RXADVANCE
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Clinical Policy Title:	bezlotoxumab
Policy Number:	RxA.330
Drug(s) Applied:	Zinplava™
Original Policy Date:	02/07/2020
Last Review Date:	09/14/2020
Line of Business Policy Applies to:	All lines of business

Background

Bezlotoxumab (Zinplava™) is a human monoclonal antibody that binds to *Clostridium difficile* toxin B. Zinplava is indicated to reduce the recurrence of *Clostridium difficile* infection (CDI) in patients 18 years of age or older who are receiving antibacterial drug treatment of CDI and are at a high risk for CDI recurrence.

Limitation(s) of use:

- Zinplava is not indicated for the treatment of CDI.
- Zinplava is not an antibacterial drug.
- Zinplava should only be used in conjunction with antibacterial drug treatment of CDI.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Bezlotoxumab (Zinplava)	Clostridium difficile infection	10 mg/kg as a single doseIV infusion over 60 minutes	10mg/kg

Dosage Forms

- Single-dose vial for injection: 1,000 mg/40 mL (25 mg/mL).

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. Clostridium difficile Infection (must meet all):

1. Diagnosis of CDI confirmed by documentation of positive *Clostridium difficile* test;
2. Age ≥ 18 years;
3. Member will receive or is currently receiving concomitant antibacterial drug treatment for CDI (e.g., metronidazole, vancomycin, fidaxomicin);
4. Member has had at least two episodes of CDI recurrence (total 3 episodes) in the previous 6 months and has been treated with appropriate treatment for CDI (e.g., metronidazole, vancomycin, fidaxomicin), including a pulsed vancomycin regimen;
   **Treatment failure for CDI may be declared in as little as 48 hours in patients with severe disease who fail to improve*
5. Dose does not exceed 10 mg/kg once;

Approval Duration
Commercial: 3 months (1 dose only)
Medicaid: 3 months (1 dose only)

II. Continued Therapy Approval

A. Clostridium difficile Infection:

1. Re-authorization is not permitted. Members must meet the initial approval criteria

Approval Duration: None

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
IDSA: Infectious Diseases Society of America
CDI: Clostridium difficile Infection

APPENDIX B: Therapeutic Alternatives
None

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None
- Boxed Warning(s):
  - None

APPENDIX D: General Information

- Zinplava is the only medication approved to reduce the recurrence of CDI.
- Zinplava was studied in two randomized placebo controlled trials in which patients received a single IV infusion of Zinplava. The efficacy of repeat courses of Zinplava therapy has not been established.
- Approximately 35% of CDI patients experience recurrence after the initial treatment and resolution of diarrhea. Of those who have a primary recurrence, 40% will have another CDI episode, and after 2 recurrences, the chances of an additional episode increases to as high as 65%.
- Per the IDSA Clinical Practice Guidelines for *Clostridium difficile* Infection 2017 Update:
  - An incident case is one with a new primary symptom onset (i.e., in the previous 8 weeks, there was not an episode of positive symptoms with positive *C. diff* result) and positive *C. diff* assay result.
  - A recurrent infection is an episode of symptom onset with a positive assay result following an episode with positive assay result in the previous 2–8 weeks.

  - Vancomycin and fidaxomicin are preferred first-line treatments for non-severe, recurrent, and severe disease in adults. Metronidazole is recommended as an alternative agent, if vancomycin and fidaxomicin are unavailable.
  - Examples of treatment regimens for recurrence:
- Vancomycin 125 mg PO QID for 10 days (may be followed by rifaximin 400 mg PO TID for 20 days)
- Tapered and pulsed regimens of vancomycin (e.g., vancomycin PO 125 mg QID for 10 to 14 days, then BID for 1 week, then QD for 1 week, then every 2 or 3 days for 2 to 8 weeks)
- Fidaxomicin 200 mg PO BID for 10 days
- Fecal microbiota transplantation

References

1. Zinplava Prescribing Information. Whitehouse Station, NJ: Merck & Co., Inc; October 2016. Available at: https://www.merck.com/product/usa/pi_circulars/z/zinplava/zinplava_pi.pdf. Accessed July 2, 2020.
2. Antimicrobial Drugs Advisory Committee. Bezlotoxumab injection briefing document (BLA 761046). Published June 9, 2016. Available athttp://www.fda.gov/downloads/advisorycommittees/committeesmeetingmaterials/drugs/antiinfectivedrugsadvisorycommittee/ucm505291.pdf. Accessed October 30, 2018.
3. Surawicz CM, Brandt LJ, Binion DG et al. Guidelines for diagnosis, treatment, and prevention of Clostridium difficile infections. Am J Gastroenterol. 2013 Apr;108(4):478-98; quiz 499. doi: 10.1038/ajg.2013.4. Epub 2013 Feb 26.
4. Zar FA, Bakkanagari SR, Moorthi KM, Davis MB. A comparison of vancomycin and metronidazole for the treatment of Clostridium difficile-associated diarrhea, stratified by disease severity. Clin Infect Dis 2007;45(3):302-7.
5. Lessa FC, Mu Y, Bamber WM et al. Burden of Clostridium difficile infection in the United States. N Engl J Med. 2015 Feb 26;372(9):825-34. doi: 10.1056/NEJMoa1408913
6. McDonald LC, Gerding DN, Johnson S, et al. Clinical practice guidelines for Clostridium difficile infection in adults and children: 2017 updated by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). Clin Infect Dis. March 2018;66(7):987-994.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established	01/2020	02/07/2020
Policy was reviewed: 1) Policy title table was updated 2) Appendices were updated 3) References were updated	07/02/2020	09/14/2020