DIFICID Is Recommended in the ACG Clinical Guidelines for Treatment of *C. diff* Infection for INITIAL and FIRST RECURRENT Episodes

Excerpts from 2021 ACG clinical guidelines: Recommendations for the treatment of *Clostridioides difficile* in adults[1]

Initial CDI Episode, Nonsevere	Recommendation[a]/ Quality of Evidence[b]
Recommend oral vancomycin 125 mg 4 times daily for 10 days	Strong/Low
Recommend oral fidaxomicin 200 mg twice daily for 10 days	Strong/Moderate
Consider in low risk patients: oral metronidazole 500 mg 3 times daily for 10 days	Strong/Moderate

Initial CDI Episode, Severe[c]	Recommendation[a]/ Quality of Evidence[b]
Recommend vancomycin 125 mg 4 times a day for 10 days	Strong/Low
Recommend fidaxomicin 200 mg twice daily for 10 days	Conditional/Very Low

First Recurrence CDI Episode	Recommendation[a]/ Quality of Evidence[b]
Recommend fidaxomicin for patients experiencing a first recurrence after an initial course of vancomycin or metronidazole	Conditional/Moderate
Suggest tapering/pulsed dose vancomycin for patients experiencing a first recurrence after an initial course of fidaxomicin, vancomycin, or metronidazole	Strong/Very Low

Special Population, Immunocompromised Patients
Suggest vancomycin or fidaxomicin be used first line for treatment of CDI in patients who are immunocompromised

[a]The strength of a recommendation is graded as strong, when the evidence shows the benefit of the intervention or treatment clearly outweighs any risk, and as conditional, when uncertainty exists about the risk-benefit ratio.

[b]The quality of the evidence is graded as follows: high if further research is unlikely to change our confidence in the estimate of the effects; moderate if further research is likely to have an important impact and may change the estimate; and low if further research is very likely to change the estimate.

[c]Severe CDI (per ACG recommendations): white blood cell ≥15,000 cells/mm^3 or serum creatinine >1.5 mg/dL.

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.*

Reference:

1. Kelly CR, Fischer M, Allegretti JR, et al. ACG Clinical Guidelines: Prevention, Diagnosis, and Treatment of *Clostridioides difficile* Infections. *Am J Gastroenterol*. 2021;10.14309/ajg.0000000000001278. doi:10.14309/ajg.0000000000001278

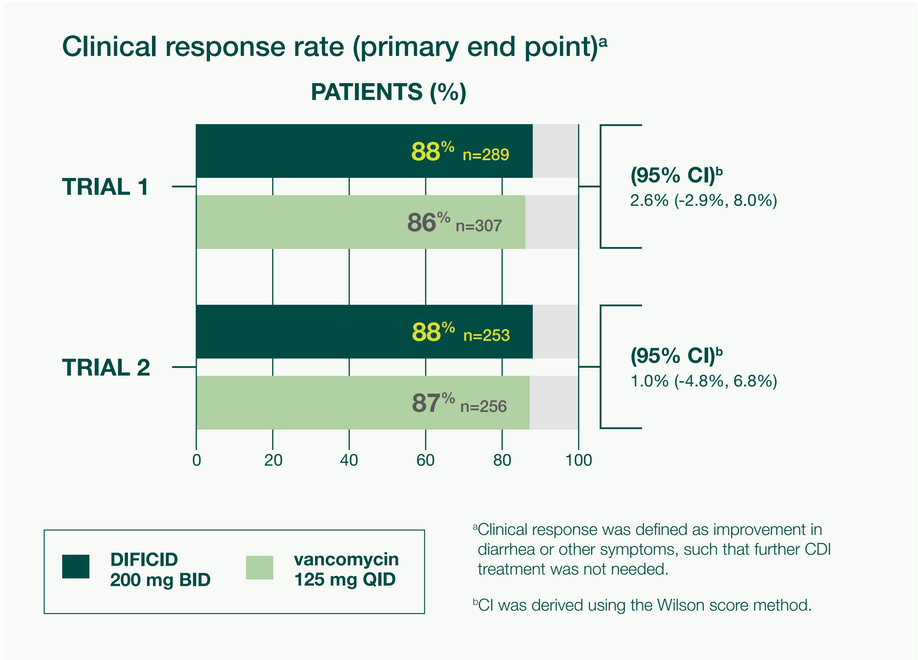
DIFICID®
(fidaxomicin)
tablets 200 mg
oral suspension 200 mg/5 ml

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).

Important Safety Information continued below.

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



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.

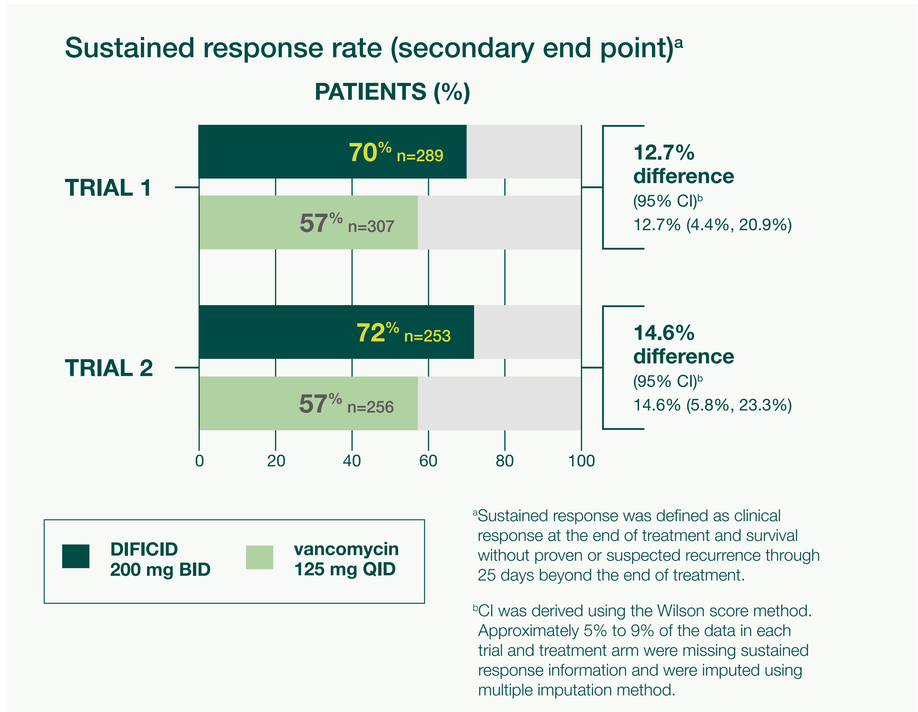
Important Safety Information *(continued)*

- 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.

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

In the same studies,

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



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 patients treated with DIFICID.

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.

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