New Drug Overview

Pivya (pivmecillinam)

PDL Category: Beta-Lactams

Introduction

Disease Background:

- Urinary tract infections (UTI) comprises cystitis and pyelonephritis (infection of the kidney/upper urinary tract) (*Gupta 2026*).
  - An uncomplicated urinary tract infection (uUTI) is an infection of the bladder (cystitis, lower urinary tract) in females who are not pregnant and who do not have functional or anatomical abnormalities in the urinary tract or other comorbidities that may lead to a more challenging infection to treat (*Gupta 2026, Orrange et al 2026*).
  - Pyelonephritis is generally characterized as a complicated UTI (cUTI) in clinical practice; however, its category may vary dependent on the professional organization (*Orrange et al 2026*).
- uUTIs and cUTIs are included as among the most common infections in outpatients overall (*Orrange et al 2026*).
  - UTIs are more common in women than men.
    - Data suggests about 50-60% of women develop a UTI at some point during their life, although prevalence differs by age.
- The common symptoms of cystitis include dysuria, urinary frequency, urinary urgency, and suprapubic pain. In addition, although not as common, gross hematuria may occur (*Orrange et al 2026*).
- Empiric antibiotic treatment is suitable when there is a robust instinct that a nonpregnant female has acute uUTI (*Orrange et al 2026*).
  - Nitrofurantoin is generally listed as a first-line treatment, along with fosfomycin or pivmecillinam.
- Pivya was FDA approved in 2024.

Pharmacology/Usage

- Pivya (pivmecillinam), a penicillin class antibacterial for oral administration, is the pro-drug containing the pivaloyloxymethyl ester of the amidino penicillanic acid, mecillinam. Pivmecillinam is rapidly hydrolyzed to mecillinam, the active antibacterial agent, by non-specific esterases present in blood, gastrointestinal mucosa and other tissues.
  - Mecillinam is a beta-lactam antibacterial drug with a targeted spectrum of activity. It is mainly active against gram-negative bacteria and works by interfering with the biosynthesis of the bacterial cell wall. Unlike the majority of other beta-lactam agents, which preferentially bind gram-negative PBP-1A, -1B, or -3, mecillinam exerts high specificity against penicillin-binding protein 2 (PBP-2) in the gram-negative cell wall

Indications

Table 1. Food and Drug Administration Approved Indications

Indication	Pivya (pivmecillinam)
• For the treatment of female patients 18 years of age and older with uncomplicated urinary tract infections (uUTI) caused by susceptible isolates of *Escherichia coli* (*E. coli*), *Proteus mirabilis*, and *Staphylococcus saprophyticus*. [a]	✔

[a] To reduce the development of drug-resistant bacteria and maintain the effectiveness of Pivya and other antibacterial drugs, Pivya should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

(Prescribing information: Pivya 2025)

- Information on indications, mechanism of action, pharmacokinetics, dosing, safety, and clinical efficacy summary has been obtained from the prescribing information for the individual products, except where noted otherwise.

Dosing and administration

Table 2. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Pivya (pivmecillinam)	Film-Coated Tablets, each containing 185mg pivmecillinam (equivalent to 200mg pivmecillinam HCl)	PO	One tablet three times a day for 3 to 7 days as clinically indicated. Administer with or without food.	• Pivya (pivmecillinam) is a prodrug of mecillinam (the active antibacterial agent). • If a dose is missed, instruct patients to take the dose as soon as possible. Do not double the dose to make up for the missed dose. • Reductions in systemic elimination as well as urinary excretion of mecillinam are anticipated with decreases in renal function. The clinical significance of these changes on efficacy is unknown. The available safety information does not suggest a need for dosage adjustment in renal impairment.

See the current prescribing information for full details.

Clinical Efficacy Summary

- Three controlled clinical trials comparing various Pivya dosing regimens to placebo (Trial 1), to another oral antibacterial drug (Trial 2), or to ibuprofen (Trial 4) assessed the efficacy of pivmecillinam for the treatment of uUTI.
  - Efficacy was assessed in the microbiological intent-to-treat (micro-ITT) population, which included all randomized subjects with a positive baseline urine culture defined as $\geq 10^5$ colony-forming units (CFU)/ml of a uropathogen where CFU count was available and no more than 2 species of microorganisms, regardless of colony count, and no baseline pathogen was non-susceptible to the active comparator.

