Clinical Policy: Infectious Disease Agents: Antibiotics - Macrolides

Reference Number: OH.PHAR.PPA.66
Effective Date: 01/01/2020
Last Review Date: 01/2022
Line of Business: Medicaid

Coding Implications
Revision Log

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

Description:

INFECTIOUS DISEASE AGENTS: MACROLIDES - ORAL

NO PA REQUIRED "PREFERRED"	PA REQUIRED "NON-PREFERRED"
AZITHROMYCIN tablets and suspension (generic of Zithromax®) CLARITHROMYCIN ER (generic of Biaxin XL®) CLARITHROMYCIN tablets and suspension (generic of Biaxin®)	ERYPED® (erythromycin ethylsuccinate) ERYTHROCIN STEARATE® (erythromycin stearate) ERYTHROMYCIN BASE ERYTHROMYCIN ETHYLSUCCINATE ERY-TAB® (erythromycin base DR) ZMAX™ (azithromycin ER) for oral suspension

FDA Approved Indication(s):
Macrolides are indicated for the treatment of:

- amebiasis
- bacterial conjunctivitis
- bacterial colonization eradication
- bowel preparation
- bronchitis
- cervicitis
- chancroid
- chlamydia infection
- community-acquired pneumonia
- diphtheria
- erythrasma
- gonorrhea
- Legionnaire's disease
- listeriosis
- lower respiratory tract infections
- Mycobacterium avium complex infection
- non-gonococcal urethritis (NGU)
- otitis media
- pelvic inflammatory disease (PID)
- pertussis
- pharyngitis

- pneumonia
- proctitis
- sinusitis
- skin and skin structure infections
- syphilis
- tonsillitis
- upper respiratory tract infections
- urethritis

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 Buckeye Health Plan, an affiliate of Centene Corporation®, that EryPed, Erythrocin Stearate, Erythromycin, and Zmax are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. PA Required Agents (must meet all)**:**

1. FDA-approved or supported by standard pharmacopeias;
2. Member must meet labeled age requirements for the medication;
3. The member meets one of the following (a, b, or c):
   a. Documentation that the infection is caused by an organism resistant to medications not requiring prior approval (note diagnosis and any culture and sensitivity reports);
   b. Documentation that there have been therapeutic failures to no less than a 3-day trial of at least one medication not requiring prior approval UNLESS there is a reason the member cannot be changed to a preferred medication. Acceptable reasons include:
      - Allergies to all medications not requiring prior approval.
      - Contraindication to or drug-to-drug interaction with medications not requiring prior approval.
      - History of unacceptable/toxic side effects to medications not requiring prior approval.
   c. Documentation that the member is completing a course of therapy with a medication requiring prior approval, which was initiated in the hospital.

Approval duration: For the date of service only; no refills**.**

B. Other diagnoses/indications:

1. There are no pharmacy and therapeutic committee approved off-label use criteria for the diagnosis;
2. Use is supported by one of the following (a, b, or c):
   a. The National Comprehensive Cancer Network (NCCN) Drug Information and Biologics Compendium level of evidence 1 or 2A;

b. Evidence from at least two high-quality, published studies in reputable peer-reviewed journals or evidence-based clinical practice guidelines that provide all of the following (i – iv):
   i. Adequate representation of the member's clinical characteristics, age, and diagnosis;
   ii. Adequate representation of the prescribed drug regimen;
   iii. Clinically meaningful outcomes as a result of the drug therapy in question;
   iv. Appropriate experimental design and method to address research questions;
c. Micromedex DrugDex® with strength of recommendation Class I, IIa, or IIb;

3. Prescribed by or in consultation with an appropriate specialist for the diagnosis;
4. Failure of an adequate trial of at least two FDA-approved drugs for the indication and/or drugs that are considered the standard of care, when such agents exist for the same indication at maximum indicated doses, unless no such drugs exist, at maximum indicated doses, unless contraindicated or clinically significant adverse effect are experienced;
5. Dosing regimen and duration are within dosing guidelines recommended by clinical practice guidelines and/or medical literature.

Approval duration: For the date of service only; no refills**.**

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

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.PMN.53 for Medicaid or evidence of coverage documents.

