SHC Clinical Pathway
Guidelines for the Treatment of *Clostridioides difficile* Infection

- **CDI Diagnosis**
  - **Fulminant? Hypotension, shock, ileus, megacolon**
    - Yes: Vancomycin 500 mg PO q6h ≥ 10 days* + Metronidazole 500 mg IV TID ≥ 10 days*
      - If ileus present and w/o megacolon: Vancomycin 500 mg PR q6h ≥ 10 days*
    - No: Initial Episode?
  - No: **Severe? WBC ≥ 15,000 OR Creatinine > 1.5 mg/dL**
    - Yes: Fidaxomicin 200 mg PO BID x 10 days
      - Alternatives: Vancomycin 125 mg PO q6h x 10 days
      - Adjunctive: Evaluate for bezlotoxumab
    - No: Initial Episode? [1 episode]
  - No: PRIOR CDI Episodes in Last 3-6 Months
    - 1 episode: Fidaxomicin 200 mg PO BID x 10 days
      - Alternatives: Vancomycin taper***
      - Adjunctive: Evaluate for bezlotoxumab
    - 2+ episodes: Consider ID consult for multiple recurrences
      - Fidaxomicin 200 mg PO BID x 10 days
      - or Vancomycin taper***
      - or Vancomycin followed by rifaximin****
        - Alternatives: Consider fecal microbiota transplant evaluation
        - Adjunctive: Evaluate for bezlotoxumab

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*Duration 10 days or longer depending on clinical improvement. Once patients are reliably taking medications by mouth and ileus has resolved, IV metronidazole and PR vancomycin can be stopped.

***Metronidazole 500 mg PO TID x 10-14 days can be used for mild initial cases of CDI only when fidaxomicin and vancomycin are unavailable.

****Vancomycin PO 125mg q6h x 10-14 days, then BID x 7 days, then daily x 7 days, then q2-3d x 2-8 weeks.

*****Vancomycin 125mg PO q6h x 10 days followed by rifaximin 400mg PO TID x 20 days. Rifaximin may require insurance prior authorization.
<table>
<thead>
<tr>
<th>Clinical Severity/Stage</th>
<th>First Line Regimen(s)</th>
<th>Alternative Regimen(s)</th>
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</thead>
<tbody>
<tr>
<td><strong>First Episode Non-Severe</strong> (WBC &lt; 15,000 AND Creatinine &lt; 1.5 mg/dL)</td>
<td>Fidaxomicin 200mg PO BID x 10 days</td>
<td>Vancomycin 125mg PO q6h x 10 days - Alternative if resources for fidaxomicin are unavailable Metronidazole 500mg PO TID x 10-14 days - Only if fidaxomicin and vancomycin are unavailable - For mild CDI cases only</td>
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<tr>
<td><strong>First Episode Severe</strong> (WBC ≥ 15,000 OR Creatinine &gt; 1.5 mg/dL)</td>
<td>Fidaxomicin 200mg PO BID x 10 days</td>
<td>Vancomycin 125mg PO q6h x 10 days - Alternative if resources for fidaxomicin are unavailable</td>
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<tr>
<td><strong>Fulminant</strong> (Hypotension, shock, ileus, or megacolon)</td>
<td>Vancomycin 500mg PO q6h PLUS Metronidazole 500mg IV TID - Surgical and ID consults indicated If ileus present and without toxic megacolon: add Vancomycin 500mg PR in 100ml NS enema q6h Duration: 10 days or longer depending on clinical improvement. Once patients are reliably taking medications by mouth and ileus has resolved, IV metronidazole and PR vancomycin can be stopped.</td>
<td>No alternative recommended</td>
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<tr>
<td><strong>First Recurrence</strong> (Non-fulminant)</td>
<td>Fidaxomicin 200mg PO BID x 10 days*</td>
<td>Vancomycin PO 125mg q6h x 10-14 days, then BID x 7 days, then daily x 7 days, then q2-3d x 2-8 weeks Adjunctive Treatment: - Evaluate for bezlotoxumab**</td>
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<tr>
<td><strong>Second or Subsequent Recurrence</strong> (Non-fulminant)</td>
<td>Fidaxomicin 200mg PO BID x 10 days* OR Vancomycin PO 125mg q6h x 10-14 days, then BID x 7 days, then daily x 7 days, then q2-3d x 2-8 weeks OR Vancomycin 125mg PO q6h x 10 days followed by rifaximin 400mg PO TID x 20 days</td>
<td>Fecal Microbiota Transplant - Can be considered for those with at least two recurrences who fail first line therapy Adjunctive Treatment: - Evaluate for bezlotoxumab** - Consider ID consult for multiple recurrences</td>
</tr>
</tbody>
</table>

*The 2021 IDSA/SHEA guidelines also suggest fidaxomicin 200 mg PO BID x 5 days, then once every other day x 20 days as another preferred regimen. However, dosing medications every other day may be logistically challenging for patients and there is currently no evidence to suggest superiority of extended-pulsed fidaxomicin over standard fidaxomicin therapy.
**Bezlotoxumab 10mg/kg IV once, should be considered as part of treatment for recurrent disease and may be used as adjunctive therapy for recurrence prevention with any stage of disease with an ID consult if criteria are met.† Bezlotoxumab may be given at any time during the 10-14 day course of antimicrobial therapy and it is preferable that the infusion be administered in the outpatient setting when possible. In patients with a history of chronic heart failure, the FDA warns that bezlotoxumab should be reserved for use when the benefit outweighs the risk.

†Bezlotoxumab Restriction Criteria

1) Recurrent disease within the last six months and unable to receive outpatient bezlotoxumab within 10 days of starting *C. difficile* treatment

OR

2) ID consult required unless in patients with an initial CDI episode being treated with oral vancomycin and ≥ 2 of the following risk factors for recurrence and unable to receive outpatient bezlotoxumab within 10 days of starting *C. difficile* treatment
   a. Age ≥ 65
   b. Meets criteria for severe CDI
   c. Immunocompromised host (hematopoietic stem cell transplant, solid organ transplant, active malignancy, use of immunosuppressive medications)
References


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