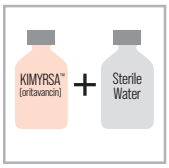
Guide to KIMYRSA® Preparation and Administration

Kimyrsa™ (oritavancin) for injection 1,200 mg

KIMYRSA® Preparation

Aseptic technique should be used to reconstitute and dilute one KIMYRSA® 1,200 mg vial. KIMYRSA® is intended for intravenous infusion.



1. Add Sterile Water

Add 40 mL of sterile water for injection to reconstitute the vial to provide a 30 mg/mL solution.

2. Swirl gently

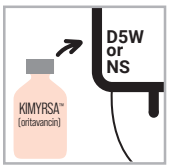
Swirl gently the contents to avoid foaming and ensure that all KIMYRSA® powder is completely dissolved to form a reconstituted solution. May not dissolve immediately.

3. Inspect

Inspect visually for particulate matter. Solution should appear to be clear, colorless to pink, and free of visible particles.

4. Withdraw and discard

Withdraw and discard 40 mL from a 250 mL intravenous bag of 0.9% sodium chloride injection (NS) or D5W.



5. Transfer

Withdraw 40 mL of the reconstituted vial of KIMYRSA® and add to the intravenous bag of NS or D5W to bring the bag volume to 250 mL. This yields a concentration of 4.8 mg/mL.

Supplies

One KIMYRSA® 1,200 mg vial
250 mL D5W or NS IV Bag
40 mL Sterile Water for Injection

Stability of Diluted IV Solution

Four hours at room temperature (20° to 25°C or 68° to 77°F)
Twelve hours refrigerated (2°C to 8°C or 36°F to 46°F).
The combined storage time (reconstituted solution in the vial and diluted solution in the bag) and 1 hour infusion time should not exceed 4 hours at room temperature or 12 hours if refrigerated.

KIMYRSA® Administration

There are two oritavancin products (KIMYRSA® and ORBACTIV®) that have differences in dose strengths, duration of infusion, reconstitution and dilution instructions, and compatible diluents.

1. Inquire

Inquire carefully about known hypersensitivity reactions to glycopeptides (vancomycin, telavancin, or dalbavancin).

NOTE: KNOWN HYPERSENSITIVITY TO KIMYRSA® (ORITAVANCIN) IS A CONTRAINDICATION.

2. Check label

Check label on IV bag, as KIMYRSA® 1-hour infusion must be completed within:

- 4 hours after dilution when stored at room temperature (20°C to 25°C or 68°F to 77°F)
- 12 hours after dilution when refrigerated (2°C to 8°C or 36°F to 46°F).

3. Use D5W or NS

Use a dedicated line.
The line should be flushed before and after infusion of KIMYRSA® with D5W or NS.

4. Infuse

Infuse 1,200 mg of KIMYRSA® in one 250 mL bag of D5W or NS over one hour.

Dosage and Administration

KIMYRSA® is administered as a single dose by IV infusion over 1 hour. Single dose KIMYRSA® does not require dose adjustment for mild-to-moderate renal* or mild-to-moderate hepatic† impairment, weight, age (≥18 years of age), race, or gender.

*Mild renal impairment CrCL 50-79 mL/min, moderate renal impairment CrCL 30-49 mL/min
†Moderate hepatic impairment (Child-Pugh Class B)

Incompatibilities

Drugs formulated at a basic or neutral pH may be incompatible with KIMYRSA®. KIMYRSA® should not be administered simultaneously with commonly used intravenous drugs through a common intravenous port. If the same intravenous line is used for sequential infusion of additional medications, the line should be flushed before and after infusion of KIMYRSA® with NS or D5W.

Please see Important Safety Information inside and accompanying Full Prescribing Information for KIMYRSA®

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INDICATION AND USAGE

Both KIMYRSA® and ORBACTIV® are oritavancin products that are indicated for the treatment of adult patients with acute bacterial skin and skin structure infections (ABSSSI) caused or suspected to be caused by susceptible isolates of the following gram-positive microorganisms: *Staphylococcus aureus* (including methicillin-susceptible [MSSA] and methicillin-resistant [MRSA] isolates), *Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus dysgalactiae, Streptococcus anginosus group* (includes *S. anginosus, S. intermedius,* and *S. constellatus*), and *Enterococcus faecalis* (vancomycin-susceptible isolates only).

To reduce the development of drug-resistant bacteria and maintain the effectiveness of oritavancin and other antibacterial drugs, oritavancin should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.

KIMYRSA® and ORBACTIV® are not approved for combination use and have differences in dose strength, duration of infusion, and preparation instructions, including reconstitution and dilution instructions and compatible diluents. Please see the full Prescribing Information for each product.

IMPORTANT SAFETY INFORMATION

Contraindications

Use of intravenous unfractionated heparin sodium is contraindicated for 120 hours (5 days) after oritavancin administration because the activated partial thromboplastin time (aPTT) test results may remain falsely elevated for approximately 120 hours (5 days) after oritavancin administration.

Oritavancin products are contraindicated in patients with known hypersensitivity to oritavancin.

Warnings and Precautions

Coagulation test interference: Oritavancin has been shown to artificially prolong aPTT for up to 120 hours, and may prolong PT and INR for up to 12 hours and ACT for up to 24 hours. Oritavancin has also been shown to elevate D-dimer concentrations up to 72 hours. For patients who require aPTT monitoring within 120 hours of oritavancin dosing, consider a non-phospholipid dependent coagulation test such as a Factor Xa (chromogenic) assay or an alternative anticoagulant not requiring aPTT.

