In patients with cIAI...

WHEN THE RESISTANCE RISK IS HIGH,

THE EMPIRIC CHOICE IS CLEAR

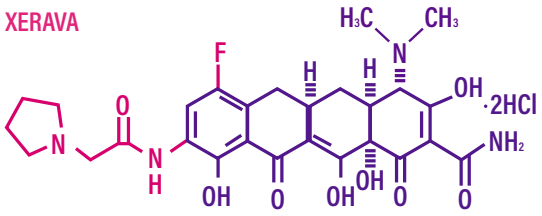
XERAVA™
(eravacycline) for injection

Key structural modifications to the tetracycline core differentiate XERAVA from other tetracyclines[1,2]

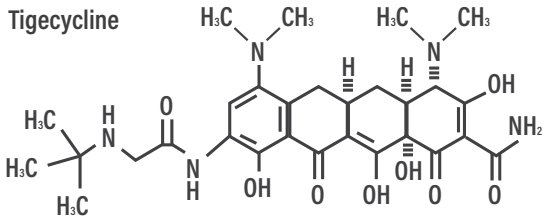
- The C7 and C9 substitutions in XERAVA are not present in any naturally occurring or semisynthetic tetracyclines[1]
- The substitution pattern imparts microbiologic activities, including in vitro activity against Gram-positive and Gram-negative strains expressing certain tetracycline-specific resistance mechanisms[1]
  - — Efflux mediated by *tet*(A), *tet*(B), and *tet*(K)
  - — Ribosomal protection as encoded by *tet*(M) and *tet*(Q)
- XERAVA was 2- to 4-fold more potent than tigecycline in vitro against Gram-positive and Gram-negative bacteria, and 2- to 8-fold more potent against most anaerobes[2]
- Low rates of nausea (6.5%), vomiting (3.7%), and diarrhea (2.3%) were among the gastrointestinal-related adverse reactions reported in 2 pivotal clinical trials[1]

Comparison of tetracycline structures[1,3]

XERAVA



Tigecycline



Indications and Usage

XERAVA is indicated for the treatment of complicated intra-abdominal infections (cIAI) caused by susceptible microorganisms: *Escherichia coli*, *Klebsiella pneumoniae*, *Citrobacter freundii*, *Enterobacter cloacae*, *Klebsiella oxytoca*, *Enterococcus faecalis*, *Enterococcus faecium*, *Staphylococcus aureus*, *Streptococcus anginosus* group, *Clostridium perfringens*, *Bacteroides* species, and *Parabacteroides distasonis* in patients 18 years or older.

Limitations of Use
XERAVA is not indicated for the treatment of complicated urinary tract infections (cUTI).

Usage

To reduce the development of drug-resistant bacteria and maintain the effectiveness of XERAVA and other antibacterial drugs, XERAVA 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.

Important Safety Information

XERAVA is contraindicated for use in patients with known hypersensitivity to eravacycline, tetracycline-class antibacterial drugs, or to any of the excipients. Life-threatening hypersensitivity (anaphylactic) reactions have been reported with XERAVA.

The use of XERAVA during tooth development (last half of pregnancy, infancy and childhood to the age of 8 years) may cause permanent discoloration of the teeth (yellow-gray-brown) and enamel hypoplasia.

The use of XERAVA during the second and third trimester of pregnancy, infancy and childhood up to the age of 8 years may cause reversible inhibition of bone growth.

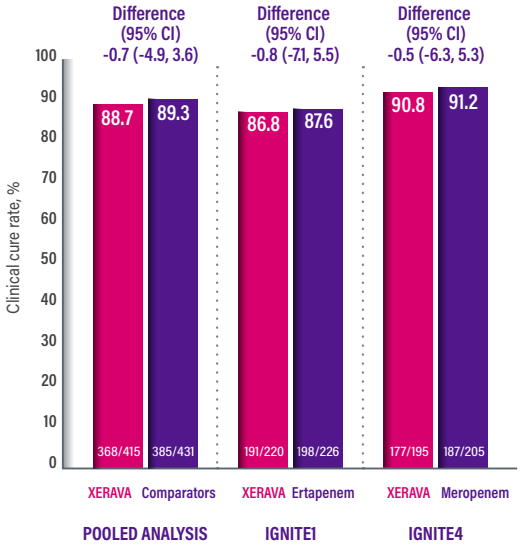
Learn more at xerava.com.

Please see additional Important Safety Information on reverse side and enclosed full Prescribing Information.

