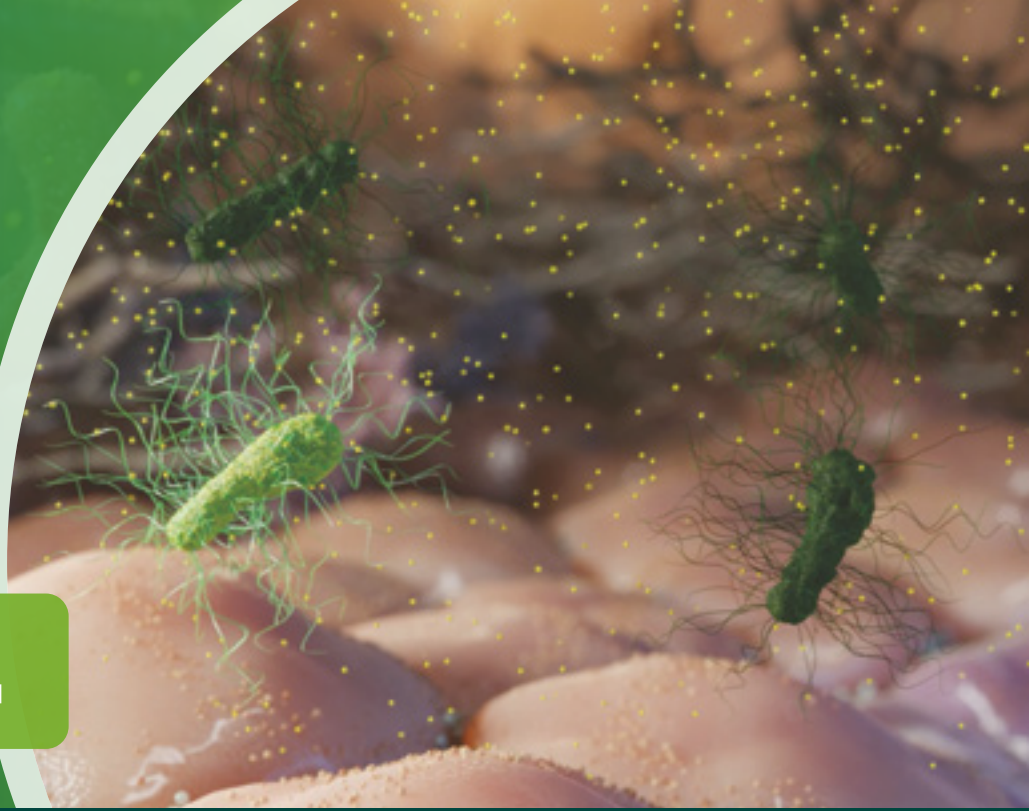
Why risk the consequences of CDI recurrence?



Take control – act early with DIFICLIR™

Prescribing information and adverse event reporting information can be found on the next page.

Indications: treatment of CDI, also known as *C. difficile*-associated diarrhoea (CDAD), in adults and paediatric patients with a bodyweight of at least 12.5 kg (film-coated tablets), in adults and paediatric patients from birth to <18 years of age (granules for oral suspension). Consideration should be given to official guidelines on the appropriate use of antibacterial agents.[1,2]

CDI, *C. difficile* infection.

1. DIFICLIR™ 200 mg film-coated tablets SmPC.
2. DIFICLIR™ 40 mg/ml granules for oral suspension SmPC.

This leaflet has been created by Tillotts Pharma.

DIFICLIR™
fidaxomicin

ZERIA GROUP
TILLOTTS PHARMA

DIFICLIR™ prescribing information

DIFICLIR 200 mg film-coated tablets
Capsule-shaped tablets, white to off-white, debossed with "FDX" on one side and "200" on the other, each containing 200mg fidaxomicin.
DIFICLIR 40 mg/ml granules for oral suspension
Granules for oral suspension. White to yellowish white granules.
INDICATIONS: Treatment of *Clostridioides difficile* infections (CDI) also known as *C. difficile*-associated diarrhoea (CDAD). Tablets: in adult and paediatric patients with a body weight of at least 12.5 kg. Granules: in adults and paediatric patients from birth to < 18 years of age.
DOSAGE AND ADMINISTRATION:
Oral use.
Tablets: Adults and elderly standard dosing: 200 mg (one tablet) administered once every 12 hours for 10 days. DIFICLIR 40 mg/ml granules for oral suspension may be used in adult patients with difficulties in swallowing tablets. **Extended-pulsed dosing:** Fidaxomicin 200 mg tablets administered twice daily for days 1-5 (no intake of a tablet on day 6) then once daily on alternate days for days 7-25.
Children weighing at least 12.5 kg: 200 mg administered once every 12 hours for 10 days using the film-coated tablets or the granules for oral suspension. Reduced doses are recommended for patients with a body weight of less than 12.5 kg, see granules below. Tablets should be swallowed whole with water.
Granules: Adults and elderly standard dosing: 200 mg (5 ml) administered once every 12 hours for 10 days. **Extended-pulsed dosing**: Fidaxomicin 40 mg/ml granules for oral suspension (5 ml) administered twice daily for days 1-5 (no intake of suspension on day 6) then once daily on alternate days for days 7-25.
Children 12.5kg or over: 200 mg (5 ml oral suspension) once every 12 hours for 10 days.