- The composite response rates (composite endpoint of clinical cure and microbiological response), as well as clinical cure and microbiological response rates of the recommended 185mg TID dosing regimen are presented in the tables below, which were adapted from the prescribing information.

- Trial 1 was a multicenter, randomized, double-blind study in Sweden assessing the efficacy of 3 dosage regimens of Pivya tablets (185mg TID X7 days, 185mg BID X 7 days [not an approved dosing regimen], and 370mg BID X3 days [not an approved dosing regimen]) compared to placebo in women 18 years of age or older with symptoms of uUTI.
  - The trial enrolled patients with a mean age of 45 years with *E. coli* as the most common baseline pathogen.
  - Pivya demonstrated efficacy for the composite response of clinical cure and microbiological response at day 8-10.
    - Clinical cure was defined as no persisting symptoms during and post-therapy.
    - Microbiological response for the initial pathogen at follow-up visits was defined as reduction in the number of bacteria to $<10^3$ CFU/mL.
    - Composite response was achieved in 85/137 (62%) of patients in the Pivya group and 14/134 (10%) in the placebo group at TOC in the micro-ITT population.
- Trial 2 was a multicenter, randomized, double-blinded study in the U.S. evaluating the efficacy and safety of Pivya (185mg TID X3 days) compared to cephalexin 250mg QID for 7 days in females 18 years of age or older with uUTI.
  - The trial enrolled patients with a mean age of 31 years, while 85% were White, and with *E. coli* as the most common baseline pathogen.
  - Clinical cure was defined as no persisting symptoms during and post-therapy.
  - Microbiological response was defined as negative urine culture ($<10^3$ CFU/mL) for the initial pathogen at day 10.
  - Composite response was achieved in 91/127 (72%) of patients in the Pivya group and 100/132 (76%) in the cephalexin group at the TOC in the micro-ITT population.
- Trial 4 was a multicenter, randomized, double-blind, non-inferiority study in Denmark, Norway, and Sweden to assess the safety and efficacy of Pivya (185mg TID X3 days) compared to ibuprofen 600mg TID X3 days in women 18 to 60 years of age with clinical symptoms of uUTI.
  - The trial enrolled patients with a mean age of 29 years with *E. coli* as the most common baseline pathogen.
    - Pivya demonstrated efficacy for the composite response (clinical cure and microbiological response) at TOC (day 14).
      - Clinical cure was defined as the patient reporting no symptoms at day 7 and reporting no symptoms at day 14.
      - Microbiological response was defined as negative urine culture ($<10^3$ CFU/mL) for the initial pathogen at day 14.
      - Composite response was achieved in 69/105 (66%) in the Pivya group and 26/119 (22%) in the ibuprofen group at TOC in the micro-ITT population.
- As discussed above, tables below, adapted from the prescribing information, present the results of the outcomes of the three trials.

Table 3. Efficacy results

	Composite Response Rates (Clinical Cure and Microbiological Response)		
Trial 1	**Pivya, n (%) (N=137)**	**Placebo, n (%) (N=134)**	**Difference**
	85 (62%)	14 (10%)	52%
Trial 2	**Pivya, n (%) (N=127)**	**Cephalexin, n (%) (N=132)**	
	91 (72%)	100 (76%)	-4%

	Composite Response Rates (Clinical Cure and Microbiological Response)		
Trial 1	**Pivya, n (%) (N=137)**	**Placebo, n (%) (N=134)**	**Difference**
Trial 4	**Pivya, n (%) (N=105)**	**Ibuprofen, n (%) (N=119)**	
	69 (66%)	26 (22%)	44%

Table 4. Efficacy results

	Clinical Cure Rates		
Trial 1	**Pivya, n (%) (N=137)**	**Placebo, n (%) (N=134)**	**Treatment Difference**
	87 (64%)	31 (23%)	40%
Trial 2	**Pivya, n (%) (N=127)**	**Cephalexin, n (%) (N=132)**	
	105 (83%)	112 (85%)	-2%
Trial 4	**Pivya, n (%) (N=105)**	**Ibuprofen, n (%) (N=119)**	
	81 (77%)	45 (38%)	39%

Table 5. Efficacy results

	Microbiological Response Rates		
Trial 1	**Pivya, n (%) (N=137)**	**Placebo, n (%) (N=134)**	**Treatment Difference**
	119 (87%)	35 (26%)	61%
Trial 2	**Pivya, n (%) (N=127)**	**Cephalexin, n (%) (N=132)**	
	97 (76%)	106 (80%)	-4%
Trial 4	**Pivya, n (%) (N=105)**	**Ibuprofen, n (%) (N=119)**	
	78 (74%)	64 (54%)	21%

