



**Tracking Form for Applicants for New Technology Add-on Payments under
the Acute Inpatient Prospective Payment System (IPPS) for Federal Fiscal
Year (FY) 2013**

1. Technology Name:

DIFICID™ (fidaxomicin) tablets

2. Manufacturer Name:

Optimer Pharmaceuticals, Inc.

3. Trade Brand of Technology:

The brand name is DIFICID™

4. Brief Description of Service or Device:

DIFICID (fidaxomicin) tablets represents the first major clinical advancement to address the *Clostridium difficile* epidemic in more than 25 years and is one of only two agents indicated by the U.S. Food and Drug Administration (FDA) to treat this disease. Even more importantly, DIFICID is the only agent proven to provide a superior sustained clinical response versus vancomycin – meaning a higher proportion of patients achieve clinical response and remain free of potentially devastating recurrences through 25 days after the end of treatment. DIFICID received priority review by the FDA and was approved on May 27, 2011 for the treatment of *Clostridium difficile*-associated diarrhea (CDAD) in adults 18 years of age and older. DIFICID was designated by the FDA as superior to vancomycin, the only other agent with an indication for *C. difficile*, in achieving sustained clinical response through 25 days beyond the end of treatment and comparable to vancomycin in initial response.

Newness Criterion

Note: To qualify for a new technology add-on payment, the technology or service must not be reflected in the data used to establish the Medicare severity diagnosis related groups (MS-DRGs).

5. Date of Food and Drug Administration (FDA) approval (or expected approval) for the device or service:

(For the complete application requirements, please see the instructions at http://www.cms.hhs.gov/AcuteInpatientPPS/08_newtech.asp#TopOfPage--.

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The DIFICID New Drug Approval Application (NDA) was approved by the FDA on May 27, 2011.

6. Was the product available on the market immediately after FDA approval? If not, please provide the date that the medical service or technology came on the market (i.e. first sales or availability) and an explanation for any delay (i.e. manufacturing issues, shelf life concerns or other reasons).

DIFICID was commercially available within 7 weeks from FDA approval.

7. Does the technology have an International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and/or ICD-10-PCS procedure code(s) or is an application pending?

Currently no ICD-9-CM diagnosis or procedure code(s) exists to uniquely identify DIFICID administration.

- a. If yes, please provide the ICD-9-CM and/or ICD-10-PCS procedure code(s) used to identify the clinical procedure(s) with which the medical service and technology is used.

N/A

- b. If there is no existing ICD-9-CM and/or ICD-10-PCS code that captures this new technology, please indicate whether you will be applying for a new code. (Refer to http://www.cms.hhs.gov/ICD9ProviderDiagnosticCodes/01_overview.asp#TopOfPage for more information.) We note that, if the product were to receive add-on payment status approval, it would need to be distinctly identifiable by ICD-9-CM and effective October 1, 2013 by ICD-10-PCS code(s) in the MedPAR claims data in order to receive add-on payment.

Per ongoing discussions with the Centers for Medicare & Medicaid (CMS) staff, Optimer is considering a request for a new ICD-9-CM procedure code for DIFICID administration to the ICD-9-CM Coordination and Maintenance Committee for discussion at the ICD-9-CM Coordination and Maintenance Committee Meeting to be held March 5-6, 2012.

8. Have you submitted an application for outpatient pass-through payments under the Medicare outpatient prospective payment system? If so, please provide the tracking number or, if it was approved, please provide the date of approval. (Please refer to http://www.cms.hhs.gov/HospitalOutpatientPPS/04_passthrough_payment.asp#TopOfPage for more information.)

N/A

Cost Criterion

(For the complete application requirements, please see the instructions at http://www.cms.hhs.gov/AcuteInpatientPPS/08_newtech.asp#TopOfPage--.

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Note: To qualify for a new technology add-on payment, the technology or service must result in average charges for cases using the technology in excess of the lesser of 75 percent of the standardized amount increased to reflect the difference between costs and charges or 75 percent of 1 standard deviation beyond the geometric mean standardized charge for all cases in the MS-DRGs to which the new technology is assigned. Table 10 from the annual final rule lists the thresholds by MS-DRG. The most recent version of Table 10 can be downloaded at: <https://www.cms.gov/AcuteInpatientPPS/FR2012/itemdetail.asp?filterType=none&filterByDID=-99&sortByDID=1&sortOrder=ascending&itemID=CMS1250507&intNumPerPage=10>.

Provide the following information to demonstrate the technology or service meets the criterion.

