Clinical Policy: Doxycycline Hyclate (Acticlate, Doryx), Doxycycline (Oracea)

Reference Number: CP.PMN.79
Effective Date: 06.01.17
Last Review Date: 05.25
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

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

FDA Approved Indication(s)

Acticlate and Doryx/Doryx MPC are 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.

Limitation(s) of use:

- The Oracea formulation of doxycycline has not been evaluated in the treatment or prevention of infections. Do not use Oracea 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. Oracea has not been evaluated for the treatment of the erythematous, telangiectatic, or ocular components of rosacea.
- To reduce the development of drug-resistant bacteria and maintain the effectiveness of Acticlate, Doryx, and Doryx MPC, these agents should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Acticlate, Doryx, Doryx MPC, doxycycline delayed release capsule, doxycycline hyclate delayed-release tablets, and Oracea are **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 doxycycline delayed release capsule (Oracea);
3. Age ≥ 18 years;
4. If request is for brand Oracea, member must use doxycycline delayed release capsule (generic Oracea), unless contraindicated or clinically significant adverse effects are experienced;
5. Failure of immediate-release doxycycline, unless contraindicated or clinically significant adverse effects are experienced;
6. Failure of ≥ 4-week trial of one additional preferred oral tetracycline antibiotic (e.g., immediate-release minocycline), unless contraindicated or clinically significant adverse effects are experienced;
7. Dose does not exceed both of the following (a and b):
   a. 40 mg per day;
   b. 1 capsule per day.

Approval duration: 16 weeks

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

1. Diagnosis of acne vulgaris;
2. Request is for Acticlate, doxycycline hyclate delayed-release tablets (Doryx), or Doryx MPC;
3. Member must use immediate-release doxycycline, unless contraindicated or clinically significant adverse effects are experienced;
4. Failure of a ≥ 4-week trial of one additional preferred oral tetracycline antibiotic (e.g., immediate-release minocycline), unless clinically significant adverse effects are experienced or all are contraindicated;
5. Dose does not exceed:
   a. Acticlate, doxycycline hyclate delayed-release tablets (Doryx): 200 mg per day;
   b. Doryx MPC: 240 mg per day.

Approval duration: 3 months

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

1. Prescribed for malaria prophylaxis;
2. Request is for Acticlate, doxycycline hyclate delayed-release tablets (Doryx), or Doryx MPC;
3. Member must use immediate-release doxycycline, unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed:
   a. Acticlate, doxycycline hyclate delayed-release tablets (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. FDA-Approved Acute Infection Indications for Acticlate, doxycycline hyclate delayed-release tablets (Doryx), Doryx MPC (must meet all)**:**

1. Prescribed for the treatment of one of the following conditions or diseases (*refer to Appendix D 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, doxycycline hyclate delayed-release tablets (Doryx), or Doryx MPC;
3. Member must use immediate-release doxycycline, unless contraindicated or clinically significant adverse effects are experienced;
4. Failure of one additional preferred oral tetracycline antibiotic (e.g., immediate-release minocycline), unless clinically significant adverse effects are experienced or the other preferred tetracycline antibiotics are not indicated for the member's diagnosis;
5. Dose does not exceed:
   a. Acticlate, doxycycline hyclate delayed-release tablets (Doryx): 200 mg per day;
   b. Doryx MPC: 240 mg per day.

Approval duration: 60 days or duration of request, whichever is less

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Request is for doxycycline delayed release capsule (Oracea);
3. Member is responding positively to therapy;
4. If request is for brand Oracea, member must use doxycycline delayed release capsule (generic Oracea), unless contraindicated or clinically significant adverse effects are experienced;
5. Member has not received doxycycline delayed release capsule (Oracea) daily for > 16 weeks;
6. If request is for a dose increase, new dose does not exceed both of the following (a and b):
   a. 40 mg per day;
   b. 1 capsule per day.

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

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Request is for Acticlate, doxycycline hyclate delayed-release tablets (Doryx), or Doryx MPC;
3. Member is responding positively to therapy;
4. If request is for a dose increase, new dose does not exceed:
   a. Acticlate, doxycycline hyclate delayed-release tablets (Doryx): 200 mg per day;
   b. Doryx MPC: 240 mg per day.

Approval duration: 3 months

C. Prophylaxis of Malaria and FDA-Approved Acute Infection Indications for Acute Infections

1. Re-authorization is not permitted. Members must meet the initial approval criteria.

Approval duration: Not applicable

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):

a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
doxycycline (Vibramycin®)	Acne vulgaris, adults: 100 mg PO every 12 hrs on day 1, followed by a maintenance dose of 100 PO QD Acne vulgaris, children 8 years and older and adolescents weighing less than 45 kg: 2.2 mg/kg/dose PO every 12 hours on day 1, then 2.2 mg/kg/dose PO QD Rosacea: 40 mg or 50 mg PO QAM Malaria (off label): 100 mg PO BID for 7 days See Full Prescribing Information for additional indication specific dosage information.	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
minocycline (Minocin)	Acne vulgaris, adults: 200 mg PO initially, then 100 mg PO every 12 hours. Alternatively, if more frequent oral doses are preferred, 100 to 200 mg PO initially, then 50 mg PO every 6 hours. Acne vulgaris, children ≥ 8 years and adolescents: 4 mg/kg PO (max: 200 mg) initially, then 2 mg/kg/dose PO every 12 hours (max: 100 mg/dose) as adjunctive therapy See Full Prescribing Information for additional indication specific dosage information	200 mg/day
tetracycline	Acne vulgaris, adult: 1 gram PO in divided doses, then decrease slowly to 125 to 500 mg PO daily or every other day. Acne vulgaris, children≥ 9 years and adolescents: 1 g/day PO in divided doses, then decrease slowly to 125 to 500 mg PO QD or QOD Rosacea: 250 to 1,500 mg PO QD Malaria (off label): 250 mg PO four times daily for 7 days. See Full Prescribing Information for additional indication specific dosage information.	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): hypersensitivity to any of the tetracyclines.
- Boxed warning(s): none reported

