General Principles

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The following guidance applies to the treatment of patients with a clinical diagnosis of *Clostridioides Difficile* Infection (CDI) and supportive microbiological evidence of CDI:

- Stop unnecessary antimicrobial therapy (if possible). If an antibiotic is still essential, consider changing to one with a lower risk of causing CDI. It is preferable to use agents with as narrow spectrum as possible. Almost all antibiotics increase the risk of CDI but clindamycin, cephalosporins, ciprofloxacin (and other fluoroquinolones) and co-amoxiclav are well-documented as having the greatest risk.
- Avoid anti-motility medications.
- Review proton pump inhibitor use.
- Ensure adequate nutrition and replacement of fluid and electrolytes.
- Record stool output daily.
- Daily clinical review to assess for progression to severe or fulminant disease with toxic megacolon, impending perforation and shock. Urgent Surgical review is essential.
- HCWs should wash hands with soap and water as alcohol-based hand sanitisers are less effective in removing *C. difficile* spores from hands.
- Patients/ residents of a healthcare facility with potentially infectious diarrhoea (i.e. no clear alternative cause) should be isolated with Standard and Contact Precautions as soon as possible.
- Test-of-cure or testing asymptomatic individuals is not recommended and asymptomatic carriers do not need treatment.
- Where diarrhoea is due to laxative administration and there is no concern for infectious diarrhoea, testing for C difficile is not recommended.

Definitions

Definitions

- **Diarrhoea** is defined as 3 or more loose stools, i.e. Bristol stool scale 6-7, in 24 hours.
- **Treatment response** is present when the patient has resolution of diarrhoea, and has had a formed or normal stool for that patient, with maintenance of resolution for the duration of therapy and at least 48 hours after the end of treatment, and no further requirement for CDI therapy, AND parameters of disease severity (clinical, laboratory, radiological) have improved and no new signs of severe disease have developed. In all other cases, treatment is considered a failure.
- **Refractory CDI:** is CDI not responding to recommended CDI antibiotic treatment, i.e. no response after 3-5 days of therapy. Refractory CDI can be part of either non-complicated or complicated CDI, which are described below.
- **Recurrence:** is present when CDI recurs within 8 weeks after a previous episode, provided the symptoms from the previous episode resolved after completion of initial treatment. It is not feasible to distinguish recurrence due to relapse (renewed symptoms from already present CDI) from recurrence due to reinfection in daily practice because genotyping is not readily available.

  Severe CDI: is characterized by one of the following factors at presentation:
  - Fever, i.e. core body temperature greater than 38.5°C,
  - Marked leucocytosis, i.e. leucocyte count greater than 15 x 10^9 /L, and
  - Rise in serum creatinine, i.e. more than 50% above the baseline.
  - Additional supporting factors, when available are distension of the large intestine, pericolonic fat stranding or colonic wall thickening (including low-attenuation mural thickening) at imaging.

  Severe-complicated CDI (or fulminant CD) : is defined by the presence of one of the following factors that needs to be attributed to CDI:
  - Hypotension, septic shock, elevated serum lactate, ileus, toxic megacolon, bowel perforation or any fulminant course of disease (i.e. rapid deterioration of the patient).

Initial Episode & First Recurrence of C. difficile Infection (CDI)

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Treatment *C. difficile infection (CDI)* in hospital setting

Drug	Dose	Duration	Notes
Non-severe CDI • **Mildly symptomatic** patients (positive test result but less than 3 episodes of diarrhoea in 24 hours):			
It is recommended to discontinue antibiotic therapy with the inciting antibiotic if possible and closely monitor the patient for 48 hours. *C. difficile* treatment should be initiated if any signs of clinical deterioration are observed.			
• Positive test results and **3 or more episodes of diarrhoea in 24 hours**, follow treatment options below:			
1st line options:			
Metronidazole oral *or*	400mg every 8 hours	10 days	
Vancomycin oral [1]	125mg every 6 hours	10 days	
Treatment option for patient at high risk of recurrence supported by age over 65 years plus the presence of one or more of these additional risk factors (healthcare associated CDI, prior hospitalisation in the last 3 months, use of concomitant antibiotics, PPI started during/after CDI diagnosis or prior CDI episode)			
Fidaxomicin oral	200mg every 12 hours	10 days	Discuss with a clinical microbiologist or infectious diseases consultant. High Tech item, see prescribing notes*
Severe CDI			
• Early surgical opinion • Patients with severe CDI should be managed by a multidisciplinary team to include a clinical microbiologist and/or infectious diseases physician, gastroenterologist, surgeon and pharmacist as needed			
1st line options:			
Vancomycin oral [1] *or*	125mg every 6 hours	10 days	
Fidaxomicin oral	200mg every 12 hours	10 days	Discuss with a clinical microbiologist or infectious diseases consultant. High Tech item, see prescribing notes*
Severe complicated/fulminant CDI			
• Early surgical opinion • Patients with severe CDI should be managed by a multidisciplinary team to include a clinical microbiologist and/or infectious diseases physician, gastroenterologist, surgeon and pharmacist as needed			
1st line option: Vancomycin oral [1] *plus* metronidazole intravenous	 500mg every 6 hours 500mg every 8 hours	10 days	
2nd line option: Other therapeutic options may be considered on a case-by-case basis and after multidisciplinary discussions. This is beyond the scope of this guidance.			

