## INTRODUCTION

The Adult *Clostridioides difficile* management guideline establishes evidence-based standards for management of *C. difficile* infection (CDI) at UCSF Medical Center. The guideline has been adapted from published consensus guidelines from the Society for Healthcare Epidemiology of America (SHEA), the Infectious Diseases Society of America (IDSA), and the American College of Gastroenterology (ACG) with input from the Antimicrobial Stewardship Program, the Infectious Diseases Management Program, and the Infectious Diseases division.

| Date | Main changes |
|---|---|
| 9/2025 update | Traditional fecal microbiota transplantation (FMT) no longer available, fecal microbiota, live-jslm (Rebyota) added to formulary (restricted) |
| 5/2025 update | Bezlotoxumab no longer available after being discontinued by the manufacturer, removed from guidelines, which are otherwise unchanged |
| 2024 update | Vowst® (fecal microbiota spores live-brpk) was added to UCSF formulary with inpatient adult restrictions for ID/ASP. The IDSA/SHEA guidelines have not yet addressed this agent, and ACG suggests use similar to current indications for FMT. This product is manufactured from human fecal matter sourced from qualified donors and is used to prevent the recurrence of CDI. |
| 2022 update | Fidaxomicin is now first-line therapy for first and second *C. difficile* episodes (non-fulminant) Added recommendation for bezlotoxumab for certain patients after the 1st episode and all patients after the 2nd episode of CDI<br>Guidelines now apply only to UCSF Health (ZSFG and SFVA have independent guidelines) |

## DEFINITIONS

| Abbreviation | Definition |
|---|---|
| **ASP** | Antimicrobial Stewardship Program (adult) |
| **CDI** | *Clostridioides difficile* infection |
| **FMT** | Fecal Microbiota Transplantation |
| **ID** | Infectious Diseases (adult) |
| **GI** | Gastroenterology |

## PRINCIPLES OF CDI MANAGEMENT

- Refer to the Hospital Epidemiology and Infection Control website for information on work-up of diarrhea and guidance on Infection Control issues pertaining to CDI at UCSF Medical Center (http://infectioncontrol.ucsfmedicalcenter.org/ucsf-clostridium-difficile-infection-prevention)
- Stop all unnecessary antibiotics, shorten antibiotic courses, and narrow the spectrum of

antibiotic activity when possible

- Stop acid suppressive medications, especially proton-pump inhibitors, when possible
- Do not use anti-peristaltic agents until acute symptoms of CDI improve

**TREATMENT OF CDI IN ADULT PATIENTS, INITIAL EPISODE**

| Clinical definition | Criteria | Treatment |
|---|---|---|
| Initial episode, non-complicated, **toxin protein negative, toxin gene positive** | | Treatment for colonization typically is not necessary<br><br>If treating, most patients: Vancomycin 125 mg po q6h x 10 days<br><br>In symptomatic patients at very high risk for relapse (advanced age, severe immunocompromise, or need for ongoing systemic antibiotics) could consider Fidaxomicin 200 mg po twice daily x 10 days* |
| Initial CDI episode, non-complicated, **toxin protein positive, toxin gene positive** | Not meeting criteria for fulminant | Fidaxomicin 200 mg po twice daily x 10 days*<br><br>Alternative: Vancomycin 125 mg po q6h x 10 days |
| **Secondary prophylaxis** after initial episode after initial episode of toxin protein positive infection | | Treat for initial episode as above<br><br>Bezlotoxumab is no longer available |
| **Fulminant** | Hypotension, shock, ileus, and/or megacolon | Vancomycin 500 mg po/ng q6h + metronidazole 500 mg IV q8h +/- rectal vancomycin<br><br>Rectal vancomycin should be considered in patients with ileus. It is given as 500 mg in 100 mL of 0.9% NaCl and instilled q6h (retain each dose for 1h)<br><br>Consult ID and General Surgery for consideration of colectomy versus diverting loop ileostomy with colonic lavage<br><br>Fidaxomicin is not studied in fulminant CDI |

* can transition to po vancomycin for completion of course if unable to obtain outpatient. If insurance does not cover fidaxomicin can try the MERCK patient assistance program at www.merckhelps.com.

