Derby and Derbyshire
Clinical Commissioning Group

DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE (JAPC)

PRESCRIBING GUIDELINE FOR *CLOSTRIDIOIDES DIFFICILE INFECTION* (CDI) IN ADULTS IN PRIMARY CARE

This guideline deals with the management and antibiotic treatment of adult patients having suspected or diagnosed **MILD** to **MODERATE** *Clostridioides difficile* infection in the community.

Severe infection – requiring urgent referral to hospital if;[1]

- WCC greater than 15 × 10^9/L
- Acutely increased serum creatinine concentration (greater than 50% increase above baseline)
- Temperature higher than 38.5 degrees Celsius
- Evidence of severe colitis (abdominal or radiological signs). Stool number may be a less reliable indicator of severity[1].

Management & Treatment [1,4,5,6]

For ALL patients with suspicion of or confirmed *Clostridiodes difficile* Infection (CDI) see below – please document any rationale for deviations from the advice outlined here.

General management

- Replace fluid & electrolyte losses. Encourage eating and drinking.
- Assess nutritional risk & manage appropriately. Give all patients & carers patient information about *C difficile* infection via https://www.nhs.uk/conditions/c-difficile/

Medications

- Discontinue current 'unnecessary' antibiotics to allow normal intestinal flora to be re-established. If this is not possible, discuss alternatives with a Consultant Microbiologist.
- Anti-motility drugs (e.g. codeine, loperamide) should be avoided in CDI (due to the risk of precipitating toxic megacolon – by slowing clearance of *C.difficile* from intestine). Including those prescribed or bought over the counter.
- Review anti-ulcer drugs (e.g. PPIs & H2 antagonists) -stop or reduce dose if possible. Evidence indicates these are a risk factor for CDI (in particular PPIs). Consider the risk/benefit to the patient. If necessary, H2- Antagonist may an alternative to PPI medication.
- Avoid prokinetic agents (e.g. metoclopramide, domperidone) as these may increase diarrhoea.
- Laxatives (e.g. lactulose, senna) are rarely indicated long term - stop in acute CDI.
- Non-steroidal anti-inflammatory drugs (e.g. ibuprofen, diclofenac) should be stopped in acute CDI.
- Review use of diuretics (e.g. furosemide, bendroflumethiazide, spironolactone) and ACE inhibitors/A2RAs (e.g. ramipril, lisinopril, losartan, valsartan) during acute CDI and withhold if appropriate due to acute kidney injuries. Remember to review ongoing need once infection has cleared.
- Review drugs where therapeutic levels may be affected by CDI (as diarrhoea can lead to altered absorption. Consider seeking advice from relevant speciality – (For example – Lithium levels increasing. Advice will need to be sought from the consultant psychiatrist, as appropriate) Remember to restart medication when appropriate
- Avoid prescribing cephalosporins, quinolones, clindamycin or co-amoxiclav / amoxicillin in future to patients who have had an episode of CDI - Discuss alternatives with a Consultant Microbiologist, if needed.
- **Do not advise people taking antibiotics to take prebiotics or probiotics to prevent *C. difficile* infection**

Special populations

- Stoma patients who require anti-motility drugs to maintain a normal stoma output should be discussed with the gastroenterologist.

Drug Treatment of mild, moderate or severe CDI[1]

Please find NICE visual summary **here**

Metronidazole is no longer recommended as first line treatment as it has been shown to be neither clinically nor cost effective compared to vancomycin[1]

Where there is a strong clinical suspicion of CDI, start treatment:

Treatment	Antibiotic, dosage and course length
First-line antibiotic for a first episode of mild, moderate or severe *C. difficile* infection	Vancomycin: 125 mg orally four times a day for 10 days *In the instance of swallowing difficulties, vancomycin liquid is available as special order in community pharmacies. More information on vancomycin use in swallowing difficulties can be found on the SPS website here*[2]
Second-line antibiotic for a first episode of mild, moderate or severe *C. difficile* infection if vancomycin is ineffective	Fidaxomicin: 200 mg orally twice a day for 10 days *In the instance of swallowing difficulties, fidaxomicin (Dificlir) granules for oral suspension is available. More information on Fidaxomicin use in swallowing difficulties can be found on the SPS website here*[3]
Antibiotics for *C. difficile* infection if first- and second-line antibiotics are ineffective	**Seek specialist advice. Specialists may initially offer:** Vancomycin: Up to 500 mg orally four times a day for 10 days, with or without metronidazole: 500 mg intravenously three times a day for 10 days

Further Episode (Relapse /Recurrent infection)[1]

A further episode of *C. difficile* infection could either be a relapse, which is more likely to be with the same *C. difficile* strain, or a recurrence, which is more likely to be with a different *C. difficile* strain. There is no agreement on the precise definition of relapse and recurrence, and it is difficult to distinguish between them in clinical practice. NICE guideline NG199 states that a relapse occurs within 12 weeks of previous symptom resolution and recurrence occurs more than 12 weeks after previous symptom resolution.

