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*Dieter Adam*

Children's Hospital, University of Munich, Munich, Germany

# Overview of the Clinical Features of Cefixime

**Key Words**
Cefixime
Bacterial infection
3rd gen. cephalosporin

**Abstract**
Third-generation cephalosporins in oral formulations have become an increasingly important first-line choice against common bacterial infections. Cefixime is one such agent, which possesses excellent efficacy against a broad spectrum of pathogens, including *Haemophilus influenzae, Streptococcus pneumoniae* and *Moraxella catarrhalis.* Clinical success rates are similar to cefaclor, clarithromycin, and other cephalosporins. Importantly, cefixime also possesses excellent activity against beta-lactamase-producing strains. The pharmacodynamic features of the drug include a half-life of 3–4 h and a $C_{max}$ of 4.4 μg/ml, well above the $MIC_{90}$ for susceptible pathogens, permitting once-daily dosing. In this brief overview, the bacteriological and clinical efficacy of cefixime is discussed, as well as its indications.

## Introduction

Cefixime is an oral 3rd gen. cephalosporin, which has become increasingly well known throughout the world. Many physicians have been using it daily in the treatment of bacterial infections in children as well as adults. In light of the increased failure rates noted with conventional antibiotics against common infections, increased awareness of regional variations in antibiotic susceptibility, and the increased use of cefixime in the outpatient setting, it is appropriate to present an overview of our current understanding of cefixime based on bacteriological and clinical studies.

In the last few years there have been changes in the pattern of resistance development in some countries, but also stabilization of resistance development, for example *Strep-*

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Prof. Dr. Dr. D. Adam
Children's Hospital
University of Munich
Lindwurmstrasse 4
D–80337 München (Germany)

**Table 1.** Comparison of $MIC_{90}$ for cefixime and other antibiotics against common infectious disease pathogens

| Agent | *H. influenzae* | | *S. pneumoniae* | | *M. catarrhalis* | | *S. pyogenes* |
|---|---|---|---|---|---|---|---|
| | β (–) | β (+) | Pen S | Pen R | β (–) | β (+) | |
| Cefixime | ≤0.06 | ≤0.06 | 0.25 | >8.0 | ≤0.12 | 0.5 | ≤0.12 |
| Cefaclor | 8.0 | ≥8 | 0.5 | >8.0 | 1.0 | 4.0 | ≤0.12 |
| Cefuroxime | 2.0 | 2.0 | ≤0.05 | 16 | 1.0 | 4.0 | ≤0.05 |
| Cefprozil | 8.0 | 32 | ≤0.05 | 16 | 1.0 | 8.0 | ≤0.05 |
| Amoxicillin clavulanate | 1.0 | 2.0 | ≤0.12 | 4.0 | ≤0.25 | 0.5 | ≤0.12 |
| Clarithromycin | 16.0 | 16 | 2.0 | 2.0 | ≤0.5 | ≤0.05 | ≤0.25 |
| Azithromycin | 2.0 | 2.0 | ≤0.25 | >32 | ≤0.25 | ≤0.05 | ≤0.23 |

Pen S: penicillin MIC ≤0.06 mg/l; Pen R: penicillin MIC ≥2.0 mg/l (100 strains in each category).

*tococcus pneumoniae,* in other countries. The overall incidence of *Haemophilus influenzae* with beta-lactamase production has increased. In North America, the incidence has increased from 16.9 to 45% from 1985 to 1994. In contrast, in Germany the rate is currently less than 5% while it reaches up to 60% in other countries. Proper strategies for the management of antibiotic usage must therefore be according to the country in which the substance is used.

