
Product Data Sheet

Product Name: Oritavancin diphosphate (LY333328 diphosphate)

Cat. No.: GC32082

Chemical Properties

Cas. No. 192564-14-0

Formula $C_{86}H_{103}Cl_3N_{10}O_{34}P_2$

M.Wt 1989.09

Solubility DMSO : 33.33 mg/mL (16.76 mM; Need ultrasonic(<60°C)) □Water□50 mg/mL (25.14 mM; Need ultrasonic) Storage 4°C, sealed storage, away from moisture

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure **Protocol****Cell experiment****[1]:**

Cell lines J774 cells

Preparation Method J774 cells were cultured in RPMI 1640 containing 10% fetal calf serum at 37°C in a 5% CO₂ humidified incubator. The cells were treated with different concentrations of Oritavancin (1, 5, 10, 20, 40, 60, 80, and 100µg/ml) for 24 hours, and then incubated in HBSS buffer containing 0.5% hydrogen peroxide for 25 minutes. The levels of ROS in the cells were evaluated.

Reaction Conditions 1, 5, 10, 20, 40, 60, 80, and 100µg/ml; 24h

Caution: Product has not been fully validated for medical applications. For research use only.

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Applications	Oritavancin treatment significantly enhanced the levels of ROS in J774 cells exposed to H ₂ O ₂ in a dose-dependent manner.
Animal experiment [2]:	
Animal models	Female BALB/c mice
Preparation Method	Female BALB/c mice (6-week-old) were housed four per cage in a soundproof room under a 12h/12h light/dark cycle (lights on at 07:00) and were fed a standard laboratory diet and tap water ad libitum. Dexamethasone was administered by subcutaneous injection at 5 mg/kg/day (6 days per week) to suppress the immune response of mice to sustain <i>M. abscessus</i> infection. All mice were infected with 10 ⁶ CFU <i>M. abscessus</i> via intravenous injection. From day 3 after infection, the infected mice were treated daily with Oritavancin for 10 days. Oritavancin, cefoxitin, and meropenem were administered via subcutaneous injection at the doses of 50mg/kg, 200mg/kg, and 100mg/kg, respectively. All the mice were sacrificed on day 10 after drug treatment, lungs were removed and homogenized. Homogenates were plated onto 7H11 agar plates to calculate CFUs for determining the bacterial loads of these organs.
Dosage form	50mg/kg/day for 10 days; s.c.
Applications	Oritavancin treatment significantly reduced the load of pulmonary <i>M. abscessu</i> in the immunosuppressed mouse models.

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References:

- [1] Lemaire S, Mingeot-Leclercq M P, Tulkens P M, et al. Study of macrophage functions in murine J774 cells and human activated THP-1 cells exposed to oritavancin, a lipoglycopeptide with high cellular accumulation[J]. Antimicrobial agents and chemotherapy, 2014, 58(4): 2059-2066.
- [2] Wang G, Tang J, Feng J, et al. Activity of oritavancin and its synergy with other antibiotics against Mycobacterium abscessus infection in vitro and in vivo[J]. International Journal of Molecular Sciences, 2021, 22(12): 6346.

Background

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Oritavancin diphosphate (LY333328 diphosphate) is a semisynthetic lipoglycopeptide analogue of vancomycin, inhibiting ArIS kinase activity with an IC₅₀ value of 5.47μM^[1]. Oritavancin can bind to the d-alanyl-d-alanine peptidoglycan termini of Lipid II, prevent the cross-linking of adjacent peptidoglycan chains, reduce the integrity of the cell wall, and cause membrane depolarization and increased permeability in intact *Staphylococcus* and *Enterococcus*^[2]. Oritavancin has been widely used to kill drug-resistant Gram-positive bacteria and alleviate acute bacterial skin and soft tissue infections^[3].

In vitro, Oritavancin (20μg/ml) treatment for 24 hours significantly promoted the production of reactive oxygen species (ROS) in J774 cells exposed to H₂O₂^[4]. Treatment with 20mg/ml Oritavancin for 72 hours resulted in the accumulation of phospholipids, free cholesterol, and esterified cholesterol in rat embryonic fibroblasts^[5].

In vivo, Oritavancin treatment via daily subcutaneous injection at a dose of 50mg/kg for 10 days significantly reduced the load of pulmonary *Mycobacterium abscessus* in the immunosuppressed mouse models^[6]. Daily intravenous administration of 10mg/kg dose of Oritavancin for 2 days significantly reduced the concentration of penicillin-resistant *Streptococcus pneumoniae* in the meningitis rabbit model and decreased inflammatory indicators^[7].

References:

- [1] Bai J, Zhu X, Zhao K, et al. The role of ArIRS in regulating oxacillin susceptibility in methicillin-resistant *Staphylococcus aureus* indicates it is a potential target for antimicrobial resistance breakers[J]. *Emerging microbes & infections*, 2019, 8(1): 503-515.
- [2] Brade K D, Rybak J M, Rybak M J. Oritavancin: a new lipoglycopeptide antibiotic in the treatment of gram-positive infections[J]. *Infectious diseases and therapy*, 2016, 5(1): 1-15.
- [3] Saravolatz L D, Stein G E. Oritavancin: a long-half-life lipoglycopeptide[J]. *Clinical Infectious Diseases*, 2015, 61(4): 627-632.
- [4] Lemaire S, Mingeot-Leclercq M P, Tulkens P M, et al. Study of macrophage functions in murine J774 cells and human activated THP-1 cells exposed to oritavancin, a lipoglycopeptide with high cellular accumulation[J]. *Antimicrobial agents and*

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chemotherapy, 2014, 58(4): 2059-2066.

[5] Van Bambeke F, Saffran J, Mingeot-Leclercq M P, et al. Mixed-lipid storage disorder induced in macrophages and fibroblasts by oritavancin (LY333328), a new glycopeptide antibiotic with exceptional cellular accumulation[J]. Antimicrobial agents and chemotherapy, 2005, 49(5): 1695-1700.

[6] Wang G, Tang J, Feng J, et al. Activity of oritavancin and its synergy with other antibiotics against Mycobacterium abscessus infection in vitro and in vivo[J]. International Journal of Molecular Sciences, 2021, 22(12): 6346.

[7] Cabellos C, Fernandez A, Maiques J M, et al. Experimental study of LY333328 (oritavancin), alone and in combination, in therapy of cephalosporin-resistant pneumococcal meningitis[J]. Antimicrobial agents and chemotherapy, 2003, 47(6): 1907-1911.

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