

**Formulary Review:** Teflaro™  
**Generic Name:** Ceftaroline  
**Manufacturer:** Eisai Inc.

**Reviewed: March 2011**

## Executive Summary

### Introduction

Ceftaroline is a broad-spectrum fifth generation cephalosporin approved to treat adults with community acquired pneumonia and bacterial skin and skin structure infections. Ceftaroline is distinct in that it has antimicrobial activity against multidrug-resistant *Staphylococcus aureus* (including methicillin-resistant *S. aureus*, vancomycin-intermediate *S. aureus* (VISA), *Streptococcus pneumoniae*, and respiratory gram-negative pathogens such as *Moraxella catarrhalis* and *Haemophilus influenzae*. There is insufficient data to recommend the use of ceftaroline for treatment of community-acquired pneumonia caused by MRSA.

### Pharmacology/ Pharmacokinetics

Ceftaroline fosamil is a cephalosporin with in vitro bactericidal action against gram-positive and gram-negative bacteria. Bactericidal action due to the inhibition of cell wall synthesis is mediated through binding to penicillin-binding proteins. Activity against *S. aureus* is due to its affinity for PBP2a, and activity against *S. pneumoniae* is due to its affinity for PBP2x in which typically beta-lactams have little binding affinity. Ceftaroline fosamil is converted into bioactive ceftaroline in plasma by a phosphate enzyme. The median volume of distribution after a single 600 mg IV dose is 20.3L. The mean serum half-life is 2.6 hours, plasma protein binding is less than 20%, and drug clearance occurs mainly by way of renal excretion, with 75% of the drug recovered in the urine.

### Clinical Efficacy

CANVAS 1 and CANVAS 2 trials: A total of 1396 adults with clinically documented complicated skin and skin structure infection were enrolled in two clinical trials comparing Teflaro (600 mg IV over 1 hour every 12 hours) to Vancomycin plus Aztreonam (1 gram Vancomycin IV over one hour followed by 1 gram aztreonam over 1 hour every 12 hours). In CANVAS I, Teflaro-treated patients had a response rate of 74% compared with a response rate of 64.6% for vancomycin plus aztreonam-treated patients. In addition, Ceftaroline obtained a clinical cure rate of 91.1% compared with a rate of 93.3% in vancomycin/aztreonam-treated patients. In CANVAS II, Teflaro-treated patients had a response rate of 74% compared with a response rate of 68.1% for vancomycin plus aztreonam-treated patients. Teflaro-treated patients had a clinical cure rate of 92.2% compared with a rate of 92.1% in vancomycin/aztreonam-treated patients.

FOCUS I and FOCUS II: studied adult patients who were hospitalized with moderate to severe CABP requiring treatment with intravenous antimicrobials. In FOCUS I, Teflaro-treated patients had a response rate of 69.6% compared with a response rate of 58.3% for ceftriaxone-treated patients. Teflaro-treated patients had a clinical cure rate of 86.6% compared with a rate of 78.2% in ceftriaxone-treated patients. In FOCUS II, Teflaro-treated patients had a response rate of 69% compared with a response rate of 61.4% for ceftriaxone-treated patients and Teflaro treated-patients had a clinical cure rate of 82.3% compared with a rate of 77.1% in ceftriaxone-treated patients.

### Adverse Drug Reactions

Anaphylactic reactions and serious skin reactions have been reported with beta-lactam antibiotics, including ceftaroline. *Clostridium difficile*-associated diarrhea, hypo/hyperkalemia, and renal failure have been reported with Teflaro.

### Drug Interactions

In vitro studies indicate that ceftaroline does not inhibit or induce the cytochrome P450 isoenzymes. Therefore there is minimal potential for drug-drug interactions with CYP450 substrates, inhibitors, or inducers.

**Dosage & Administration**

*For the treatment of acute bacterial skin and skin structure infections:*

Adults: 600 mg IV every 12 hours for 5—14 days by IV infusion over 1 hour

*For the treatment of bacterial community-acquired pneumonia:*

Adults: 600 mg IV every 12 hours for 5—7 days by IV infusion over 1 hour

Dose adjustments should be made in renal impairment as follows:

Estimated CrCl <sup>a</sup> (mL/min)	Recommended Dosage Regimen for Teflaro
> 50	No dosage adjustment necessary
> 30 to ≤ 50	400 mg IV (over 1 hour) every 12 hours
≥ 15 to ≤ 30	300 mg IV (over 1 hour) every 12 hours
End-stage renal disease, including hemodialysis <sup>b</sup>	200 mg IV (over 1 hour) every 12 hours <sup>c</sup>

**Summary**

Ceftaroline is a fifth generation cephalosporin that is clinically effective for the treatment of complicated skin and skin structure infections and community-acquired bacterial pneumonia, and it has distinctive activity against some difficult-to-treat multidrug-resistant gram-positive organisms making the drug a cornerstone cephalosporin.

**Formulary status****Non-formulary**