Clinical Policy Title:	doxycycline
Policy Number:	RxA.004
Drug(s) Applied:	Acticlate®
Original Policy Date:	02/07/2020
Last Review Date:	01/17/2022
Line of Business Policy Applies to:	All lines of business

Background

Doxycycline (Acticlate®) is a tetracycline-class drug. It 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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
doxycycline hyclate (Acticlate®)	All indications listed in the FDA-approved indications section	Acticlate® • Adults: 200 mg orally on the first day of treatment (administered 100 mg every 12 hours) followed by a maintenance dose of 100 mg orally daily. In the management of more severe infections (particularly chronic infections of the urinary tract), 100 mg orally 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 orally.	200 mg/day

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
		• 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 orally 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) orally. • For pediatric patients weighing over 45 kg: the usual adult dose should be used.	

Dosage Forms

- doxycycline hyclate (Acticlate®):
  - Tablets: 75 mg, 150 mg
  - Capsules: 75 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. **Initial Approval Criteria**

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

1. Diagnosis of acne vulgaris;
2. Medical justification supports inability to use immediate-release doxycycline (e.g., member experienced clinically significant adverse effects or has contraindication(s) to the excipients in immediate-release doxycycline);
3. Failure of at least 4-week trial of one additional preferred oral tetracycline antibiotic, unless clinically significant adverse effects are experienced;
4. Dose does not exceed 200 mg/day;

Approval duration

Commercial: 3 months

Medicaid: 3 months

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

1. Prescribed for malaria prophylaxis;
2. Medical justification supports inability to use immediate-release doxycycline (e.g., member experienced clinically significant adverse effects or has contraindication(s) to the excipients in immediate-release doxycycline);
3. Dose does not exceed 100 mg/day;

Approval duration

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

Medicaid: 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® (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. Medical justification supports inability to use immediate-release doxycycline (e.g., member experienced clinically significant adverse effects or has contraindication(s) to the excipients in immediate release doxycycline);
3. 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;
4. Dose does not exceed 200 mg/day;

Approval duration

Commercial: 2 months

Medicaid: 2 months

II. **Continued Therapy Approval**

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

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 200 mg/day;

Approval duration

Commercial: 3 months

Medicaid: 3 months

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

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

Approval duration

Not applicable.

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

FDA: Food and Drug Administration

APPENDIX B: Therapeutic Alternatives

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Maximum Dose
doxycycline (Vibramycin®)	Adults: 200 mg orally on the first day of treatment (administered 100 mg every 12 hours) followed by a maintenance dose of 100 mg/day. See Full Prescribing Information for additional indication specific dosage information. <u>Rosacea:</u> 40 mg or 50 mg orally once daily.	300 mg/day
minocycline	Adults: 200 mg orally initially, then 100 mg orally every 12 hours. Alternatively, if more frequent oral doses are preferred, 100 to 200 mg orally initially, then 50 mg orally every 6 hours.	300 mg on day 1, then 200 mg/day
tetracycline	Adults: 500 mg orally twice daily or 250 mg four times daily. See Full Prescribing Information for additional indication specific dosage information.	2 gram/day

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

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Hypersensitivity to doxycycline or other tetracyclines.

- Boxed Warning(s):
  - None reported.

*Contraindications listed reflect direct statements made in the manufacturer's package insert; for additional uses, warnings, and precautions, refer to clinical guidelines.

APPENDIX D: General Information

Other FDA-approved acute infection indications for 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 Rickettsia
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

FDA-Approved Indications	Applicable Conditions or Diseases
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

References

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Review/Revision History	Review/Revision Date	P&T Approval Date
Policy was established	01/2020	02/07/2020
2Q2020 P&T Review; No updates, references reviewed and updated	04/2020	05/20/2020
Policy was reviewed: 1. Clinical policy title table was updated. 2. Dosing information section was updated to consolidate dosing regimen for Acticlate® and Doryx®. 3. Dosage forms section was updated. 4. Added "one of the following" to maximum dosing criteria in initial and continued therapy criteria. 5. Continued therapy approval criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…". 6. Approval duration sections were updated for initial and continued therapy approval. For I.A, to 4 months from 16 weeks, for I.D to 2 months from 60 days or duration of request, whichever is less, and for II.A, 4 months from up to 16 weeks of treatment (total). 7. Appendix B standard verbiage was updated to "Below are suggested therapeutic alternatives…". 8. References were updated.	02/01/2021	03/09/2021
Policy was reviewed: 1. Statement about provider sample ''The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. 2. Drug(s) Applied, Background, Dosing Information, Dosage forms, Clinical Policy , Appendix C remove Doryx®, Doryx® MPC, Oracea® as they no longer require Prior Authorization. 3. Initial Approval Criteria, I.B.5.a, I.C.4.a,	11/18/2021	01/17/2022

I.D.5.a: Updated dosing criteria from Acticlate®230 mg/day to Acticlate®200 mg/day. 4. Continued Therapy Approval Criteria II.A.1 and II.B.1 were rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 5. Continued Therapy Approval, II.B.4.a: Updated dosing criteria from Acticlate® 300 mg/day to Acticlate® 200 mg/day. 6. Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 7. Disclaimer about contraindications," Contraindications listed reflect statements made in the manufacturer's package insert.." was added to Appendix C. 8. References were reviewed and updated.		