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Take CME Exams

Live Fecal Microbiota Oral Capsules (*Vowst*) for Prevention of CDI Recurrence

The FDA has approved *Vowst* (Seres Therapeutics/Nestle HealthScience), an oral capsule containing live fecal microbiota spores, for prevention of additional recurrences of *Clostridioides difficile* infection (CDI) in adults. *Vowst* is the first orally administered microbiota-based treatment to be approved for this indication. A rectally-administered live fecal microbiota-based suspension *(Rebyota)* was approved in 2022 for the same indication.[1] Neither product is approved for acute treatment of CDI.

Pronunciation and Abbreviation Key
***Vowst*:** vowst
CDI = *Clostridioides difficile* infection

Key Points: *Vowst*

- **Description:** Oral capsule containing live fecal microbiota spores manufactured from human donor fecal matter.
- **Indication:** Prevention of additional recurrences of *Clostridioides difficile* infection (CDI) in adults.
- **Efficacy:** In one small trial, the rate of CDI recurrence up to 8 weeks after treatment was lower with *Vowst* than with placebo (12% vs 40%) in patients with ≥3 recurrences within 12 months.
- **Adverse Effects:** Flatulence, abdominal distension, abdominal pain, fatigue, constipation, chills, and diarrhea can occur.
- **Dosage:** 4 capsules once daily for 3 days started 2-4 days after the last dose of antibiotics for treatment of CDI.
- **Cost:** A 3-day course of treatment costs $17,500.
- **Conclusion:** *Vowst* reduced the risk of recurrent CDI compared to placebo. Its long-term efficacy remains to be established.

INITIAL EPISODES OF CDI — All adults with an initial episode of nonfulminant CDI should receive 10 days of oral treatment with fidaxomicin *(Dificid)* or standard-dose vancomycin. Use of fidaxomicin is preferred; compared to vancomycin, it has a narrower spectrum of activity, which limits its effect on the gut microbiome, and it is associated with higher rates of sustained response and fewer recurrences.[2,3]

RECURRENT CDI — Most CDI recurrences develop within 60 days after stopping antibacterial treatment; the risk is greatest in the first 2 weeks. The recurrence rate after treatment of an initial episode is typically 20-25%. Patients who have one recurrent episode are at increased risk of additional recurrences; the risk of having multiple recurrences has increased in recent years.[4]

PREVENTION OF RECURRENCES — Addition of a single IV dose of the anti-*C. difficile* toxin B antibody **bezlotoxumab** *(Zinplava)* to antibacterial therapy is recommended to prevent further recurrences in adults who have a recurrence of CDI within 6 months of a previous episode. Use of bezlotoxumab can be considered following antibacterial treatment of a first episode of CDI in patients who have risk factors for disease recurrence (e.g., age ≥65 years, severe CDI, immunosuppression).[5] In two trials in patients receiving antibacterial treatment for primary or recurrent CDI, the recurrence rate with addition of bezlotoxumab was significantly lower than that with addition of placebo (16-17% vs 26-28%).[6] Bezlotoxumab may exacerbate heart failure.

A single dose of ***Rebyota*** (live fecal microbiota rectal suspension) was modestly more effective than placebo in preventing a recurrence of CDI within 8 weeks after treatment of recurrent CDI (estimated treatment success rate of 70.6% vs 57.5%).[1]

Fecal microbiota transplantation (FMT), a process (not FDA-approved) in which donor feces is administered to the recipient via colonoscopy, upper endoscopy, nasoenteric tube, sigmoidoscopy, an enema, or an oral capsule, has been used for patients with multiple recurrences of CDI.[7,8]

CLINICAL STUDIES — FDA approval of *Vowst* was based on the results of a trial (ECOSPOR III) in 182 adults with recurrent CDI (≥3 recurrences within 12 months) who received 10-21 consecutive days of standard antibacterial therapy (vancomycin or fidaxomicin) with improvement in CDI symptoms. Patients were randomized to receive *Vowst* or placebo for 3 days. Up

Table 1. Some Drugs for Prevention of CDI Recurrence

	Zinplava	*Rebyota*	*Vowst*
Generic Name	Bezlotoxumab	Fecal microbiota, live-jslm	Fecal microbiota spores, live-brpk
Formulation	1000 mg/40 mL single-dose vial	Suspension for rectal administration; contains $1x10^8$ to $5x10^{10}$ CFU/mL of fecal microbes	Capsule; each capsule contains $1x10^6$ to $3x10^7$ firmicutes spore CFU
Administration	IV infusion over 60 minutes	Rectally by a healthcare provider	Orally by patient
Dosage	Single 10 mg/kg dose	Single 150-mL dose	4 capsules once daily x 3 days
Cost[1]	$3,800	$9000	$17,500

CFU = colony forming units

1. Approximate WAC for one treatment course (one dose of *Zinplava* for a 70-kg patient, one dose of *Rebyota*, and 12 capsules of *Vowst*). WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. May 5, 2023. Reprinted with permission by First Databank, Inc. All rights reserved. ©2023. www.fdbhealth.com/policies/drug-pricing-policy.

to 8 weeks after treatment, the rate of CDI recurrence was lower with *Vowst* than with placebo (12% vs 40%; RR 0.32; number needed to treat [NNT] 3.6).[9] The rate of recurrence at 24 weeks, a secondary endpoint, was 21.3% with *Vowst* and 47.3% with placebo.[10]

No trials directly comparing *Vowst* with bezlotoxumab, *Rebyota*, or FMT for prevention of CDI recurrence are available.

ADVERSE EFFECTS — The most common adverse effects of *Vowst* in ECOSPOR III were flatulence, abdominal distension, abdominal pain, fatigue, constipation, chills, and diarrhea; most were mild to moderate in severity. *Vowst* is manufactured from human donor fecal matter that has been tested for a panel of transmissible pathogens, but not for food allergens; the label states that *Vowst* may transmit infectious agents to the recipient.

DRUG INTERACTIONS — *Vowst* contains live bacterial spores; concurrent administration of antibacterial drugs is not recommended.

PREGNANCY AND LACTATION — No adequate human or animal data on the use of *Vowst* during pregnancy are available.

DOSAGE AND ADMINISTRATION — *Vowst* should be started 2-4 days after completing antibacterial treatment for recurrent CDI and at least 8 hours (preferably 24 hours) after drinking 10 ounces of magnesium citrate (to prevent inactivation of bacterial spores in *Vowst* by residual fidaxomicin or vancomycin in the GI tract). The recommended dosage is 4 capsules taken once daily before the first meal of the day for 3 consecutive days. The capsules should be swallowed whole.

CONCLUSION — In one small trial, a 3-day course of oral live fecal microbiota spores *(Vowst)* was more effective than placebo in preventing a recurrence of *Clostridioides difficile* infection (CDI) within 8 weeks of treatment in patients who had at least 3 recurrences within 12 months. Its long-term efficacy remains to be established. No head-to-head trials comparing *Vowst* with the anti-*C. difficile* toxin B antibody bezlotoxumab *(Zinplava)*, a rectally-administered, live fecal microbiota suspension *(Rebyota)*, or fecal microbiota transplant (FMT) are available. ■

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