Clinical guidelines

- Infectious Diseases Society of America (IDSA) notes that updated uUTI guidelines are in development. It is unknown whether Pivya will be included in these guidelines (*IDSA website*).
- **IDSA 2024 Guidance on the Treatment of Antimicrobial-Resistant Gram-Negative Infections** (*Tamma et al 2024*)

- Preferred antibiotics for the treatment of uncomplicated cystitis caused by extended-spectrum β-lactamase-producing Enterobacterales (ESBL-E) include nitrofurantoin and trimethoprim-sulfamethoxazole (TMP/SMX).
- Alternatives include ciprofloxacin, levofloxacin, and carbapenems; although effective, use is discouraged when nitrofurantoin or TMP/SMX are active.
- An aminoglycoside (as a single dose) and oral fosfomycin (for *E. coli* only) are also alternative treatments for uUTI caused by ESBL-E.

- **International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America (IDSA) and the European Society for Micobiology and Infectious Disease** (*Gupta et al 2011*).
  - These guidelines are limited to the treatment of UTI in premenopausal, nonpregnant women with no known urological abnormalities or comorbidities.
  - In women with acute uncomplicated cystitis (eg, absence of fever, flank pain, or other suspicion for pyelonephritis), antimicrobials should be considered based on (1) availability, (2) allergy history, and (3) tolerance.
  - Guideline-recommended first-line antibiotics include nitrofurantoin, TMP/SMX DS, fosfomycin, and pivmecillinam. The decision on which agent to use should be individualized.

Safety summary

- **Contraindications:**
  - In patients who have experienced a serious hypersensitivity reaction to Pivya or other beta-lactam antibacterial drugs (eg, penicillins and cephalosporins).
  - In patients with primary or secondary carnitine deficiency resulting from inherited disorders of mitochondrial fatty acid oxidation and carnitine metabolism, and other inborn errors of metabolism.
  - In patients suffering from porphyria as pivmecillinam has been associated with acute attacks of porphyria.

- **Box Warning:** None.

- **Warnings and precautions:**
  - Serious hypersensitivity reactions have been reported in patients treated with Pivya. These reactions are more likely to occur in individuals with a history of penicillin, cephalosporin, or carbapenem hypersensitivity or a history of sensitivity to multiple allergens.
    - Before starting treatment, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, carbapenems, and other beta-lactams because cross-hypersensitivity has been reported.
  - Severe Cutaneous Adverse Reactions (SCAR) including Acute Generalized Exanthematous Pustulosis (AGEP), Drug Reactions with Eosinophilia and Systemic Symptoms (DRESS), Stevens-Johnson Syndrome (SJS), and Toxic Epidermal Necrolysis (TEN) have been reported with Pivya. Monitor patients closely and discontinue Pivya at the first signs or symptoms of SCAR or other signs of hypersensitivity.
  - Clinical manifestations of carnitine depletion may occur with pivalate-containing compounds, including Pivya. No clinical effects of decreased carnitine have been associated with short-term treatment of Pivya. Clinically significant hypocarnitinemia has been observed in patients receiving long term treatment with pivmecillinam. Pivya is not recommended when prolonged antibacterial treatment is necessary. The effects of carnitine concentrations of repeated short-term courses of Pivya are not known.
    - In patients at risk for reductions in serum carnitine (eg, patients with significant renal impairment or decreased muscle mass), consider alternative antibacterial therapies.

    - Avoid concurrent treatment with valproic acid, valproate, or other pivalate-generating drugs due to increased risk of carnitine depletion.
  - Pivya is contraindicated in patients suffering from porphyria as pivmecillinam has been associated with acute attacks of porphyria. These episodes may be life-threatening, and include symptoms and signs such as anxiety, confusion, limb or abdominal pain, hyponatremia, seizures, and muscle weakness.
  - *Clostridioides difficile*-associated diarrhea (CDAD) has been reported for nearly all systemic antibacterial agents, including Pivya, and may range in severity from mild diarrhea to fatal colitis. CDAD must be considered in all patients who present with diarrhea following antibacterial use. Careful medical history is necessary because CDAD has been reported to occur over 2 months after the administration of antibacterial agents.
    - If CDAD is suspected or confirmed, ongoing antibacterial drug use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplement, antibacterial drug treatment of *C. difficile*, and surgical evaluation should be started as clinically indicated.
  - Prescribing Pivya in the absence of a proven or strongly suspected bacterial infection or for prophylaxis is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.
  - Treatment of a pregnant individual with Pivya prior to delivery may cause a false positive test for isovaleric acidemia in the newborn as part of newborn screening. Prompt follow-up of a positive newborn screening result for isovaleric acidemia is recommended.

