



Management of *Clostridioides* *difficile* Infection in Wales

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1.0 Aims and scope

This guidance presents updated learning from previous and current UK guidelines and peer-reviewed publications to provide an evidence-based, accessible, antimicrobial prescribing strategy for *Clostridioides difficile* Infection (CDI), previously known as *Clostridium difficile*¹⁻⁴. This guideline is not intended to replace NICE guidance, but to supplement current guidance and provide a short summary for use by Welsh health boards. The recommendations in this guideline are for managing CDI in adults. Advice from a specialist in paediatric infectious diseases or paediatric gastroenterology should be sought for children and young adults in both community and hospital settings, with the choice of antibiotic being based on what is recommended and available for adults, but also what is licensed for paediatric use. This guideline does not cover pathogenesis, diagnosis or prevention of *C. difficile* which have been well described elsewhere⁵⁻⁸. See local Health Board Infection, Prevention and Control guidelines for more information.

2.0 Assessment of symptoms

A multidisciplinary clinical team with input from microbiology, infectious diseases, antimicrobial pharmacy, infection prevention and control, gastroenterology, general surgery and dieticians should follow existing UK guidance when diagnosing and managing patients with suspected or confirmed CDI. Severity should be assessed as per NICE guideline (NG199) *Clostridioides difficile* infection: antimicrobial prescribing (Box 1). Mild-to-moderate CDI may be suitable for treatment in primary care, but severe CDI should always be referred to secondary care.

Box 1: Severity of CDI¹:

Mild: not associated with an increased white cell count (WCC).

Typically associated with fewer than three episodes of loose stools (defined as loose enough to take the shape of the container used to sample them) per day.

Moderate: associated with an increased WCC (but less than 15×10^9 per litre).

Typically associated with three to five loose stools per day.

Severe: associated with a WCC greater than 15×10^9 per litre, or an acutely increased serum creatinine concentration (greater than 50% increase above baseline), or a temperature higher than 38.5°C , or evidence of severe colitis (abdominal or radiological signs). The number of stools may be a less reliable marker of severity.

Life threatening: signs and symptoms include hypotension, partial or complete ileus, toxic megacolon, or CT evidence of severe disease.

3.0 Review of medication and prescribing considerations

Promptly review the following concurrent medications, with the aim of **de-escalating or suspending** their prescribing, with referral to appropriate specialists (microbiology, gastroenterology, acute pain team and others) as necessary:

- All existing antibiotics. If antibiotics are required to treat a concurrent infection, choose narrow spectrum agents where possible to minimize the risk of exacerbating CDI;
- Gastric acid suppressing agents, such as proton pump inhibitors (PPI) and histamine (H₂) receptor antagonists;
- Gut motility agents and opiates;
- Medicines that may cause problems in dehydrated patients, for example non-steroidal anti-inflammatory drugs (NSAID), angiotensin converting enzyme (ACE) inhibitors, angiotensin-II receptor antagonists and diuretics;
- Laxatives.

Antibiotics should **not** be used to prevent CDI, and patients taking antibiotics should **not** be advised to take prebiotics or probiotics to prevent CDI. Anti-motility agents such as loperamide are contraindicated as they increase the risk of toxic megacolon.

4.0 Hydration and preventing spread

Alongside review of medication, patients with suspected or confirmed CDI should be managed as for gastroenteritis, with advice to drink sufficient fluids to avoid dehydration. Consider the use of oral electrolyte solutions to aid hydration.

Medical staff, patients and carers must comply with strict hand hygiene using soap and water to help prevent the spread of CDI. Alcohol-based hand rub solutions are ineffective for CDI and should not be used in isolation. A diagnosis of CDI must be recorded in patient notes and in any transfer documentation to inform further antimicrobial prescribing especially when patients are moved across care settings.

Advice on effective methods for the prevention and control of CDI were published in 2008 with good antimicrobial stewardship summarised in 2015 to decrease the incidence and spread of CDI^{5,6}.

5.0 Referral and specialist advice

Prompt referral for specialist advice for patients with suspected or confirmed CDI is vital to manage CDI:

- Patients in primary care should be promptly referred to hospital if their symptoms are severe, or worsen rapidly or significantly. Red flags for referral to secondary care include: high WCC, high temperature, signs of hypotension and acute dehydration. Patients in primary care with CDI recurrence or relapse should be discussed with a specialist in microbiology or infectious disease.
- Patients in hospital with suspected or confirmed CDI should be promptly assessed by an infection specialist or general surgeon if symptoms worsen rapidly or significantly or the patient relapses. Specialist advice should be sought for patients considered at high risk of complications or recurrence because of their age, frailty or comorbidities.

6.0 Treating suspected or confirmed CDI

An oral antibiotic should be prescribed to treat suspected or confirmed CDI in **adults aged 18 years and over** (Table 1). Specialist advice should be sought when prescribing for **children and young adults**. Refer to Box 1 for severity of treatment and treat accordingly using Table 1 below. In primary care, consider discussing with a specialist in microbiology or infectious diseases before starting treatment.

