BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

VOWST™ (fecal microbiota spores, live-brpk) oral Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Vowst (fecal microbiota spores, live-brpk) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Gastroenterologist or Infectious Disease Specialist

2. Individual is 18 years of age or older

3. Individual has a confirmed diagnosis of history of recurrences of *Clostridioides difficile* infection (CDI) following standard-of-care antibacterial treatment for recurrent CDI (rCDI)

4. CDI episodes are documented as having diarrhea (3 or more unformed stools per day for at least 2 consecutive days) and a positive *C. difficile* stool sample using a toxin assay

5. Individual has a history of 3 or more CDI episodes (initial plus two recurrences) within 12 months

6. Individual has at least **ONE** of the following other risk factors for recurrent CDI:
    a. Individual is greater than 65 years of age
    b. Individual is immunocompromised (e.g., active hematologic malignancy, uses an antineoplastic or immunomodulating agent, uses corticosteroids, has received a solid organ transplant, is asplenic, or has an immunodeficiency condition, etc.)
    c. Episodes are described as clinically severe CDI
    d. Infection is due to a hypervirulent *Clostridioides difficile* strains (ribotypes 027, 078 or 244)

7. Individual currently will complete a standard-of-care antibacterial treatment for CDI and has CDI symptom resolution defined as less than 3 unformed stools in 24 hours for 2 or more consecutive days

8. Vowst treatment for prevention of CDI will begin 2-4 days after the end of standard-of-care antibacterial for CDI

9. Individual will not be using Vowst for the treatment of CDI

10. Individual has **NONE** of the following:
    a. Neutropenia (absolute neutrophil count of <500 cells/mm^3)
    b. History of fecal microbiota transplantation (FMT)
    c. Taking antibacterial therapy other than standard-of-care antibacterial for the most recent episode of CDI
    d. Toxic megacolon
    e. Small bowel ileus
    f. History of irritable bowel syndrome
    g. History of active inflammatory bowel disease (ulcerative colitis, Crohn's disease, microscopic colitis) with diarrhea believed to be caused by active inflammatory bowel disease in the past 12 months
    h. Major gastrointestinal surgery (e.g., significant bowel resection or diversion) within the previous 3 months or any history of total colectomy or bariatric surgery

11. Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for IV Zinplava (bezlotoxumab)

12. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

13. Will not be used in combination with other fecal transplants or preventative measures (e.g., Rebyota (fecal microbiota, live-jslm), Zinplava (bezlotoxumab injection))

Initial approval duration: 1 dose (4 capsules) orally, once daily for 3 consecutive days,
1 fill of 12 capsules in a 6 month period

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- **Criteria for continuation of coverage (renewal request):** Vowst (fecal microbiota spores, live-brpk) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Gastroenterologist or Infectious Disease Specialist

  2. Continuation of therapy requires meeting **ALL** of the Criteria for Initial Therapy and other criteria described below

  3. Individual has been adherent with the medication

  4. Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for IV Zinplava (bezlotoxumab)

  5. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

  6. Will not be used in combination with other fecal transplants or preventative measures (e.g., Rebyota (fecal microbiota, live-jslm), Zinplava (bezlotoxumab injection))

  Renewal duration: 1 dose (4 capsules) orally, once daily for 3 consecutive days,
  1 fill of 12 capsules in a 6 month period

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

  1. **Off-Label Use of Non-Cancer Medications**

  2. **Off-Label Use of Cancer Medications**

Description:

VOWST (fecal microbiota spores, live-brpk) is indicated to prevent the recurrence of *Clostridioides difficile* infection (CDI) in individuals 18 years of age and older following antibacterial treatment for recurrent CDI (rCDI). VOWST is not indicated for treatment of CDI.

*Clostridioides (*formerly *Clostridium) difficile (C. difficile)* infection is a bacterium causing symptoms ranging from diarrhea to more serious intestinal conditions such as colitis. CDI is one of the most common hospital-acquired infections and is an increasingly frequent cause of morbidity and mortality among older adult hospitalized individuals. *C. difficile* colonizes the human intestinal tract after the normal gut flora has been altered by antibiotic therapy and is the causative organism of antibiotic-associated pseudomembranous colitis.

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Clinical symptoms vary widely, from asymptomatic colonization to pseudomembranous colitis with bloody diarrhea, fever, severe abdominal pain, toxic megacolon, sepsis, bowel perforation and death. *C. difficile* infection is defined by the presence of symptoms, usually diarrhea, and either a stool test positive for *C. difficile* toxins (toxigenic *C. difficile*) or colonoscopic or histopathologic findings revealing pseudomembranous colitis.

The incidence of recurrent Clostridium difficile infection is reported to be 5-30% (mean 20%) of patients, usually within the first eight weeks after treatment of the infection.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Clostridium difficile infection (CDI): A bacterium causing symptoms ranging from diarrhea to more serious intestinal conditions such as colitis

Clinical cure: Cure of the baseline episode of Clostridium difficile infection after a standard-of-care (SOC) antimicrobial regimen with no reported diarrhea (≤ 2 loose stools per 24 hours) on the 2 days immediately following the last day of SOC treatment

CDI recurrence: Resolution of CDI symptoms while on appropriate therapy, followed by reappearance of symptoms, usually within two months of discontinuing treatment. Recurrence can represent either relapse or reinfection. Relapse is a recurrence with the original isolate. Reinfection is a recurrence with a new isolate.

***C. difficile* treatment failure:** Failure of treatment is not defined by development of a recurrent episode. Treatment failure is an inadequate response with unresolved *C. difficile* infection.

Per Vowst package insert:

	CDI Recurrence		
After treatment	VOWST	Placebo	Difference from Placebo
Through 8 weeks	12.4%	39.8%	27.4%
Through 12 weeks	18.0%	46.2%	28.2%
Through 24 weeks	21.3%	47.3%	26.0%

Resources:

Vowst (fecal microbiota spores, live-brpk) capsule product information, revised by Aimmune Therapeutics, Inc. 04-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 20, 2024.

Brody TJ, Ramrakha S. Fecal microbiota transplantation for treatment of *Clostridioides difficile* infection. In: UpToDate, Lamont JT, Bogorodskaya M, Robson KM (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through June 2024. Topic last updated on March 19, 2024. AccessedJuly 20, 2024.

Kelly CP, Lamont JT, Bakken JS. *Clostridioides difficile* infection in adults: Treatment and prevention. In: UpToDate, Calderwood SB, Bogorodskaya M (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through June 2024. Topic last updated on May 11, 2023 March 19, 2024. Accessed July 20, 2024.

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Johnson S, Lavergne V, Skinner AM, et al.: Clinical Practice Guideline by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA): 2021 Focused Update Guidelines on Management of *Clostridioides difficile* Infection in Adults. CID 2021:73 (1 September): e1029. Accessed June 01, 2023. Re-evaluated July 20, 2024.

Feuerstadt P, Louie TJ, Lashner B, et al: SER-109, an Oral Microbiome Therapy for Recurrent *Clostridioides difficile* Infection. NEJM 2022 Jan 20;386 (3):220-229. Accessed May 17, 2023. Re-evaluated July 20, 2024.

ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT03183128: A Phase 3 Multicenter, Randomized, Double Blind, Placebo Controlled, Parallel Group Study to Evaluate the Safety, Tolerability, & Efficacy of SER-109 vs. Placebo to Reduce Recurrence of *Clostridium Difficile Infection* (CDI) in Adults. Available from: http://clinicaltrials.gov. Last update posted April 27, 2023. Last verified June 2021. Accessed May 17, 2023. Re-evaluated July 20, 2024.