for Acticlate, Doryx or Doryx MPC;
3. Member experienced clinically significant adverse effects to immediate-release doxycycline or has contraindication(s) to the excipients in immediate-release doxycycline;
4. Failure of ≥ 4 week trial of one additional PDL oral tetracycline antibiotic, unless clinically significant adverse effects are experienced;
5. Dose does not exceed:
    a. Acticlate, Doryx: 300 mg/day;
    b. Doryx MPC: 240 mg/day.

Approval duration: 3 months

C. Prophylaxis of Malaria (must meet all)**:**

1. Prescribed for malaria prophylaxis;
2. Request is for Acticlate, Doryx or Doryx MPC;
3. Member experienced clinically significant adverse effects to immediate-release doxycycline or has contraindication(s) to the excipients in immediate-release doxycycline;
4. No documentation of hypersensitivity to tetracyclines;
5. Dose does not exceed:
    a. Acticlate, Doryx: 100 mg per day;
    b. Doryx MPC: 120 mg per day.

Approval duration: 4 months or duration of travel and up to 4 weeks after member leaves the malarious area (whichever is less)

D. Other FDA Approved Indications for Acticlate, Doryx/Doryx MPC (must meet all)**:**

1. Prescribed for the treatment of one of the following conditions or diseases (refer to Appendix B for conditions or diseases that are applicable):
    a. Rickettsial infections;
    b. Sexually transmitted infections;
    c. Respiratory tract infections;
    d. Specific bacterial infections;
    e. Ophthalmic infections;
    f. Anthrax, including inhalational anthrax (post-exposure);
    g. Selected infections when penicillin is contraindicated;
    h. Acute intestinal amebiasis;
2. Request is for Acticlate, Doryx or Doryx MPC;

3. Member experienced clinically significant adverse effects to immediate-release doxycycline or has contraindication(s) to the excipients in immediate release doxycycline;
4. Failure of one additional PDL oral tetracycline antibiotic, unless clinically significant adverse effects are experienced *or* the other PDL tetracycline antibiotics are not indicated for the member's diagnosis;
    5. Dose does not exceed:
        a. Acticlate, Doryx: 300 mg/day;
        b. Doryx MPC: 240 mg/day.
6. .

Approval duration: 60 days or duration of request (whichever is less)

E. Other diagnoses/indications

1. Refer to PA.CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Rosacea (must meet all)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Request is for Oracea;
3. Documentation of positive response to therapy;
4. Member has not received Oracea daily for ≥ 16 weeks;
5. Dose does not exceed 40 mg/day (1 capsule/day).

Approval duration: up to 16 weeks of treatment (total)

B. Acne Vulgaris (must meet all)**:**

1. Request is for Acticlate, Doryx/Doryx MPC;
2. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
3. Documentation of positive response to therapy.
4. If request is for a dose increase, new dose does not exceed:
    a. Acticlate, Doryx: 300 mg/day;
    b. Doryx MPC: 240 mg/day.

Approval duration: 3 months

C. Other Indications for Acute Infections and Malaria Prophylaxis (must meet all)**:**

1. Therapy for **Acticlate** or Doryx/Doryx MPC may not be renewed. Member must meet initial approval criteria for approval of **Acticlate** or Doryx/Doryx MPC.or the Continuity of Care policy (PA.LTSS.PHAR.01) applies

Approval duration: N/A

D. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

Approval duration: 3 months or duration of request (whichever is less)

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – PA.CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
PDL: preferred drug list
N/A: not applicable

Appendix B: Other FDA Approved Indications for Doryx/Doryx MPC

FDA approved indications	**Applicable conditions or diseases**
Rickettsial infections	Rocky Mountain spotted fever, typhus fever and the typhus group, Q fever, rickettsialpox, and tick fevers caused by Rickettsiae
Sexually transmitted infections	Uncomplicated urethral, endocervical or rectal infections caused by Chlamydia trachomatis Nongonococcal urethritis caused by Ureaplasma urealyticum Lymphogranuloma venereum caused by Chlamydia trachomatis Granuloma inguinale caused by Klebsiella granulomatis Uncomplicated gonorrhea caused by Neisseria gonorrhoeae Chancroid caused by Haemophilus ducreyi.
Respiratory tract infections	Respiratory tract infections caused by Mycoplasma pneumoniae Psittacosis (ornithosis) caused by Chlamydophila psittaci Doxycycline is indicated for treatment of infections caused by the following micro- organisms, when bacteriological testing indicates appropriate susceptibility to the drug: Respiratory tract infections caused by Haemophilus influenzae Respiratory tract infections caused by Klebsiella species Upper respiratory infections caused by Streptococcus pneumoniae
Specific bacterial infections	Relapsing fever due to Borrelia recurrentis 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 Doxycycline is indicated for treatment of infections caused by the following gram- negative microorganisms, when bacteriological testing indicates appropriate susceptibility to the drug: Escherichia coli, Enterobacter aerogenes, Shigella species, Acinetobacter species, urinary tract infections caused by Klebsiella species
Ophthalmic infections	Trachoma caused by Chlamydia trachomatis Inclusion conjunctivitis caused by Chlamydia trachomatis
Anthrax including inhalational anthrax (post-exposure)	Anthrax due to Bacillus anthracis, including inhalational anthrax (post-exposure)
Alternative treatment for selected infections when penicillin is contraindicated	Syphilis caused by Treponema pallidum Yaws caused by Treponema pallidum subspecies pertenue Vincent's infection caused by Fusobacterium fusiforme Actinomycosis caused by Actinomyces israelii Infections caused by Clostridium species
Adjunctive therapy for acute intestinal amebiasis	N/A

