Baxdela (delafloxacin)
Policy Number: C16332-A

CRITERIA EFFECTIVE DATES:

ORIGINAL EFFECTIVE DATE	LAST REVIEWED DATE	NEXT REVIEW DUE BY OR BEFORE
7/19/2019	11/18/2020	1/26/2022
J CODE	**TYPE OF CRITERIA**	**LAST P&T APPROVAL/VERSION**
C9462-injection, delafloxacin, 1mg	RxPA	Q1 2021 20210127C16332-A

PRODUCTS AFFECTED:
Baxdela (delafloxacin)

DRUG CLASS:
Fluoroquinolone antibiotic

ROUTE OF ADMINISTRATION:
Oral, Intravenous

PLACE OF SERVICE:
Retail Pharmacy, Buy and Bill
The recommendation is that IV medications in this policy will be for medical benefit coverage and the product is administered in a place of service that is a non-hospital facility based location (i.e., home infusion provider, provider's office, free-standing ambulatory infusion center) unless the therapy/member meets the Site of Care exceptions. (See appendix for excerpt from Specialty Medication Administration Site of Care Policy) the oral medication will be for pharmacy benefit coverage and self-administered.

AVAILABLE DOSAGE FORMS:
Oral tablets: 450 mg, For injection: 300 mg single dose vials

FDA-APPROVED USES:
Baxdela (delafloxacin) is indicated for the treatment of adults with the following infections caused by designated susceptible bacteria:

- Acute Bacterial Skin and Skin Structure Infections (ABSSSI)
- Community-Acquired Bacterial Pneumonia (CABP)

To reduce the development of drug-resistant bacteria and maintain the effectiveness of BAXDELA and other antibacterial drugs, BAXDELA should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria

COMPENDIAL APPROVED OFF-LABELED USES:
None

COVERAGE CRITERIA: INITIAL AUTHORIZATION

DIAGNOSIS:
Acute bacterial skin and skin structure infection (ABSSSI), community-acquired bacterial

pneumonia (CABP)

REQUIRED MEDICAL INFORMATION:

A. ACUTE BACTERIAL SKIN AND SKIN STRUCTURE INFECTION AND COMMUNITY ACQUIRED PNEUMONIA:

1. Documentation member has an infection caused by or strongly suspected to be caused by a type of pathogen and site of infection within the FDA label or compendia supported.
   AND
2. (a) Documentation of inadequate treatment response, intolerance, contraindication or non-susceptibility to a first-line antibiotic treatments, such as a macrolide, fluoroquinolone, beta-lactam, or tetracycline
   OR
   (b) Request is for a continuation of therapy that was started at an in-patient setting (within the last 14 days) and member is at time of request transitioning to an outpatient site of care [DISCHARGE DOCUMENTATION REQUIRED WHICH INCLUDES INFECTIOUS DISEASE PRESCRIBER RECOMMENDED DURATION OF THERAPY; START AND END DATE]
   AND
3. FOR IV REQUESTS ONLY: Member must have medical documentation of medically necessary use of IV Baxdela (delafloxacin) for the current active infection instead of oral Baxdela (delafloxacin)
   AND
4. Provider attestation that member's renal function (eGFR) has been evaluated within the previous 30 days and that the requested dose is appropriate based on member's renal function

DURATION OF APPROVAL:

Up to a total treatment duration of 14 days

QUANTITY:

Dosage, frequency, and total treatment duration must be supported by FDA label or compendia supported dosing for prescribed indication

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with an infectious disease specialist

AGE RESTRICTIONS:

18 years of age or older

CONTINUATION OF THERAPY:

NA: each new infection treatment should be a new review

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Baxdela (delafloxacin) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications include known hypersensitivity to Baxdela or other fluoroquinolones.

Clostridium difficile-associated diarrhea (CDAD) has been reported in users of nearly all systemic antibacterial drugs, including Baxdela, with severity ranging from mild diarrhea to fatal colitis. Treatment with antibacterial agents can alter the normal flora of the colon and may permit overgrowth of C. difficile. If CDAD is suspected or confirmed, ongoing antibacterial use not directed against C. difficile should be discontinued, if possible. Appropriate measures such as fluid and electrolyte management, protein supplementation, antibacterial treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated

Black Box Warning: Serious adverse reactions: Fluoroquinolones are associated with disabling and potentially irreversible serious adverse reactions that have occurred together, including tendinitis and tendon rupture, peripheral neuropathy, and CNS effects. Discontinue delafloxacin immediately and avoid the use of fluoroquinolones in patients who experience any of these serious adverse reactions. Exacerbation of myasthenia gravis: Fluoroquinolones may exacerbate muscle weakness in patients with myasthenia gravis. Avoid delafloxacin in patients with known history of myasthenia gravis.

OTHER SPECIAL CONSIDERATIONS:
Patients with renal impairment (eGFR 15-29 ml/min) should have their IV dose reduced to 200 mg every 12 hours, or 400 mg per day. No adjustment is needed with the oral dosage form.

BACKGROUND:
Patients with renal impairment (eGFR 15-29 ml/min) should have their IV dose reduced to 200 mg every 12 hours, or 400 mg per day. No adjustment is needed with the oral dosage form.