8. What is the anticipated average standardized charge per case involving this new technology? For details how to standardize charges please refer to the technical appendix of the application form.

Optimer estimates the average standardized charge per case involving DIFICID is \$58,066.

9. **A.** What is the total estimated cost per case for the service or technology (this will include all costs involved in the case, including the cost of the service or device)?

Trade secret information.

B. What is the cost of the technology per patient? Please provide a breakdown how the cost of the technology is calculated (i.e. **Drugs**- Average dosage or number of units per patient (ml/kg/hr); **Devices**- breakdown of the cost of all components used in the new technology, clearly showing which components are the “new” ones).

Trade secret information.

10. List the Medicare severity diagnosis-related groups (MS-DRGs) to which cases involving this new technology will most likely be assigned.

Medicare cases involving CDI are spread widely across the MS-DRG system. The 2009 MedPAR analysis showed that CDI occurred in 161,999 total cases that mapped to 538 MS-DRGs. Of these, MS-DRGs 371-373 contain the highest frequency of CDI cases.

These DRG totals are the result, in large part, of CDI's status as a top occurring hospital-acquired infection. CDI is often transmitted from contaminated surfaces by patients, caregivers, or providers by the fecal-oral route and can be spread via transient contamination. As such, CDI often develops post-procedure or as a secondary diagnosis, leading to wide mapping under CMS' GROUPER system.

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11. What is the anticipated volume of Medicare cases involving of this technology in FY 2013 (by MS-DRG)?

Optimer estimates 40,138 DIFICID cases among the Medicare beneficiary population in FY 2013.

Clinical Improvement Criterion

Note: To qualify for a new technology add-on payment, the technology or service must represent a substantial clinical improvement over existing technologies or services.

12. Please provide a short synopsis of the following clinical issues added to the new technology. Use the regular application to submit full details.
 - a. Briefly describe how the new service or technology represents a substantial clinical improvement over existing services or technologies:

DIFICID is the only FDA-approved antibacterial drug proven to be superior to vancomycin in achieving sustained clinical response through 25 days beyond the end of treatment for CDAD and represents a significant clinical improvement over existing CDAD treatments. By providing a superior sustained clinical response and lower risk of CDAD recurrence, DIFICID has the potential to decrease hospitalizations, physician office visits, and/or need for new or repeat prescriptions for CDAD recurrence.

Specifically:

- DIFICID demonstrates comparable efficacy on initial clinical response and superior efficacy over vancomycin on sustained clinical response through 25 days post treatment. Differences in sustained clinical response were due to lower rates of proven or suspected CDAD recurrence during the follow up period. Thus, DIFICID patients experience a higher durability of cure compared with vancomycin, the only other agent FDA approved for the treatment of this disease.
- DIFICID significantly lowers the rate of CDAD recurrence compared with vancomycin.
- DIFICID has the potential to decrease hospitalizations, physician office visits, and/or need for new or repeat prescriptions for CDAD recurrence by providing a superior sustained clinical response and lower risk of CDAD recurrence.
- DIFICID has the potential to improve CDAD patients' quality of life by decreasing time to resolution of diarrhea, providing a superior sustained clinical response, and decreasing the rate of recurrence.
- DIFICID is an important treatment for geriatric patients who are at increased risk of experiencing CDAD and recurrent episodes.

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- DIFICID has longer acting antimicrobial activity compared with vancomycin.
 - In patients with CDAD who require concomitant antibiotics for other infections, DIFICID treatment results in higher initial clinical response, higher sustained clinical response, and lower recurrence rates compared to vancomycin.
 - DIFICID has minimal impact on normal gut flora.
 - DIFICID treatment is associated with a lower risk of acquisition of vancomycin-resistant Enterococcus (VRE).
 - DIFICID inhibits spore production in *C. difficile* in vitro. *C. difficile* cells produce spores when exposed to air, so transmission of infection occurs even when the cells themselves are killed. DIFICID inhibits spore production in *C. difficile* in vitro.
- b. List all published peer-reviewed articles relevant to the new service or technology.

Select peer-reviewed articles relevant to DIFICID.

