Zinplava

(bezlotoxumab)

New Product Slideshow

MPR

Introduction

- **Brand name:** Zinplava
- **Generic name:** Bezlotoxumab
- **Pharmacological class:** Human IgG1 monoclonal antibody
- **Strength and Formulation:** 25mg/mL; solution for IV infusion after dilution; preservative-free
- **Manufacturer:** Merck
- **How supplied:** Single-dose vial (40mL)—1
- **Legal Classification:** Rx

Indications

- To reduce recurrence of *Clostridium difficile* infection (CDI) in patients who are receiving antibacterial drug treatment of CDI and are at high risk for CDI recurrence

Limitations of Use

- **Not** for treating CDI
- Use only in conjunction with antibacterial drug treatment of CDI

Dosage & Administration

- Infuse over 60 minutes
- ≥18 years: a single dose of 10mg/kg

Considerations for Special Populations

- **Pregnancy:** Adequate and well controlled studies not conducted in pregnant women
- **Nursing mothers:** Consider the need and adverse effects on the infant
- **Pediatric:** <18 years: not established
- **Elderly:** No overall differences observed in safety or efficacy

Warnings/Precautions

- History of congestive heart failure (CHF)

Adverse Reactions

- Nausea
- Pyrexia
- Headache
- Infusion-related reactions
- Heart failure

Mechanism of Action

- Bezlotoxumab is a **human monoclonal antibody** that binds *C. difficile* toxin B with an equilibrium dissociation constant (K_d) of $<1x10^{-9}M$
- Bezlotoxumab inhibits the binding of toxin B and prevents its effects on mammalian cells
- *In vitro* studies in cell-based assays using Vero cells or Caco-2 cells, suggest that bezlotoxumab neutralizes the toxic effects of toxin B

Clinical Trials

- The safety and efficacy of Zinplava were studied in 2 randomized, double-blind, placebo-controlled, multicenter, Phase 3 trials **(Trials 1 and 2)** in patients receiving standard of care antibacterial drugs for treatment of CDI (SoC)

- Study randomization was based on SoC (metronidazole, vancomycin, or fidaxomicin) and hospitalization status (inpatient vs. outpatient) at the time of study entry

Clinical Trials

- Enrolled patients had a confirmed diagnosis of CDI and a positive stool test no more than 7 days before study entry
- They received a 10–14 day course of oral SoC and a single infusion of Zinplava or placebo during the course of SoC
- Patients receiving oral vancomycin or oral fidaxomicin were able to also receive intravenous metronidazole

Clinical Trials

- **Trial 1** included 403 patients randomized to Zinplava and 404 patients randomized to placebo
- **Trial 2** included 407 patients randomized to Zinplava and 399 patients randomized to placebo
- Enrolled patients were assessed for clinical cure of the presenting CDI episode, defined as no diarrhea for 2 consecutive days following the completion of a ≤14 day SoC regimen
- Patients who achieved clinical cure were then evaluated for CDI recurrence through 12 weeks following administration of Zinplava or placebo

Clinical Trials

- **CDI recurrence** was defined as a new episode of diarrhea associated with a positive stool test for toxigenic *Clostridium difficile* following clinical cure of the presenting CDI episode

- **Sustained clinical response** was defined as clinical cure of the presenting CDI episode and no CDI recurrence through 12 weeks after infusion

Clinical Trials

- In **Trial 1**, sustained clinical response was seen in **60.1%** of patients in the Zinplava with SoC group vs. **55.2%** of patients in the placebo with SoC group (adjusted difference 4.8, 95% CI:−2.1, 11.7)
- **CDI recurrence** was seen in 17.4% of patients in the Zinplava with SoC group vs. 27.6% in the placebo with SoC group
- The clinical cure rate of the presenting CDI episode was lower in the Zinplava arm vs. the placebo arm

Clinical Trials

- In **Trial 2**, sustained clinical response was seen in **66.8%** of patients in the Zinplava with SoC group vs. **52.1%** of patients in the placebo with SoC group (adjusted difference 14.6, 95% CI: 7.7, 21.4)
- **CDI recurrence** was seen in 15.7% of patients in the Zinplava with SoC group vs. 25.7% of patients in the placebo with SoC group
- The clinical cure rate was lower in the placebo arm vs. the Zinplava arm

Clinical Trials

- Efficacy results in patients at high risk for CDI recurrence (eg, patients aged ≥65yrs, with a history of CDI in the past 6 months, immunocompromised state, severe CDI at presentation, or *Clostridium difficile* ribotype 027) were consistent with the efficacy results in the overall trial population in Trials 1 and 2

- For more clinical trial data, see full labeling

New Product Monograph

- For more information view the product monograph available at:

  http://www.empr.com/zinplava/drug/34650/