








## ***Clostridioides (formerly Clostridium) difficile* infection (CDI) in adults**

Healthcare workers should use the “**SIGHT**” mnemonic when managing suspected potentially infectious diarrhoea. Use the **Bristol Stool Chart** to monitor frequency and severity of diarrhoea.

<b>S</b>	<b>Suspect</b> that the diarrhoea may have an infective cause where there is no clear alternative cause for diarrhoea (drugs eg laxatives, underlying bowel disease) – if you suspect CDI on clinical grounds, start treatment for CDI empirically pending test results and then review that treatment when the results become available
<b>I</b>	<b>Isolate</b> the patient immediately - consult the bed managers or infection control team (ICT), if necessary, particularly if no isolation facilities available
<b>G</b>	<b>Gloves</b> and aprons must be used for all contacts with the patient and their environment (in the patient “zone”)
<b>H</b>	<b>Hand washing</b> with soap and water should be carried out before and after each contact with the patient and the patient’s environment
<b>T</b>	<b>Test</b> the stool for evidence of toxigenic <i>Clostridioides difficile</i> , by sending a specimen immediately

The Bristol Stool Form Scale (Bristol Stool Chart)

Type 1		Separate hard lumps, like nuts (hard to pass)
Type 2		Sausage-shaped but lumpy
Type 3		Like a sausage but with cracks on its surface
Type 4		Like a sausage or snake, smooth and soft
Type 5		Soft blobs with clear-cut edges (passed easily)
Type 6		Fluffy pieces, a mushy stool
Type 7		Watery, no solid pieces ENTIRELY LIQUID

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**Table 1. Initial assessment / management including empirical CDI treatment pending confirmation**

**If CDI is suspected, send a stool (faeces) specimen to microbiology and start empirical CDI antibiotic treatment with VANCOMYCIN 125mg po qds immediately (see appendix 2). If concern of life-threatening infection/fulminant infection add METRONIDAZOLE 500mg iv tds.**

### **Assess clinical severity of CDI when laboratory confirmed (use “stickers”) and then daily**

**Mild CDI:** not associated with a raised White Cell Count (WCC) ; typically associated with less than 3 stools of types 6–7 per day

**Moderate CDI:** associated with a raised WCC (but less than  $15 \times 10^9/L$ ); typically with 3–5 stools of types 6–7 per day

**Severe CDI** if any of the following:

- WCC count greater than  $15 \times 10^9/L$
- Acutely rising blood creatinine (e.g. greater than 50% increase above baseline)
- Temperature higher than  $38.5^\circ C$
- Evidence of severe colitis (abdominal signs, radiology)

**Life-threatening / fulminant CDI** includes hypotension, ileus, toxic megacolon or CT evidence of severe disease. **Note: If the patient has ileus diarrhoea may be absent in life-threatening / fulminant CDI**

**Discuss with consultant medical microbiologist and request early gastroenterology and/or surgical and/or critical care review in severe / life-threatening / fulminant CDI**

Fluid & electrolyte replacement and nutrition review as necessary

Isolate patient in a single room if not already isolated

Review the need to continue any other antibiotics or other diarrhoea causing drugs if possible

Avoid anti-motility medicines (e.g. loperamide)

Review the need to continue with Proton pump inhibitors (PPIs) unless required acutely

**Table 2. Specific antibiotic therapy for laboratory confirmed CDI i.e. detection of toxigenic *C. difficile* in stool or histopathological evidence of CDI.**

Note: If *C.difficile* toxin is not detected but the sample is positive for *C.difficile* toxin gene then results may reflect either carriage or genuine CDI. Assess patient to decide whether carriage or clinical CDI, initiate treatment only if assessed as clinical CDI.

Review CDI therapy if initial test result is negative, if symptoms continue despite a negative result, and suspicion of CDI remains, repeat stool testing after 5 days. Repeat CDI testing during therapy or as “test of cure” or within 28 days of laboratory confirmed CDI is not recommended.

### **First episode of CDI : Mild, Moderate or Severe infection**

**First-line : VANCOMYCIN 125mg po (or via NG tube) qds for 10 days see (appendix 2)**

DAILY REVIEW ESSENTIAL

If increasing severity of CDI **OR** no response to therapy within 7 days **OR** based on clinical judgement, switch to:

**Second-line : FIDAXOMICIN 200mg po bd for 10 days (see appendix 2 for NG administration)**

If increasing severity of CDI **OR** no response to therapy within 7 days **OR** based on clinical judgement, switch to:

- Discuss with consultant medical microbiologist (See appendix 1)
- Obtain surgical / gastroenterology / critical care review as appropriate