1. Babakhani F, Gomez A, Robert N, Sears P. Postantibiotic effect of fidaxomicin and its major metabolite, OP-1118, against *Clostridium difficile*. *Antimicrob Agents Chemother.* 2011;Sep;55(9):4427-9.
2. Babakhani F, Gomez A, Robert N, Sears P. Killing kinetics of fidaxomicin and its major metabolite, OP-1118, against *Clostridium difficile*. *J Med Microbiol.* 2011;Aug;60(Pt 8):1213-7.
3. Biedenbach DJ, Ross JE, Putnam SD, Jones RN. In vitro activity of fidaxomicin (OPT-80) tested against contemporary clinical isolates of Staphylococcus spp. and Enterococcus spp. *Antimicrob Agents Chemother.* 2010;May;54(5):2273-5
4. Cocanour CS. Best strategies in recurrent or persistent *Clostridium difficile* infection. *Surg Infect (Larchmt).* 2011;Jun;12(3):235-9.
5. Crook D, Weiss K, Cornely O, Miller M, Esposito R, Gorbach S. Randomized clinical trial (RCT) in *Clostridium difficile* infection (CDI) confirms equivalent cure rate and lower recurrence rate of fidaxomicin (FDX) versus vancomycin (VCN). Poster presented at the 20th European congress of clinical microbiology and infectious diseases - April 10-13, 2010; Vienna, Austria.
6. Dolgin E. 'Game changer' antibiotic and others in works for superbug. *Nat Med.* 2011;Jan;17(1):10.

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7. Dubberke, ER, Chen YJ, Ackerman, SJ, Owens, R, Johnson, S. Economic burden of *Clostridium difficile* infection among elderly patients in the United States: An analysis using Medicare claims data. 40th annual meeting of the Infectious Disease Society of America (IDSA). October 20-23, 2011; Boston, MA.
8. Goldstein EJ, Citron DM, Sears P, Babakhani F, Sambol SP, Gerding DN. Comparative Susceptibilities to Fidaxomicin (OPT-80) of Isolates Collected at Baseline, Recurrence, and Failure from Patients in Two Phase III Trials of Fidaxomicin against *Clostridium difficile* Infection. *Antimicrob Agents Chemother.* 2011;Nov;55(11):5194-9.
9. Hardesty JS, Juang P. Fidaxomicin: a macrocyclic antibiotic for the treatment of *Clostridium difficile* infection. *Pharmacotherapy.* 2011;Sep;31(9):877-86.
10. Hausmann J, Zeuzem S, Schröder O. Fidaxomicin-the next step? A new narrow-spectrum macrocyclic antibiotic for the management of *clostridium difficile* infection. *Gastroenterology.* 2011;Sep;141(3):1116-8.
11. Louie TJ, Emery J, Krulicki W, et al. OPT-80 eliminates *Clostridium difficile* and is sparing of bacteroides species during treatment of *C. difficile* infection. *Antimicrob Agents Chemother.* 2009;Jan;53(1):261-3.
12. Louie TJ, Miller MA, Mullane KM, Weiss K, Lentnek A, Golan Y, et al. Fidaxomicin versus vancomycin for *Clostridium difficile* infection. *N Engl J Med.* 2011;364(5):422-431.
13. McFarland LV. Emerging therapies for *Clostridium difficile* infections. *Expert Opin Emerg Drugs.* 2011;Sep;16(3):425-39.
14. Mullane, KM, Gorbach, S. Fidaxomicin: first-in-class macrocyclic antibiotic. *Expert Rev Anti Infect Ther.* 2011;Jul;9(7):767-77.
15. Mullane KM, Miller MA, Weiss K, Lentnek A, Golan Y, Sears PS, Shue YK, Louie TJ, Gorbach SL. Efficacy of fidaxomicin versus vancomycin as therapy for *Clostridium difficile* infection in individuals taking concomitant antibiotics for other concurrent infections. *Clin Infect Dis.* 2011;Sep;53(5):440-7.
16. Musgrave CR, Bookstaver PB, Sutton SS, Miller AD. Use of alternative or adjuvant pharmacologic treatment strategies in the prevention and treatment of *Clostridium difficile* infection. *Int J Infect Dis.* 2011;Jul;15(7):e438-48

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17. Prabaker K, Weinstein RA. Trends in antimicrobial resistance in intensive care units in the United States. *Curr Opin Crit Care.* 2011;Oct;17(5):472-9.
18. Tannock GW, Munro K, Taylor C, Lawley B, Young W, Byrne B, Emery J, Louie T. A new macrocyclic antibiotic, fidaxomicin (OPT-80), causes less alteration to the bowel microbiota of Clostridium difficile-infected patients than does vancomycin. *Microbiology.* 2010;Nov;156(Pt 11):3354-9.
19. van Nispen tot Pannerden CM, Verbon A, Kuipers EJ. Recurrent Clostridium difficile infection: what are the treatment options? *Drugs.* 2011;May 7;71(7):853-68.

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