## Update of the Microbiological Situation of Cefixime

Cefixime is active against beta-lactamase-positive *H. influenzae,* beta-lactamase-positive *Moraxella catarrhalis* and penicillin-sensitive *S. pneumoniae,* although not against penicillin-resistant *S. pneumoniae*. In addition to its broad-spectrum activity, the pharmacokinetic profile of cefixime makes it an ideal preparation for a number of infections. Oral absorption is 40–50%, and excretion is about 16–26% in urine and 10% in bile. When considering serum concentration compared with the $MIC_{90}$ values of common pathogens, most strains are found to be covered with a normal dose of 400 mg (table 1) [1]. Peak serum concentration is reached after 4 h, with a $C_{max}$ of 4.4 μg/ml and a half-life of 3–4 h. Taken together, this makes it possible to administer cefixime once daily. In addition, there are strong correlations between concentrations of cefixime in specific tissues and the sites where infection occurs. For example, cefixime levels are high in tonsil, maxillary sinus, sputum, bronchial mucosa, middle ear fluid, bile, gall bladder, urine and inflamed tissues. The substance penetrates well compared to all other beta-lactams, and is similar to other cephalosporins and penicillins. Macrolides and quinolones, however, still have superior penetration characteristics. When considering the pharmacokinetics of other oral cephalosporins, a once-daily dose of 400 mg cefixime provides steadier plasma levels over a longer period of time. Cefuroxime 500 mg, cefprozil 500 mg, cefpodoxime 400 mg, and ceftibuten 400 mg have half-lives of 1.3, 1.3, 2.5 and 2.0 h, respectively, in comparison to 3.5 h for cefixime.

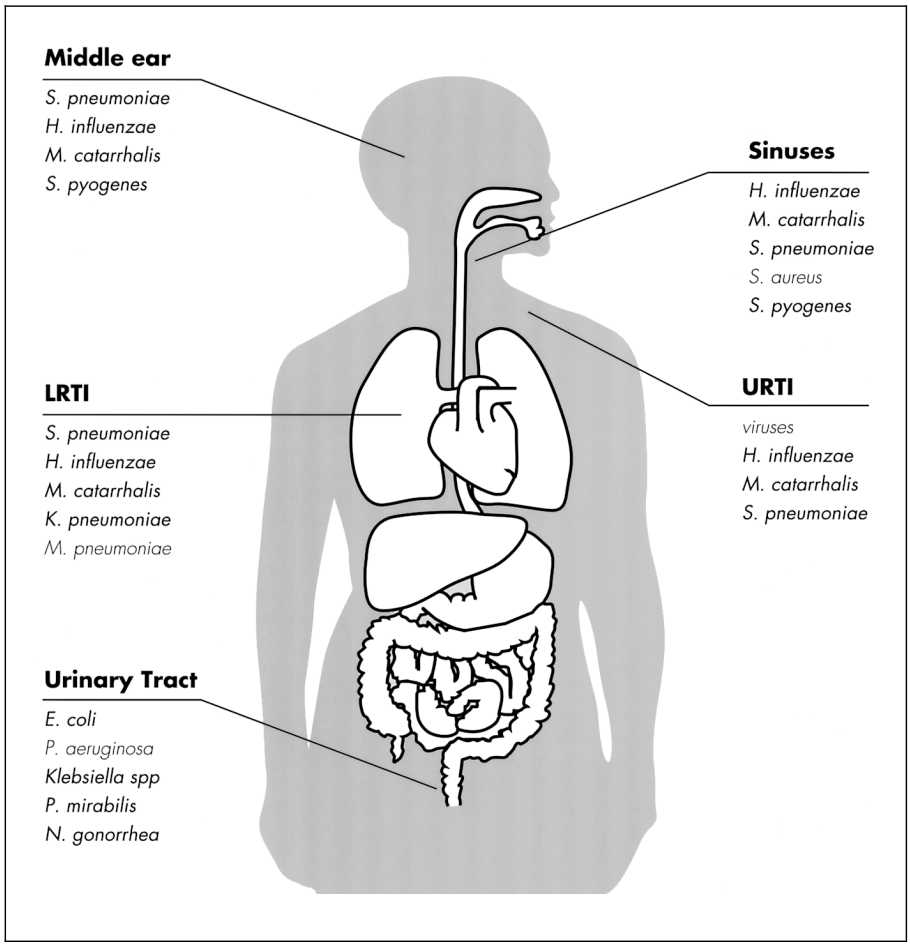


**Fig. 1.** Major bacterial pathogens responsible for infection.

## Clinical Experience with Cefixime

Cefixime covers several bacterial infections that are commonly encountered by the physician in daily practice. The indications for cefixime are bronchitis, acute exacerbations of chronic bronchitis, tonsillitis, pharyngitis, sinusitis, otitis media, gonorrhea and urinary tract infections. For all indications in adults the dosage is fixed at 400 mg/day, with 1 or 2 divided doses possible. In pediatrics the dose is also fixed at 8 mg/kg/day, in 1 or 2 divided doses for all indications. Figure 1 lists the bacterial pathogens most commonly associated with infection in various sites of the body. Most bacteria that are responsible for infection, excluding mycoplasma or chlamydia, which are the domain of the macrolides, can be reached by third-generation cephalosporins. This includes cefixime, which is absolutely stable to beta- lactamases, and which is very active against *H. influenzae.* In daily

