NTAP GRANTED: Effective October 1, 2020

New technology add-on payment (NTAP) available for Fetroja[1]

As of October 1, 2020, additional NTAP reimbursement is available for qualifying cases—up to 75% ($7919.86) of the average cost of Fetroja[1]

CMS developed the Qualified Infectious Disease Product (QIDP) pathway to increase access to innovative antibacterials for hospital inpatients beginning in FY2021. As a QIDP, Fetroja qualified for NTAP under this new pathway[1,2]

- NTAP is designed to provide additional Medicare inpatient reimbursement on top of the MS-DRG for innovative new products such as Fetroja[1,2]
- NTAP reimbursement is made available while CMS recalibrates the DRG reimbursement to account for these new therapies[1,2]
- NTAP helps ensure adequate payment for new medical services and technologies[1,2]

CMS=Centers for Medicare & Medicaid Services; DRG=diagnosis-related group; FY=fiscal year; MS-DRG=Medicare Severity-Diagnosis Related Group.

INDICATIONS

Fetroja® (cefiderocol) is indicated in patients 18 years of age or older for the treatment of complicated urinary tract infections (cUTIs), including pyelonephritis caused by the following susceptible Gram-negative microorganisms: *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, and *Enterobacter cloacae* complex.

Fetroja is indicated in patients 18 years of age or older for the treatment of hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia, caused by the following susceptible Gram-negative microorganisms: *Acinetobacter baumannii* complex, *Escherichia coli*, *Enterobacter cloacae* complex, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Serratia marcescens*.

USAGE

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

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Fetroja is contraindicated in patients with a known history of severe hypersensitivity to cefiderocol or other beta-lactam antibacterial drugs, or any other component of Fetroja.

Please see Important Safety Information throughout this brochure and accompanying Full Prescribing Information for Fetroja, or visit Fetroja.com.

Fetroja® (cefiderocol) for injection

Fetroja NTAP reimbursement available: Additional payment up to 75% of the average cost of Fetroja

To support the availability of new antibacterials, CMS increased the NTAP for QIDPs from 50% to 75%[2]

- NTAP offers hospitals timely access to new and innovative technologies and services, such as Fetroja[2]
- CMS now covers up to 75% of the estimated cost of QIDPs or 75% of the difference between the full DRG payment and the hospital's estimated cost[2]
- This add-on payment will be incremental to the MS-DRG reimbursement for qualifying Medicare inpatient cases[1,2]

Fetroja is one of the 5 antibacterials granted NTAP for FY2021[1]

Drug Name	Maximum NTAP for FY2021
Fetroja (cefiderocol)	**$7919.86**
Recarbrio™ (imipenem/cilastatin/relebactam)	$3532.78
Zerbaxa® (ceftolozane/tazobactam)	$1836.98
Nuzyra® (omadacycline)	$1552.50
Xenleta™ (lefamulin)	$1275.75

NTAP approval for Fetroja reinforces Shionogi's commitment to making novel, effective treatments accessible for patients

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Increase in All-Cause Mortality in Patients with Carbapenem-Resistant Gram-Negative Bacterial Infections

An increase in all-cause mortality was observed in patients treated with Fetroja as compared to best available therapy (BAT) in a multinational, randomized, open-label trial in critically ill patients with carbapenem-resistant Gram-negative bacterial infections (NCT02714595). Patients with nosocomial pneumonia, bloodstream infections, sepsis, or cUTI were included in the trial. BAT regimens varied according to local practices and consisted of 1 to 3 antibacterial drugs with activity against Gram-negative bacteria. Most of the BAT regimens contained colistin.

The increase in all-cause mortality occurred in patients treated for nosocomial pneumonia, bloodstream infections, or sepsis. The 28-Day all-cause mortality was higher in patients treated with Fetroja than in patients treated with BAT [25/101 (24.8%) vs 9/49 (18.4%), treatment difference 6.4%, 95% CI (-8.6, 19.2)]. All-cause mortality remained higher in patients treated with Fetroja than in patients treated with BAT through Day 49 [34/101 (33.7%) vs 10/49 (20.4%), treatment difference 13.3%, 95% CI (-2.5, 26.9)].

