Clinical Policy: Bezlotoxumab (Zinplava)

Reference Number: CP.PHAR.300
Effective Date: 11.16.16
Last Review Date: 02.18
Line of Business: Commercial, Medicaid

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 the 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 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 (including 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 ≥ 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 (3 episodes) in the previous 6 months and has been treated with appropriate treatment for CDI (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.

Approval duration: 1 dose only (3 months)

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 (must meet all)**:**

1. Zinplava will not be approved for continued therapy. Subsequent request should be reviewed using initial approval criteria. The efficacy of repeat courses of Zinplava therapy has not been established.

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
IDSA: Infectious Diseases Society of America

Appendix B: Therapeutic Alternatives
Not applicable.

Appendix B: General Information

- Zinplava is the only medication approved to reduce the recurrence of CDI.
- 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%.
- The IDSA Clinical Practice Guidelines for Clostridium difficile Infection in Adults 2010 Update state that a new primary infection is one with no positive *C.diff* assay result within the previous 8 weeks since CDI symptoms began (e.g., diarrhea). A recurrent infection is one with a positive assay result within the previous 2–8 weeks since CDI symptoms began.
- Recurrent episodes of CDI are treated with metronidazole, vancomycin, or Dificid. The first recurrence should be treated with the same treatment as the initial episode. The

second recurrence should be treated with vancomycin in a pulsed regimen and the third recurrence with a pulsed regimen and consideration for fecal microbiata transplant.
    - Metronidazole: 500 mg orally 3 times per day for 10 - 14 days
    - Vancomycin: 125 mg orally 4 times per day for 10 days
    - Fidaxomicin: 200 mg orally twice daily for 10 days
- Pulsed Vancomycin: 10 days course of vancomycin at 125 mg four times per day, followed 125 mg daily pulsed every 3 days for 10 doses
- 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.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Clostridium Difficile Infection (CDI)	10 mg/kg as an IV infusion over 60 minutes	10 mg/kg

VI. Product Availability

Vial: 1,000 mg/40 mL (25 mg/mL)

VII. References

1. Zinplava Prescribing Information. Whitehouse Station, NJ: Merck & Co., Inc; October 2016. Available at http://www.merck.com. Accessed November 3, 2017.
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 November 3, 2017.
3. 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/ucm505290.pdf. Published June 9, 2016. Accessed November 3, 2017.
4. Cohen SH, Gerding DN, Johnson S et al. Clinical practice guidelines for Clostridium difficile infection in adults: 2010 update by the society for healthcare epidemiology of America (SHEA) and the infectious diseases society of America (IDSA). Infect Control Hosp Epidemiol. 2010 May;31(5):431-55. doi: 10.1086/651706.
5. 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.
6. 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.
7. 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

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

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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.