University of Nebraska Medical Center
Nebraska Medicine

Formulary Update: Cefpodoxime

Situation

Cefpodoxime has replaced cefdinir on Nebraska Medicine's inpatient drug formulary as the preferred oral 3rd generation cephalosporin given its more favorable pharmacokinetic profile. Nebraska DHHS has also accepted our proposal to add cefpodoxime to the state Medicaid formulary.

Background

Cefdinir does not reliably achieve therapeutic levels in the blood or at most sites of infection, increasing treatment failure risk. Clinical evidence for cefdinir suffers from the Pollyanna phenomenon or "false optimism" due to high baseline spontaneous remission rates in the studied outpatient indications.

Assessment

Table 1: Comparison of Pharmacokinetics and Pharmacodynamics

PK Parameter	**Cefdinir**	**Cefpodoxime**
Absorption	16-25%	50%
Protein Binding	60-70%	21-33%
Half-life	1.7 hours	1.7-3.3hours
Urine excretion unchanged	12-18%	29-33%

Comparison of Pharmacokinetics and Pharmacodynamics

- The probability of achieving target concentrations necessary for efficacy with cefpodoxime is better than cefdinir. The European organization establishing susceptibility breakpoints removed all interpretive criteria for cefdinir due its inability to reach/maintain adequate concentrations for efficacy across the wild-type distributions of minimum inhibitory concentrations (MIC). Results from the Survey of Antibiotic Resistance (SOAR) 2018–21: data based on CLSI, EUCAST (dose-specific) and pharmacokinetic/pharmacodynamic (PK/PD) breakpoints are below.

Figure 1: Comparison table of IV ceftriaxone with oral penicillin and cephalosporin antibiotics

Beta-lactams	*S. pneumoniae* MIC_{90} (mcg/mL)	%Non-Susceptible	Likelihood of Achieving 50% fT>MIC
Ceftriaxone	1	1	>95%
Amoxicillin (30mg/kg TID)	1	4	>95%
Amoxicillin (45 mg/kg BID)	1	4	~90%
Cefprozil	≥8	20	62-70%
Cefuroxime	8	21	62-72%
Cefpodoxime	2	18	75-80%
Cefixime	32	48	52-62%
Cefdinir	4	14	58-68%

- High-dose amoxicillin remains the most effective oral agent for infections due to *Streptococcus pneumoniae*. In situations where amoxicillin cannot be utilized, alternative oral options on formulary at UNMC include:
    - Cefuroxime – formulary 2nd generation cephalosporin oral tablet
    - Cefprozil – formulary 2nd generation cephalosporin oral suspension
    - Cefpodoxime – formulary 3rd generation cephalosporin (tablet and suspension)
- Supportive evidence
    - Cephem antibiotics: Wise use today preserves cure for tomorrow - Pubmed
    - IDSA Complicated UTI guidelines: Cefpodoxime 200-400mg PO BID is considered an alternative option for oral therapy following IV lead-in treatment following clinical improvement in patients with complicated UTIs (including those with bacteremia) due to *Enterobacterales* (e.g., *E. coli, Klebsiella pneumoniae*) susceptible to 3rd generation cephalosporins.
    - For uncomplicated UTIs, Cefpodoxime 100mg PO BID x 3 days achieved similarly high rates of clinical and microbiological cure compared to 3-days of PO TMP-SMX in a prospective, randomized trial of women.
    - Recent clinical evidence with cefdinir for uncomplicated UTIs observed significantly more treatment failures vs. cephalexin recipients (23.4% vs 12.5%, OR 1.9; 95% CI: 1.1-3.4).
        - Cephalexin is substantially more bioavailable and achieves higher urinary concentrations compared to cefdinir.

Recommendation

Cefpodoxime is now the preferred oral 3rd generation cephalosporin at Nebraska Medicine and cefdinir is no longer on inpatient formulary. Orders for cefdinir will automatically be interchanged to the standard dose of cefpodoxime 200mg po BID per MP 51. A higher dose of cefpodoxime 400mg po BID can be considered when transitioning from IV beta-lactams in systemic Gram-negative infections.