Pharmacology Matters

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BEZLOTOXUMAB: A NEW DRUG FOR THE TOXIC EFFECTS OF *CLOSTRIDIUM DIFFICILE*

Clostridium difficile (*C. diff*) is a non-native bacterium that colonizes the intestinal tract and spreads by spores that can be found in the feces. It is communicated from person to person by fecal to mouth route. Patients who have been receiving antibiotics appear to be at particular risk of *C. diff* infection likely due to the suppression of natural intestinal bacteria flora. Treatment has been conducted using antibiotics, but has proved difficult due to *C. diff*'s antibiotic resistance and protective spore coating. Symptoms include abdominal pains accompanied by several distinctive foul-smelling, loose, watery stools for more than 1 day (Surawicz et al., 2013; Taylor, McHale, Saenz, & Plaxe, 2017).

Hospital-acquired *C. diff* is largely responsible for infections. Estimated cases of *C. diff* infections per year in the United States are 453,000, with a mortality rate of 6.5% (Lessa et al., 2015). The most dangerous strains of *C. diff* release endotoxins (A and B) that inflame and damage intestinal mucosa. Treatment includes the antibiotics vancomycin, fidaxomicin, or metronidazole; probiotics; and fecal transplant (Cairns et al., 2017). Prevention appears to be effective with frequent caregiver hand washing, private room, and equipment cleaning between patients (Surawicz et al., 2013).

Recently, a new drug has been approved by the Food and Drug Administration (FDA) to treat *C. diff* infection. Bezlotoxumab (Zinplava; Merck & Co., Kenilworth, NJ) is a monoclonal antibody that attaches to toxin B, rendering that toxin unable to bind to intestinal cells (Orth et al., 2014). Monoclonal antibodies are specifically engineered, identical Y-shaped proteins that target a particular part of an antigen. An antigen is a chemical structure that harms cells and activates the immune system. Antibodies (Ab) in the body are also called immunoglobulins (Ig). These protein antibodies

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are secreted by specialized white blood cells called plasma cells (Nutt, Hodgkin, Tarlinton, & Cororan, 2015). Through a complex immune response system, plasma cells are instructed to produce specific antibodies that attach to a particular molecular structure and may destroy or label that structure for other immune cells to respond (Nutt et al., 2015). *C. diff* toxin B is the antigen targeted by bezlotoxumab. Once bezlotoxumab attaches to toxin B, it is unable to attach to and harm intestinal cells (Figure 1). It appears that bezlotoxumab exerts its action not by destroying toxin B, but rather by occupying the binding site, rendering it unable to attach and exert its harmful effects ("FDA briefing document," 2016).

Bezlotoxumab is intended to bind and lessen *C. diff*'s tissue-damaging toxin B. It is not intended to treat the underlying disease cause, as it is not an antibacterial drug. Antibacterial drugs should remain a part of *C. diff*'s treatment. Bezlotoxumab requires dilution before administration. It is prepared as 1,000 mg/40 ml (25 mg/ml) vial. Administration is as a single 10 mg/kg dose diluted in an appropriate amount of 0.9% sodium chloride injection, or 5% dextrose injection, to make a final concentration of 1–10 mg/ml. Infusion should be over 60 minutes (Zinplava PI, 2017).

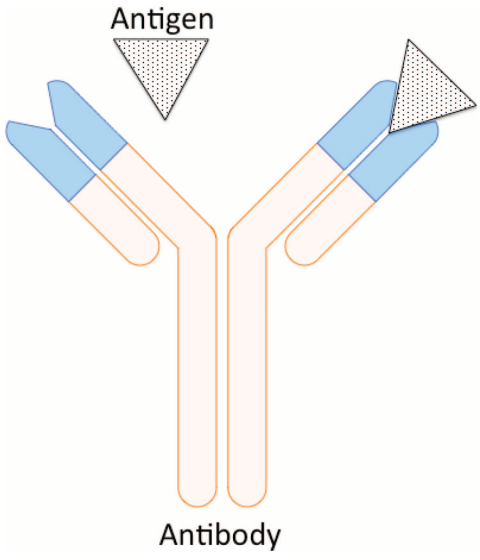

FIGURE 1. Y-shaped antibody attached to antigen (triangle).

Bezlotoxumab is relatively contraindicated in patients with congestive heart failure, as patients with this condition in clinical trials had an increased risk of heart failure (12.7% vs. 4.8%) and death (19.5% vs. 12.5%) compared with patients not receiving this drug (placebo group). Other adverse reactions include nausea, pyrexia, and headache, which occurred with a higher incidence than that with placebo in clinical studies (Zinplava PI, 2017).

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