Appendix D: Other FDA-Approved Acute Infection Indications for Doryx/Doryx MPC and Acticlate

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

FDA-approved indications	Applicable conditions or diseases
	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	Not applicable

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Doxycycline hyclate (Acticlate), doxycycline hyclate delayed-release (Doryx, Doryx MPC)	All indications listed in the FDA-approved indications section	Acticlate *Adults:* 200 mg PO on the first day of treatment (administered 100 mg every 12 hours) followed by a maintenance dose of 100 mg PO daily. In the management of more severe infections (particularly chronic infections of the urinary tract), 100 mg PO every 12 hours is recommended. *For all pediatric patients weighing less than 45 kg with severe or life-threatening infections (e.g., anthrax, Rocky Mountain spotted fever):* 2.2 mg per kg of body weight administered every 12 hours PO. *For pediatric patients with less severe disease (greater than 8 years of age and weighing less than 45 kg):* 4.4 mg per kg of body weight PO divided into two doses on the first day of treatment, followed by a maintenance dose of 2.2 mg per kg of body weight (given as a single daily dose or divided into two doses) PO. *For pediatric patients weighing over 45 kg:* the usual adult dose should be used. Doryx *Adults:* 200 mg PO on the first day of treatment (administered 100 mg every 12 hours) followed by a maintenance dose of 100 mg PO daily. In the management of more severe infections (particularly chronic infections of the urinary tract), 100 mg every 12 hours PO is recommended. *For children above eight years of age:* The recommended dosage schedule for children weighing 45 kg or less is 4.4 mg/kg of body weight PO 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 PO on subsequent days. For more severe infections up to 2.2 mg/kg of body weight administered every 12 hours may be used.	200 mg/day Doryx MPC: 240 mg/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
		For children over 45 kg, the usual adult dose should be used. Doryx MPC *Adults:* 240 mg PO 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 PO is recommended. *For all pediatric patients weighing less than 45 kg with severe or life threatening infections (e.g., anthrax, Rocky Mountain spotted fever):* 2.6 mg per kg of body weight administered PO every 12 hours. *For pediatric patients with less severe disease (greater than 8 years of age and weighing less than 45 kg):* 5.3 mg per kg of body weight divided into two doses on the first day of treatment PO, 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) PO. *For pediatric patients weighing over 45 kg:* the usual adult dose should be used.	
Doxycycline capsule (Oracea)	Inflammatory lesions (papules and pustules) of rosacea	40 mg PO QD	40 mg/day

VI. Product Availability

Drug Name	Availability
Doxycycline hyclate (Acticlate)	Tablets: 75 mg, 150 mg Generic: 20 mg, 50 mg, 75 mg, 100 mg, 150 mg
Doxycycline hyclate delayed-release tablets (Doryx, Doryx MPC)	Delayed-release tablets: 50 mg, 80 mg, 200 mg Delayed-release tablets (MPC): 60 mg, 120 mg Generic: 50 mg, 75 mg, 80 mg, 100 mg, 150 mg, 200 mg
Doxycycline (Oracea)	Delayed-release capsule: 40 mg

VII. References

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11. Del Rosso JQ, Tanghetti E, Webster G. Update on the Management of Rosacea from the American Acne & Rosacea Society. J Clin Aesthet Dermatol. 2019;12(6):17-24.
12. Reynolds RV, Yeung H, Cheng CE, et al. Guidelines of care for the management of acne vulgaris. J Am Acad Dermatol. 2024 May; 90(5): 1006.e1-1006.e30.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2021 annual review: no significant changes; updated IR doxycycline prior trial requirement to "must use" language; revised HIM.PHAR.21 to HIM.PA.154; adjusted max dose of Acticlate and Doryx to match labeling for these two products; references reviewed and updated.	03.01.21	05.21
2Q 2022 annual review: no significant changes; references reviewed and updated.	02.14.22	05.22

Reviews, Revisions, and Approvals	Date	P&T Approval Date
RT4: Doryx MPC 60 mg strength added to policy. Template changes applied to other diagnoses/indications and continued therapy section.	08.30.22	
2Q 2023 annual review: no significant updates; references reviewed and updated.	02.14.23	05.23
For rosacea, added requirement that member must use delayed release doxycycline (generic Oracea).	07.12.23	
2Q 2024 annual review: no significant changes; references reviewed and updated.	01.10.24	05.24
2Q 2025 annual review: no significant changes; added references to generic Oracea and Doryx; references reviewed and updated.	01.22.25	05.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible

for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.