Dose by bodyweight:

Table 1: Dosing instruction for the oral suspension Weight band of patient	Mg per dose (every 12 hours)	Volume of fidaxomicin oral suspension (every 12 hours)
< 4.0 kg	40 mg	1 ml
4.0 - < 7.0 kg	80 mg	2 ml
7.0 - < 9.0 kg	120 mg	3 ml
9.0 - < 12.5 kg	160 mg	4 ml
≥ 12.5 kg	200 mg	5 ml

For oral use (ingestion or via an enteral feeding tube using a syringe), with or without food. Caution in patients with severe renal impairment, moderate to severe hepatic impairment.
Reconstitution must be done by a healthcare professional. For instructions see Section 6.6 of the Summary of Product Characteristics. Oral suspension to be taken from the refrigerator 15 minutes prior to administration, shaken, and administered using the oral syringe and adaptor provided by the healthcare professional. Refrigerate after each use. Once reconstituted, use within 27 days.
Tablets and granules: If a dose is forgotten, take the missed dose as soon as possible, or if nearly time for the next dose, skip the missed dose.
CONTRAINDICATIONS: Hypersensitivity to the active substance or any excipients.
SPECIAL WARNINGS AND PRECAUTIONS: Reported: Hypersensitivity reactions including severe angioedema, discontinue immediately. Caution: in patients with a known macrolides allergy, patients with severe renal impairment or moderate to severe hepatic impairment, patients with pseudomembranous colitis, fulminant or life- threatening CDI, patients below 6 months of age. Not recommended/caution advised: Co-administration of potent P-glycoprotein inhibitors such as cyclosporine, ketoconazole, erythromycin, clarithromycin, verapamil, dronedarone and amiodarone is not recommended.
Testing for *C. difficile* colonization or toxin is not recommended in children younger than 1 year due to high rates of asymptomatic colonisation unless severe diarrhoea is present in infants with risk factors for stasis such as Hirschsprung disease, operated anal atresia or other severe motility disorders. Alternative aetiologies should always be sought and *C. difficile* enterocolitis be proven.
Granules: contains less than 1 mmol sodium (23 mg) per 5 ml suspension: essentially 'sodium-free'. Contains 2.5 mg sodium benzoate (E 211) in each ml oral suspension. May increase jaundice in babies up to 4 weeks old.
INTERACTIONS: Potent inhibitors of P-gp, such as cyclosporine, ketoconazole, erythromycin, clarithromycin, verapamil, dronedarone and amiodarone may increase Cmax and AUC of fidaxomicin. Fidaxomicin is a mild to moderate inhibitor of intestinal P-gp; e.g. digoxin, dabigatran etexilat. Paediatric population: no interaction data.
USE DURING PREGNANCY AND LACTATION: Pregnancy: no data available, not recommended. Breast-feeding: no data available, risk to the infant cannot be excluded. Discontinue breast-feeding or discontinue/abstain from fidaxomicin therapy. Animal data showed no effect on fertility.
UNDESIRABLE EFFECTS:
Common: vomiting (1.2%), nausea (2.7%) and constipation (1.2%). Uncommon: rash, pruritus, decreased appetite, dizziness, headache, dysgeusia, abdominal distention, flatulence, dry mouth. Frequency not known: hypersensitivity reactions (angioedema, dyspnea). Paediatric: profile as for adults, urticaria (2 cases) reported. Refer to Summary of Product Characteristics for details.
MA HOLDER: Tillotts Pharma GmbH, Warmbacher Strasse 80, DE-79618 Rheinfelden, Germany.
LEGAL CATEGORY: POM.
MARKETING AUTHORISATION NUMBER: Tablets EU/1/11/733/003-004. Granules EU/1/11/733/005.
DATE OF PREPARATION: July 2025.
FULL PRESCRIBING INFORMATION AVAILABLE ON REQUEST FROM THE MARKETING AUTHORISATION HOLDER OR FROM TILLOTTS PHARMA LIMITED, SPACES, 1ST FLOOR BUILDING 2, THE GREEN, DUBLIN AIRPORT CENTRAL, DUBLIN AIRPORT, SWORDS, COUNTY DUBLIN, K67 E2H3, TEL: (00 353 1) 294 2015. Dificlir® is a trademark.

