

Blujepa[®] (gepotidacin)

Policy # 00963

Original Effective Date: 05/01/2026

Current Effective Date: 05/01/2026

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. These services are excluded from coverage under benefits.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Uncomplicated Urinary Tract Infection

Based on review of available data, the Company may consider Blujepa^{®†} (gepotidacin) for the treatment of uncomplicated urinary tract infections (uUTI) to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for Blujepa (gepotidacin) for the treatment of uncomplicated urinary tract infections (uUTI) will be considered when the following criteria are met:

- Patient has a diagnosis of uncomplicated UTI caused by one of the following susceptible microorganisms: *Escherichia coli*, *Klebsiella pneumoniae*, *Citrobacter freundii* complex, *Staphylococcus saprophyticus*, or *Enterococcus faecalis*; AND
- Patient is 12 years of age or older; AND
- Patient is a female weighing at least 40 kg; AND
- Patient has tried and failed (e.g., intolerance or inadequate response) ONE of the following alternatives to which the microorganism is susceptible: ciprofloxacin, fosfomycin, levofloxacin, nitrofurantoin, sulfamethoxazole-trimethoprim or a beta-lactam antibiotic (e.g., amoxicillin-clavulanate, cefdinir, cefpodoxime) unless there is clinical evidence or patient history that suggests the alternatives will be ineffective or cause an adverse reaction to the patient.

*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

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Urogenital Gonorrhea Infection

Based on review of available data, the Company may consider Blujepa (gepotidacin) for the treatment of uncomplicated urogenital gonorrhea to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility for Blujepa (gepotidacin) for the treatment of uncomplicated urogenital gonorrhea will be considered when the following criteria are met:

- Patient has a diagnosis of uncomplicated urogenital gonorrhea; AND
- Patient is 12 years of age or older; AND
- Patient weights at least 45 kg; AND
- Patient has tried and failed (e.g., intolerance or inadequate response) ONE of the following alternatives: ceftriaxone intramuscular injection, cefixime capsules, OR gentamicin intramuscular injection plus oral azithromycin unless there is clinical evidence or patient history that suggests the alternatives will be ineffective or cause an adverse reaction to the patient.

*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of Blujepa (gepotidacin) for the treatment of uUTI when the patient has not tried and failed ciprofloxacin, fosfomycin, levofloxacin, nitrofurantoin, sulfamethoxazole-trimethoprim, OR a beta-lactam antibiotic to be **not medically necessary**.**

Based on review of available data, the Company considers the use of Blujepa (gepotidacin) for the treatment of uncomplicated urogenital gonorrhea when the patient has not tried and failed ceftriaxone intramuscular injection, cefixime capsules, OR gentamicin intramuscular injection plus oral azithromycin to be **not medically necessary**.**

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of Blujepa (gepotidacin) when patient selection criteria are not met (with the exception of those denoted as **not medically necessary****) to be * **investigational**.*

Background/Overview

Blujepa is indicated for the treatment of uncomplicated urinary tract infections (uUTI) caused by susceptible microorganisms in female adult and pediatric patients 12 years of age and older weighing at least 40 kilograms, and for the treatment of uncomplicated urogenital gonorrhea caused by susceptible microorganisms in adult and pediatric patients 12 years of age and older weighing at

least 45 kilograms who have limited or no alternative treatment options (approval for the gonorrhea indication is based on limited clinical safety data). Blujepa contains gepotidacin, a triazaacenaphthylene bacterial type II topoisomerase inhibitor. The recommended dosage for uUTI is 1,500 mg (two 750 mg tablets) taken orally twice daily (approximately 12 hours apart) for 5 days. For uncomplicated urogenital gonorrhea, the recommended dosage is 3,000 mg (four 750 mg tablets) taken orally, followed by a second 3,000 mg dose approximately 12 hours later. Blujepa is supplied as 750 mg tablets and should be taken after a meal. Blujepa should be used only to treat infections that are proven or strongly suspected to be caused by bacteria to reduce the development of drug-resistant bacteria and maintain the effectiveness of Blujepa and other antibacterial drugs. According to the prescribing information, use of Blujepa should be avoided in patients with severe renal impairment (estimated glomerular filtration rate [eGFR] < 30 mL/min, including those receiving dialysis) and in patients with severe hepatic impairment (Child-Pugh Class C).

Uncomplicated UTI

Urinary tract infections (UTIs) are generally classified as either uncomplicated (uUTI) or complicated (cUTI); however, the definitions of these classifications have been inconsistent. In 2025, Infectious Disease Society of America (IDSA) issued new treatment guidelines for cUTIs and revised the classification. According to the update, infection confined to the bladder in afebrile men or women is classified as uncomplicated. Local bladder signs and symptoms associated with a uUTI may include dysuria, urgency, frequency, and suprapubic pain. Systemic signs of illness, such as fever or bacteremia, suggest that the infection has extended beyond the bladder and is thus defined as a complicated UTI. Evidence of renal parenchymal involvement (e.g., costovertebral angle tenderness), or a prostatic abscess, would also demonstrate that the infection has extended beyond the bladder. Subsequent discovery of obstruction in the upper urinary tract, such as from a stone, would render the infection complicated. The guidelines cite that all patients diagnosed with UTI need to have signs or symptoms related to the organisms in the bladder (or spreading beyond the bladder); otherwise, the patient has asymptomatic bacteriuria (ASB) and does not need antibiotic treatment. The guidelines note that the classifications of uncomplicated and complicated UTI are intended to guide management of UTI, not diagnosis.

