

Clinical Policy: Bezlotoxumab (Zinplava)

Reference Number: ERX.SPA.03

Effective Date: 04.01.17

Last Review Date: 02.18

[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 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 (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Envolve Pharmacy Solutions[™] 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 (3 episodes total) in the previous 6 months and has been treated with an appropriate treatment for CDI (metronidazole, vancomycin, fidaxomicin), including a pulsed vancomycin regimen;
Failure 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 ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Clostridium Difficile Infection

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

Approval duration: N/A

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 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 C: 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 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, followed 125 mg daily pulsed every 3 days for 10 doses
 - 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
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 <https://www.merckconnect.com/zinplava/overview.html>. 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.	11.16	02.17
1Q18 annual review: - Added age requirement in accordance with prescribing information. - 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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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