

**Amber with Guidance (Amber-G)** = To be recommended or initiated by a specialist\* with follow up prescribing and monitoring by primary care clinicians.

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## **Fidaxomicin for the treatment of *Clostridioides difficile* infections (CDI) in adults aged 18 and over.**

The details of side-effects, cautions, contraindications and interactions are not a complete list and the current BNF (<https://www.medicinescomplete.com/#/>) and the SPC (<https://www.medicines.org.uk/emc/>) remain authoritative.

<b>Background Information</b> <sup>1,2,3</sup>	<p>Fidaxomicin should be initiated in line with the NICE guidance NG199: <a href="https://www.nice.org.uk/guidance/ng199">Clostridioides difficile infection: antimicrobial prescribing (nice.org.uk)</a></p> <p>Fidaxomicin is a topically acting macrocyclic antibacterial that cannot be used to treat systemic infections, as it is poorly absorbed from the gastro-intestinal tract.</p>
<b>BNF therapeutic class</b>	<p>5.1.5 Antibacterial drugs; macrolide antibacterial</p>
<b>Indication</b> <sup>1</sup>	<p>Licensed for treatment of <i>Clostridioides difficile</i> infections (CDI) also known as <i>C. difficile</i>-associated diarrhoea (CDAD) in adults aged 18 years and over.</p> <p>In line with NICE guidance NG199, when treating adults aged 18 years and over:</p> <ul style="list-style-type: none"> <li>• Fidaxomicin can be used as a second-line antibiotic for a first episode of mild, moderate or severe <i>C. difficile</i> infection if vancomycin is ineffective</li> <li>• Fidaxomicin can be used for a further episode of <i>C. difficile</i> infection within 12 weeks of symptom resolution (relapse)</li> <li>• Fidaxomicin can be used as one of two options for a further episode of <i>C. difficile</i> infection more than 12 weeks after symptom resolution (recurrence).</li> </ul> <p>Refer to Table 1 in the NICE guidance for further information (link above).</p> <p>(Treatment of paediatric patients with Fidaxomicin is outside the scope of this guidance)</p>
<b>Dosage and administration</b> <sup>1,4</sup>	<p><b><u>Fidaxomicin 200 mg tablets:</u></b></p> <p><u>Adults</u>          The recommended dose is 200 mg (one tablet) administered twice daily (once every 12 hours) for 10 days.</p> <p>Fidaxomicin 40 mg/ml granules for oral suspension may be used in adult patients with difficulties in swallowing tablets (see below). More information on Fidaxomicin use in swallowing difficulties can be found on the <a href="#">SPS</a> website and in <a href="#">NEWT</a> guidelines.</p> <p><u>Administration</u></p> <p>The tablets should be administered whole with water. They can be taken with or without food.</p> <p><b><u>Fidaxomicin 40 mg/ml granules for oral suspension (for swallowing difficulties only):</u></b></p> <p><u>Adults</u>          The recommended dose is 200 mg (5 ml) administered twice daily (once every 12 hours) for 10 days.</p>

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	<p><u>Administration</u></p> <p>The granules for oral suspension can be taken with or without food.</p> <p>The bottle should be taken from the refrigerator 15 minutes prior to administration and approximately 10 times gently shaken.</p> <p>Once reconstituted*, the oral suspension should only be administered using the oral syringe and adaptor provided by the healthcare professional. The bottle should be stored in a refrigerator after each use.</p> <p>The reconstituted suspension is stable for 12 days in a refrigerator (2°C – 8°C).</p> <p>*NB. <u>SPC</u> states that purified water should be used for reconstitution of the granules.</p>
<p><b>Cautions and Contraindications</b> 1</p>	<p><u>Cautions:</u></p> <p>Some patients with hypersensitivity reactions reported a history of allergy to macrolides. Fidaxomicin should be used with caution in patients with a known macrolides allergy.</p> <p>Due to limited clinical data, fidaxomicin should be used with caution in patients with severe renal impairment or moderate to severe hepatic impairment.</p> <p>Due to limited clinical data, fidaxomicin should be used with caution in patients with pseudomembranous colitis, fulminant or life threatening CDI.</p> <p>Co-administration of potent P-glycoprotein inhibitors such as cyclosporine, ketoconazole, erythromycin, clarithromycin, verapamil, dronedarone and amiodarone is not recommended (see interactions below).</p> <p><u>Contra-indications:</u></p> <p>Hypersensitivity to the active substance or to any of the excipients - please see the SPC<sup>1</sup> for the list of excipients.</p>
<p><b>Pregnancy and breast feeding</b> 1</p>	<p><u>Pregnancy</u></p> <p>There are no data available from the use of fidaxomicin in pregnant women. Animal studies did not indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of fidaxomicin during pregnancy.</p> <p><u>Breast-feeding</u></p> <p>It is unknown whether fidaxomicin and its metabolites are excreted in human milk. Although no effects on the breastfed newborns/infants are anticipated since the systemic exposure to fidaxomicin is low, a risk to the newborns/infants cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from fidaxomicin therapy, taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.</p>
<p><b>Adverse Drug Reactions</b> 1</p>	<p>The most common (<math>\geq 1/100</math> to <math>&lt; 1/10</math>) adverse reactions are vomiting (1.2%), nausea (2.7%) and constipation (1.2%).</p> <p>See SPC<sup>1</sup> for full list of adverse reactions.</p> <p>Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme: <a href="http://www.mhra.gov.uk/yellowcard">www.mhra.gov.uk/yellowcard</a></p>