Table 1: Antibiotics for adults aged 18 years and over:

Antibiotic choice		Duration of treatment
First line antibiotic for a first episode of mild, moderate or severe suspected or confirmed <i>C. difficile</i> infection.	Vancomycin 125 mg PO QDS (IV powder for solution for oral use, or capsules)	10 days
Second line antibiotic for a first episode of <i>C. difficile</i> if vancomycin is ineffective.	Fidaxomicin 200 mg PO BD	10 days
Antibiotic for <i>C. difficile</i> not responding to a first or second-line antibiotic.	Seek specialist advice. Specialists may initially offer:	
	Vancomycin Up to 500 mg PO QDS With or without: Metronidazole 500 mg IV TDS	10 days
Antibiotic for a further episode of <i>C. difficile</i> infection within 12 weeks of symptom resolution (relapse).	Fidaxomicin 200 mg PO BD	10 days
Antibiotics for a further episode of <i>C. difficile</i> infection more than 12 weeks of symptom resolution (recurrence).	Vancomycin 125 mg PO QDS Or Fidaxomicin 200 mg PO BD	10 days
Antibiotics for life-threatening <i>C. difficile</i> infection.	Seek urgent specialist advice including general surgery. Medical specialists may initially offer:	
	Vancomycin 500 mg PO QDS With Metronidazole 500 mg IV TDS	10 days
BD = twice-daily; IV = intravenous; PO = by mouth (per os); QDS = four times daily; TDS = three times daily.		

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Alternative routes for administering antibiotics (for example, a nasogastric tube or rectal catheter) can be used for patients unable to take medicines orally. Patients in primary care will need to be admitted to hospital if unable to tolerate oral medication.

Consider treating with faecal microbiota transplantation (FMT) after discussion with Microbiology and follow [NICE guidance](#) for adults who have had two or more episodes of CDI that have not responded to antibiotics.

Patients with severe disease that progresses to possible ileus or toxic megacolon should be referred urgently for discussion with Microbiology and reviewed by General Surgery.

7.0 Reassessment

Patients with suspected or confirmed CDI should be reassessed after commencement of antibiotic therapy, for example, after 3-5 days, and again on completing the course. Use clinical judgement to determine whether antibiotic treatment of CDI is ineffective. It is not usually possible to determine this until day 7 because diarrhoea may take one to two weeks to resolve. Daily assessment is recommended for in-patients if symptoms or signs do not improve as expected, or worsen rapidly or significantly at any time. If antibiotics have been started for suspected CDI, and subsequent stool sample tests do not confirm CDI, consider reviewing the need for antibiotics (see [Public Health England's guidance on diagnosis and reporting](#) for recommendations on stool sample tests⁷). Samples taken after commencing antibiotics may return a negative result due to the effect of the antibiotics, therefore clinical judgement should be used when stopping antibiotics.

Bezlotoxumab should not be used to prevent recurrence of CDI as it is not cost effective¹.

References

1. National Institute for Health and Care Excellence. NICE Guideline, NG199. Clostridioides difficile infection: antimicrobial prescribing. 23 July 2021. Available at: <https://www.nice.org.uk/guidance/ng199>. Accessed September 2021.
2. Public Health England. Updated guidance on the management and treatment of C. difficile infection. 23 July 2021. Available at: <https://www.gov.uk/government/publications/clostridium-difficile-infection-guidance-on-management-and-treatment>. Accessed September 2021.
3. Health Protection Scotland. Guidance on Prevention and Control of Clostridium difficile Infection in health and social care settings in Scotland. September 2017. Available at: <https://www.hps.scot.nhs.uk/web-resources-container/guidance-on-prevention-and-control-of-clostridium-difficile-infection-cdi-in-health-and-social-care-settings-in-scotland/>. Accessed September 2021.
4. National Institute for Health and Care Excellence. Evidence summary, ESMPB1. Clostridium difficile infection: risk with broad-spectrum antibiotics. 17 March 2015. Available at: <https://www.nice.org.uk/advice/esmpb1/chapter/full-evidence-summary-medicines-and-prescribing-briefing>. Accessed September 2021.
5. Health Protection Agency. Clostridium difficile infection: How to deal with the problem. December 2008. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/340851/Clostridium_difficile_infection_how_to_deal_with_the_problem.pdf. Accessed September 2021.
6. National Institute for Health and Care Excellence. NICE Guideline, NG15. Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use. 18 August 2015. Available at: <https://www.nice.org.uk/guidance/ng15>. Accessed September 2021.
7. Department of Health and Social Care. Updated guidance on the diagnosis and reporting of Clostridium Difficile. March 2012. Available at: <https://www.gov.uk/government/publications/updated-guidance-on-the-diagnosis-and-reporting-of-clostridium-difficile>. Accessed September 2021.
8. Borriello SP. Pathogenesis of Clostridium difficile infection. *Journal of Antimicrobial Chemotherapy*. 1998;41 Suppl C:13–19. Available at: https://doi.org/10.1093/jac/41.suppl_3.13. Accessed November 2021.