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Fetroja® (cefiderocol) for injection

Eligibility and reimbursement for NTAP

Who qualifies for NTAP[1]:

Eligible Facilities	Setting of Care	Qualified Patients
Acute care hospitals paid through the IPPS	Inpatient care settings	Medicare fee-for-service beneficiaries who are administered Fetroja in the inpatient setting

ICD-10-PCS codes describing Fetroja administration for NTAP reimbursement claims[3]:

ICD-10-PCS Code	Description
XW033A6	Introduction of Cefiderocol Anti-Infective Into Peripheral Vein, Percutaneous Approach, New Technology Group 6
XW043A6	Introduction of Cefiderocol Anti-Infective Into Central Vein, Percutaneous Approach, New Technology Group 6

The appropriate ICD-10-PCS codes for Fetroja must be included when billing to qualify for NTAP[2]

ICD-10-PCS=International Classification of Diseases, 10th Revision, Procedure Coding System; IPPS=Inpatient Prospective Payment System.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (cont'd)

Increase in All-Cause Mortality in Patients with Carbapenem-Resistant Gram-Negative Bacterial Infections (cont'd)

Generally, deaths were in patients with infections caused by Gram-negative organisms, including non-fermenters such as *Acinetobacter baumannii* complex, *Stenotrophomonas maltophilia*, and *Pseudomonas aeruginosa*, and were the result of worsening or complications of infection, or underlying comorbidities. The cause of the increase in mortality has not been established.

Closely monitor the clinical response to therapy in patients with cUTI and HABP/VABP.

Hypersensitivity Reactions

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions and serious skin reactions have been reported in patients receiving beta-lactam antibacterial drugs. Hypersensitivity was observed in Fetroja-treated patients in clinical trials. These reactions are more likely to occur in individuals with a history of beta-lactam hypersensitivity and/or a history of sensitivity to multiple allergens. There have been reports of individuals with a history of penicillin hypersensitivity who have experienced severe reactions when treated with cephalosporins.

Before therapy with Fetroja is instituted, inquire about previous hypersensitivity reactions to cephalosporins, penicillins, or other beta-lactam antibacterial drugs. Discontinue Fetroja if an allergic reaction occurs.

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Learn more about Fetroja at Fetroja.com

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (cont'd)

Clostridioides difficile-associated Diarrhea (CDAD)

Clostridioides difficile-associated diarrhea (CDAD) has been reported for nearly all systemic antibacterial agents, including Fetroja. CDAD may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of *C. difficile*.

Careful medical history is necessary because CDAD has been reported to occur more than 2 months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, antibacterial drugs not directed against *C. difficile* may need to be discontinued. Manage fluid and electrolyte levels as appropriate, supplement protein intake, monitor antibacterial treatment of *C. difficile*, and institute surgical evaluation as clinically indicated.

Seizures and Other Central Nervous System (CNS) Adverse Reactions

Cephalosporins, including Fetroja, have been implicated in triggering seizures. Nonconvulsive status epilepticus (NCSE), encephalopathy, coma, asterixis, neuromuscular excitability, and myoclonia have been reported with cephalosporins particularly in patients with a history of epilepsy and/or when recommended dosages of cephalosporins were exceeded due to renal impairment. Adjust Fetroja dosing based on creatinine clearance. Anticonvulsant therapy should be continued in patients with known seizure disorders. If CNS adverse reactions including seizures occur, patients should undergo a neurological evaluation to determine whether Fetroja should be discontinued.

Development of Drug-Resistant Bacteria

Prescribing Fetroja in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

ADVERSE REACTIONS

The most common adverse reactions occurring in (≥2%) of patients receiving Fetroja compared to imipenem/cilastatin in the cUTI trial were: diarrhea (4% vs 6%), infusion site reactions (4% vs 5%), constipation (3% vs 4%), rash (3% vs <1%), candidiasis (2% vs 3%), cough (2% vs <1%), elevations in liver tests (2% vs <1%), headache (2% vs 5%), hypokalemia (2% vs 3%), nausea (2% vs 4%), and vomiting (2% vs 1%). The most common adverse reactions occurring in (≥4%) of patients receiving Fetroja compared to meropenem in the HABP/VABP trial were: elevations in liver tests (16% vs 16%), hypokalemia (11% vs 15%), diarrhea (9% vs 9%), hypomagnesemia (5% vs <1%), and atrial fibrillation (5% vs 3%).

References: 1. Centers for Medicare & Medicaid Services. *Fed Regist*. Published May 29, 2020. Available at: https://www.federalregister.gov/documents/2020/05/29/2020-10122/medicare-program-hospital-inpatient-prospective-payment-systems-for-acute-care-hospitals-and-the. Accessed July 6, 2020. **2.** Centers for Medicare & Medicaid Services. *MLN Matters*. Published January 21, 2020. Available at: https://www.cms.gov/files/document/se20004.pdf. Accessed July 6, 2020. **3.** Centers for Medicare & Medicaid Services. Updated May 28, 2020. Available at: https://www.cms.gov/medicare/icd-10/2021-icd-10-pcs. Accessed July 6, 2020.

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