For use in:	Adult patients
By:	Medical and Nursing Staff
For:	Patients who are *Clostridium difficile* toxin positive, previously positive or *Clostridium difficile* toxigenic gene positive Wards where Supportive Measures apply Surgical Prophylaxis
Division responsible for document:	Clinical Support Division
Key words:	Diarrhoea, glutamate dehydrogenase (GDH), *Clostridium difficile* toxin, *Clostridium difficile* PCR
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Assessed and approved by:	Clinical Guidelines Assessment Panel (CGAP)
Date of approval:	22/11/2021
Ratified by or reported as approved to (if applicable)**:**	Clinical Safety and Effectiveness Sub-Board
To be reviewed before: This document remains current after this date but will be under review	22/11/2024
To be reviewed by:	Caroline Hallam
Reference and / or Trustdocs ID No:	CA5116 – ID No: 9400
Version No:	7
Compliance links: *(is there any NICE related to guidance)*	Clostridioides difficile infection: antimicrobial prescribing NICE guideline (NG199) Published: 23 July 2021
If Yes – does the strategy/policy deviate from the recommendations of NICE? **If so, why?**	No

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Version and Document Control:

Version Number	Date of Update	Change Description	Author
5.2	21/07/2021	No clinical changes. Addition of key people. Will review again when NICE have finalised their guidelines.	Caroline Hallam
6	14/10/2021	Reviewed as per the NICE guidelines	Caroline Hallam
7	22/11/2021	Replaced a drug name – ranitidine to famotidine	Caroline Hallam

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Section 1: Initial Assessment

For people with suspected or confirmed C. *difficile* toxin infection assess;

Whether it's the first or further episode (relapse or recurrence) of C *difficile* infection:

Relapse: Usually occurs within 12 weeks of previous symptom resolution. Likely to be with the same C.*difficile* strain.

Recurrence: Usually occurs more than 12 weeks after previous symptom resolution. Likely to be a different C. *difficile* strain.

The Severity of the C *difficile:*

Individual factors such as age, frailty or comorbidities that may affect the risk of complications or recurrence.

Type of infection	Definition
Mild	No increase in white cell count Typically associated with < 3 episodes of loose stools (defined as loose enough to take the shape of the container used to sample them) per day
Moderate	Increase in white cell count (but less than 15 x 10^9 per litre). Typically 3-5 stools a day
Severe	White cell count > 15 x 10^9 per litre OR An acutely increased serum creatinine (>50% increase above baseline) OR A temperature > 38.5^{0}C OR Evidence of severe colitis (abdominal or radiological signs). The number of stools may be a less reliable indicator.
Life Threatening	Symptoms and signs include hypotension, partial or complete ileus, toxic megacolon or CT evidence of severe disease.

Concurrent Antimicrobial Treatment:

Review existing antimicrobial treatment and stop it unless essential. If an antibiotic is essential consider changing to one with a lower risk of causing C.*difficile* if possible. See page 8 for more details. Contact Microbiology for advice if needed.

Review other medication:

Review the need to continue PPIs, other medicines with gastrointestinal activity or adverse effects such as laxatives, medicines that can cause problems with dehydration such as NSAIDs, ACEI or Angiotensin 2 receptor antagonists and diuretics. See page 5 for more details

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Section 2: Antimicrobial Treatment of *C. difficile* toxin Positive Patients

Treatment	Recommendation
First Line Antibiotic for first episode (mild, moderate or severe)	Vancomycin 125mg PO qds 10 days
Second Line Antibiotic for first episode if vancomycin is ineffective (use clinical judgement to determine this, not usually possible to determine until day 7 as diarrhoea may take 1-2 weeks to resolve) (mild, moderate or severe)	Contact Microbiology
Relapse (further episode of C. *difficile* infection ≤12 weeks of symptom resolution)	Contact Microbiology
Recurrence (further episode of C. *difficile* infection > 12 weeks of symptom resolution	Vancomycin 125mg PO qds 10 days
LifeThreatening C.*difficile*	Seek urgent specialist advice from Microbiology and Gastroenterology Usual treatment: Vancomycin 500mg qds PO 10 days + Metronidazole 500mg tds IV 10 days

Section 3: General Prescribing Points in C. *difficile* toxin positive patients

Non *C. difficile* Antibiotics

Non *C. difficile* antibiotics should only be continued if clinically essential. High risk antibiotics e.g. ciprofloxacin, cephalosporins and clindamycin and moderate risk antibiotics e.g. amoxicillin, co-amoxiclav, tazocin and meropenem should be switched to those with a lower risk if possible. If the antibiotic is to be continued it is imperative that this is clearly documented in the medical notes. The antibiotic should be kept under regular review, both in the medical notes and on EPMA. EPMA should be regularly reviewed and the stop/review date updated every 24/48 hours.