- **Common adverse drug reactions**:
  - Listed % incidence for adverse drug reactions= reported % incidence for drug (Pivya) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or less than placebo.
    - The most frequently reported adverse events included nausea (2.2%), diarrhea (1.4%), vulvovaginal candidiasis (1.8%), genital pruritus (0.4%), and headache (1.1%).

- **Drug interactions:**
  - Avoid concurrent treatment with valproic acid, valproate, or other pivalate-generating drugs. If concomitant use with Pivya is necessary, counsel patients to monitor adverse reactions associated with carnitine depletion.
  - Clearance of methotrexate from the body can be reduced by concurrent use of drugs in the penicillin class, including Pivya. Where possible, consider alternative therapy.

- **Special populations:**
  - There is no pregnancy category for this medication; however, the risk summary indicates that published observational studies on use during the first trimester do not indicate an increased risk of major birth defects. There are limited studies on use during pregnancy that assess the risk of miscarriage and other adverse maternal or fetal outcomes. These studies have methodological limitations hindering interpretation. No dose adjustment is required in pregnant women.
  - The safety and efficacy of use in the pediatric population have not been established.

Conclusion

- Urinary tract infections (UTI) comprises cystitis and pyelonephritis (infection of the kidney/upper urinary tract) (*Gupta 2026*).
  - An uncomplicated urinary tract infection (uUTI) is an infection of the bladder (cystitis, lower urinary tract) in females who are not pregnant and who do not have functional or anatomical abnormalities in the urinary tract or other comorbidities that may lead to a more challenging infection to treat (*Gupta 2026, Orrange et al 2026*).

- Pivya is a penicillin class antibacterial indicated for the treatment of female patients 18 years of age and older with uncomplicated urinary tract infections (uUTI) caused by susceptible isolates of *Escherichia coli*, *Proteus mirabilis*, and *Staphylococcus saprophyticus*.
  - To reduce the development of drug-resistant bacteria and maintain the effectiveness of Pivya and other antibacterial drugs, Pivya should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.
- The efficacy of Pivya was assessed in 3 controlled clinical trials comparing various Pivya dosing regimens to placebo (Trial 1), to another oral antibacterial (Trial 2), or to ibuprofen (Trial 4) for the treatment of uUTI.
  - Pivya demonstrated efficacy for the composite response of clinical cure and microbiological response in Trial 1 and Trial 4. The composite response rate in Trial 2 was 72% with Pivya and 76% in the cephalexin group.
- Guidelines were published prior to Pivya being FDA approved; however, guideline-recommended first-line antibiotics include nitrofurantoin, TMP/SMX DS, fosfomycin, and pivmecillinam for acute cystitis. The decision on which agent to use should be individualized.

- There is no evidence to suggest that Pivya is safer or more effective than other currently preferred, more cost-effective medications. It is therefore recommended that Pivya remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

- **PDL Placement:**
  - ☐ Preferred
  - ☒ Non-Preferred

References

- Gupta K. Acute simple cystitis in female adults. UpToDate Website. Updated April 24, 2026. Accessed June 12, 2026. www.uptodate.com.
- 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 Diseases Society of America and the European Society for Microbiology and Infectious Disease. *Clin Infect Dis*. 2011:52(5):e103-e120.
- Infectious Diseases Society of America (IDSA). IDSA practice guideline highlights and status. IDSA. 2026. Accessed June 12, 2026. https://www.idsociety.org/practice-guideline/guideline-highlights/.
- Orrange S, Nseyo U, Munsiff SS, et al. Uncomplicated urinary tract infection (UTI) in female adults. Dynamed Website. Updated May 7, 2026. Accessed June 12, 2026. www.dynamed.com.
- Pivya. Package insert. Alembic Pharmaceuticals Inc; October 2025.
- Tamma PD, Heil EL, Justo JA, et al. Infectious Diseases Society of America 2024 guidance on the treatment of antimicrobial-resistant gram-negative infections. *Clin Infect Dis*. 2024;ciae403. [Online ahead of print].

Publication Date: June 2026.