Adverse events should be reported.
Reporting forms and information can be found at HPRA Pharmacovigilance at www.hpra.ie - Adverse events should also be reported to Tillotts Pharma Ireland Ltd. Tel: +353 1 2942015

Every recurrent episode of CDI brings with it increasingly serious and costly complications[1–6]

For patients...

- Hospitalisations become frequent[1]
- Length of hospital stay is prolonged[1,4]
- Quality of life decreases[5]
- Risk of death increases[2,6]
- Other treatments or operations may be postponed[7]

For you...

- Pressure on resources intensifies[1,4,6]
- Burden on bed capacity escalates[1,4]
- Costs of management increase[1,2,4]
- Contamination control measures need to be implemented[7]
- Patient transfers may be interrupted[7]

What are the biggest risk factors for recurrence?

Age >65 years plus ≥1 of the following:[8]

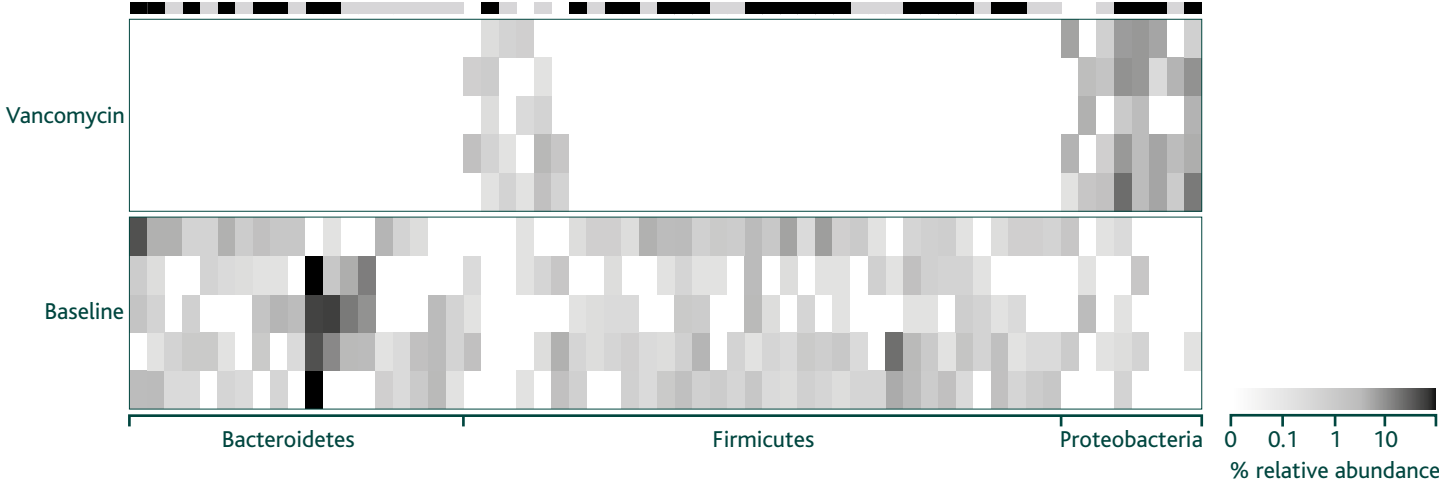
- Healthcare-associated CDI
- Prior hospitalisation in the last 3 months
- Use of concomitant non-CDI antibiotic after the diagnosis of CDI
- PPI started during/after CDI diagnosis
- Prior CDI episode

CDI, *C. difficile* infection; PPI, proton pump inhibitor.