Serious hypersensitivity reactions, including anaphylaxis, have been reported with the use of oritavancin products. Discontinue infusion if signs of acute hypersensitivity occur. Closely monitor patients with known hypersensitivity to glycopeptides.

Infusion related reactions: Infusion reactions characterized by chest pain, back pain, chills and tremor have been observed with the use of oritavancin products, including after the administration of more than one dose of oritavancin during a single course of therapy. Stopping or slowing the infusion may result in cessation of these reactions.

Clostridioides difficile-associated diarrhea: Evaluate patients if diarrhea occurs.

Concomitant warfarin use: Oritavancin has been shown to artificially prolong PT/INR for up to 12 hours. Patients should be monitored for bleeding if concomitantly receiving oritavancin products and warfarin.

Osteomyelitis: Institute appropriate alternate antibacterial therapy in patients with confirmed or suspected osteomyelitis.

Prescribing oritavancin products in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of development of drug-resistant bacteria.

Adverse Reactions

The most common adverse reactions (≥3%) in patients treated with oritavancin products were headache, nausea, vomiting, limb and subcutaneous abscesses, and diarrhea. The adverse reactions occurring in ≥2 patients receiving KIMYRSA® were hypersensitivity, pruritis, chills and pyrexia.

Please see Full Prescribing Information for ORBACTIV® (oritavancin).

Please see Full Prescribing Information for KIMYRSA® (oritavancin).

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MEDICAL INFORMATION

For medical inquiries or to report an adverse event, other safety-related information, or product complaints, please contact Medical Information.

1-844-MED-MLNT (1-844-633-6568)

medinfo@melinta.com

melintamedicalinformation.com

References: 1. Kimyrsa. Package Insert. Melinta Therapeutis; 2021 **2.** Dalvance. Package insert. Allergan Pharmaceuticals Limited; 2021 **3.** Vancomycin. Package insert. ANI Pharmaceuticals, Inc; 2017 **4.** Telavancin. Package insert. Cumberland Pharmaceuticals Inc; 2023 **5.** Hoover RK, Krsak M, Molina KC, Shah K, Redell M. Kimyrsa, an oritavancin-containing product: clinical study and review of properties. *Open Forum Infect Dis.* 2022;9(5):ofac090 doi:10.1093/ofid/ofac090 **6.** Orbactiv. Package insert. Melinta Therapeutics; 2019. **7.** Redell M, Moeck G, Lucasti C, et al. A real-world patient registry for oritavancin demonstrates efficacy and safety consistent with the phase 3 SOLO program. *Open Forum Infect Dis.* 2018;5(6):ofy051. doi:10.1093/ofid/ofy051 **8.** Saddler K, Zhang J, Sul J, et al. Improved economic and clinical outcomes with oritavancin versus a comparator group for treatment of acute bacterial skin and skin structure infections in a community hospital. *Plos One.* 2021. doi: 10.1371/journal.pone.0248129 **9.** Corey GR, Arhin FF, Wikler MA, et al. Pooled analysis of single-dose oritavancin in the treatment of acute bacterial skin and skin-structure infections caused by gram-positive pathogens, including a large patient subset with methicillin-resistant *Staphylococcus aureus. Inter J Antimicrob Agents.* 2016;48(5):528-534.

Please see Important Safety Information and accompanying Full Prescribing Information for KIMYRSA®

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Administration Safety

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Infusion-related reactions (IRR) are possible with glycopeptide antibiotic therapies, including oritavancin, dalbavancin, vancomycin and telavancin.[1-4] However, certain strategies may help manage IRRs should they occur.[1,6,8]

IRRs are a known side effect of the glycopeptide class of antibiotics[1]

- **Glycopeptide infusion-related symptoms**[1]
  - Upper body flushing
  - Urticaria
  - Puritus
  - Rash
- Chest pain, back pain, chills and tremor have also been observed with oritavancin, including after the administration of more than 1 dose during a single course of therapy[1†]

Well Established Tolerability Profile

- **A low incidence of IRRs and hypersensitivity** has been established in a PK trial of KIMYRSA® and in studies of ORBACTIV® (oritavancin).*[5-7]
  - Oritavancin-related IRRs were typically mild, and most patients completed the full 1200-mg dose.[5,7,9]

* Safety profile demonstrated in:

ORBACTIV clinical trials: 1.9% (19/976) of patients receiving oritavancin experienced IRR compared to 3.5% (34/983) of patients receiving vancomycin.[9]

PK trial: 4% (2/50) of patients receiving KIMYRSA® experienced hypersensitivity or IRR compared with 3.8% (2/52) of patients receiving ORBACTIV.[5]

CHROME retrospective, real-world study: 1.7% of patients (2/112) experienced mild hypersensitivity reactions.[7]

Potential IRR Management Strategies

- **Slowing or stopping the glycopeptide infusion** may lead to the cessation of these reactions[1]
- Real-world treatment protocols often include **pre-treatment with antihistamines** such as diphenhydramine to address the reported side effect of infusion-related reactions. The clinical benefit of pre-treatment has not been evaluated or established[8]

† The safety and efficacy of multiple doses in one course is not established.

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