Please see Important Safety Information on next page

Dear Valued Customer,

We hope this message finds you well. We recognize the healthcare challenges caused by the national shortage of large-volume parenteral solutions exacerbated by Hurricane Helene and have received multiple inquiries from the ID Community on Melinta's products.

To assist institutions that are developing action plans aimed at conserving IV fluids, we are sharing information about the fluid volume requirements for our medications and the available administration options:

Medication	Drug Class	Dosing Frequency	Fluid Volume per Dose
REZZAYO® (rezafungin for injection)	Echinocandin antifungal	1 infusion per week	• 250-mL IV bag • Fluid options for dilution: 0.9% sodium chloride, 0.45% sodium chloride, or 5% dextrose in water
KIMYRSA® (oritavancin)	Lipoglycopeptide antibiotic	Single dose	• 250-mL IV bag • Fluid options for dilution: 0.9% sodium chloride, 5% dextrose in water
ORBACTIV® (oritavancin)	Lipoglycopeptide antibiotic	Single dose	• 1000-mL IV bag • Fluid for dilution: 5% dextrose in water
VABOMERE® (meropenem and vaborbactam)	Carbapenem antibiotic and beta-lactamase inhibitor	Every 8 hours	• As low as 250-mL, up to 1000-mL IV bag • Fluid options for dilution: 0.9% sodium chloride (normal saline)
MINOCIN® (minocycline) for injection	Tetracycline antibiotic	Every 12 hours	• As low as 100-mL, up to 1000-mL IV bag • Fluid options for dilution: 0.9% sodium chloride (normal saline), dextrose injection, or dextrose and sodium chloride • Alternatively, 250-mL to 1000-mL Lactated Ringer's

Please let us know if we can help answer any questions. We are proud partners of the Infectious Diseases and medical community and remain committed to making our products available to those impacted by acute and life-threatening illnesses.

Thank you for your continued dedication and service.

Warm Regards,

Melinta Therapeutics

REZZAYO® (rezafungin for injection) Indication and Important Safety Information

INDICATION AND USAGE

REZZAYO® (rezafungin for injection) is an echinocandin antifungal indicated in patients 18 years of age or older who have limited or no alternative options for the treatment of candidemia and invasive candidiasis. Approval of this indication is based on limited clinical safety and efficacy data.

Limitations of Use

REZZAYO® has not been studied in patients with endocarditis, osteomyelitis, and meningitis due to *Candida*.

IMPORTANT SAFETY INFORMATION

Contraindications

REZZAYO® is contraindicated in patients with known hypersensitivity to rezafungin or other echinocandins.

Warnings and Precautions

- Infusion-related Reactions: REZZAYO® may cause infusion-related reactions, including flushing, sensation of warmth, urticaria, nausea, or chest tightness. If these reactions occur, slow or pause the infusion.
- Photosensitivity: REZZAYO® may cause photosensitivity. Advise patients to use protection from sun exposure and other sources of UV radiation.
- Hepatic Adverse Reactions: Abnormalities in liver tests have been seen in clinical trial patients treated with REZZAYO®. Monitor patients who develop abnormal liver tests and evaluate patients for their risk/benefit of continuing REZZAYO® therapy.

Adverse Reactions

Most common adverse reactions (incidence ≤5%) are hypokalemia, pyrexia, diarrhea, anemia, vomiting, nausea, hypomagnesemia, abdominal pain, constipation, and hypophosphatemia.

Please see full Prescribing Information for REZZAYO® (rezafungin for injection).

KIMYRSA® (oritavancin) Indication and Important Safety Information

INDICATION AND USAGE

KIMYRSA® (oritavancin) for injection is 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 KIMYRSA® and other antibacterial drugs, KIMYRSA® should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.

IMPORTANT SAFETY INFORMATION

Contraindications

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

KIMYRSA® is contraindicated in patients with known hypersensitivity to oritavancin products.

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 KIMYRSA® 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 including KIMYRSA®. 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 (e.g. KIMYRSA®), 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 KIMYRSA® and warfarin.

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

Prescribing KIMYRSA® 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, pruritus, chills and pyrexia.

Please see Full Prescribing Information for KIMYRSA®.

