Orlynvah™ (sulopenem etzadroxil/probenecid) – New drug approval

- On October 25, 2024, Iterum Therapeutics announced the FDA approval of Orlynvah (sulopenem etzadroxil/probenecid), for the treatment of uncomplicated urinary tract infections (uUTI) caused by the designated microorganisms *Escherichia coli*, *Klebsiella pneumoniae*, or *Proteus mirabilis* in adult women who have limited or no alternative oral antibacterial treatment options.

- Orlynvah is not indicated for the treatment of:

    - Complicated urinary tract infections (cUTI) or as step-down treatment after intravenous antibacterial treatment of cUTI
    - Complicated intra-abdominal infections (cIAI) or as step-down treatment after intravenous antibacterial treatment of cIAI.

- Orlynvah is the first FDA approved oral carbapenem.

- The efficacy of Orlynvah was established in a randomized, double-blind study in 2,222 adult women with uUTI. Patients were randomized to Orlynvah or amoxicillin/clavulanate for 5 days. The composite response (combined microbiological response and clinical cure rates) was determined by comparing the response rate of Orlynvah to amoxicillin/clavulanate at the test-of-cure visit (12 days after randomization) in the microbiological modified intent-to-treat (micro-MITT) population as well as in two sub-populations: a) micro-MITTS (micro-MITT population with baseline pathogens susceptible to amoxicillin/clavulanate) and b) micro-MITTR (micro-MITT population with baseline pathogens non-susceptible to amoxicillin/clavulanate).

    - Orlynvah demonstrated efficacy in the micro-MITTS population. The micro-MITTR population was small (N = 67) and had insufficient power to draw conclusions regarding efficacy.
    - In the micro-MITTS population, composite response was achieved in 61.7% and 55.0% of patients with Orlynvah and amoxicillin/clavulanate, respectively (difference 6.7, 95% CI: 0.3, 13.0).

- The efficacy of Orlynvah was also established in a separate randomized, double-blind study in 1,660 adult women with uUTI. Patients were randomized to Orlynvah for 5 days or ciprofloxacin for 3 days. The composite response (combined microbiological response and clinical cure) was determined by comparing the response rate of Orlynvah to ciprofloxacin at the test-of-cure visit (12 days after randomization) in two primary populations: a) micro-MITTS (micro-MITT population with baseline pathogens susceptible to ciprofloxacin) and b) micro-MITTR (micro-MITT population with baseline pathogens non-susceptible to ciprofloxacin).

    - Orlynvah demonstrated efficacy in the micro-MITTR population but did not demonstrate efficacy in the micro-MITTS population.
    - In the micro-MITTR population, composite response was achieved in 48.1% and 32.9% of patients with Orlynvah and ciprofloxacin, respectively (difference 15.3, 95% CI: 4.3, 25.8; p = 0.006).

- Orlynvah is contraindicated in patients with:

    - A history of hypersensitivity to the components of Orlynvah or other beta-lactam antibacterial drugs
    - Known blood dyscrasias

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  - Known uric acid kidney stones
  - Concomitant use of ketorolac tromethamine.

- Warnings and precautions for Orlynvah include hypersensitivity reactions, *Clostridioides difficile*-associated diarrhea, risk of uric acid kidney stone development, exacerbation of gout, and development of drug-resistant bacteria.

- The most common adverse reactions (≥ 2%) with Orlynvah use were diarrhea, nausea, vulvovaginal mycotic infection, headache, and vomiting.

- The recommended dose of Orlynvah is one tablet (sulopenem etzadroxil 500 mg and probenecid 500 mg) orally twice daily for 5 days.

- Iterum Therapeutics' launch plans for Orlynvah are pending. Orlynvah will be available as a tablet containing 500 mg sulopenem etzadroxil and 500 mg probenecid.