1. Feuerstadt P *et al.* J Med Econ 2020;23:603–609. **2.** Feuerstadt P *et al.* SAGE Open Med 2021;9:1–8. **3.** Whitney L *et al.* Antibiotics 2023;12:106. **4.** Wilcox MH *et al.* J Antimicrob Chemother 2017;72:2647–2656. **5.** Lurienne L *et al.* J Patient Rep Outcomes 2020;4:14. **6.** Enoch DA *et al.* J Hosp Infect 2020;106:793–803. **7.** National Clinical Guidelines on the Surveillance, Diagnosis and Management of *C. difficile* Infection in Ireland. June 2014. www.hpsc.ie/a-z/microbiologyantimicrobialresistance/clostridioidesdifficile/guidelines/File,13950,en.pdf (accessed August 2025). **8.** HSE. Antibiotic Prescribing. Clostridioides difficile infection. www.hse.ie/eng/services/list/2/gp/antibiotic-prescribing/conditions-and-treatments/gastro/clostridium-difficile/clostridium-difficile.html (accessed August 2025).

The impact of vancomycin on the microbiome could put patients at risk of recurrent CDI[1]

With vancomycin treatment, the abundance of most intestinal bacterial taxa is altered[1]



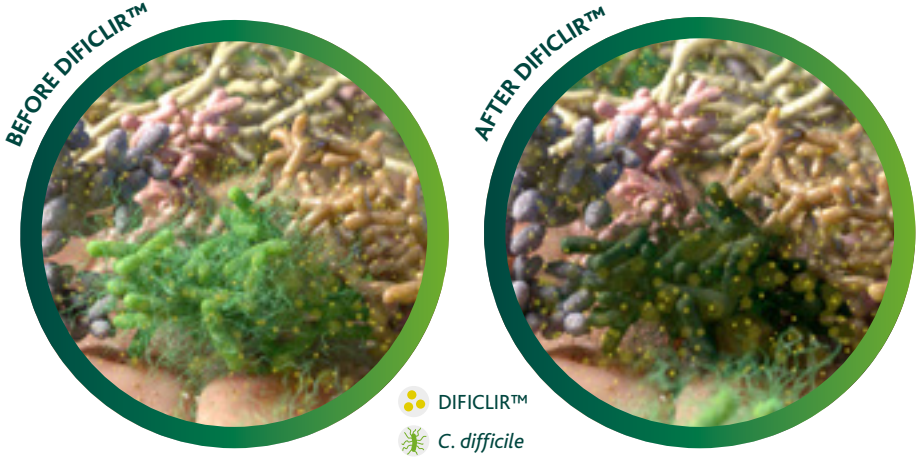
The short- and long-term effects of vancomycin on the human intestinal microbiota was investigated through high-throughput sequencing up to 22 weeks post-antibiotic cessation. The clinical relevance of the observed microbiota perturbations was studied in mice. The heatmap represents the relative abundance (%) of OTUs present in ≥50% of patients at baseline or after vancomycin treatment, showing a depletion of all prevalent bacteroidete OTUs and most firmicute OTUs. Black squares indicate significant changes ($p<0.05$, FDR<0.1); grey squares indicate close to significant changes ($p<0.073$, FDR<0.1); two-tailed Wilcoxon test. N=5.[1]

CDI, *C. difficile* infection; FDR, false discovery rate; OTU, operational taxonomic unit.

1. Isaac S *et al*. J Antimicrob Chemother 2017;72:128–136.

Minimise the risk, and consequences, of CDI recurrence with DIFICLIR™

DIFICLIR™ kills *C. difficile* without disrupting the natural microbiome, which may help protect against recurrence[1–3]



By inhibiting RNA polymerase, DIFICLIR™ reduces both the vegetative and spore forms of *C.difficile* during and after treatment to prevent its growth and survival[1,2]

Take control – act early with DIFICLIR™

- HSE recommends DIFICLIR™ as a first-line option for patients with:[4]
  - Non-severe CDI at high risk of recurrence
  - Severe CDI
  - First recurrence of CDI
- ESCMID recommends DIFICLIR™ first line for a first CDI episode and second line for CDI recurrence[5]

CDI, *C. difficile* infection; ESCMID, European Society of Clinical Microbiology and Infectious Diseases; HSE, Health Service Executive; RNA, ribonucleic acid.

1. Louie TJ *et al*. Clin Infect Dis 2012:55:S132–142. **2.** DIFICLIR™ 200 mg film-coated tablets SmPC. **3.** Cao X *et al*. Nature 2022;604:541–545. **4.** HSE. Antibiotic Prescribing. Clostridioides difficile infection. www.hse.ie/eng/services/list/2/gp/antibiotic-prescribing/conditions-and-treatments/gastro/clostridium-difficile/clostridium-difficile.html (accessed August 2025). **5.** van Prehn J *et al*. Clin Microbiol Infect 2021;27:S1–S21.

