EXCERPTS FROM THE UPDATED IDSA/SHEA CLINICAL PRACTICE GUIDELINES

DIFICID® (fidaxomicin) tablets 200 mg

The IDSA/SHEA guidelines recommend fidaxomicin over metronidazole[1]

- For INITIAL episodes of *C difficile* infection (CDI), the updated guidelines recommend using either fidaxomicin or vancomycin
- For the FIRST CDI RECURRENCE, the updated guidelines recommend considering a different regimen than that used to treat the INITIAL episode

Recommendations for the Treatment of *Clostridioides difficile* Infection in Adults [1,a,*]

INITIAL episode, non-severe	
Recommended Treatment[b]	**Strength of Recommendation/Quality of Evidence[c]**
Vancomycin 125 mg given 4 times per day, for 10 days, or	Strong/High
Fidaxomicin 200 mg given twice daily for 10 days	Strong/High
Alternate if above agents are unavailable: metronidazole, 500 mg 3 times per day by mouth for 10 days	Weak/High
INITIAL episode, severe[d]	
Recommended Treatment[b]	**Strength of Recommendation/Quality of Evidence[c]**
Vancomycin 125 mg given 4 times per day, for 10 days, or	Strong/High
Fidaxomicin 200 mg given twice daily for 10 days	Strong/High
FIRST RECURRENCE	
Recommended Treatment[b]	**Strength of Recommendation/Quality of Evidence[c]**
Vancomycin 125 mg given 4 times daily for 10 days if metronidazole was used for the INITIAL episode, or	Weak/Low
Use a prolonged tapered and pulsed vancomycin regimen if a standard regimen was used for the initial episode (eg, 125 mg 4 times per day for 10–14 days, 2 times per day for a week, once per day for a week, and then every 2 or 3 days for 2–8 weeks), or	Weak/Low
Fidaxomicin 200 mg given twice daily for 10 days if vancomycin was used for the INITIAL episode	Weak/Moderate

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[a]For recommendations for treatment of multiple recurrences and fulminant disease, please see full updated guidelines.

[b]All randomized trials have compared 10-day treatment courses, but some patients (particularly those treated with metronidazole) may have delayed response to treatment and clinicians should consider extending treatment duration to 14 days in those circumstances.

[c]For IDSA definitions on strength and quality of evidence, please see full updated guidelines.

[d]The criteria proposed for defining severe *Clostridioides difficile* infection (CDI) are based on expert opinion. These may need to be reviewed in the future upon publication of prospectively validated severity scores for patients with CDI.

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*.

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.

Important Safety Information *(continued)*

- The most common reactions in adults reported in clinical trials are nausea (11%), vomiting (7%), abdominal pain (6%), gastrointestinal hemorrhage (4%), anemia (2%), and neutropenia (2%).
- 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%).
- 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 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 atleast 4 kg) is twice daily for 10 days.

Additional Important Safety Information continues on other side.

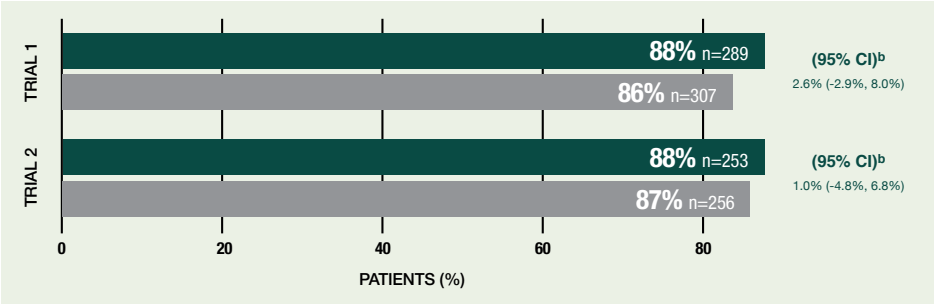
Reference:

1. McDonald LC, Gerding DN, Johnson S, et al. Clinical Practice Guidelines for *Clostridium difficile* Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). *Clin Infect Dis.* 2018;66(7):e1-e48.

DIFICID: COMPARABLE INITIAL CLINICAL RESPONSE RATE VS VANCOMYCIN AT END OF 10-DAY TREATMENT

DIFICID® (fidaxomicin) tablets 200 mg

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. 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.

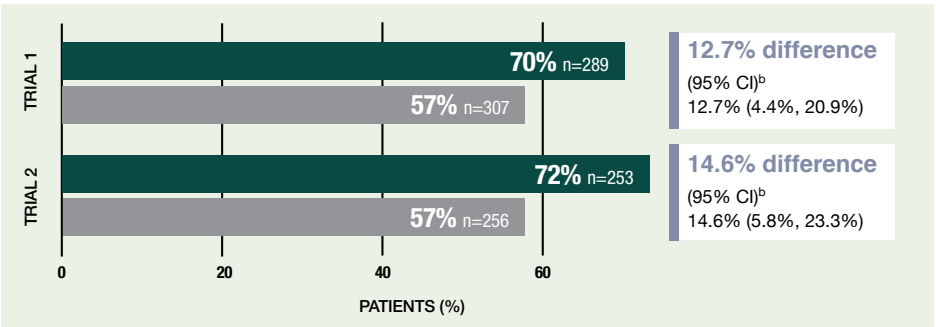
Study description: Two Phase 3, randomized, double-blind, noninferiority studies (N=1,105) comparing the efficacy and safety of oral DIFICID 200 mg BID vs oral vancomycin 125 mg QID for 10 days in the treatment of adults (aged ≥18 years) with CDI (defined as >3 unformed bowel movements or >200 mL of 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.

In the same studies,

DIFICID: SUPERIOR SUSTAINED RESPONSE RATE VS VANCOMYCIN THROUGH 25 DAYS AFTER END OF TREATMENT

Sustained response rate (secondary end point)[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.

Important Safety Information *(continued)*

- 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.