

Clinical Policy Title:	bezlotoxumab
Policy Number:	RxA.330
Drug(s) Applied:	Zinplava™
Original Policy Date:	02/07/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Bezlotoxumab (Zinplava™) is a human monoclonal antibody that binds to *Clostridium difficile* toxin B. It 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.
- It is not an antibacterial drug.
- It should only be used in conjunction with antibacterial drug treatment of CDI.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
bezlotoxumab (Zinplava™)	Clostridium difficile infection	10 mg/kg as a single dose intravenous infusion over 60 minutes	10mg/kg

Dosage Forms

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

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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 (total 3 episodes) in the previous 6 months and

This clinical policy has been developed to authorize, modify, or determine coverage for individuals with similar conditions. Specific care and treatment may vary depending on individual need and benefits covered by the plan. This policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. This document may contain prescription brand name drugs that are trademarks of pharmaceutical manufacturers that are not affiliated with RxAdvance.

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

Commercial: 3 months (1 dose only)

Medicaid: 3 months (1 dose only)

II. Continued Therapy Approval

A. Clostridium difficile Infection:

1. Re-authorization is not permitted. Members must meet the initial approval criteria.

Approval Duration

Not applicable

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

FDA: Food and Drug Administration

IDSA: Infectious Diseases Society of America

CDI: Clostridium difficile Infection

APPENDIX B: Therapeutic Alternatives

None.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
 - None reported.
- Boxed Warning(s):
 - 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 orally four times a day for 10 days (may be followed by rifaximin 400 mg orally three times daily for 20 days)
- Tapered and pulsed regimens of vancomycin (e.g., vancomycin orally 125 mg four times daily for 10 to 14 days, then twice daily for 1 week, then once daily for 1 week, then every 2 or 3 days for 2 to 8 weeks)
- Fidaxomicin 200 mg orally twice daily for 10 days.
- Fecal microbiota transplantation.

References

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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.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established	01/2020	02/07/2020
Policy was reviewed: 1) Policy title table was updated 2) Appendices were updated 3) References were updated	07/02/2020	09/14/2020
Policy was reviewed: 1) Statement about provider sample “The provision of provider samples does not guarantee coverage...” was added to Clinical Policy. 2) References were reviewed and updated.	05/28/2021	9/14/2021