# UTILITY therapeutics Ltd.

**PRESS RELEASE**

**UTILITY Therapeutics Announces FDA Approval of PIVYA™ for Uncomplicated Urinary Tract Infections (uUTI)**

- 1st new antibiotic in over 20 years to earn FDA approval for uUTI
- PIVYA represents a New 1st-Line option for the treatment of uUTI
- UTILITY expects PIVYA to be made available to prescribing physicians in 2025

**April 24, 2024**: UTILITY therapeutics Ltd., a biotechnology company focused on the development and commercialization of two European-approved antibiotics for the treatment of urinary tract infections (UTIs) in the U.S., today announced that the U.S. Food and Drug Administration (FDA) has approved PIVYA. 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.*

PIVYA is the first antibiotic in approximately 20 years to earn FDA approval for uUTI, a common bacterial infection that afflicts millions of women annually. Pivmecillinam has been widely available in Europe for more than 40 years under the brand name SELEXID. In more than 30 million courses of treatment administered across Europe, oral pivmecillinam has demonstrated strong clinical cure rates with no serious adverse events observed in clinical trials. PIVYA represents a unique mechanism of action for the US, which targets the cell wall of gram-negative bacteria.

"The approval of PIVYA represents a milestone in women's health and a major advancement in the battle against antimicrobial resistance," said Tom Hadley, President and CEO of UTILITY therapeutics. "As resistance continues to diminish the efficacy of current therapies used to treat uUTIs, PIVYA is a timely addition to clinicians' armamentarium of antibiotics. We are excited by the approval and grateful to LEO Pharma A/S for their continued support, the support of the AMR Action Fund, which was instrumental in helping us bring PIVYA for FDA review, as well as all of our investors."

"Rates of UTIs caused by resistant pathogens are rising and the need for physicians to be good stewards of antimicrobials has never been greater. Bringing PIVYA to the U.S. gives prescribers a new, effective option with a proven safety record for patients suffering from uUTIs caused by susceptible bacteria," said Keith S. Kaye, MD, MPH, Chief, Division of Allergy, Immunology and Infectious Diseases, Professor of Medicine at the Robert Wood Johnson Medical School.

UTILITY has previously received the FDA's qualified infectious disease product (QIDP) designation for pivmecillinam for the treatment of uUTI. The FDA's QIDP designation is for antibacterial and antifungal drug candidates intended to treat serious or life-threatening infections, and it provides an additional five years of market exclusivity.

"We are very pleased that the FDA approved PIVYA for uUTI," Professor Morten Sommer, co-founder of UTILITY, added. "This positive decision marks a notable achievement for UTILITY and could help change the treatment dynamics for a significant medical need in the US."

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About PIVYA (pivmecillinam oral tablets 185mg)

PIVYA is the first antibiotic in approximately 20 years to earn FDA approval for uUTI, a common bacterial infection that afflicts millions of women annually. Pivmecillinam is an oral prodrug of mecillinam that has been widely available in Europe for more than 40 years under the brand name SELEXID. It has a unique mechanism of action that targets the cell wall of gram-negative bacteria.

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*.

Mecillinam demonstrated in *vitro activity* against Enterobacterales in the presence of some beta-lactamases and extended-spectrum beta-lactamases (ESBL) of the following groups: CTX-M, SHV, TEM, AmpC. The inhibitory action of mecillinam on PBP-2 results in low cross-resistance with certain beta-lactams. The frequency of resistance to mecillinam in *E. coli* range from $8\times10^{-8}$ to $2\times10^{-5}$ when exposed to 32-256 times MIC.

PIVYA has been proven safe and effective in 3 clinical trials with the most common Adverse Reactions Occurring in ≥1% of Patients Receiving PIVYA (Adjusted for Study Size); Nausea (4.3%), Diarrhea (2.1%), Vulvovaginal candidiasis (1.8%), Genital pruritus (1.8%), and Headache (1.4%).

PIVYA demonstrated strong response in three controlled clinical trials comparing different PIVYA dosing regimens to placebo (Trial 1), to another oral antibacterial drug (Trial 2), or to ibuprofen (Trial 4) evaluated 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 $\geq10^5$ 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 185 mg three times daily dosing regimen.

