Clinical Policy: Bezlotoxumab (Zinplava)

Reference Number: CP.PHAR.300
Effective Date: 01/17
Last Review Date: 01/17

Coding Implications
Revision Log

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

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for bezlotoxumab (Zinplava™).

Policy/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 *Clostridium difficile (C. difficile)* infection (CDI) confirmed by documentation of positive *C. difficile* test;
2. 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 (see Appendix B) including a pulsed vancomycin regimen;
3. Will receive or is currently receiving concomitant antibacterial drug treatment for *CDI* (e.g. metronidazole, vancomycin, fidaxomicin).

Approval duration: one dose/3 months
Re-authorization will not be approved.
Initial approval criteria must be met for new episodes of CDI.

B. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy

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.

Formulations:
Zinplava: Intravenous injectable formulation

- Single-use vial containing 1,000 mg/40 mL (25 mg/mL) solution

FDA Approved Indications:
Zinplava is a human monoclonal antibody/intravenous infusion indicated to:

- Reduce recurrence of CDI in patients 18 years of age or older who are receiving antibacterial drug treatment of *CDI* and are at a high risk for recurrence.

Limitation of use:

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

Appendices

Appendix A: Abbreviation Key

CDI: *Clostridium difficile* infection

Appendix B: Treatment for CDI recurrent episodes

Recurrent episodes of CDI are treated with metronidazole, vancomycin, or fidaxomicin. 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 microbiota 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 by 125 mg daily pulsed every 3 days for 10 doses

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
Policy created.	1/17	01/17

References

1. Zinplava Prescribing Information. Whitehouse Station, NJ: Merck & Co., Inc; October 2016. Available at http://www.merck.com. Accessed November 2, 2016.
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/antiinfectivedrugsadvisorycommittee/ucm505291.pdf. Accessed November 10, 2016.
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/antiinfectivedrugsadvisorycommittee/ucm505290.pdf. Published June 9, 2016. Accessed November 9, 2016.

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.

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.

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.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.