Introduction

The *Clostridioides difficile* management guideline establishes evidence-based standards for management of *C. difficile infection* (CDI) at Zuckerberg San Francisco General Hospital. 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 Infectious Diseases, Clinical pharmacy, and Antimicrobial Subcommittee.

Abbreviations Used in this Guideline

- *Clostridioides difficile* infection (CDI)
- Bone Marrow Transplant (BMT)
- Graft vs. Host Disease (GVHD)
- Fecal Microbiota Transplantation (FMT)
- Infectious Diseases (ID)

Principles of CDI Management

- Refer to the ZSFG Infection Control website for information on work-up of diarrhea and guidance on Infection Control issues pertaining to CDI
- 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

Table 1. Treatment of CDI in Adult Patients, Initial Episode

Clinical Definition	Criteria	Treatment
Initial, non-complicated Toxin protein **negative**, toxin gene positive		**Treatment for colonization is typically not necessary** If electing to treat: vancomycin 125 mg PO QID x 10 days
Initial, non-complicated Toxin protein **positive**, toxin gene positive	Does not meet criteria for high-risk or fulminant disease	**Vancomycin 125 mg PO QID x 10 days**

	IF high-risk for CDI recurrence* OR non-response to oral vancomycin** *High risk for recurrence: • Age ≥ 65 OR • Age < 65 and ongoing need for high-risk antibiotics (**See Table 3**) OR • Significant immunosuppression (ex. Active chemotherapy, receipt of solid organ transplant, HIV with CD4 < 200) OR • Inflammatory bowel disease (e.g. ulcerative colitis, Crohn's disease) **Non-response: • Ongoing fever, elevated WBC, and/or abdominal pain after 5 or more days of treatment	**Fidaxomicin 200 mg PO BID x 10 days**
Initial, non-complicated (continued)	IF patient meets any of the following: • Heme malignancy & ANC < 500 for > 30 days • Recent BMT or GVHD • Solid organ transplant < 3 month ago	ADD **bezlotoxumab† 10 mg/kg IV x 1** to antibiotic above, if available
Fulminant	Hypotension, shock, ileus, and/or megacolon	**Vancomycin 500 mg PO/NG q6h + metronidazole 500 mg IV q8h +/- rectal vancomycin** Rectal vancomycin (500 mg in 100 mL NS instilled q6h) should be considered in patients with ileus. Consult ID and General Surgery for consideration of colectomy versus diverting loop ileostomy with colonic lavage

Table 2. 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.

For recurrent episode meeting criteria for fulminant disease, refer to **Table 1** for treatment.

Clinical Definition	Treatment
1st Recurrence i.e. 2nd episode within 8 weeks	**Fidaxomicin 200 mg PO BID x 10 days**

	IF ≥ 1 additional risk factor for recurrence: • Age ≥ 65 years • Severe immunocompromise ADD **bezlotoxumab† 10 mg/kg IV x 1** if available and not yet given
≥ 2nd Recurrence i.e. 3rd or subsequent episode within 8 weeks of most recent prior episode	**Vancomycin PO taper** AND consideration of FMT AND **bezlotoxumab† 10 mg/kg IV x 1** if available and not yet given Taper schedule: 125 mg PO QID x 14 days 125 mg PO BID x 7 days 125 mg PO 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)
Frequent CDI episodes with > 8 weeks between episodes	Consider ID consult and/or consideration of **FMT**

Table 3. Antibiotics Associated with High-Risk for CDI

Cefepime	Ciprofloxacin (IV & PO)	Meropenem
Ceftaroline	Clindamycin (IV & PO)	Moxifloxacin (IV & PO)
Ceftazidime	Ertapenem	Piperacillin-tazobactam
Ceftazidime-avibactam	Imipenem-cilastatin	
Ceftriaxone	Levofloxacin (IV & PO)	

Table 4. C. difficile Therapeutics

	Dose	**Warnings/ Precautions**	**Comments**
Fidaxomicin	200 mg PO BID x 10 days	Avoid in patients with macrolide allergy	**Confirmation of outpatient insurance coverage prior to discharge is strongly recommended
Bezlotoxumab† †Discontinued by manufacturer in early 2025. Contact ID Pharm to determine if supply available	10 mg/kg IV x 1 Repeat doses have not been studied; based on PK, re-dosing after 1 year is reasonable	Increased adverse events in patients with congestive heart failure. Reserve for use when benefit outweighs risk.	Dose may be administered while inpatient or at 4C after discharge, but ideally should be given during CDI treatment

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.

References

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