Therapeutic options for the treatment of uUTI depend upon the bacteria causing the infection, resistance patterns, patient medical history, and allergies. First-line oral agents commonly used for the treatment of acute uUTI include nitrofurantoin 100 mg twice daily for five days, trimethoprim-sulfamethoxazole (TMP-SMX) 160/800 mg twice daily for three days (only if local resistance rates for *E. coli* are below 20% or susceptibility is confirmed), and fosfomycin trometamol as a single 3 gram dose. Pivmecillinam may be considered where available. When these therapies cannot be used, fluoroquinolones (e.g., ofloxacin, ciprofloxacin, and levofloxacin) or beta-lactams (e.g., amoxicillin-clavulanate, cefdinir, cefaclor, and cefpodoxime proxetil) are second-line options. The Infectious Diseases Society of America (IDSA) archived its 2010 guidelines for the treatment of uncomplicated urinary tract infections (UTIs), as new guidelines are under development. The American Urological Association established guidelines for recurrent uUTI in women (2019). For the treatment of symptomatic UTIs in women, use of a first-line therapy (i.e., nitrofurantoin, TMP-SMX, fosfomycin) based on the local antibiogram is recommended.

Uncomplicated urogenital gonorrhea

Gonorrhea, an infection caused by the gram-negative coccus *Neisseria gonorrhoeae*, is a major cause of morbidity among sexually active individuals worldwide. The Centers for Disease Control and Prevention (CDC) has reported gonorrhea as the second most commonly reported bacterial communicable disease in the United States. Genital infections are the most common clinical manifestations; however, *N. gonorrhoeae* can also infect the rectum and pharynx (extragenital infection), and infections at these anatomic sites are often asymptomatic. Rarely, bacteremic spread from a mucosal site can result in disseminated gonococcal infection. *N. gonorrhoeae* may also cause an aggressive conjunctivitis in adults and adolescents, including transmission through nonsexual contact. Clinical presentation varies by anatomic site and patient factors. Urethral infection in males is commonly asymptomatic, though symptomatic disease is more frequent than in female patients; consequently, males may transmit infection without awareness. Clinical manifestations may include dysuria and copious purulent urethral discharge. Acute unilateral epididymitis, with testicular pain and swelling, can occur as a complication. In females, infection is commonly asymptomatic or minimally symptomatic and may not be recognized until complications develop. Symptomatic cervical infection can present with vaginal pruritus and a mucopurulent cervical discharge. Some patients may also have symptomatic involvement of the urethra (dysuria) or perilabial pain. Cervical infection can ascend to involve the upper reproductive tract, resulting in pelvic inflammatory disease (PID); PID can cause tubal scarring and may lead to infertility or ectopic pregnancy.

The CDC's Sexually Transmitted Infections (STI) Treatment Guidelines (2021) recommend ceftriaxone as first-line therapy for uncomplicated gonococcal infections among adolescents and adults. The recommended regimen is ceftriaxone 500 mg administered intramuscularly (IM) in a single dose for persons weighing <150 kg; for persons weighing ≥150 kg, ceftriaxone 1 g IM should be administered as a single dose. If ceftriaxone administration is not available or not feasible, cefixime 800 mg orally in a single dose is recommended. For patients with a cephalosporin allergy, the CDC recommends gentamicin 240 mg IM in a single dose plus azithromycin 2 g orally in a single dose. If chlamydial infection has not been excluded, providers should also treat for chlamydia with doxycycline 100 mg orally twice daily for 7 days.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

In March of 2025, Blujepa was FDA approved for the treatment female adult and pediatric patients 12 years of age and older weighing at least 40 kilograms for the treatment of uncomplicated urinary tract infections (uUTI) caused by the following susceptible microorganisms: *Escherichia coli*, *Klebsiella pneumoniae*, *Citrobacter freundii* complex, *Staphylococcus saprophyticus*, and *Enterococcus faecalis*. In December of 2025, Blujepa received FDA approval for the treatment of uncomplicated urogenital gonorrhea caused by susceptible strains of *Neisseria gonorrhoeae* in adult and pediatric patients 12 years of age and older weighing at least 45 kilograms who have limited or no alternative treatment options. Approval for the treatment of uncomplicated urogenital gonorrhea is based on limited clinical safety data.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