First recurrence of CDI			
1st line options: Vancomycin oral [1] *or*	125mg every 6 hours	10 days	Only use if metronidazole was used for treatment of the first episode
Fidaxomicin oral	200mg every 12 hours	10 days	Discuss with a clinical microbiologist or infectious diseases consultant. High Tech item, see prescribing notes* If initial CDI episode was treated with fidaxomicin, seek micro/ID advice.

[1] Vancomycin: If a person has swallowing difficulties or a nasogastric or PEG tube for enteral administration, vials of vancomycin powder for injection may be used to make an extemporaneous oral solution. Vancomycin (oral) adult – includes information for dispensing pharmacists on how to make extemporaneous oral solution.

*Fidaxomicin prescribing: Fidaxomicin should only be initiated on the recommendation of a Consultant Microbiologist or Infectious Diseases Physician. Fidaxomicin is only available from community pharmacies through the High Tech Arrangements. A GP may prescribe fidaxomicin, but must state the name and base hospital of the consulting Consultant Microbiologist or Infectious Diseases Physician on the prescription in order for the community pharmacy to process through the High Tech Arrangements. For hospital patients, follow the normal procedure for prescriptions of High Tech drugs.

Source: *HSE AMRIC Clostridioides difficile infection treatment guidance (version 2.0) 2023*

Additional Comments:

- Vancocin® (Vancomycin) Matrigel Capsules 125 mg are now included on the GMS Reimbursement List (i.e. a High Tech Prescription is no longer required) and thus any prescriber is able to prescribe it in line with treatment options set out in the CDI treatment guidance.
- Oral vancomycin is not absorbed from the GIT and therefore should never be used as systemic therapy. Its sole use is in the treatment of CDI. Therapeutic drug monitoring is not required.
- Fidaxomicin has not been tested in pregnant or breastfeeding women or in patients with a history of inflammatory bowel disease. It is also a reserve agent, and thus must be discussed with Clinical Microbiologist prior to prescribing.

Multiple (≥2nd) Recurrence CDI

Multiple (≥2nd) Recurrence CDI

Please discuss with Clinical Microbiologist or Infectious Diseases.

For non-severe & severe CDI, treatment options are:

- Fidaxomicin 200mg BD 10 days (if initial treatment with oral vancomycin) or
- Vancomycin 125mg QDS orally 10 days, or
- Vancomycin tapering regimen:

125mg orally QDS for two weeks

125mg orally BD for one week

125mg orally OD for one week

125mg orally every 48 hours for one week

125mg orally every 72 hours for one week

- Early surgical review for severe CDI
- Consider referral for faecal microbiota transplantation if available (MDT discussion required)

For severe-complicated/fulminant CDI:

- Vancomycin 500mg QDS oral PLUS Metronidazole 500mg TDS IV
- Urgent surgical review essential
- In patients with ileus (or any condition preventing vancomycin reaching the colon) and not responding to enteral therapy, consider administering intracolonic vancomycin. This carries a risk of colonic perforation and should only be performed by personnel trained in administering enemas.

Other adjunctive therapies such as Tigecycline IV may be considered in severe, severe-complicated/fulminant CDI in addition to standard therapy. Please discuss with Clinical Microbiologist or Infectious Diseases.

References

References

1. *HSE AMRIC Clostridioides difficile infection treatment guidance (version 2.0) 2023*
2. *European Society of Clinical Microbiology and Infectious Diseases: 2021 update on the treatment guidance document for Clostridioides difficile infection in adults.* *https://doi.org/10.1016/j.cmi.2021.09.038*
3. *NICE Guideline [NG199] Clostridioides difficile infection: antimicrobial prescribing. 2021.* *https://www.nice.org.uk/guidance/ng199*
4. *IDSA and SHEA: 2021 focused update guidelines on management of Clostridioides difficile infection in adults. Clinical Infectious Diseases. 2021.* *https://doi.org/10.1093/cid/ciab549*