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
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 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 If treating, most patients: Vancomycin 125 mg po q6h x 10 days 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* Alternative: Vancomycin 125 mg po q6h x 10 days
Secondary prophylaxis after initial episode after initial episode of toxin protein positive infection	Toxin protein positive, no history of heart failure AND meets one of the following: 1. Hematologic cancer with neutropenia expected > 30 days 2. Recent bone-marrow transplant or treatment for GVHD 3. Solid-organ transplant < 3 months 4. Otherwise not an FMT candidate	Treat for initial episode as above Bezlotoxumab 10 mg/kg as a single dose if not previously administered
Fulminant	Hypotension, shock, ileus, and/or megacolon	Vancomycin 500 mg po/ng q6h + metronidazole 500 mg IV q8h +/- rectal vancomycin 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) Consult ID and General Surgery for consideration of colectomy versus diverting loop ileostomy with colonic lavage

* 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 Alternative: Vancomycin taper: 125 mg po 4x daily x 14 days 125 mg po 2x daily x 7 days 125 mg po 1x daily x 7 days 125 mg po every other day x 8 days (4 doses) 125 mg po every 3 days x 2 weeks (5 doses)
Secondary prophylaxis after 1st recurrence		Treat for initial episode as above Bezlotoxumab 10 mg/kg as a single dose if not previously administered
≥ 2 CDI recurrence (non-fulminant)		Vancomycin taper: 125 mg po 4x daily x 14 days 125 mg po 2x daily x 7 days 125 mg po 1x daily x 7 days 125 mg po every other day x 8 days (4 doses) 125 mg po every 3 days x 2 weeks (5 doses) PLUS Evaluate for secondary prophylaxis with fecal microbiota spores, live-brpk (Vowst®) (alternative: fecal microbiota transplant (FMT)) Consult ID, GI

Secondary prophylaxis after ≥ 2nd CDI recurrence		Initiate fecal microbiota spores, live-brpk (Vowst®, 4 capsules po daily x 3 days) 2-4 days AFTER completing antibacterial treatment for recurrent CDI Preferentially administer prior to consideration of FMT

SPECIAL SITUATIONS

Bezlotoxumab (see clinical criteria above)

- Do not give in congestive heart failure
- 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 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-time dose (not studied outside of this)

Fecal microbiota spores, live-brpk (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

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 FMT, who relapsed after FMT x 2, or who require ongoing or frequent courses of antibiotics, suppressive oral vancomycin may be used to prevent further recurrences.

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