Composite Response Rates (Clinical Cure and Microbiological Response) at TOC in the uUTI trials (Micro ITT Population)

| | **Composite Response Rates (Clinical Cure and Microbiological Response)** | | |
|---|---|---|---|
| **Trial 1** | PIVYA N=137, n (%) | Placebo N=134, n(%) | Difference (95% CI) |
| | 85 (62) | 14 (10) | 52 (41,62) |
| **Trial 2** | PIVYA N=127, n (%) | Cephalexin N=132 n(%) | |
| | 91 (72) | 100 (76) | -4(-16, +7) |
| **Trial 4** | PIVYA N=105, n (%) | Ibuprofen N=119 n(%) | |
| | 69 (66) | 26 (22) | 44 (31, 57) |

Clinical Cure Rates (Micro-ITT Population)

| | Clinical Cure Rates | | |
|---|---|---|---|
| **Trial 1** | PIVYA N=137, n (%) | Placebo N=134, n(%) | Treatment Difference (95% CI) |
| | 87 (64) | 31 (23) | 40 (29, 52) |
| **Trial 2** | PIVYA N=127, n (%) | Cephalexin N=132 n(%) | |
| | 105 (83) | 112 (85) | -2 (-12, +8) |
| **Trial 4** | PIVYA N=105, n (%) | Ibuprofen N=119 n(%) | |
| | 81 (77) | 45 (38) | 39 (27, 52) |

Microbiological Response Rates (Micro-ITT Population)

| | Microbiological Response Rates | | |
|---|---|---|---|
| **Trial 1** | PIVYA N=137, n (%) | Placebo N=134, n(%) | Treatment Difference (95% CI) |
| | 119 (87) | 35 (26) | 61 (51,71) |
| **Trial 2** | PIVYA N=127, n (%) | Cephalexin N=132 n(%) | |
| | 97 (76) | 106 (80) | -4 (-15, +7) |
| **Trial 4** | PIVYA N=105, n (%) | Ibuprofen N=119 n(%) | |
| | 78 (74) | 64 (54) | 21 7, 34) |

Contraindications

- Serious hypersensitivity reactions (e.g., anaphylaxis or Stevens-Johnson syndrome) to PIVYA or to other beta-lactam antibacterial drugs (e.g., penicillins and cephalosporins).
- Primary or secondary carnitine deficiency resulting from inherited disorders of mitochondrial fatty acid oxidation and carnitine metabolism such as carnitine transporter defect or other inborn errors of metabolism (e.g., methylmalonic aciduria, or propionic academia).
- Acute porphyria.

Warnings and precautions

- Hypersensitivity Reactions: Serious hypersensitivity reactions including anaphylaxis have been reported in patients receiving PIVYA. If hypersensitivity reactions occur, discontinue treatment with PIVYA and institute appropriate therapy.
- Severe Cutaneous Adverse Reactions (SCAR): Acute Generalized Exanthematous Pustulosis (AGEP), Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) have been reported with PIVYA. Monitor closely and discontinue PIVYA at the first signs or symptoms of SCAR or other signs of hypersensitivity.
- Carnitine Depletion: In patients at risk for reductions in serum carnitine, e.g., significant renal impairment or decreased muscle mass, consider alternative antibacterial therapies. PIVYA is not

recommended when prolonged antibacterial treatment is necessary. Avoid concurrent treatment with valproic acid, valproate or other pivalate-generating drugs due to increased risk of carnitine depletion.

- *Clostridioides difficile*-Associated Diarrhea (CDAD): This has been reported with nearly all systemic antibacterial agents, including PIVYA. Evaluate if diarrhea occurs.
- Interference with Newborn Screening Test: 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.

About UTILITY therapeutics Ltd.

UTILITY has exclusive U.S. commercial rights to two European-approved antibiotics, pivmecillinam and mecillinam, for the treatment of urinary tract infections (UTI). Pivmecillinam is an oral prodrug of mecillinam that is being developed for uncomplicated UTI (uUTI), and it has a unique mechanism of action for infections caused by Gram-negative bacteria, including extended-spectrum beta-lactamases. Mecillinam, an intravenous (IV) formulation, is being developed as a first-line therapy for complicated UTI (cUTI) in the hospital setting.

UTILITY has received the FDA's qualified infectious disease product (QIDP) designation for pivmecillinam for the treatment of uUTI, and IV mecillinam followed by oral pivmecillinam as step-down, carbapenem-sparing therapy for cUTI. This therapeutic regimen allows patients to complete their treatment outside of hospital and reduces the economic burden of cUTI to both patients and payers. The FDA's QIDP designation is for antibacterial and antifungal drug candidates intended to treat serious or life-threatening infections, and provides an additional five years of market exclusivity and potentially includes Priority Review.

For additional information, please visit www.utilitytherapeutics.com, www.PIVYA.com, or https://www.fda.gov.

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