practice, one of the most common presentations is lower respiratory tract infection. A double-blind, randomized study has demonstrated equivalent efficacy of cefixime 400 mg once daily (n = 110) to clarithromycin 500 mg twice daily (n = 103), with cure or improvement rates of 86 and 88%, respectively [2].

## New Developments

One recent development in the treatment of infection is intravenous switch therapy, brought about both by the recent availability of oral cephalosporins with excellent activity and by the pressure placed on hospitals to reduce costs. The concept of switch therapy is as follows: upon hospital admission for a serious infection, the physician prescribes empiric therapy consisting of an intravenous third-generation cephalosporin, then after a few days switches to an oral third generation cephalosporin, following which the patient is discharged. Cefixime has proved itself a potent switch-down agent for a number of indications.

In addition, cefixime has proved itself a potent agent in short-course therapy. In one of our studies, treatment of patients with group A beta-hemolytic streptococcal (GABHS) pharyngitis was compared. Cefixime 8 mg/kg/day qd for 5 days (n = 65) versus penicillin V 200,000 IU/kg tid for 10 days (69%) resulted in clinical cure rates of 86.7 and 90.8%, respectively [3–5]. These were administered under study conditions, which indicates that the situation was controlled and that the penicillin was given for the full 10 days. Normally, however, patients tend to stop treatment after 5 or 6 days with penicillin V, reducing the actual efficacy rate. A recent study of 5,500 GABHS pharyngitis patients in Germany, indicated no difference between 5-day treatment with a cephalosporin or a macrolide and a standard 10-day course of penicillin V. In the future, it may be possible to recommend 5-day cefixime treatment of GABHS pharyngitis, following approval from the regulatory authorities. We are therefore now planning a study of 5-day penicillin treatment. If relapse or failure occurs more frequently with the penicillin V treatment, then it will support the use of one of the third-generation cephalosporins, such as cefixime, or macrolides for 5 days. It is of interest to note that one 4-day study in GABHS pharyngitis patients showed resolution with cefixime at 2.2 days and with penicillin V at 2.7 days, although it is still recommended to use 5-day treatment. Additional studies are required to clarify optimum treatment regimens.

## Safety Profile of Cefixime

As with other cephalosporins, the most significant adverse events with cefixime relate to the gastrointestinal tract and the skin. There are no specific problems associated with cefixime that are not reported for other cephalosporins. A recent postmarketing survey involving over 47,000 patients in Germany, the US and Canada has shown side effect incidences of between 1.6 and 11.5%, which is also comparable to those reported for other cephalosporins. In a US study of safety profile, 5.5% children and 7.7% adults had to discontinue therapy. In France and Germany the rates are much lower (0.7 and 0.9%, respectively), which likely reflects the differences from country to country in interpreting what constitutes a side effect and event. Patient compliance with cefixime is expected to be superior to that observed with other preparations that require multiple daily dosing, as supported by the finding that in general once-daily dosage results in the best compliance, at about 85%, while it decreases to 60% with

3-times daily dosing. If a substance has to be given 3 times daily, it goes down to 60%, with the mid-day dose in most cases not being given in children, for example, resulting in insufficient tissue concentrations throughout the day. A further advantage of cefixime is the well-tolerated liquid suspension available for pediatric patients, which has a favorable taste.

In summary, the clinical features of cefixime make it an important first-line choice for physicians against a variety of common infections encountered in daily practice. These include its efficacy against a wide range of pathogens, well-proven safety, a long half-life allowing once-daily dosing, fixed dosage for all indications, excellent beta- lactamase stability, and good tasting pediatric suspension.

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