Proton Pump Inhibitors (PPIs)

PPIs reduce gastro intestinal acidity which can delay resolution of C. *difficile* infection (CDI). Review the use of PPI's if there is no clear indication for use.

Discontinue if non-essential or reduce the dose / switch to a H2 receptor antagonist e.g. famotidine.
Generally should not be withdrawn in

- Current or past peptic ulcer bleed
- Gastro protection with NSAIDs/aspirin/anticoagulants/steroids
- Previous oesophageal stricture
- Recent (< 2 weeks upper GI endoscopic or surgical intervention predisposing to ulceration)

Other drugs

Other medication can delay resolution of diarrhoea by altering gastrointestinal motility and/or gastric intestinal flora or affecting other defence mechanisms. The medication outlined below should be stopped or withheld where possible.

1. Anti-peristaltic agents (opioids [although it will not be possible to stop opioids in patients who have been on them long term], anti-diarrhoeal agents etc.)
2. Pro-motility / pro-kinetic agents (laxatives, stool bulking agents etc.)
3. Iron
4. Other medications that may have detrimental effects if people are acutely ill and dehydrated e,g, NSAIDs, ACEI, Angiotensin 2 receptor antagonists and diuretics.

The patients should also be reviewed daily with regard to fluid resuscitation, electrolyte replacement and nutrition.

Section 4 : Management of C. *difficile* toxigenic gene PCR positive Patients

Patients identified to be colonised with *C. difficile* i.e. toxigenic gene PCR positive, toxin negative are at risk of progressing to active CDI.

If CDI is likely based on frequency of diarrhoea, inflammatory markers, abdominal signs and antibiotic history etc. (bearing in mind that the toxin test is not 100% sensitive), then commence treatment with vancomycin or discuss with Duty Microbiologist. Review other medication as below.

To prevent progression to active CDI, review medications as below. Stop unnecessary antibiotics or choose narrow spectrum / low risk antibiotics if indicated.

Prescribing Antibiotics:

High risk:
Quinolones e.g. ciprofloxacin
Cephalosporins e.g .cefuroxime
Clindamycin

Moderate Risk:
Amoxicillin
Co-amoxiclav
Meropenem
Tazocin (Piperacillin/Tazobactam)

If non *C. difficile* antibiotics are prescribed, they should be kept under regular review in the medical notes. EPMA should be reviewed daily and a regular stop/review date updated on EPMA.

General Prescribing Measures:

Proton Pump Inhibitors (PPIs)
PPIs reduce gastro intestinal acidity which can increase the risk of active *C. difficile* toxin positive diarrhoea.

Discontinue if non-essential or reduce the dose
Generally should not be withdrawn in

- Current or past peptic ulcer bleed
- Gastro protection with NSAIDs/aspirin/anticoagulants/steroids
- Previous oesophageal stricture
- Recent (<2 weeks upper GI endoscopic or surgical intervention predisposing to ulceration)

  Review **antiperistaltic** agents (opioids [although it will not be possible to stop opioids in patients who have been on them long term], anti-diarrhoeal agents etc.)

  Review **promotility/prokinetic** agents (laxatives, stool bulking agents etc.)

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Section 5: General Information and Prescribing Advice for Wards on 'Supportive Measures'

Following a period of increased incidence of *Clostridium difficile* infection (CDI) in a particular clinical area, 'supportive measures' will apply for a period of time as directed by Infection Control. This document offers advice / guidance to follow during this time.

Prescribing antimicrobials

HIGH RISK	MODERATE RISK
• Quinolones	Co-amoxiclav
Cephalosporins	Meropenem
Clindamycin	Amoxicillin
	Tazocin
(Piperacillin/Tazobactam)	

- **There is no evidence to support the use of Tazocin in preference to Co-amoxiclav. Both have a moderate risk of CDI and should be avoided where possible.**
- **Where oral Co-amoxiclav is considered for step down, consider alternatives.**
- **Cephalosporins, Quinolones, Clindamycin, Tazocin and Co-amoxiclav should only be prescribed on the advice of a consultant and according to policy.**
- **Review all antibiotic prescriptions with a senior doctor daily if possible.**
- **Review IV antibiotics with a view to step down to oral antibiotics at 48 hours.**

- **Respiratory**
  - For community acquired pneumonia, use benzyl penicillin and clarithromycin. If a broad spectrum penicillin is required use co-amoxiclav unless the patient is on the Sepsis pathway. Consider doxycycline as oral stepdown or as first choice if oral therapy possible.
  - Use amoxicillin and metronidazole for community acquired aspiration pneumonia.
  - Use amoxicillin, metronidazole and gentamicin for hospital acquired pneumonia/aspiration. Consider doxycycline as oral stepdown.
  - Only use Tazocin if the patient has sepsis with an NEWS2 is 5 or more or > 3 in any one parameter or is immunocompromised.