### **First episode of CDI : Life-threatening / Fulminant infection**

**VANCOMYCIN 500mg po qds (or via NG tube qds) (see appendix 2) PLUS METRONIDAZOLE 500mg iv tds for 10 days**

DAILY REVIEW ESSENTIAL

- Discuss with consultant medical microbiologist and gastroenterologist (See appendix 1)
- Obtain surgical / gastroenterology / critical care review as appropriate
- Note that therapeutic drug monitoring of Vancomycin is required with this dose of oral Vancomycin. Pre-dose (trough) Vancomycin levels should be maintained below 20mg/L. Please refer to [the TDM requirements for oral Vancomycin used for the treatment of CDI in adults](#)

### **Further episodes of CDI within 12 weeks after symptom resolution (relapse) : Mild, Moderate or Severe infection**

**FIDAXOMICIN 200mg po bd for 10 days (see appendix 2 for NG administration)**

DAILY REVIEW ESSENTIAL

If increasing severity of CDI **OR** no response to therapy within 7 days **OR** based on clinical judgement, switch to:

- Discuss with consultant medical microbiologist and gastroenterologist (See appendix 1)

### **Further episodes of CDI within 12 weeks after symptom resolution (relapse) : Life-threatening / Fulminant infection**

**Manage as Life-threatening / Fulminant infection above, but continue antibiotics for 14 days.**

### **Further episodes of CDI more than 12 weeks after symptom resolution (recurrence) : Mild, Moderate infection**

**VANCOMYCIN 125mg po (or via NG tube qds for 10 days (see appendix 2)**

DAILY REVIEW ESSENTIAL

If increasing severity of CDI **OR** no response to therapy within 7 days **OR** based on clinical judgement, switch to:

- Discuss with consultant medical microbiologist and gastroenterologist (See appendix 1)
- **Obtain gastroenterology review for all cases of recurrent CDI.**

### **Further episodes of CDI more than 12 weeks after symptom resolution (recurrence) : Severe infection**

**FIDAXOMICIN 200mg po bd for 10 days (see appendix 2 for NG administration)**

DAILY REVIEW ESSENTIAL

If increasing severity of CDI **OR** no response to therapy within 7 days **OR** based on clinical judgement, switch to:

- Discuss with consultant medical microbiologist and gastroenterologist (See appendix 1)
- **Obtain gastroenterology review for all cases of recurrent CDI.**

### **Further episodes of CDI more than 12 weeks after symptom resolution (recurrence): Life-threatening / Fulminant infection**

**Manage as Life-threatening / Fulminant infection above, but continue antibiotics for 14 days.**

## **Appendix 1**

### **Potential additional / alternative therapy options**

Following discussion with consultant medical microbiologist or gastroenterologist, these include:

- **Vancomycin po / NG up to 500mg qds.** If 500mg qds used then perform Vancomycin therapeutic drug monitoring (TDM) as in [high dose oral Vancomycin policy for CDI](#). Pre-dose (trough) Vancomycin levels should be maintained below 20mg/L. Note that lower doses of oral / NG Vancomycin do not require TDM.
- **A 6 week tapering po Vancomycin regime** (125 mg qds for one week, 125 mg tds for one week, 125 mg bd for one week, 125 mg od for one week, 125 mg on alternate days for one week, 125 mg every third day for one week)
- **Pulsed Fidaxomicin, 200mg po bd days 1 to 5 then 200mg once every 2 days** from day 7 to day 25
- In life-threatening / fulminant CDI, **intracolonic Vancomycin (500 mg** in 100–500 ml saline 4–12-hourly, given as retention enema: 18 gauge Foley catheter with 30 ml balloon inserted per rectum; vancomycin instilled; catheter clamped for 60 minutes; deflate and remove). If used then perform Vancomycin therapeutic drug monitoring (TDM) as in Vancomycin policy: [https://www.gloshospitals.nhs.uk/media/documents/Vancomycin\\_policy\\_adults\\_.pdf](https://www.gloshospitals.nhs.uk/media/documents/Vancomycin_policy_adults_.pdf)

Patients may be considered for **Faecal Microbiota Transplant (FMT)**, local protocol available at: [https://www.gloshospitals.nhs.uk/media/documents/A0321\\_CDI7.pdf](https://www.gloshospitals.nhs.uk/media/documents/A0321_CDI7.pdf). FMT should be strongly considered in recurrent CDI (three or more separate episodes of laboratory confirmed CDI).

### Other indications for FMT

Other conditions where FMT can be considered include:

- Severe CDI. As outlined in recent National guidelines (Mullish et al., Gut, 2018) and a recent European Consensus position paper on FMT (Cammarota et al., 2017).
- Refractory CDI. Patients who have received a course of vancomycin and have not had clinical resolution of diarrhoea. Although not NICE approved FMT can be considered for use in patients with refractory CDI as outlined in recent National guidelines (Mullish et al., Gut, 2018) and a recent European Consensus position paper on FMT (Cammarota et al., 2017)
- CDI cure rate from a single FMT treatment approaches 80% and exceeds 90% with a second treatment (Quraishi et al. AP&T, 2017). Patients in whom a single infusion is unsuccessful in resolving symptoms of CDI or have a relapse in symptoms within 7 days should be considered for a second infusion. Consideration of a second infusion would require a new application to be made with the relevant clinical details and outcomes.

