

Clinical Policy: Bezlotoxumab (Zinplava)

Reference Number: CP.PHAR.300

Effective Date: 11.16.16

Last Review Date: 02.19

Line of Business: Commercial, Medicaid

[Coding Implications](#)
[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

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

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 health plans affiliated with Centene Corporation[®] 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 \geq 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: 3 months (1 dose only)

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

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 Centene benefit and documentation supports positive response to therapy.
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial and CP.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

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

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
<i>Clostridium difficile</i> infection (CDI)	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; October 2016. Available at: https://www.merck.com/product/usa/pi_circulars/z/zinplava/zinplava_pi.pdf. Accessed October 30, 2018.
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
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.

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	P&T Approval Date
Policy created.	01.01.17	01.17
1Q18 annual review: combined for Medicaid and commercial lines of business; no significant change from previously approved corporate policy; age added per safety guidance endorsed by Centene Medical Affairs; references reviewed and updated.	11.03.17	02.18
1Q19 annual review: no significant changes; references reviewed and updated.	10.30.18	02.19

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. The Health Plan 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. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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