Vowst (fecal microbiota spores, live-brpk) Prior Authorization with Quantity Limit Program Summary

This program applies to Medicaid.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
1/1/2024	1/1/2024

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Vowst™ (fecal microbiota spores, live-brpk caps) Capsule	To prevent the recurrence of Clostridioides difficile infection (CDI) in individuals 18 years of age and older following antibacterial treatment for recurrent CDI (rCDI). Limitation of Use: VOWST is not indicated for treatment of CDI.		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Clostridioides difficile infection (CDI)	Clostridioides difficile is a bacterium that can cause potentially life-threatening diarrheal illness in individuals with an unhealthy mixture of gut bacteria, known as dysbiosis, and can cause recurrent infections in nearly a third of infected individuals. Recurrent CDI (rCDI) is usually defined as an episode of CDI occurring within 8 weeks of a previous episode. rCDI may be due to relapse of the previous CDI by the same strain or reinfection by a different strain. About 15% to 30% of patients who initially respond to antimicrobial therapy experience rCDI. After the first recurrence has improved, the risk of further recurrence significantly increases. A second recurrence rate of 40% has been reported among patients with resolved first recurrence. The subsequent recurrence rate of patients who have already recurred more than twice is approximately 45% to 65%. The high recurrence rate of CDI contributes to increased health care costs. The traditional treatment of rCDI includes antibiotics, which may further exacerbate dysbiosis. Fecal microbiota transplantation (FMT) has proven to be a highly efficacious therapeutic modality to prevent recurrent CDI and increasing data support its use in severe or refractory cases.(3,4,5) The gut is estimated to contain 1000 bacterial species containing 100-fold more genes than the human genome. Viruses, bacteriophages, archaea, and fungi contribute to this microbial community, which functions as an "organ" with an immense impact on human health and disease, including host metabolism, physiology, nutrition, and immune function. Recent evidence demonstrates long-term engraftment of donor microbes into the recipients of FMT. Animal models and human studies indicate that manipulation of gut microbiota can affect host susceptibility to diseases such as obesity and inflammatory bowel disease (IBD).(5) Infectious Diseases Society of America (IDSA) guidelines are as follows(2): • For patients with an initial Clostridioides difficile infection (CDI) episode, we suggest using fidaxomicin rather than a standard course of vancomycin (conditional recommendation, moderate certainty of evidence).

	○ Comment: This recommendation places a high value in the beneficial effects and safety of fidaxomicin, but its implementation depends upon available resources. Vancomycin remains an acceptable alternative. • In patients with recurrent CDI episodes, we suggest fidaxomicin (standard or extended-pulsed regimen) rather than a standard course of vancomycin (conditional recommendation, low certainty evidence). ○ Comment: Vancomycin in a tapered and pulsed regimen or vancomycin as a standard course are acceptable alternatives for a first CDI recurrence. For patients with multiple recurrences, vancomycin in a tapered and pulsed regimen, vancomycin followed by rifaximin, and fecal microbiota transplantation are options in addition to fidaxomicin. • Fecal Microbiota Transplantation (FMT): Appropriate antibiotic treatments for at least 2 recurrences (i.e., 3 CDI episodes) should be tried prior to offering FMT Vowst contains bacterial spores; therefore, antibacterials should not be administered concurrently with Vowst.(1)
Fecal Microbiota Transplantation (FMT) Efficacy (5)	The American Gastroenterological Association (AGA) Institute, in partnership with other professional organizations, has developed an FMT National Registry to collect clinical and patient-reported outcomes. This registry primarily aims to assess the short-term and long-term safety of FMT and other gut-related microbiota products. The current report is based on the first 259 participants enrolled in the FMT National Registry. Of the 259 participants, 123 had both 1-month and 6-month follow-up within the prespecified windows. Of the 112 participants cured at 1-month and with follow-up at the 6-month point, 4 participants (4%) had developed recurrent CDI at a median of 8 weeks (range, 8–14 weeks) post FMT. Of the 11 participants failing initial FMT who were followed to 6 months, 7 (64%) were reported as cured at this later point. Treatments administered to these 7 participants included metronidazole and/or vancomycin (n = 6 [86%]) or repeat FMT (n = 1 [14%]). CDI cure rates were excellent at approximately 90%, and were in line with those reported in RCTs of FMT. CDI cure could be achieved with only 1 FMT in virtually all cases with recurrence in the 6 months after successful FMT seen in only 4% of participants, occurring most often within 2 months. For those with unsuccessful FMT at 1 month, most could still achieve cure by 6 months using standard antibiotic therapy or after repeated FMT. Infectious complications after FMT appear remarkably rare, as was reported in a recent systematic review that showed infections occurred in only 2.5% of more than 1000 patients treated. Even high-risk immunocompromised patients appear to have a low risk of contracting an infection related to FMT. Understanding FMT effectiveness and safety in real-world clinical settings is important because many recurrent CDI patients are not eligible for clinical trials due to common comorbidities, such as IBD and immunocompromised status, and because interest in FMT for other indications is increasing.
Vowst Efficacy (1)	The efficacy of Vowst was evaluated in a randomized placebo-controlled multi-center study (Study 1). The primary objective was to demonstrate the reduction of Clostridioides difficile infection (CDI) recurrence. Enrolled participants were 18 years of age or older and had a confirmed diagnosis of recurrent CDI (with a total of greater than or equal to 3 episodes of CDI within 12 months). CDI episode at the study entry was defined as diarrhea (greater than or equal to 3 unformed stools per day for at least 2 consecutive days) and a positive C. difficile stool sample using a toxin assay. Participants were required to have symptom resolution, defined as <3 unformed stools in 24 hours for 2 or more consecutive days prior to randomization, following 10 to 21 days of standard-of-care antibacterial treatment with vancomycin or fidaxomicin. Participants were stratified by antibacterial received (vancomycin or fidaxomicin) and age (<65 years or greater than or equal to 65 years) and randomized 1:1 to receive a dose of Vowst or placebo once daily for 3 consecutive days. The primary efficacy endpoint was CDI recurrence through 8 weeks after completion of treatment. Participants were assessed for recurrence, which was defined as greater than or equal