XERAVA WAS PROVEN AS EFFECTIVE AS CARBAPENEMS IN 2 PIVOTAL COMPARATIVE cIAI CLINICAL TRIALS

Efficacy demonstrated as monotherapy[1,4-6]

Clinical response in micro-ITT population at the TOC visit

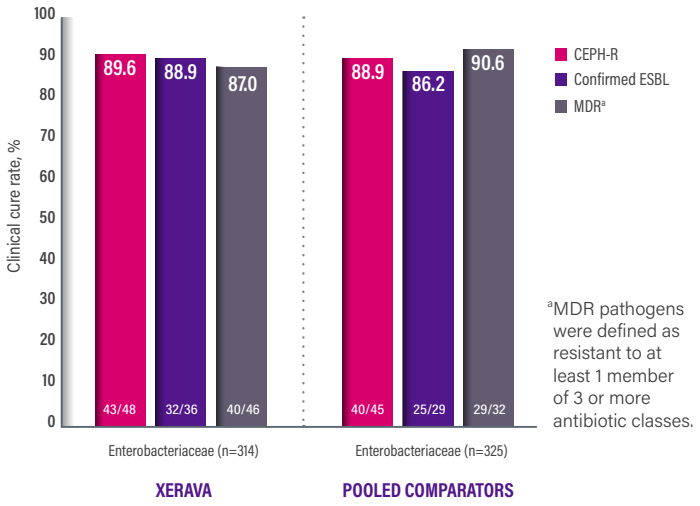


Concurrent bacteremia was present in 32 patients in the XERAVA group and 31 patients in the comparator group in the pooled micro-ITT population; the rates of clinical response were 87.5% for XERAVA and 77.0% for comparators.[7]

Non-inferior to ertapenem (IGNITE1) and meropenem (IGNITE4)

Clinically effective against resistant Enterobacteriaceae[8]

Clinical cure rate in micro-ITT population at the TOC visit



[a]MDR pathogens were defined as resistant to at least 1 member of 3 or more antibiotic classes.

Pooled data from IGNITE1 and IGNITE4

Study Design

Primary endpoint: Clinical cure was defined as complete resolution or significant improvement of signs or symptoms of the index infection at the TOC visit, which occurred 25 to 31 days after randomization.[1]

IGNITE1: Phase 3, randomized, double-blind, double-dummy, multicenter, prospective study in subjects with cIAI to demonstrate the non-inferiority of XERAVA compared with ertapenem.[4]

IGNITE4: Phase 3, randomized, double-blind, double-dummy, multicenter, prospective study in subjects with cIAI to demonstrate the non-inferiority of XERAVA compared with meropenem.[5]

CEPH-R, cephalosporin-resistant; cIAI, complicated intra-abdominal infection; ESBL, extended-spectrum beta-lactamase; IGNITE, Investigating Gram-Negative Infections Treated with Eravacycline; MDR, multidrug-resistant; micro-ITT, microbiologic intent-to-treat; TOC, Test of Cure.

Important Safety Information (cont'd)

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, and may range in severity from mild diarrhea to fatal colitis.

The most common adverse reactions observed in clinical trials (incidence ≥3%) were infusion site reactions (7.7%), nausea (6.5%), and vomiting (3.7%).

XERAVA is structurally similar to tetracycline-class antibacterial drugs and may have similar adverse reactions. Adverse reactions including photosensitivity, pseudotumor cerebri, and anti-anabolic action which has led to increased BUN, azotemia, acidosis, hyperphosphatemia, pancreatitis, and abnormal liver function tests, have been reported for other tetracycline-class antibacterial drugs, and may occur with XERAVA. Discontinue XERAVA if any of these adverse reactions are suspected.

To report SUSPECTED ADVERSE REACTIONS, contact Tetraphase Pharmaceuticals Inc., at 1-833-7-XERAVA (1-833-793-7282) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see full Prescribing Information for XERAVA at www.XERAVA.com.

References: 1. XERAVA [prescribing information]. Watertown, MA: Tetraphase Pharmaceuticals, Inc.; 2018. **2.** Zhanel GG, Cheung D, Adam H, et al. Review of eravacycline, a novel fluorocycline antibacterial agent. *Drugs*. 2016;76(5):567-588. **3.** Tygacil [prescribing information]. Philadelphia, PA: Wyeth Pharmaceuticals, Inc.; 2018. **4.** Solomkin J, Evans D, Slepavicius A, et al. Assessing the efficacy and safety of eravacycline vs ertapenem in complicated intra-abdominal infections in the Investigating Gram-Negative Infections Treated with Eravacycline (IGNITE 1) trial: a randomized clinical trial. *JAMA Surg*. 2017;152(3):224-232. **5.** Solomkin JS, Gardovskis J, Lawrence K, et al. IGNITE4: results of a phase 3, randomized, multicenter, prospective trial of eravacycline vs meropenem in the treatment of complicated intraabdominal infections [published online December 18, 2018]. *Clin Infect Dis*. doi:10:1093/cid/ciy1029. **6.** Data on file. Watertown, MA: Tetraphase Pharmaceuticals, Inc.; 2018. **7.** Demuth J, Lawrence K, Izmailyan S, Tsai L. Efficacy of eravacycline in secondary bacteremia: a post hoc analysis of two phase 3 studies of complicated intra-abdominal infection. Poster presented at: IDWeek; October 3-7, 2018; San Francisco, CA. P1978. **8.** Ditch K, Newman J, Izmailyan S, Fyfe C, Tsai L. Microbiological efficacy of eravacycline against Enterobacteriaceae and *Acinetobacter baumannii*, including MDR isolates: a pooled analysis from IGNITE1 and IGNITE4, two phase 3 trials of complicated intra-abdominal infection. Poster presented at: ASM Microbe; June 7-11, 2018; Atlanta, GA. P629.

TETRAPHASE PHARMACEUTICALS

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Learn more at xerava.com.

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