

INTRODUCTION

The Adult *Clostridioides difficile* management guideline establishes evidence-based standards for management of *C. difficile* infection (CDI) at UCSF Medical Center. The protocol 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
2022 update	Fidaxomicin now first-line therapy for first and second <i>C. difficile</i> episodes (non-fulminant) Added recommendation for bezlotoxumab for certain patients after the 1 st episode and all patients after the 2 nd episode of CDI Guidelines now apply only to UCSF Health (ZSFG and SFVA have independent guidelines)

DEFINITIONS

Abbreviation	Definition
CDI	<i>Clostridioides difficile</i> infection
FMT	Fecal Microbiota Transplantation
ID	Infectious Diseases
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 <u>negative</u>, 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 <u>positive</u>, 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	Toxin antigen protein positive AND meets one of the following: <ol style="list-style-type: none"> 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 5. Patient does not have history of heart failure 	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.

Clinical definition	Criteria	Treatment
1 st 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 1 st recurrence		Treat for initial episode as above Bezlotoxumab 10 mg/kg as a single dose if not previously administered
≥ 2 nd 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 fecal microbiota transplant (FMT) if ≥ 3 episodes Consult ID, GI

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
- Only may receive one-time dose (not studied outside of this)

Pediatric patients

Refer to: <https://idmp.ucsf.edu/pediatric-guidelines-gastrointestinal-infections-clostridium-difficile-associated-diarrhea>

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

REFERENCES

Carignan A, *et al.* Efficacy of Secondary Prophylaxis With Vancomycin for Preventing Recurrent *Clostridium difficile* Infections. *Am J Gastroenterol.* 2016 Dec;111(12):1834-1840.

Caroff DA, *et al.* Oral vancomycin prophylaxis during systemic antibiotic exposure to prevent *Clostridioides difficile* infection relapses. *Infect Control Hosp Epidemiol.* 2019 Jun;40(6):662-667. doi: 10.1017

Cornely OA, *et al.* Treatment of first recurrence of *Clostridium difficile* infection: fidaxomicin versus vancomycin. *Clin Infect Dis* 2012; 55(s2): S154-161.

Johnson S, *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. *Clinical Infectious Diseases*, ciab549, <https://doi.org/10.1093/cid/ciab549>

Kelly CP and LaMont JT. *Clostridium difficile*—more difficult than ever. *N Engl J Med* 2008; 359: 1932-1940.

Celly CR et al. ACG Clinical Guidelines: Prevention, Diagnosis, and Treatment of *Clostridioides difficile* Infections *Am J Gastroenterol* 2021;116:1124–1147. <https://doi.org/10.14309/ajg.0000000000001278>

McDonald LC, Gerding DN, Johnson S, et al. Clinical Practice Guidelines for *Clostridium difficile* Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). *Clin Infect Dis*. 2018 Mar 19;66(7):987-994. doi: 10.1093/cid/ciy149.

Mullane KM et al. A Randomized, Placebo-controlled Trial of Fidaxomicin for Prophylaxis of *Clostridium difficile*-associated Diarrhea in Adults Undergoing Hematopoietic Stem Cell Transplantation. *Clin Infect Dis*. 2019 Jan 7;68(2):196-203. doi: 10.1093/cid/ciy484.

Surawicz CM, et al. Guidelines for diagnosis, treatment, and prevention of *Clostridium difficile* infections. *Am J Gastroenterol* 2013; 108: 478-498.

Van Hise NW et al. Efficacy of Oral Vancomycin in Preventing Recurrent *Clostridium difficile* Infection in Patients Treated With Systemic Antimicrobial Agents. *Clin Infect Dis* 2016; 63 (5): 651-3

Wilcox MH et al. Bezlotoxumab for Prevention of Recurrent *Clostridium difficile* Infection. *N Engl J Med* 2017; 376:305-317. DOI: 10.1056/NEJMoa1602615

Original guideline prepared by:

UCSFMC: Sarah Doernberg, MD, MAS; Catherine Liu, MD; Jennifer Babik, MD, PhD; Rachel Wattier, MD; Alexandra Hilt-Horeczko, PharmD; Jonathan Faldasz, PharmD

SFVA team: Harry Lampiris, MD; Daniel Maddix, PharmD

ZSFG team: Lisa Winston, MD; Gregory Melcher, MD; Camille Beauduy, PharmD

2019 revision prepared by:

UCSFMC: Sarah Doernberg, MD, MAS

SFVA: Jennifer Mulliken, MD; Sean Chow, PharmD

ZSFG: Lisa Winston, MD; Camille Beauduy, PharmD

2022 revision prepared by:

Ripal Jariwala, PharmD

Sarah Doernberg, MD, MAS

Approved by:

Group	Date
IDMP	2.29.16
Clinical ID group at VAMC	2.29.16
Clinical ID group at ZSFG	2.29.16
Trihospital group meeting	8.19.19
IDMP	9.10.19
IDMP	08.10.21
UCSF P&T	02.09.22