Efficacy
The PROCEED studies were two phase III, multicenter, multinational, double-blind, double- dummy, non-inferiority trials that assessed the efficacy of Baxdela versus vancomycin 15 mg/kg actual body weight plus aztreonam in adults with ABSSSI. Patients in Trial 1 received 300 mg Baxdela via intravenous infusion every 12 hours for five to 14 days. The mean duration of treatment with delafloxacin was 5 days, and 5.5 days in the vancomycin plus aztreonam group. In Trial 2, patients received Baxdela 300 mg via intravenous infusion for six doses then made a mandatory switch to oral Baxdela 450 mg every 12 hours for a total treatment duration of five to 14 days. The primary efficacy outcome for both trials was the clinical response at 48 to 72 hours after treatment was initiated, which was defined as a 20% or greater decrease in lesion size measured at the leading edge of erythema. In Trial 1, 78.2% (259/331) of patients in the Baxdela group had a clinical response at 48 to 72 hours compared to 80.9% (266/329) of patients in the vancomycin plus aztreonam group. In Trial 2, 83.7% (354/423) of patients in the Baxdela group had a clinical response at 48 to 72 hours compared to 80.6% (344/427) of patients in the vancomycin plus aztreonam group. Baxdela met non-inferiority criteria with similar clinical response rates in either treatment arm of both trials. The secondary endpoint was investigator-assessed success, defined as complete or near resolution of signs and symptoms with no further antibacterial needed, at the follow-up visit (Day 14 ± 1) and late follow-up visit (Days 21–28). Success rates were similar between Baxdela and vancomycin plus aztreonam. In Trial 1, the Baxdela group had an 81.6% (270/331) success rate compared to 83.3% (274/329) in the vancomycin plus aztreonam group. In Trial 2, the Baxdela group had an 87.2% (369/423) success rate compared to 84.8% (362/427) in the vancomycin plus aztreonam group.

Safety
Serious adverse reactions occurred in 3/741 (0.4%) of patients treated with Baxdela and in 6/751 (0.8%) of patients treated with vancomycin plus aztreonam. Baxdela was discontinued due to an adverse reaction in 7/741 (0.9%) patients and vancomycin plus aztreonam was discontinued due to an adverse reaction in 21/751 (2.8%) patients. The most commonly reported adverse reactions leading to study discontinuation in the Baxdela arm included urticaria (2/741; 0.3%) and hypersensitivity (2/741; 0.3%). Among both trials, there was one death in the Baxdela treatment arm and three deaths in the vancomycin plus aztreonam arm; none of the deaths were considered related to treatment. Among all patients in the Baxdela treatment arm (N=741), the most common adverse reactions were nausea (8%), diarrhea (8%), headache (3%), transaminase elevations (3%),

and vomiting (2%). Baxdela has a black box warning as fluoroquinolones have been associated with disabling and potentially irreversible serious adverse reactions that have occurred together, including tendinitis and tendon rupture, peripheral neuropathy, and central nervous system effects. Baxdela should be discontinued immediately and fluoroquinolones should be avoided in patients who have experienced these adverse reactions. Baxdela should be avoided in patients with a known history of myasthenia gravis.

APPENDIX:

None

Molina Healthcare, Inc. covers injectable/infused treatment in a hospital outpatient setting or at a hospital-affiliated infusion suite* when the level of care is determined to be medically necessary. Considerations used to determine if an alternative level of care is not suitable may include the following findings:

1. The member is clinically unstable based on documented medical history and susceptible to complication with drug administration (e.g., cardiopulmonary, or renal dysfunction, risk for fluid overload)
2. The requested medication is administered as part of a chemotherapy regimen (e.g., anti-neoplastic agent, colony stimulating factor, erythropoiesis-stimulating agent, anti-emetic) for treatment of cancer or with dialysis
3. The member exhibits physical or cognitive impairment and a capable caregiver is not available to assist with safe administration of prescribed medication in the home
4. It is the patient's first dose of the medication or it is being re-initiated after at least 12 months*
5. The member has experienced adverse events with past administration of the drug and cannot be managed by premedication or resources available at an non-hospital facility based location (NHFBL)
6. Documented history of difficulty establishing and maintaining patent vascular access, or is not a candidate for a mode of long-term vascular access during the duration of prescribed treatment

Note: a hospital outpatient setting or a hospital-affiliated infusion suite is expected to have immediate access to specific services of a medical center/hospital setting, including having emergency resuscitation equipment and personnel (ACLS protocol), emergency services, and inpatient admission or intensive care, if necessary

Documentation Requirements:

Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

REFERENCES:

1. Baxdela Prescribing Information. Melinta Therapeutics, Inc. Lincolnshire, IL. October 2020.
2. Adler A, Chaudhry S, Goldberg T. BaxdelaTM (Delafloxacin): A Novel Fluoroquinolone for the

Treatment of Acute Bacterial Skin and Skin Structure Infections. P T. 2018 Nov;43(11):662-666.
3. Pullman J, Gardovskis J, Farley B, Sun E, Quintas M, Lawrence L, Ling R, Cammarata S; PROCEED Study Group. Efficacy and safety of delafloxacin compared with vancomycin plus aztreonam for acute bacterial skin and skin structure infections: a Phase 3, double-blind, randomized study. J Antimicrob Chemother. 2017 Dec 1;72(12):3471-3480. doi: 10.1093/jac/dkx329.
4. O'Riordan W, McManus A, Teras J, Poromanski I, Cruz-Saldariagga M, Quintas M, Lawrence L, Liang S, Cammarata S; PROCEED Study Group. A Comparison of the Efficacy and Safety of Intravenous Followed by Oral Delafloxacin With Vancomycin Plus Aztreonam for the Treatment of Acute Bacterial Skin and Skin Structure Infections: A Phase 3, Multinational, Double-Blind, Randomized Study. Clin Infect Dis. 2018 Aug 16;67(5):657-666. doi: 10.1093/cid/ciy165.