ORBACTIV® (oritavancin) Indication and Important Safety Information

INDICATION AND USAGE

ORBACTIV® (oritavancin) for injection is 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 -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 ORBACTIV® and other antibacterial drugs, ORBACTIV® should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.

IMPORTANT SAFETY INFORMATION

Contraindications

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

ORBACTIV® is contraindicated in patients with known hypersensitivity to oritavancin products.

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, including ORBACTIV®. Discontinue infusion if signs of acute hypersensitivity occur. Closely monitor patients with known hypersensitivity to glycopeptides.

Infusion Related Reactions: Administer ORBACTIV® over 3 hours to minimize infusion-related reactions. Infusion reactions characterized by chest pain, back pain, chills and tremor have been observed with the use of oritavancin products (e.g. ORBACTIV®), 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 ORBACTIV® and warfarin.

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

Prescribing ORBACTIV® 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 ORBACTIV® were headache, nausea, vomiting, limb and subcutaneous abscesses, and diarrhea.

Please see Full Prescribing Information for ORBACTIV®.

VABOMERE® (meropenem and vaborbactam) Indication and Important Safety Information

INDICATION AND USAGE

VABOMERE® (meropenem and vaborbactam) is indicated for the treatment of patients 18 years of age and older with complicated urinary tract infections (cUTI) including pyelonephritis caused by the following susceptible microorganisms: *Escherichia coli*, *Klebsiella pneumoniae*, and *Enterobacter cloacae species* complex.

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

IMPORTANT SAFETY INFORMATION

Contraindications

VABOMERE is contraindicated in patients with known hypersensitivity to any components of VABOMERE (meropenem and vaborbactam), or to other drugs in the same class or in patients who have demonstrated anaphylactic reactions to beta-lactam antibacterial drugs.

Warnings and Precautions

Hypersensitivity reactions were reported in patients treated with VABOMERE in the clinical trials. Serious and occasionally fatal hypersensitivity (anaphylactic) reactions and serious skin reactions have been reported in patients receiving therapy with beta-lactam antibacterial drugs. There have been reports of individuals with a history of penicillin hypersensitivity who have experienced severe hypersensitivity reactions when treated with another beta-lactam antibacterial drug. If an allergic reaction to VABOMERE occurs, discontinue the drug immediately.

Seizures and other adverse Central Nervous System (CNS) experiences have been reported during treatment with meropenem, which is a component of VABOMERE. Close adherence to the recommended dosage regimens is urged, especially in patients with known factors that predispose to convulsive activity.

Clostridioides difficile-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including VABOMERE, and may range in severity from mild diarrhea to fatal colitis. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents. If CDAD is suspected or confirmed, ongoing antibacterial drug use not directed against *C. difficile* may need to be discontinued.

The concomitant use of VABOMERE and valproic acid or divalproex sodium is generally not recommended. Case reports in the literature have shown that co-administration of carbapenems, including meropenem, to patients receiving valproic acid or divalproex sodium results in a reduction in valproic acid concentrations. The valproic acid concentrations may drop below the therapeutic range as a result of this interaction, therefore increasing the risk of breakthrough seizures. If administration of VABOMERE is necessary, consider supplemental anticonvulsant therapy.

In patients with renal impairment, thrombocytopenia has been observed in patients treated with meropenem, but no clinical bleeding has been reported.

Alert patients receiving VABOMERE on an outpatient basis regarding adverse reactions such as seizures, delirium, headaches and/or paresthesias that could interfere with mental alertness and/or cause motor impairment.

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

As with other antibacterial drugs, prolonged use of VABOMERE may result in overgrowth of nonsusceptible organisms.

Adverse Reactions

The most frequently reported adverse reactions occurring in ≥3% of patients treated with VABOMERE were headache, phlebitis/infusion site reactions, and diarrhea.

Please see Full Prescribing Information for VABOMERE®.

MINOCIN® (minocycline) for injection Indication and Important Safety Information

INDICATION

MINOCIN® (minocycline) for Injection is indicated for the treatment of infections due to susceptible isolates of designated microorganisms, including *Acinetobacter* species bacteria. For the full list of indications and designated susceptible pathogens, please see the Full Prescribing Information.

IMPORTANT SAFETY INFORMATION

Contraindications

MINOCIN® (minocycline) for Injection is contraindicated in persons who have shown hypersensitivity to any of the tetracyclines or to any of the components of the product formulation.

