EXCERPTS FROM:

2021 IDSA/SHEA Clinical Practice Guidelines suggest DIFICID as preferred for INITIAL CDI episode rather than vancomycin[1]

DIFICID® (fidaxomicin)
tablets 200 mg
oral suspension 200 mg/5 ml

Recommendations for the Treatment of *Clostridioides difficile* Infection (CDI) in Adults[1,*]

INITIAL CDI episode	
Recommended and Alternative Treatments	**Strength of Recommendation/Certainty of Evidence[a]**
Preferred: Fidaxomicin[b]	Conditional/Moderate
Alternative: Vancomycin	
Alternative for non-severe CDI[c], if above agents are unavailable: *Metronidazole*	

FIRST RECURRENT CDI episode	
Recommended and Alternative Treatments	**Strength of Recommendation/Certainty of Evidence[a]**
Preferred: Fidaxomicin	Conditional/Low
Alternative: Vancomycin	

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[a] For IDSA definitions on strength of recommendation and certainty of evidence, please refer to 2021 IDSA/SHEA Clinical Practice Guidelines update.

[b] Implementation depends upon available resources.

[c] Definition of non-severe CDI is supported by the following laboratory parameters: White blood cell count of ≤15,000 cells/μL and a serum creatinine level <1.5 mg/dL

For detailed information, including recommended dosing regimens and recommendations for treatment of second/subsequent CDI recurrence and fulminant CDI, please refer to the full 2021 IDSA/SHEA Clinical Practice Guidelines.

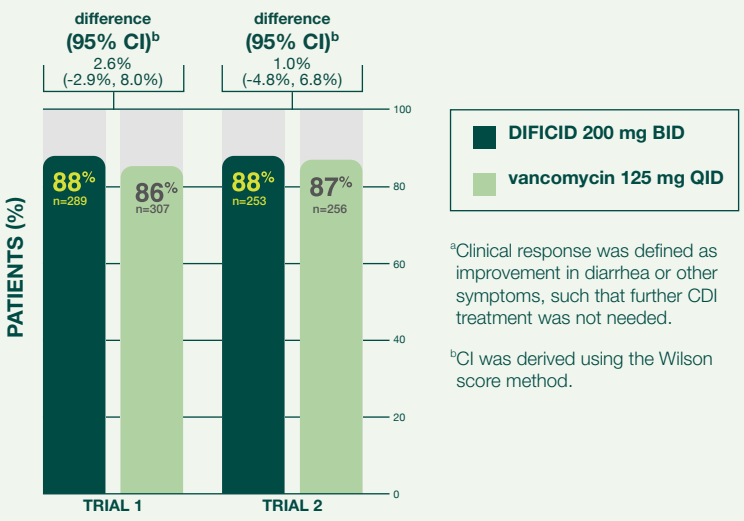
Indication

DIFICID is a macrolide antibacterial drug indicated in adult and pediatric patients 6 months of age and older for treatment of *Clostridioides difficile*-associated diarrhea (CDAD).

To reduce the development of drug-resistant bacteria and maintain the effectiveness of DIFICID and other antibacterial drugs, DIFICID should be used only to treat infections that are proven or strongly suspected to be caused by *C. difficile.*

DIFICID: Comparable initial clinical response rate[a] vs vancomycin at end of 10-day treatment

Clinical response rate (primary end point)[a]



[a] Clinical response was defined as improvement in diarrhea or other symptoms, such that further CDI treatment was not needed.

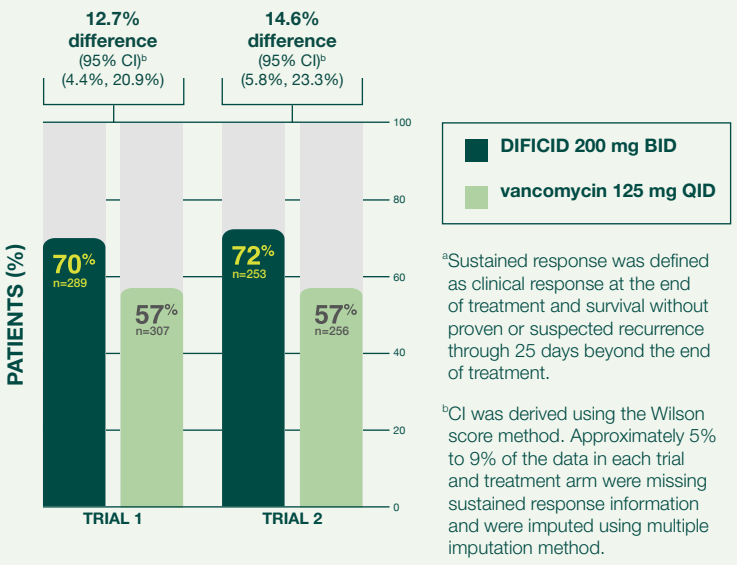
[b] CI was derived using the Wilson score method.