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
ER: Extended Release
FDA: Food and Drug Administration
NGU: Non-Gonococcal Urethritis
PA: Prior Authorization
PID: Pelvic Inflammatory Disease

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
azithromycin (Zithromax)	**Mild to moderate acute bacterial exacerbations of chronic bronchitis in patients with COPD** 500 mg once daily for 3 days or 500 mg on first day of therapy, followed by 250 mg once daily for 4 days.	500 mg/day is FDA-approved dosage; however, doses up to 1,200 mg/day are used off-label; 2 g when given as single dose.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
azithromycin (Zithromax) - continued	**Community-acquired pneumonia (CAP)** 500 mg on day 1, followed by 250 mg once daily for at least 5 days. **Uncomplicated skin and skin structure infections** 500 mg on first day of therapy, followed by 250 mg once daily for 4 days. **Uncomplicated gonorrhea** 1 g as a single dose plus ceftriaxone 250 mg IM as a single dose **Mycobacterium avium complex infection in HIV-infected patients** 500 to 600 mg once daily plus ethambutol. **Primary Mycobacterium avium complex prophylaxis in HIV-infected patients** 1,200 mg once weekly or 600 mg twice weekly. **Acute bacterial sinusitis** 500 mg once daily for 3 days.	500 mg/day is FDA-approved dosage; however, doses up to 1,200 mg/day are used off-label; 2 g when given as single dose.
clarithromycin Extended Release (Biaxin XL)	**Acute exacerbations of chronic bronchitis** 1000 mg every 24 hours for 7 days. **Community-acquired pneumonia (CAP)** 1,000 mg once daily for at least 5 days. **Sinusitis** 1,000 mg every 24 hours for 14 days.	1 g/day
clarithromycin (Biaxin)	**Acute exacerbations of chronic bronchitis** 250 to 500 mg every 12 hours for 7 to 14 days. **Community-acquired pneumonia (CAP)** 500 mg every 12 hours for at least 5 days. **Sinusitis** 500 mg every 12 hours for 14 days.	1.5 g/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
clarithromycin (Biaxin) - continued	**Uncomplicated skin and skin structure infections** 250 mg every 12 hours for 7 to 14 days. **Mycobacterium avium complex infection in HIV-infected patients** 500 mg twice daily plus ethambutol. **Primary Mycobacterium avium complex prophylaxis in HIV patients** 500 mg twice daily.	1.5 g/day

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):
  - Hepatitis
  - Jaundice
  - Macrolide Hypersensitivity

IV. Dosage and Administration

- Varies by drug product. See FDA approved dosing and administration AND Appendix B.

V. Product Availability

Drug Name	Availability
Azithromycin	Oral suspension: 100 mg/5 mL, 200 mg/5 mL, 1 g single-dose
Azithromycin	Tablets: 250 mg, 500 mg, 600 mg
Clarithromycin	Oral suspension: 125 mg/5 mL, 250 mg/5 mL
Clarithromycin	Tablets: 250 mg, 500 mg
Clarithromycin	Extended-Release Tablets: 500 mg
EryPed	Oral suspension: 200 mg/5 mL, 400 mg/5 mL
Erythrocin Stearate	Tablets: 250 mg
Erythromycin Base	Delayed-Release Capsules: 250 mg
Erythromycin Base	Tablets: 250 mg, 500 mg
Erythromycin Base	Delayed-Release Tablets: 250 mg, 333 mg, 500 mg
Erythromycin Ethylsuccinate	Oral suspension: 200 mg/5 mL, 400 mg/5 mL
Erythromycin Ethylsuccinate	Tablets: 400 mg
Zmax	Oral suspension (extended-release): 2 g

VI. References

- Azithromycin. Clinical Pharmacology. Elsevier. Tampa, FL. Available at https://www.clinicalpharmacology-ip.com. Accessed November 18, 2019.

- Clarithromycin. Clinical Pharmacology. Elsevier. Tampa, FL. Available at https://www.clinicalpharmacology-ip.com. Accessed November 18, 2019.
- Erythromycin. Clinical Pharmacology. Elsevier. Tampa, FL. Available at https://www.clinicalpharmacology-ip.com. Accessed November 18, 2019.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
New policy created.	10.19	N/A
Policy updated.	11.20	N/A
Annual review. Approval duration changed from 28 days to date of service only.	10.21	N/A
ODM Q4 P&T update. Added Erythromycin products to list of non-preferred medications.	01.22	N/A

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.

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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.