- **Urinary Tract**
  - Use gentamicin for moderate / severe urinary tract infection if the patient has good renal function unless the patient is on the sepsis pathway.
    Only use oral co-amoxiclav for a urinary tract infection if trimethoprim and nitrofurantoin are inappropriate.

NB This also applies to patients who are transferred or treated elsewhere in the hospital.

Other high risk medication

- **Proton pump inhibitors e.g. lansoprazole**
- **Laxatives**
- **Antidiarrhoeal agents e.g loperamide**
- **Iron**
- **Prokinetic agents e.g. Metoclopramide**

This list highlights other drugs which can increase the risk of developing CDI. This medication should be reviewed carefully in all patients on the ward, but particularly in patients on high / moderate risk antibiotics. If possible anything that is not required in the short term should be stopped / withheld.

Section 6: Prescribing Advice for Patients who have previously had C. *difficile*

Antibiotics are an important risk factor in precipitating *C. difficile* and should be used cautiously in patients who have had a previous episode. Other pre-disposing factors include increasing age, underlying illness, recent gastro-intestinal surgery and nasogastric feeding. All antibiotics pose some risk but some are riskier than others.

Prescribing Antibiotics

High risk:	**Moderate Risk**:
Quinolones e.g. ciprofloxacin	Amoxicillin
Cephalosporins e.g .cefuroxime	Co-amoxiclav
Clindamycin	Meropenem
	Tazocin (Piperacillin/Tazobactam)

In these patients a low risk antibiotic should be prescribed where possible. The antibiotic should be kept under regular review in the medical notes. EPMA should be reviewed daily and a regular stop/review date updated on EPMA.

General Prescribing Measures

Proton Pump Inhibitors (PPIs)
PPIs reduce gastro intestinal acidity which can increase the risk of C. *difficile* diarrhoea.

Discontinue if non-essential or reduce the dose
Generally should not be withdrawn in

- Current or past peptic ulcer bleed
- Gastro protection with NSAIDs/aspirin/anticoagulants/steroids
- Previous oesophageal stricture
- Recent (<2 weeks upper GI endoscopic or surgical intervention predisposing to ulceration)

Review antiperistaltic agents (opioids [although it will not be possible to stop opioids in patients who have been on them long term], anti-diarrhoeal agents etc.)

Review promotility/prokinetic agents (laxatives, stool bulking agents etc.)
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Section 7: Surgical Prophylaxis for Patients with a previous history of C. *difficile*

For patients with a history of *C.difficile,* cephalosporins and quinolones should be avoided, as should co-amoxiclav if possible. Many surgical prophylaxis regimens do not include these antibiotics. BUT in patients who have a history of CDI please use a regimen that includes the appropriate selection from gentamicin, teicoplanin and metronidazole.

There will however be particular patients and procedures in whom the risk of *C.difficile* is outweighed by the benefit of using particular antibiotics, but this should be an explicit decision made by the consultant in charge of the patient. Microbiology can also help in these difficult cases.

Wards on Supportive Measures due to a period of increased incidence of *C. difficile*

If the ward is on Supportive Measures due to a Period of Increased Incidence (PII) of C.*difficile* then patients from the ward who are to be given antibiotic prophylaxis should have the same regimens as patients who have a previous history of C. *difficile.*

Section 8: Appendix 1

Administration of Vancomycin Injection orally

Vancomycin preparation for injection is now licensed for oral use and is cheaper than the capsules. It is also easier to swallow. The contents of vials for parenteral administration may be used for oral administration. After initial reconstitution of the vial, the selected dose may be diluted in 30 mL of water and given to the patient to drink, or the diluted material may be administered via an enteral feeding tube.

Instructions

1. Reconstitute 500mg vial with 10mL of water for injection to give a concentration of 125mg/2.5mL.

2. Withdraw the required volume for the dose into a medicine gallipot, this may be diluted with water up to 30mLs before administration.

3. Write the patient's name on an IV additive label plus the date and time of expiry (24 hours after opening) and attach the label to the vial.

4. Store the solution in the fridge.

5. Vials are for single patient use only and should not be shared.

References

NICE guidelines (NG199) Published: 23 July 2021: Clostridioides difficile infection: antimicrobial prescribing