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Effective Date: 04/14/2022

Zinplava™ (bezlotoxumab)

HCPCS: J0565

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

- A. Coverage of the requested drug is provided when all the following are met:
 - a. Prescribed by or in consultation with a gastroenterologist or infectious disease specialist
 - b. Patient greater than 18 years of age
 - c. Patient with a confirmed diagnosis of CDI and a positive stool test
 - d. Patient at high risk for CDI recurrence e.g.
 - i. Patients aged 65 years and older
 - ii. History of CDI in the past 6 months
 - iii. Immunocompromised state
 - iv. Severe CDI at presentation
 - v. Clostridium difficile ribotype 027
 - e. Used in conjunction with standard of care antibacterial agents (i.e. metronidazole or vancomycin)
- B. Quantity Limitations, Authorization Period and Renewal Criteria
 - a. Quantity Limit: One infusion per lifetime
 - b. Initial Authorization Period: 1 month
 - c. Renewal Criteria: No further authorizations required. Safety and efficacy of repeat administration of Zinplava in patients with CDI has not been studied

***Note: Coverage may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at <http://www.cms.hhs.gov/>. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information

- CDI is one of the most common hospital-acquired (nosocomial) infections and is an increasingly frequent cause of morbidity and mortality among older adult hospitalized patients
- *Clostridium difficile* colonizes the human intestinal tract after the normal gut flora has been altered by antibiotic therapy and is the causative organism of antibiotic-associated pseudomembranous colitis

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- Patients taking antibiotics are 7 to 10 times more likely to contract CDI
- The overprescribing of antibiotics combined with poor hygiene and infection control on the part of healthcare workers make CDI a scourge in the nation's hospitals and nursing homes
- The Centers for Disease Control and Prevention estimated that CDI caused almost 500,000 illnesses and 29,000 deaths within one month of the initial diagnosis in 2011
- Estimates suggest that recurrence of CDI occurs within 30 days after completion of treatment in 20.9% of patients with an initial hospital-associated infection and 13.5% of those with an initial community-associated infection
- The frequency of recurrence has been shown to increase with each subsequent episode, with a 45% chance of recurrence after the first recurrent episode and a 65% chance following a second recurrent episode
- The incidence of recurrent CDI is higher in certain patient populations, including people 65 years of age or older and those with compromised immune systems
- Toxins A and B are the major virulence factors of *Clostridium difficile*
- Toxins A and B mediate disease by disrupting the cytoskeletal structure of intestinal epithelial cells, resulting in inflammation and cell death
- Toxin A ("enterotoxin") causes inflammation leading to mucosal injury and intestinal fluid secretion
- Toxin B ("cytotoxin") is essential for the virulence of *Clostridium difficile* and is more potent than toxin A in mediating colonic mucosal damage
- Zinplava binds to and neutralizes toxin B, the one considered central to the life-threatening virulence of the bacteria.

References:

1. Zinplava [prescribing information package insert] Merck Sharp and Dohme, Corp.; October 2016
2. Bezlotoxumab (BEZ) Alone and With Actoxumab (ACT) for Prevention of Recurrent *C. difficile* Infection (rCDI) in Patients on Standard of Care (SoC) Antibiotics: Integrated Results of 2 Phase 3 Studies (MODIFY I and MODIFY II) Open Forum Infect Disease, Fall 2015, Vol 2, issue suppl 1.
3. Wilcox MH, Gerding D, Poxton I, et al. Bezlotoxumab alone and with actoxumab for prevention of recurrent *C. difficile* infection in patients on standard of care antibiotics: Integrated results of two Phase III studies (MODIFY I and MODIFY II) [oral presentation]. ID Week; San Diego, CA; October 7-11, 2015
4. Guidelines for Diagnosis, Treatment, and Prevention of *Clostridium difficile* Infections. The American Journal of Gastroenterology, Volume 108, April 2013.
5. FDA approves Zinplava for preventing return of C diff. Available at <http://www.medscape.com/viewarticle/870887>. Accessed January 19, 2017.
6. FDA Briefing Document. Bezlotoxumab Injection Meeting of the Antimicrobial Drugs Advisory Committee (AMDAC) [cited June 9, 2016] available from <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Anti-InfectiveDrugsAdvisoryCommittee/UCM505290.pdf>

Policy History		
#	Date	Change Description
1.1	Effective Date: 04/14/2022	Annual review of criteria was performed, no changes were made.
1.0	Effective Date: 01/01/2022	Effective as of date on policy.

* The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or <http://dailymed.nlm.nih.gov/dailymed/index.cfm>.