	to 3 unformed stools per day for 2 consecutive days with continued diarrhea until antibacterial treatment was initiated, a positive C. difficile test on a stool sample determined by a toxin assay, and assessment by the Investigator that the clinical condition of the participant warranted antibacterial treatment. Through 8 weeks after treatment, CDI recurrence in Vowst-treated participants was lower compared to that in placebo-treated participants (12.4% compared to 39.8%). Through 12 weeks after treatment, the recurrence rates for Vowst and placebo recipients were 18.0% (16/89) and 46.2% (43/93), respectively. Through 24 weeks after treatment, recurrence rates for Vowst and placebo recipients were 21.3% (19/89) and 47.3% (44/93), respectively.
Safety(1)	Vowst has no FDA labeled contraindications for use.

REFERENCES

Number	Reference
1	Vowst prescribing information. Seres Therapeutics, Inc. April 2023.
2	Johnson, S., Lavergne, V., Skinner, et.al. (2021). 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. Clinical Infectious Diseases, 73(5), e1029–e1044. https://doi.org/10.1093/cid/ciab549
3	Minkoff NZ, Aslam S, Medina M, Tanner-Smith EE, Zackular JP, Acra S, Nicholson MR, Imdad A. Fecal microbiota transplantation for the treatment of recurrent Clostridioides difficile (Clostridium difficile). Cochrane Database of Systematic Reviews 2023, Issue 4. Art. No.: CD013871. DOI: 10.1002/14651858.CD013871.pub2.
4	Song JH, Kim YS. Recurrent *Clostridium difficile* Infection: Risk Factors, Treatment, and Prevention. Gut Liver. 2019 Jan 15;13(1):16-24. doi: 10.5009/gnl18071.
5	Kelly, C. R., Yen, E. F., Grinspan, A., et.al. (2021). Fecal Microbiota Transplantation Is Highly Effective in Real-World Practice: Initial Results From the FMT National Registry. Gastroenterology, 160(1), 183-192.e3. https://doi.org/10.1053/j.gastro.2020.09.038

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Vowst	fecal microbiota spores, live-brpk caps		M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Vowst	fecal microbiota spores, live-brpk caps		12	Capsules	12	MONTHS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Vowst	fecal microbiota spores, live-brpk caps		Medicaid

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Vowst	fecal microbiota spores, live-brpk caps		Medicaid

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Target Agent(s) will be approved when ALL of the following are met: 1. The requested agent will be used to prevent the recurrence of Clostridioides difficile infection (CDI) **AND** 2. The patient has a diagnosis of recurrent CDI as defined by ALL of the following: A. Greater than or equal to 3 episodes of CDI in a 12 month period **AND** B. A positive C. difficile stool sample **AND** C. A CDI episode of diarrhea greater than or equal to 3 unformed stools per day for at least 2 consecutive days **AND** 3. The patient has completed a standard of care oral antibiotic regimen (e.g., vancomycin, fidaxomicin) for recurrent CDI at least 2 to 4 days before initiating treatment with the requested agent **AND** 4. The patient has had an adequate clinical response to a standard of care oral antibiotic regimen (e.g., vancomycin, fidaxomicin) as defined by less than 3 unformed stools in 24 hours for 2 or more consecutive days **AND** 5. The patient will NOT be using the requested agent in combination with any antibiotic regimen for any indication **AND** 6. If the patient has an FDA approved indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND** 7. The prescriber is a specialist in the area of the patient's diagnosis (e.g., infectious disease, gastroenterologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 8. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** One course per 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Quantity limit for the Target Agent(s) will be approved when the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **Length of Approval:** One course every 12 months