Clinical Policy: Bezlotoxumab (Zinplava)

Reference Number: LA.PHAR.300
Effective Date: 02.22.24
Last Review Date: 03.03.25
Line of Business: Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

****Please note: This policy is for medical benefit****

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

FDA Approved Indication(s)
Zinplava is indicated to reduce recurrence of Clostridioides difficile infection (CDI) in adults and pediatric patients 1 year of age and older who are receiving antibacterial drug treatment for 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
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Louisiana Healthcare Connections 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 ≥ 1 year;
3. Member will receive or is currently receiving concomitant antibacterial drug treatment for CDI (e.g., vancomycin, fidaxomicin);
4. Member has had at least one episode of CDI recurrence (total 2 episodes) in the previous 6 months and has been treated with appropriate treatment for CDI (e.g., 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: 3 months (1 dose only)

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy LA.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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – LA.PMN.53 for Medicaid or evidence of coverage documents.

IV. 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
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Dificid® (fidaxomicin)	200 mg PO BID for 10 days; for recurrences, may use alternative regimen of 200 mg PO BID for 5 days, followed by QOD for 20 days	See regimen
vancomycin	Adult: 125 mg PO QID for 10 days; for recurrences, may use a tapered and pulsed regimen Pediatric: 10 mg/kg/dose PO QID	See regimen

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: General Information

- The new term *Clostridioides difficile* was introduced in 2019. It may be used interchangeably with *Clostridium difficile*.
- 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 chance 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.
- Per the IDSA 2021 Focused Update for *Clostridium difficile* Infection in adults:
  - Fidaxomicin (standard or extended-pulsed regimen) is the preferred first-line treatment for patients with recurrent CDI episode(s).
  - Vancomycin in a tapered and pulsed regimen or as a standard course are acceptable alternatives for first CDI recurrence. For patients with multiple recurrences, vancomycin in a tapered and pulsed regimen, vancomycin followed by rifaximin, and fecal microbiota transplantation are options in addition to fidaxomicin.
- Examples of treatment regimens for recurrence:
  - Adult: Vancomycin 125 mg PO QID for 10 days (may be followed by rifaximin 400 mg PO TID for 20 days)
  - Pediatric: Vancomycin 10 mg/kg PO QID for 10 days (may be followed by rifaximin* for 20 days)
    ** rifaximin is not FDA-approved for use in children <12 years of age*
  - 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)
  - Adult: Fidaxomicin 200 mg PO BID for 10 days
  - Adult: Fidaxomicin 200 mg PO BID for 5 days followed by once every other day for 20 days
  - Fecal microbiota transplantation

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CDI recurrence	10 mg/kg as a single dose IV infusion over 60 minutes	10 mg/kg

VI. Product Availability

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

VII. References

1. Zinplava Prescribing Information. Whitehouse Station, NJ: Merck & Co., Inc; May 2023. Available at: https://www.merck.com/product/usa/pi_circulars/z/zinplava/zinplava_pi.pdf. Accessed October 22, 2024.
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 31, 2024.
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.
7. Johnson S, Lavergne V, Skinner AM, et al. Clinical Practice Guideline by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA): 2021 Focused Update Guidelines on Management of *Clostridioides difficile* Infection in Adults. CID 2021; 73 (1 September): e1029-1044.
8. Kelly CR, Fischer M, Allegretti JR, et al. ACG Clinical Guidelines: Prevention, Diagnosis, and Treatment of *Clostridioides difficile* Infections. Am J Gastroenterol 2021;116:1124 - 1147.
9. Clinical Pharmacology [database online]. Tampa, FL: Elsevier; 2023. URL: www.clinicalkey.com/pharmacology.

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
J0565	Injection, bezlotoxumab, 10 mg

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Converted corporate to local policy.	11.22.23	01.23.24
Annual review: updated CDI age requirement from ≥18 years to ≥ 1 year per FDA pediatric expansion; references reviewed and updated.	06.14.24	09.04.24
Annual review: no significant changes; references reviewed and updated	03.03.25	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

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