Warnings

Tooth Development

MINOCIN®, like other tetracycline-class antibacterials, can cause fetal harm when administered to a pregnant woman. If any tetracycline is used during pregnancy, or if the patient becomes pregnant while taking these drugs, the patient should be apprised of the potential hazard to the fetus. The use of drugs of the tetracycline class 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).

This adverse reaction is more common during long-term use of the drugs but has been observed following repeated short-term courses. Enamel hypoplasia has also been reported. Tetracycline drugs, therefore, should not be used during tooth development unless other drugs are not likely to be effective or are contraindicated.

Skeletal Development

All tetracyclines form a stable calcium complex in any bone-forming tissue. A decrease in the fibula growth rate has been observed in premature human infants given oral tetracycline in doses of 25 mg/kg every six hours. This reaction was shown to be reversible when the drug was discontinued.

Results of animal studies indicate that tetracyclines cross the placenta, are found in fetal tissues, and can have toxic effects on the developing fetus (often related to retardation of skeletal development). Evidence of embryotoxicity has been noted in animals treated early in pregnancy.

Dermatologic Reaction

Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) including fatal cases have been reported with minocycline use. If this syndrome is recognized, the drug should be discontinued immediately.

Anti-anabolic Action

The anti-anabolic action of the tetracyclines may cause an increase in BUN. While this is not a problem in those with normal renal function, in patients with significantly impaired function, higher serum levels of tetracycline may lead to azotemia, hyperphosphatemia, and acidosis. Under such conditions, monitoring of creatinine and BUN is recommended, and the total daily dosage should not exceed 200 mg in 24 hours. If renal impairment exists, even usual oral or parenteral doses may lead to systemic accumulation of the drug and possible liver toxicity.

Photosensitivity

Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking tetracyclines. This has been reported with minocycline.

Central Nervous System Effects

Central nervous system side effects including light-headedness, dizziness or vertigo have been reported. Patients who experience these symptoms should be cautioned about driving vehicles or using hazardous

machinery while on minocycline therapy. These symptoms may disappear during therapy and usually disappear rapidly when the drug is discontinued.

Clostridium difficile Associated Diarrhea

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including MINOCIN®, and may range in severity from mild diarrhea to fatal colitis. If CDAD is suspected or confirmed, ongoing antibacterial use not directed against *C. difficile* may need to be discontinued.

Intracranial Hypertension

Intracranial hypertension (IH, pseudotumor cerebri) has been associated with the use of tetracyclines including MINOCIN®. Clinical manifestations of IH include headache, blurred vision, diplopia, and vision loss; papilledema can be found on fundoscopy. Women of childbearing age who are overweight or have a history of IH are at greater risk for developing tetracycline associated IH. Concomitant use of isotretinoin and MINOCIN® should be avoided because isotretinoin is also known to cause pseudotumor cerebri.

Although IH typically resolves after discontinuation of treatment, the possibility for permanent visual loss exists. If visual disturbance occurs during treatment, prompt ophthalmologic evaluation is warranted. Since intracranial pressure can remain elevated for weeks after drug cessation patients should be monitored until they stabilize.

PRECAUTIONS

As with other antibacterial preparations, use of this drug may result in overgrowth of nonsusceptible organisms, including fungi. If superinfection occurs, the antibacterial should be discontinued and appropriate therapy instituted.

Hepatotoxicity has been reported with minocycline; therefore, minocycline should be used with caution in patients with hepatic dysfunction and in conjunction with other hepatotoxic drugs.

Incision and drainage or other surgical procedures should be performed in conjunction with antibiotic antibacterial therapy when indicated.

MINOCIN® (minocycline) for Injection contains magnesium sulfate heptahydrate. Because magnesium is excreted primarily by the kidney, serum levels of magnesium should be monitored in patients with renal impairment.

Because MINOCIN® (minocycline) for Injection contains magnesium, close monitoring is recommended in patients with heart block or myocardial damage.

Prescribing MINOCIN® (minocycline) for Injection 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 the development of drug-resistant bacteria.

Adverse Reactions

For a complete list of adverse reactions that have been observed in patients receiving tetracyclines, consult the full prescribing information for MINOCIN® (minocycline) for injection.

Please see Full Prescribing Information for MINOCIN®.