DUHS Treatment of Suspected or Documented *Clostridioides difficile* Infection (CDI) in Adult Patients

General Principles of Treatment

- Evaluate use of laxatives and other causes for diarrhea when considering testing and diagnosis for *C. difficile* infection.
- Discontinue antibiotics and proton-pump inhibitors (such as pantoprazole) as soon as clinically appropriate.
- If possible, **avoid use of anti-peristaltic agents**, e.g. loperamide, as they may obscure symptoms and precipitate toxic megacolon. Use of cholestyramine is not recommended as it may bind anti-*C difficile* therapies.
- Response assessment should be based on resolution of signs/symptoms, and NOT repeated PCR testing. Do not test for "cure".
- ID consultation is recommended for management of fulminant or recurrent infection
- **Preferred vancomycin preparation is the commercial oral capsules.** Oral solution reserved for those who cannot swallow capsules or require administration via tube. Oral administration of vancomycin is NOT systemically absorbed and should NOT replace IV vancomycin for treatment of concomitant systemic Gram-positive infections. **Vancomycin IV should NOT be used to treat *C. difficile* infection.**

Cost & Access Considerations

- Access to **fidaxomicin** in the outpatient setting may be **cost-prohibitive**. Patient's ability to pay for complete course of therapy in the outpatient setting must be assessed at the time of starting fidaxomicin.
- **Fecal microbiota transplantation (FMT)** access may be subject to availability. Recommend Gastroenterology (GI) consultation to assess patient candidacy and clarify availability.
- Merck **discontinued production of bezlotoxumab** as of **1/31/25**. DUHS has purchased extra doses; however, supply will be limited & likely eventually depleted in 2025-2026.

Occurrence/Severity	Recommendations
First Occurrence	Vancomycin 125mg PO QID for 10 days **OR** Fidaxomicin* 200mg PO BID for 10 days <u>Fidaxomicin should be considered for patients at increased risk of CDI recurrence (list not all-inclusive)</u>: • Age > 65 years old • Moderate-severe immune compromise • Concomitant moderate-high risk systemic antibiotic use anticipated for ≥ 5 days during CDI treatment
Recurrent Episode	<u>If vancomycin was used for the initial episode:</u> Vancomycin in tapered and pulsed regimen[A] **OR**

	Fidaxomicin* 200mg PO BID for 10 days <u>If fidaxomicin was used for the initial episode:</u> Vancomycin in tapered and pulsed regimen[A] <u>If metronidazole was used for the initial episode:</u> Vancomycin 125mg PO QID for 10 days **OR** fidaxomicin* 200mg PO BID for 10 days
Second or Subsequent Recurrent Episode	Fidaxomicin* 200mg BID for 10 days **OR** Vancomycin in tapered and pulsed regimen[A] **NOTE:** if considering ambulatory fecal microbiota transplantation (FMT) for the prevention of recurrent CDI, consider placing an E-communication to Infectious Disease (ID) or ambulatory referral to GI. For urgent outpatient FMT questions please staff message Amy Barto, MD (medical director of the Duke FMT program).
Fulminant Disease	Vancomycin: 500mg PO QID (*If vancomycin unable to be given PO, use NG tube*) **AND** Metronidazole 500mg IV Q8H <u>If ileus is present:</u> Consider adding vancomycin enema 500mg/100mL of normal saline Q6H <u>For patients with fulminant CDI refractory to standard therapy:</u> Recommend GI and ID consult. Consider fecal microbiota rectal suspension [REBYOTA][B] administered via colonoscopy <u>If FMT is performed for the treatment of fulminant CDI</u>: 1. Anti-CDI antibiotics should be continued until pseudomembranes are no longer detected on colonoscopy and the patient has clinically improved following FMT (*i.e.* improvement in CDI-related symptoms, WBC, and CRP). 2. For subjects with pseudomembranes on colonoscopy after FMT, consider continuing anti-CDI antibiotics for 5 additional days after FMT. Longer durations may be required to bridge to eventual microbiome-based treatments (*e.g.* VOWST or REBYOTA enema) as an outpatient if symptoms are slow to resolve. Please note that colonoscopy-assisted FMT via Rebyota is not currently available for outpatients at Duke. 3. The optimal choice of anti-CDI antibiotic after FMT for fulminant CDI remains unknown; however, fidaxomicin may be preferred as vancomycin is more disruptive to the newly transplanted microbiota

C. difficile Prophylaxis: Agents for Use & Recommendations	
Bezlotoxumab[C]	Bezlotoxumab 10 mg/kg IV once[C] as adjunctive therapy with active CDI treatment for patients at increased risk for CDI recurrence (*i.e.* age > 65 yrs, immunocompromised, severe CDI, and/or NAP1 strain) **NOTE**: Merck discontinued production of bezlotoxumab as of **1/31/25**. DUHS has purchased extra doses, but supply will likely be depleted in 2025-2026.
Oral vancomycin prophylaxis (OVP)	Dose: vancomycin PO 125 mg daily for secondary prophylaxis in select patients Duration: while receiving high-risk systemic antibiotics PLUS 5 days after antibiotic cessation **Evidence for efficacy of OVP remains limited and largely observational**. Some studies have found benefit with OVP; however, this is not consistent across studies. Additionally, one case series found OVP may not reduce CDI incidence but rather just delay disease onset. One meta-analysis suggests no benefit when used as primary prophylaxis. Refer to Vancomycin (PO) | Duke CustomID for a detailed summary of available evidence. **Clinicians may consider OVP for secondary prophylaxis in select individuals at high risk of recurrence (example cases below):** • For example, history of recurrent or severe CDI within the past 6 months AND concomitant use of high-risk systemic antibiotics, such as fluoroquinolones, clindamycin, or 3rd/4th generation cephalosporins. • History of prior fecal microbiota therapy in the last 12 months. Oral vancomycin prophylaxis is NOT recommended for ANY of the following patient populations: • Low-risk systemic antibiotic use (*e.g.* tetracyclines, macrolides, penicillin/amoxicillin alone, nitrofurantoin) • Absence of recurrent CDI episode in the past 6 months (*e.g.* primary prophylaxis) • Metronidazole-containing systemic antibiotic regimens due to anti-CDI activity of metronidazole

[A]Tapered and pulsed vancomycin regimen example: 125mg PO QID for 10-14 days, BID for 7 days, QD for 7 days, then every 2 or 3 days for 2-8 weeks.

[B]Fecal microbiota rectal suspension [REBYOTA] is restricted to Gastroenterology (GI) or Infectious Diseases (ID) consult. Prior to use, REBYOTA must be thawed for ~24 hours.

[C]Bezlotoxumab is restricted to ID or GI consult. Preferred as outpatient administration.

*Patient's ability to pay for complete course of therapy in outpatient setting must be assessed at the time of starting fidaxomicin. Fidaxomicin should not be used for fulminant disease.

References:

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Developed by: ASET
Origination Date: April 2018; revised October 2021, May 2023, March 2025
DUHS PMMC approval: May 2018; August 2019; November 2021; June 2023; April 2025

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