Uncomplicated Urinary Tract Infections

A total of 3,136 female patients with uncomplicated urinary tract infections were randomized in 2 multicenter, parallel-group, double-blind, double-dummy, non-inferiority trials (Trial 1 and Trial 2). Both trials compared Blujepa 1,500 mg (administered orally twice daily with food for 5 days) to nitrofurantoin 100 mg (administered orally twice daily for 5 days). Patients entered the trials with at least 2 symptoms consistent with uUTI (dysuria, frequency, urgency, or lower abdominal pain) and with evidence of urinary nitrite or pyuria. Patients with any medical condition or presentation suggestive of a complicated UTI, or an upper UTI (e.g., pyelonephritis, urosepsis) were excluded. Efficacy was assessed as a composite of clinical cure and microbiological response at the Test-of-Cure (TOC) Visit (study day 10 to 13) in the microbiological ITT nitrofurantoin-susceptible (micro-ITTS) population, which included all patients who received at least 1 dose of study medication, had at least 1 baseline qualifying uropathogen (≥ 10 colony-forming units [CFU]/mL), and excluded patients with organisms not susceptible to nitrofurantoin. Clinical cure was defined as resolution of all 5 signs and symptoms of acute cystitis present at baseline and no new signs and symptoms without the patient receiving other systemic antimicrobials. Microbiological response was defined as having all qualifying uropathogens found at baseline at $\geq 10^5$ CFU/mL reduced to $< 10^3$ CFU/mL without the patient receiving other systemic antimicrobials. Both trials demonstrated non-inferiority of Blujepa to nitrofurantoin for composite response. In Trial 1, the micro-ITTS population consisted of 634 female patients with uUTI (n = 336 BLUJEPa; n = 298 nitrofurantoin). The composite response rate was 51.8% with Blujepa and 47.0% with nitrofurantoin, for a treatment difference of 5.3 percentage points (95% confidence interval [CI]: -2.4,13.0). In Trial 2, the micro-ITTS population consisted of 567 female patients with uUTI (n = 292 Blujepa; n = 275 nitrofurantoin). The composite response rate was 58.9% with Blujepa and 44.0% with nitrofurantoin, for a treatment difference of 14.4 percentage points (95% CI: 6.4 to 22.4).

Uncomplicated Urogenital Gonorrhea

A total of 628 patients with suspected uncomplicated urogenital gonorrhea due to *Neisseria gonorrhoeae* were randomized in an open-label, active-controlled, multicenter, multinational trial. Patients were randomized 1:1 to receive either Blujepa (3,000 mg taken orally followed by a second dose of 3,000 mg approximately 12 hours later), or a combination of a single intramuscular 500 mg dose of ceftriaxone and single 1 gram oral dose of azithromycin. Patients were eligible for enrollment if they were ≥ 12 years old and > 45 kg. Patients with confirmed or suspected complicated or disseminated gonorrhea were excluded from the study. The microbiological intent-to-treat (micro-ITT) population, which included patients who had urogenital *N. gonorrhoeae* isolated at baseline and who were not infected with a strain that was nonsusceptible to ceftriaxone at baseline, consisted of 406 patients (n = 202 Blujepa; n = 204 ceftriaxone/azithromycin). The primary efficacy endpoint was microbiological success as determined by confirmed bacterial eradication of *N.*

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gonorrhoeae at the urogenital body site at the test of cure (TOC) visit (Day 4 to 8) without receipt of other systemic antimicrobials and was assessed in the micro-ITT population. Trial 3 demonstrated non-inferiority of Blujepa to the combination of ceftriaxone and azithromycin. In Trial 3 (micro-ITT population), microbiological success was 92.6% with Blujepa and 91.2% with ceftriaxone/azithromycin, for a treatment difference of -0.1 percentage points (95% CI: -5.6 to 5.5).

References

1. Blujepa (Gepotidacin) [prescribing information]. Durham, NC. GlaxoSmithKline. Updated December 2025.
2. UpToDate. Acute simple cystitis in female adults. Ghanem KG, ed. UpToDate, Wolters Kluwer; Updated January 9, 2026. Accessed March 24, 2026.
3. UpToDate. Clinical manifestations and diagnosis of *Neisseria gonorrhoeae* infection in adults and adolescents. Ghanem KG, ed. UpToDate, Wolters Kluwer; Updated March 6, 2026. Accessed March 24, 2026.
4. Gupta K, Hooton TM, Naber KG, et al. International Clinical Practice Guidelines for the Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women: A 2010 Update by the Infectious Disease Society of America (IDSA) and the European Society for Microbiology and Infectious Diseases. *Clinical Infectious Diseases*. 2011; 52(5): e103-120.
5. Centers for Disease Control and Prevention (CDC). Sexually Transmitted Infections Treatment Guidelines, 2021. Available at <https://www.cdc.gov/std/treatment-guidelines/toc.htm>. Accessed: January 14, 2026.

Policy History

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04/02/2026 Medical Policy Committee review

04/10/2026 Medical Policy Implementation Committee approval. New policy.

Next Scheduled Review Date: 04/2027

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 1. Consultation with technology evaluation center(s);

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2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

****Medically Necessary (or “Medical Necessity”)** - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan’s authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan’s pharmacy benefit.