**TREATMENT OF CDI IN ADULT PATIENTS, RECURRENT DISEASE**

Recurrence is defined as the re-appearance of symptoms and signs of CDI within 8 weeks after completion of therapy for prior CDI episode for which symptoms and signs had resolved, and assumes toxin gene AND toxin protein positive in all instances.

| Clinical definition | Criteria | Treatment |
|---|---|---|
| **1st CDI recurrence** (non-fulminant) | | Fidaxomicin 200 mg po q12h x 10 days<br><br>Alternative:<br>Vancomycin taper:<br>125 mg po 4x daily x 14 days<br>125 mg po 2x daily x 7 days<br>125 mg po 1x daily x 7 days<br>125 mg po every other day x 8 days (4 doses)<br>125 mg po every 3 days x 2 weeks (5 doses) |
| **Secondary prophylaxis after 1st recurrence** | | Treat as above<br><br>Bezlotoxumab is no longer available<br><br>Can consider evaluating for secondary prophylaxis in high risk patients with fecal microbiota spores, live-bprk (Vowst ®) as an outpatient (alternative: fecal microbiota, live-jslm (Rebyota)) |
| **≥ 2 CDI recurrence** (non-fulminant) | | Vancomycin taper:<br>125 mg po 4x daily x 14 days<br>125 mg po 2x daily x 7 days<br>125 mg po 1x daily x 7 days<br>125 mg po every other day x 8 days (4 doses)<br>125 mg po every 3 days x 2 weeks (5 doses)<br><br>PLUS<br><br>Evaluate for secondary prophylaxis with fecal microbiota spores, live-brpk (Vowst®): 4 capsules po daily x 3 days 2-4 days AFTER completing antibacterial treatment for recurrent CDI (alternative: fecal microbiota, live-jslm (Rebyota))<br><br>Consult ID, GI |

SPECIAL SITUATIONS

**Oral fecal microbiota spores, live-brpk (Vowst, see clinical criteria above)**

- Avoid concurrent use with antibacterials
- Treat for episode of *C. difficile* with fidaxomicin or oral vancomycin as above
- Administer as an outpatient if possible
- Prior to administration of this biotherapeutic, the patient should drink 296 mL (10 oz) of magnesium citrate on the day before and at least 8 hours prior to taking the first dose of fecal microbiota spores, live-brpk
    - For patients with impaired renal function, the clinical study participants received polyethylene glycol electrolyte solution (250 mL)
- Criteria for inpatient administration: Must be expected to be hospitalized > 14 days after *C. difficile* episode
    - All use requires ID/ASP approval
    - This agent is not routinely stocked in inpatient pharmacy. Contact pharmacy purchasing team several days in advance to initiate order.
- Only may receive one course (currently not studied outside of this)
- Avoid in patients with severe immunocompromise

**Fecal microbiota spores, live-jslm (Rebyota, see clinical criteria above)**

- Now available in lieu of traditional fecal microbiota transplantation, which is not currently commercially available
- Degree to which prior traditional fecal microbiota transplantation data would apply to this product is not clear
- Avoid concurrent use with antibacterials
- Treat for episode of *C. difficile* with fidaxomicin or oral vancomycin as above
- Administer as an outpatient if possible
- Criteria for inpatient administration: Must be expected to be hospitalized > 14 days after *C. difficile* episode
    - All use requires GI and/or ID consultation
    - To be administered colonoscopically
- Avoid in patients with severe immunocompromise

**Bezlotoxumab**: No longer available after being discontinued by manufacturer, previously used as secondary prophylaxis

**Comment on probiotics**

Mixed data exist regarding use of probiotics for primary prevention of CDI. There is insufficient data to support use for secondary prophylaxis. Can consider use based on patient and provider preference. Relatively contraindicated in immunocompromised populations.

**Comment on duration of therapy in patients receiving ongoing antibiotics**

Extension of CDI therapy in patients receiving ongoing systemic antibiotics is not routinely recommended. Can consider use based on patient and provider preference.

**Comment on secondary antibiotic prophylaxis for CDI**

Do not routinely use prophylaxis if treating with fidaxomicin as the benefit of this therapy is to preserve the microbiome.

Mixed data exist regarding use of vancomycin for secondary prevention of CDI. Can consider use based on patient and provider preference.

For patients with recurrent CDI who are not candidates for commercially available fecal microbiota products (Vowst, Rebyota), relapsed after commercially available fecal microbiota products, or require ongoing or frequent courses of antibiotics, suppressive oral vancomycin may be used to prevent further recurrences.

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