Minimise the risk of CDI recurrence with DIFICLIR™ vs vancomycin[1–8]

DIFICLIR™

Narrow spectrum activity **selectively kills *C. difficile*** without disrupting the natural microbiome[2–4]

Potent inhibition of *C. difficile* sporulation in an *in vitro* study[5]

Significantly **fewer hospitalised patients with *C. difficile*-contaminated room surfaces** (36.8%; 25/68)[6*]...

Significantly **lower CDI recurrence rates** after 30 days in 2 double-blind, randomised, parallel group studies of 15.4% (39/253)[7] and 12.7% (28/221)[8†]...

Non-inferior clinical cure rates in 2 double-blind, randomised, parallel group studies of 88.2% (253/287)[7] and 87.7% (221/252)[8†]...

Significantly **higher sustained response rates** (clinical cure without recurrence) in 2 double-blind, randomised, parallel group studies of 74.6% (214/287)[7] and 76.6% (193/252)[8†]...

Similar safety profiles in 2 double-blind, randomised, parallel group studies[7,8†]

*Surfaces in the rooms of 66 hospitalised patients treated with vancomycin and/or metronidazole, and 68 hospitalised patients treated with DIFICLIR™, were sampled and analysed via enzyme immunoassay and polymerase chain reaction.[6]

†Multicentre, double-blind, randomised phase 3 trials evaluating the efficacy and safety of DIFICLIR™ and vancomycin to treat patients with CDI across Europe, Canada and the USA. A total of 629 and 535 patients were randomised 1:1 to receive oral DIFICLIR™ (200 mg twice daily) or oral vancomycin (125 mg four times daily) for 10 days.[7,8]

The most common adverse reactions with DIFICLIR™ are vomiting, nausea and constipation.[3]

Vancomycin

Broad spectrum activity **induces drastic changes in the microbiome**[1]

No inhibition of *C. difficile* sporulation in the *in vitro* study[5]

...vs **more patients with contaminated rooms** (57.6%; 38/66) when treated with vancomycin and/or metronidazole (p=0.02)[6]*

...vs **higher CDI recurrence rates** of 25.3% (67/265; p=0.005)[7] and 26.9% (60/223; p=0.0002),[8†] respectively (secondary endpoints)

...vs **similar clinical cure rates** of 85.8% (265/309)[7] and 86.8% (223/257),[8†] respectively (mITT populations; primary endpoints)

...vs **lower sustained response rates** of 64.1% (198/309; p=0.006)[7] and 63.4% (163/257; p=0.001),[8†] respectively (mITT populations; secondary endpoints)

Similar safety profiles in 2 double-blind, randomised, parallel group studies[7,8†]

CDI, *C. difficile* infection; mITT, modified intention-to-treat; USA, United States of America.

1. Isaac S *et al.* J Antimicrob Chemother 2017;72:128–136.
2. Louie TJ *et al.* Clin Infect Dis 2012:55:S132–142.
3. DIFICLIR™ 200 mg film-coated tablets SmPC.
4. Cao X *et al.* Nature 2022;604:541–545.
5. Babakhani F *et al.* Clin Infec Dis 2012;55:S162–169. **6.** Biswas JS *et al.* J Hosp Infect 2015;90:267–270.
7. Louie TJ *et al.* N Engl J Med 2011;364:422–431.
8. Cornely OA *et al.* Lancet Infect Dis 2012;12:281–289.

Target CDI with conviction – act early with DIFICLIR™

Compared to vancomycin, DIFICLIR™ has demonstrated:

Non-inferior clinical cure rates[1,2]

Greater reductions in CDI recurrence rates[1,2]

Higher sustained response rates[1,2]

Similar safety profiles[1,2]

Selective killing of *C. difficile* while preserving the natural microbiome[3–6]

Reduced environmental contamination[7]*

Contact your local Tillotts representative to find out more

*Vs vancomycin and/or metronidazole.

CDI, *C. difficile* infection.

1. Louie TJ *et al.* N Engl J Med 2011;364:422–431. **2.** Cornely OA *et al.* Lancet Infect Dis 2012;12:281–289. **3.** Isaac S *et al.* J Antimicrob Chemother 2017;72:128–136. **4.** Louie TJ *et al.* Clin Infect Dis 2012:55:S132–142. **5.** DIFICLIR™ 200 mg film-coated tablets SmPC. **6.** Cao X *et al.* Nature 2022;604:541–545. **7.** Biswas JS *et al.* J Hosp Infect 2015;90:267–270.

PM-DIF200-IE-00010 | AUGUST 2025