Study description: Two Phase 3, randomized, double-blind, noninferiority studies (N=1,105) comparing the efficacy and safety of oral DIFICID 200 mg BID vs oral vancomycin 125 mg QID for 10 days in the treatment of adults (aged ≥18 years) with CDI (defined as >3 unformed bowel movements or >200 mL of unformed stool for subjects having rectal collection devices in the 24 hours before randomization and presence of either *C. difficile* toxin A or B in the stool within 48 hours of randomization).

- The primary end point was clinical response rate at the end of 10-day treatment.
- An additional efficacy end point was a sustained response 25 days after the end of treatment. Sustained response was evaluated only for patients who were clinical successes at the end of treatment.

DIFICID: Superior sustained response rate[a] vs vancomycin through 25 days after end of treatment

Sustained response rate (additional efficacy endpoint)[a]



[a] Sustained response was defined as clinical response at the end of treatment and survival without proven or suspected recurrence through 25 days beyond the end of treatment.

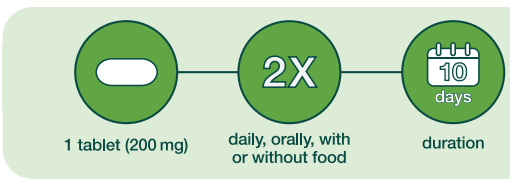
[b] CI was derived using the Wilson score method. Approximately 5% to 9% of the data in each trial and treatment arm were missing sustained response information and were imputed using multiple imputation method.

- Since clinical success at the end of treatment and mortality rates were similar across treatment arms (approximately 6% in each group), differences in sustained response were due to lower rates of proven or suspected CDI during the follow-up period in DIFICID patients.

Efficacy in BI isolates

- In patients infected with a BI isolate, similar rates of clinical response at the end of treatment and during the follow-up period were seen in fidaxomicin-treated and vancomycin-treated patients. However, DIFICID did not demonstrate superiority in sustained response when compared with vancomycin in these patients.

DIFICID: Dosing in adults



Before prescribing DIFICID, please read the accompanying Prescribing Information. The Patient Information also is available.

Important Safety Information

- DIFICID is contraindicated in patients who have known hypersensitivity to fidaxomicin or any other ingredient in DIFICID.
- Acute hypersensitivity reactions, including dyspnea, rash, pruritus, and angioedema of the mouth, throat, and face have been reported with DIFICID. If a severe hypersensitivity reaction occurs, DIFICID should be discontinued and appropriate therapy should be instituted.
- DIFICID is not expected to be effective for the treatment of other types of infections due to minimal systemic absorption of fidaxomicin. DIFICID has not been studied for the treatment of infections other than CDAD. DIFICID should only be used for the treatment of CDAD.
- Only use DIFICID for infection proven or strongly suspected to be caused by *C. difficile*. Prescribing DIFICID in the absence of a proven or strongly suspected *C. difficile* infection is unlikely to provide benefit to the patient and increases the risk of development of drug-resistant bacteria.
- The most common adverse reactions in adults reported in clinical trials are nausea (11%), vomiting (7%), abdominal pain (6%), gastrointestinal hemorrhage (4%), anemia (2%), and neutropenia (2%).
- Among adult patients receiving DIFICID, 33 (5.9%) withdrew from trials as a result of adverse reactions. Vomiting was the primary adverse reaction leading to discontinuation of dosing (incidence of 0.5% for both DIFICID and vancomycin patients).
- The most common adverse reactions in pediatric patients treated with DIFICID are pyrexia (13.3%), abdominal pain (8.2%), vomiting (7.1%), diarrhea (7.1%), constipation (5.1%), increased aminotransferases (5.1%), and rash (5.1%).
- The safety and effectiveness of DIFICID in patients <6 months of age have not been established.
- The recommended dose of DIFICID for adults and pediatric patients weighing at least 12.5 kg and able to swallow tablets is one 200 mg tablet orally twice daily for 10 days, with or without food. The recommended weight-based dosage of the oral suspension in pediatric patients (weighing at least 4 kg) is twice daily for 10 days.
- No dose adjustment is recommended for patients ≥65 years of age.
- No dose adjustment is recommended for patients with renal impairment.
- No dosage adjustments are recommended when co-administering fidaxomicin with substrates of P-gp or CYP enzymes.
- The impact of hepatic impairment on the pharmacokinetics of fidaxomicin has not been evaluated; however, because fidaxomicin and its active metabolite (OP-1118) do not appear to undergo significant hepatic metabolism, elimination of fidaxomicin and OP-1118 is not expected to be significantly affected by hepatic impairment.

Reference:

1. Johnson S, Lavergne V, Skinner AM, et al. Clinical Practice Guideline by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA): 2021 Focused Update Guidelines on Management of *Clostridioides difficile* Infection in Adults. *Clin Infect Dis*. 2021. https://doi.org/10.1093/cid/ciab549

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