Clinical Policy: Bezlotoxumab (Zinplava)

Reference Number: PA.CP.PHAR.300
Effective Date: 01/18
Last Review Date: 07/18

Coding Implications
Revision Log

Description
Bezlotoxumab (Zinplava™) is a human monoclonal antibody that binds to *Clostridium difficile* toxin B.

FDA Approved Indication(s)
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.

Policy/Criteria
It is the policy of Pennsylvania Health and Wellness ® that Zinplava is **medically necessary** when the following criteria are met:

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. Patient is at high risk for recurrence: age greater than or equal to 65, clinically severe CDI (as defined by ZAR score greater than or equal to 2), at least one previous episode of CDI within the past 6 months, immunosuppression, or the presence of a hypervirulent strain of CDI bacteria;
5. Dose does not exceed 10 mg/kg once.

Approval duration: 3 months(1 dose only)

Re-authorization will not be approved.
Initial approval criteria must be met for new episodes of CDI.

B. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Therapy

A. *Clostridium difficile* Infection:

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

Approval duration: Not applicable

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PMN.53

Background

Description/Mechanism of Action:

Bezlotoxumab is a human monoclonal antibody that binds *C. difficile* toxin B with an equilibrium dissociation constant (Kd) of $<1\times10^{-9}$M. Bezlotoxumab inhibits the binding of toxin B and prevents its effects on mammalian cells. Bezlotoxumab does not bind to *C. difficile* toxin A.

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CDI: *Clostridium difficile* infection
FDA: Food and Drug Administration
IDSA: Infectious Diseases Society of America

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

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

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Clostridium difficile infection (CDI)	10 mg/kg as a single dose IV infusion over 60 minutes	10 mg/kg

V. Product Availability

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

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
N/A	

Reviews, Revisions, and Approvals	Date	Approval Date
Age added per safety guidance endorsed by Centene Medical Affairs. References reviewed and updated.	02/18	
1Q19 annual review: references reviewed and updated.	01/19	

References

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2. Antimicrobial Drugs Advisory Committee. Bezlotoxumab injection briefing document (BLA 761046). Published June 9, 2016. Available at http://www.fda.gov/downloads/advisorycommittees/committeesmeetingmaterials/drugs/anti-infectivedrugsadvisorycommittee/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
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