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GEPOTIDACIN, A NEWLY FIRST IN CLASS FDA-APPROVED ANTIBIOTIC FOR TREATMENT OF UNCOMPLICATED URINARY TRACT INFECTION

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BACKGROUND

- Urinary tract infections (UTIs) are among the most common bacterial infections in females worldwide; the rising antimicrobial resistance of uropathogens limits the effectiveness of the current oral treatment options.
- Gepotidacin is the first new oral antibiotic with a unique mechanism approved by the FDA in March 2025 for treatment of uncomplicated UTIs in females and adolescents ≥12 years and ≥40 kg.

OBJECTIVE

This review provides an overview of current scientific literature on gepotidacin, focusing on:

- Mechanism of action
- Phase III trial data
- Pharmacokinetics and pharmacodynamics
- Adverse effects and precautions
- Clinical relevance against resistant uropathogens.
- Antimicrobial stewardship implications and future research directions

METHODOLOGY

Literature Search Strategy

- **Databases Searched:** PubMed, Scopus, and ClinicalTrials.gov.
- **Search Terms:** *"Gepotidacin," "uncomplicated urinary tract infection," "antimicrobial resistance," "pharmacokinetics," "efficacy,"* and *"safety profile."*

Inclusion Criteria

- Peer-reviewed clinical trials, reviews, and FDA reports focusing on human subjects with uncomplicated urinary tract infections (uUTIs) treated with gepotidacin.

Exclusion Criteria

- Preclinical or animal-only studies without human clinical data.
- Publications in languages other than English.

Data Extraction

Extracted key information on:

- Mechanism of action and antibacterial spectrum.
- Pharmacokinetic and pharmacodynamic profiles.
- Phase II and III clinical trial outcomes.
- Safety data, drug interactions, and adverse events.
- Efficacy against antimicrobial-resistant uropathogens.

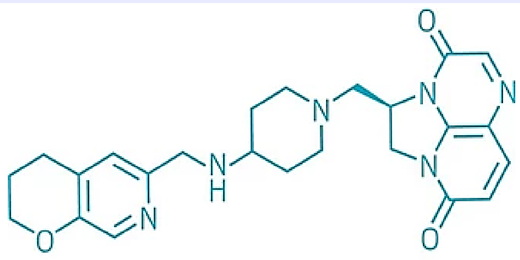
Data Synthesis and Analysis

- Data were organized under the core categories of the research.

RESULTS

Chemical Structure

- Triazaacenaphthylene core linked to a pyranopyridine moiety via a piperidinyl bridge.



RESULTS

Mechanism of Action

- First-in-class triazaacenaphthylene antibiotic that inhibits DNA gyrase and topoisomerase IV via a unique binding, requiring dual mutations for resistance.

Pharmacokinetics and Pharmacodynamics

- Metabolized primarily via CYP3A4, minimal renal excretion.
- Oral bioavailability allows twice-daily dosing (1,500 mg BID for 5 days).

Safety Profile

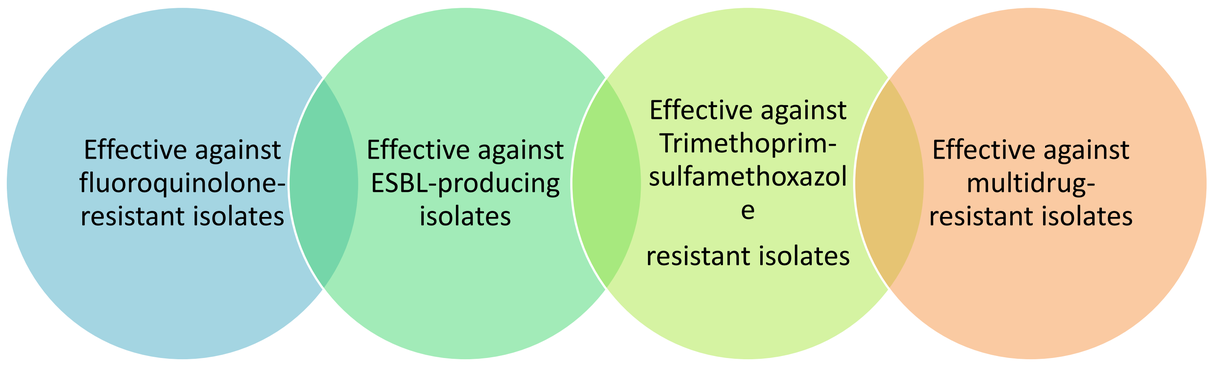
Well-tolerated adverse events include diarrhea, nausea, headache, abdominal discomfort.

Serious events rare; QTc prolongation, cholinergic effects, hypersensitivity.

Clinical Implications

- Supports antimicrobial stewardship by offering a targeted novel oral option for uncomplicated UTIs with a reduced risk of resistance.

Activity Against Resistant Phenotypes of E.coli Strains



Future Roles of Gepotidacin

Gepotidacin activity against MDR E. coli supports its future role in treatment of complicated UTI and pyelonephritis.

Sequential oral–IV transition strategies could position Gepotidacin as an outpatient step-down therapy for resistant infections.

Ongoing trials are exploring Gepotidacin for uncomplicated gonorrhea.

CONCLUSION

- ❑ Gepotidacin is the first novel oral antibiotic class in over two decades approved for uncomplicated urinary tract infections (uUTIs).
- ❑ Demonstrated non-inferior or superior efficacy to nitrofurantoin across global Phase III trials with a favorable safety profile.
- ❑ Retains potent activity against multidrug-resistant (MDR), ESBL-producing, and fluoroquinolone-resistant E. coli isolates.
- ❑ Offers an effective oral option for community and outpatient management of resistant infections, potentially reducing the need for IV therapy.
- ❑ Future directions include expanded indications (gonorrhea, complicated UTI), combination strategies, and integration into antimicrobial stewardship programs.

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