Recurrence occurs in about 20% of patients, and is more common in elderly patients, with risk of further recurrence of nearly 50%[6].

Treatment	Antibiotic, dosage and course length
Further episode of *C. difficile* infection ***within*** 12 weeks of symptom resolution (relapse)	Fidaxomicin: 200 mg orally twice a day for 10 days
Further episode of *C. difficile* infection ***more than*** 12 weeks after symptom resolution (recurrence)	Vancomycin: 125 mg orally four times a day for 10 days Or Fidaxomicin: 200 mg orally twice a day for 10 days

For second and subsequent recurrences, contact consultant microbiologist for advice on appropriate antibiotic treatment. The same management and monitoring should be performed as outlined above.

Ineffective treatments / life threatening infection[1]

In the event of 1st and 2nd line treatments being ineffective, specialist advice should be sought (if not already advising.) Treatment options may involve Vancomycin up to 500mg four times a day for 10 days ± Metronidazole 500mg IV three times a day for 10 days**.** This regime may also be initially offered in life threatening CDI, however surgery may be included. It is likely that patients in these categories will already have been referred to/ admitted to secondary care (see referral pathway in NICE visual summary).

Treatment	Antibiotic, dosage and course length
Antibiotics for life-threatening *C. difficile* infection	Seek urgent specialist advice, which may include surgery. Antibiotics that specialists may initially offer are: Vancomycin: 500 mg orally four times a day for 10 days with metronidazole: 500 mg IV three times a day for 10 days

Obtaining Vancomycin & Fidaxomicin

Urgency of treatment

Advice from local Lead Antimicrobial Pharmacist is a mild case should be able to wait until the next day to start treatment, with appropriate safety netting advice. A moderate case should start treatment the same day. Severity assessment is important and is dependent on clinical judgement. Microbiologist advice is to send blood for WBC when sending the stool sample, with an aim to start treatment within an hour of a positive result. It is likely that severe to life threatening cases would be admitted to hospital, however treatment should be started whilst awaiting admission, if clinical suspicion of CDI.

Patients should be advised to have their prescriptions dispensed at a community pharmacy in the first instance. If the medication is not immediately available, it can be ordered in for the afternoon if presented in the morning and for the next day if presented in the afternoon. If a patient has a prescription for vancomycin that community pharmacy cannot obtain in a timely manner, patients can have their prescription dispensed at the pharmacy at local acute trusts (UHDB/ CRH). Both acute trusts also stock a liquid formulation of Vancomycin – if a patient is unable to swallow capsules.

UHDB: https://www.uhdb.nhs.uk/service-pharmacy
There is a hospital pharmacist on duty 24 hours per day for 7 days per week, so this can be dealt with at any time. At weekends and evenings, please ask switchboard to bleep the on-call pharmacist.

Chesterfield Royal Hospital: https://www.chesterfieldroyal.nhs.uk/our-services/pharmacy
Opening times are Mon-Fri 8.30am-6pm; Sat 9am-1.00pm; Sun 10am-12 noon.

Fidaxomicin

Fidaxomicin at dose 200mg twice daily for 10 days is the reserved treatment option for 2nd line treatment where vancomycin is ineffective[1]. It is also used in severe CDI in patients with multiple comorbidities who are receiving concomitant antibiotics or for recurrence of CDI[1]. Stock is not usually kept at community pharmacies but is available from wholesalers. If unable to obtain fidaxomicin in a timely manner, follow same advice for obtaining vancomycin above.

Document update	Date
Fidaxomicin (Dificlir) granules oral suspension for swallowing difficulties added	Sept 2022

References

1. NICE (July 2021) *Clostridioides difficile infection: antimicrobial prescribing* Available at : https://www.nice.org.uk/guidance/ng99/resources/clostridioides-difficile-infection-antimicrobial-prescribing-pdf-66142090546117

2. SPS (May 2021) *Choosing between oral Vancomycin options* Available at: https://www.sps.nhs.uk/articles/choosing-between-oral-vancomycin-options/

3. SPS (October 2021) *Choosing between oral Fidaxomicin options* Available at: https://www.sps.nhs.uk/articles/choosing-between-oral-fidaxomicin-options/

4. Department of Health (March 2012) *Clostridium difficile: updated guidance on diagnosis and reporting.* https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/215135/dh_133016.pdf

5. Department of Health / Health Protection Agency (December 2008) *Clostridium difficile : how to deal with the problem* 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

6. Nottinghamshire Area Prescribing committee (August 2021) *GASTRO-INTESTINAL TRACT INFECTIONS : Clostridioides difficile* Available at : https://www.nottsapc.nhs.uk/media/1379/25-clostridium-difficle-iv-kr.pdf