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<p><b>Monitoring</b></p>	<p>Patients will be reviewed by the Community IPC Team.</p> <p>If any evidence of severe disease or their symptoms or signs worsens rapidly or significantly at any time, the patient should be referred for urgent admission and consultant microbiologist review.</p> <p>Severe disease if ANY of the following regardless of stool frequency:</p> <ul style="list-style-type: none"> <li>• Temperature &gt;38.5°C</li> <li>• WCC &gt;15 X 10<sup>9</sup> /L</li> <li>• Tachycardia &gt;100 beats/min</li> <li>• rising serum creatinine (&gt;50% from baseline)</li> <li>• signs/symptoms of severe colitis (abdominal pain/distension, hypotension, ileus, radiology)</li> </ul>
<p><b>Interactions <sup>1</sup></b></p>	<p><u>P-glycoprotein inhibitors</u></p> <p>Avoid with potent P-glycoprotein inhibitors, such as cyclosporine, ketoconazole, erythromycin, clarithromycin, verapamil, dronedarone and amiodarone.</p> <p><u>P-glycoprotein substrates</u></p> <p>Fidaxomicin may be a mild to moderate inhibitor of intestinal P-gp.</p> <p>Fidaxomicin (200 mg twice daily) had a small but not clinically relevant effect on digoxin exposure. However, a larger effect on P-gp substrates with lower bioavailability more sensitive to intestinal P-gp inhibition such as dabigatran cannot be excluded.</p> <p>Please see the SPC<sup>1</sup> and BNF<sup>2</sup> for further information on interactions.</p>
<p><b>Ordering information</b></p>	<p>Fidaxomicin is licensed in the UK and is available via standard wholesalers, but it is not usually stocked in community pharmacies. If the medication is not immediately available, it can be ordered in for the next working day.</p> <p>If a supply is required more urgently than the next working day, note that Asda Pharmacy, Old Mill Lane, Barnsley, S71 1LN, Tel: 01226 704810, stocks 1 box of 20 fidaxomicin 200mg tablets.</p> <p>Opening hours Asda Pharmacy, Old Mill Lane:  Monday: 8am - 11pm  Tuesday - Friday: 7am - 11pm  Saturday: 7am - 10pm  Sunday: 10am - 4pm</p>

## Contact names and details

Contact Details	Telephone number	Email
Medicines Information (BHNFT)	01226 432857	<a href="mailto:gilliansmith2@nhs.net">gilliansmith2@nhs.net</a>
Dr J. Rao	01226 432749	<a href="mailto:j.rao@nhs.net">j.rao@nhs.net</a>
Dr Y. Pang	01226 434986	<a href="mailto:y.pang@nhs.net">y.pang@nhs.net</a>

<https://www.barnsleyhospital.nhs.uk/pathology/microbiology/>

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## **References**

1. Summary of Product Characteristics, SPC. Available at: [Home - electronic medicines compendium \(emc\)](#) Dificlir 200mg tablets and Dificlir 40mg/ml granules for oral suspension Accessed 13.09.22
2. British National Formulary, BNF, Available at: [www.medicinescomplete.com](http://www.medicinescomplete.com) Accessed 13.09.22
3. NICE Clinical Guidelines [NG199]. Clostridioides difficile infection: antimicrobial prescribing. Available at: <https://www.nice.org.uk/guidance/ng199> Accessed 13.09.22
4. Specialist Pharmacy Service, SPS, Available at: <https://www.sps.nhs.uk/articles/choosing-between-oral-fidaxomicin-options/> Accessed 13.09.22

## **Development Process**

*This guidance has been produced by Claire Pendleton (clinical pharmacy technician) and Joanne Howlett (medicines management pharmacist) following an AMBER-G classification status of Fidaxomicin by the Barnsley Area Prescribing Committee. This guideline has been subject to consultation and endorsement by the consultant microbiologists and was ratified by the Area Prescribing Committee on 14<sup>th</sup> December 2022.*