FMT for these conditions patients must be referred, reviewed and agreed by Gastroenterology.

The use of FMT for the management of diverse pathologies is currently the subject of numerous clinical trials, most particularly in IBD. Under the conditions of a “specials licence” it is possible for clinicians to request FMT for patients with conditions other than CDI, where the clinician considers the use of FMT to be justified and appropriate for the individual patient. These requests will be considered on a case-by-case basis by the UoBMTC Clinical Team. In the case of FMT for the treatment of ulcerative colitis this would most likely require treatment at our facility in Birmingham according to our published trial protocol. Payment for this treatment would be discussed on a case by case basis

### Requesting FMT

For CDI requests meeting the NICE indications (patients who have suffered from  $\geq 3$  episodes of CDI and failed to respond to standard antibiotic treatment) or have refractory CDI FMT requests for patient treatment should be ALL agreed by **the Infection Prevention and Control Team, a Consultant Gastroenterologist and Consultant Microbiologist**; and Consultant Gastroenterologist can be a requestor for FMT on the FMT request form (FMTDON-009; see appendix) and order form (FMT-DON-010; see appendix),

A request for FMT is submitted by email, using the FMT request form (FMTDON-009) (see appendix) sent together with order form (FMT-DON-010- see appendix), to the University of Birmingham Microbiome Treatment centre (UoBMTC) via [bhs-tr.FMT@nhs.net](mailto:bhs-tr.FMT@nhs.net).

For all other requests outside of the NICE indications, an agreement to treat the patient should be confirmed after a clinical discussion with one of the UoBMTC clinical consultants regarding appropriateness of FMT. Once agreed the request for patient treatment should be submitted by email, using the FMT request form, to the UoBMTC via [bhs-tr.FMT@nhs.net](mailto:bhs-tr.FMT@nhs.net)

On receipt of completed request and order form accepting the UoB Terms and Conditions for supply, the UoBMTC clinical team will assess information on request form against approved indications for FMT

If the FMT request is ratified by the UoBMTC a delivery date and time will be discussed with the requesting clinician. In the case of ground for rejection of the request the requesting clinician will be contacted by email to explain why the proposed FMT treatment is inappropriate or to obtain further clinical information.

The address for delivery of FMT for Gloucester Royal Hospital is Pathology Reception, Great Western Road, Gloucester, Gloucestershire, GL1 3NN.

The address for delivery of FMT for Cheltenham General Hospital is Pathology Department, Sandford Road, Cheltenham, Gloucestershire, GL53-7AN

FMT will be supplied at room temperature, will be ready to use 3 hours following dispatch from UoBMTC and should be used no more than 9 hours from dispatch as described on the accompanying validation certificate. FMT cannot be given out of hours as there is no service provision during this time.

Questions relating to transport/delivery can be sent to UoBMTC Email: [bhs-tr.FMT@nhs.net](mailto:bhs-tr.FMT@nhs.net) or call 0121 414 4547

### **FMT Follow up**

As stipulated in the UoBMTC terms and conditions follow up data on patient clinical outcomes is required at 7 days post FMT (or upon patient discharge, whichever is earliest) and post 90 days after FMT administration.

The 7 days post FMT follow up form is accessed on: <http://tiny.cc/Uobmtc>

The 90 days follow up form can be found on: [https://www.gloshospitals.nhs.uk/media/documents/FMT-DON-013\\_FMT\\_Clinical\\_90\\_days\\_follow\\_up\\_form\\_v2.0.pdf](https://www.gloshospitals.nhs.uk/media/documents/FMT-DON-013_FMT_Clinical_90_days_follow_up_form_v2.0.pdf). It should be sent via email to [bhs-tr.FMT@nhs.net](mailto:bhs-tr.FMT@nhs.net) once completed.

All patients will continue to be monitored internally by the Trust for 12 months.

### **Appendix 2**

#### **Oral and NG administration of vancomycin**

Vancomycin 500mg injection can be used orally/enterally - some brands are licensed for this use - (Wockhardt, Flynn and Bowmed Ibisqus)

Reconstitute 500mg vial with 10mls of water for injection. At the time of administration each dose can be further diluted to 30ml if desired to aid administration (some brands allow flavouring syrups to be added - Wockhardt and Flynn). Keep reconstituted vial in fridge for maximum 24hrs for subsequent doses.

#### **NG administration of fidaxomicin**

Cut the tablet in half, crush well and disperse in water to administer via enteral tubes.

There is limited information available regarding this.

Note: Link to full IPC guidance: [http://ghtsp07.glos.nhs.uk/sites/gnhhsft\\_policy\\_library/WPP/A0321.aspx](http://ghtsp07.glos.nhs.uk/sites/gnhhsft_policy_library/WPP/A0321.aspx)