Antimicrobial Stewardship *Clostridium difficile* treatment guidelines complement the multidisciplinary Montefiore CDI Management Guidelines. The following are based on national guidelines, adapted to local policies and practices.

1. Stop, deescalate or shorten antibiotics whenever possible.

2. Avoid antiperistaltic agents such as loperamide. Decrease usage of medications with anti-motility properties such as morphine and its analogues.

3. Stop acid suppressive therapy, such as PPIs and H₂ receptor antagonists, whenever possible; avoid routine PPI prescribing to reduce risk of adverse effects.

4. Do not order laxatives and stool softeners in CDI patients. Consider alternative diagnosis for diarrhea in patients already receiving laxatives/stool softeners; avoid testing these patients.

5. PLEASE NOTE: Due to recent updates to national CDI guidelines, oral vancomycin 125mg Q6h will NOT require approval for CDI treatment within the first 72 hours.

**Stewardship/ID approval will be required:**

1) After 72 hours of use (ongoing dosing based on *C.diff* result and clinical response)

2) For CDI prophylaxis if required (see page 4 for indications)

3) For higher PO vancomycin doses >125mg
Treatment of Initial Episode:

**Initial Episode**

**Non-severe Disease**
(WBC <15,000 cells/mL and minimal, if any, renal impairment)

*Preferred*: Vancomycin 125 mg PO q6h for 10 days

Please note: Metronidazole is no longer recommended as first-line therapy, but can consider metronidazole 500 mg PO q8h for 10 days if patients cannot obtain PO vancomycin due to cost or insurance issues. Contact stewardship if unsure.

**Severe Disease**
(WBC ≥15,000 cells/mL or significant acute renal impairment)

*Preferred*: Vancomycin 125 mg PO/NG q6h for 10 days

If limited GI motility/ileus: Use metronidazole 500 mg IV q8h; consider adding vancomycin 500 mg PR q6h.*

If patients have ≥3 unfavorable prognostic features (see below), also consider surgical evaluation.

- Temperature >101°F
- WBC >20,000 cells/mL
- Albumin <2.5 mg/dL
- Decreasing bicarbonate
- Increasing SCr
- >60 years old
- Severe abdominal pain, tenderness, or distention

**Fulminant Disease**
(hypotension, shock, ileus, or megacolon)

*Preferred*: Vancomycin 500 mg PO/NG q6h (duration as per ID consult)

If ileus or reduced gut motility due to shock:
Add metronidazole 500 mg IV q8h +/-vancomycin 500 mg PR q6h* as PO vancomycin alone might not be effective.

Obtain STAT Surgical and Infectious Diseases consults

*Vancomycin 500 mg PR q6h = Vancomycin 500mg in NS 100 mL q6h via rectal tube. Retention enema – clamp rectal tube for 1 hour. PLEASE NOTE: drug accumulation can occur with high PO/PR doses of vancomycin, close monitoring required.*
**Treatment of 1st Recurrence:**

Non-fulminant* 1st Recurrence

- If Non-fulminant Initial Episode:
  - Vancomycin 125 mg PO q6h for 10 days

Fulminant* 1st Recurrence

- If Fulminant Initial Episode:
  - Vancomycin 125 mg PO q6h for 14 days followed by tapering doses of PO vancomycin over 6 weeks:
    - Week 1: 125 mg PO q8h
    - Week 2: 125 mg PO q12h
    - Week 3: 125 mg PO q24h
    - Week 4: 125 mg PO q48h
    - Weeks 5, 6: 125 mg PO every 3 days

*Treat as fulminant disease (see treatment of initial episode)

*Fulminant = CDI with hypotension, shock, ileus, or megacolon

**Treatment of Multiple Recurrences:**

- Infectious Diseases or Gastroenterology should be consulted. **Fecal transplant** should be considered in consultation with Gastroenterology. Fecal transplant offers highest chance of cure compared to other available treatments.

- PO vancomycin 125 mg q6h for 14 days followed by 6 week taper should be considered. (Refer to 1st recurrence chart for taper instructions.)

- For patients at **high risk for further recurrence who do not currently have fulminant disease:**
  - Fidaxomicin may be considered in **consultation with Infectious Diseases (requires approval 24/7)** in confirmed *C. difficile* recurrence if they have at least one of the following:
    a. Solid organ or hematopoietic stem cell transplant recipients
    b. Patients with HIV infection or AIDS
    c. Patients on immune-modulating agents
    d. Advanced age
    e. Hemodialysis or advanced CKD
    f. Prior fulminant CDI
  - Please note: fidaxomicin is non-formulary at MMC and may not be covered by various types of insurance.
**Additional Treatment Notes:**

- Dual therapy with PO vancomycin plus PO metronidazole has no proven additional benefit over PO vancomycin monotherapy.

- There is no added benefit of higher dose PO vancomycin 250mg.

- There is not enough evidence in favor of adjunctive probiotics according to the IDSA 2018 CDI guidelines. Pharmacy does not carry any probiotics on formulary as per the Pharmacy and Therapeutic Committee.

- Adjunctive therapy with IVIG for CDI has limited data. It may be helpful in patients with hypogammaglobulinemia - use for this indication requires formal consultation by Infectious Diseases (and required approval 24/7). IVIG dose will be determined in conjunction with ID and ASP-ID Pharmacists.

- IV vancomycin is not efficacious for the treatment of *C. difficile* diarrhea or colitis, and should never be used.

- Cholestyramine binds to a variety of drugs in the gastrointestinal tract including PO vancomycin, thereby rendering effective agents potentially ineffective. Efficacy data for cholestyramine is questionable. If it is used, it must be timed so that doses are not given within two hours of other oral CDI treatment.

- Currently, there are not enough clinical data to support the routine use of nitazoxanide (non-formulary), rifampin, or rifaximin in the treatment of *C. difficile* diarrhea or colitis.

- **Monoclonal antibody** against *Clostridium difficile* toxin B has been FDA approved but is non-formulary at MMC; use can be considered in complicated cases in consultation with ID and GI.

- Data on **prophylactic PO vancomycin** in patients concurrently on systemic antibiotics is limited. Low doses of PO vancomycin can be considered in certain patients in this setting. When selecting patients for secondary prophylaxis, consider the length of time since previous CDI treatment, number of previous CDI episodes, severity of previous episodes, and underlying comorbidities. Stewardship or ID approval is required for PO vancomycin prophylaxis.

- For questions about appropriate C. difficile testing, please refer to relevant sections of the MMC CDI management guidelines or contact antimicrobial stewardship.

*This guideline was prepared by the Antimicrobial Stewardship Program and ID faculty, and approved by the antibiotic subcommittee and P&T.*