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Acne vulgaris and other FDA approved indications	Doryx *Adults*: The usual dose of oral doxycycline 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. *For 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	Based on weight and indication.

	Doryx MPC *Adults:* The usual dosage is 240 mg on the first day of treatment (administered 120 mg every 12 hours) followed by a maintenance dose of 120 mg daily. In the management of more severe infections (particularly chronic infections of the urinary tract), 120 mg every 12 hours is recommended. *Pediatrics:* 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 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 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. See Full Prescribing Information for additional indication specific dosage information	
Malaria prophylaxis	Doryx *Adults:* The recommended dose is 100 mg daily. *For children over 8 years of age:* The recommended dose is 2 mg/kg given once daily up to the adult dose. Doryx MPC *Adults:* The recommended dose is 120 mg daily. *For pediatric patients 8 years of age and older*: The recommended dosage is 2.4 mg per kg of body weight administered once daily. *Pediatric patients weighing 45 kg or more*: should receive the adult dose**.** Prophylaxis should begin 1 or 2 days before travel to the malarious area. Prophylaxis should be continued daily during travel in the malarious area and for 4 weeks after the traveler leaves the malarious area.	Doryx 100 mg/day Doryx MPC Adults, adolescents, and children 8 years and older weighing 45 kg or more: 120 mg/day Children 8 years and older and adolescents weighing less than 45 kg: 2.4 mg/kg/dose/day
Rosacea	Oracea	40 mg/day

	Adults: 40 mg orally once daily	

VI. Product Availability

Drug	Availability
Doryx	Delayed-release tablets: 50 mg, 200 mg
Doryx MPC	Delayed-release tablets: 120 mg
Oracea	Capsules: 40 mg

VII. References

1. Oracea Prescribing Information. Fort Worth, TX: Galderma Laboratories, L.P.; December 2014. Available at: www.oracea.com. Accessed January 11, 2017.
2. Doryx Prescribing Information. Greenville, NC: Mayne Pharma; July 2015. Available at: www.doryx.com. Accessed January 29, 2018.
3. Doryx MPC Prescribing Information. Greenville, NC: Mayne Pharma; May 2018. Available at: https://dailymed.nlm.nih.gov/dailymed/. Accessed January 29, 2018.
4. Acticlate Prescribing Information. Exton, PA: Aqua Pharmacueticals; October 2017. Available at: https://dailymed.nlm.nih.gov/dailymed/. Accessed January 30, 2018.
5. Schaller M, Almeida LM, Bewley A, et al. Rosacea treatment update: recommendations from the global ROSacea COnsensus (ROSCO) panel. Br J Dermatol. 2017 Feb;176(2):465-471.
6. Oge LK, Muncie HL, Phillips-Savoy AR. Rosacea: Diagnosis and Treatment. Am Fam Physician. 2015;92(3):187-196.
7. Del Rosso JQ, Thiboutot D, Gallo R. Consensus Recommendations from the American Acne & Rosacea Society on the Management of Rosacea, Part 5: A Guide on the Management of Rosacea. Cutis. 2014 March;93(3):134-138.
8. Zaenglein AL, Pathy AL, Schlosser BJ, et al. Guidelines of care for the management of acne vulgaris. J Am Acad Dermatol. 2016;74(5):945-973.
9. Arguin \PM, Tan KR. Chapter 3. Infectious diseases related to travel. Malaria. In. Centers for Disease Control and Prevention. 2014 Yellow Book - Traveler's Health. Atlanta: U.S. Department of Health and Human Services, Public Health Service. 2014. Available at: http://wwwnc.cdc.gov/travel/yellowbook/2014/chapter-3-infectious-diseases-related-to-travel/malaria.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2018 annual review: added Acticlate to the policy; Removed criteria related to hypersensitivity to tetracyclines per safety guidance; Rosacea: added age requirement; removed criteria related to topical treatments; Acne vulgaris: removed criteria related to topical treatments; added max dose; Other FDA approved indications: added max dose. References reviewed and updated.	1.29.18	