Drug Class Review Monograph – GPI Class 02 – Cephalosporins

Review Time Frame: 02/2016 – 04/2017
Previous Class Review: 05/2016

Background:
Cephalosporins are beta-lactam antibiotics that inhibit the third and final stage of bacterial cell wall synthesis by preferentially binding to specific penicillin-binding proteins (PBPs) that are located inside the bacterial cell wall. Cephalosporins' ability to interfere with PBP-mediated cell wall synthesis ultimately leads to cell lysis. There are five classifications of cephalosporins.

- First generation: active against most gram-positive cocci (including penicillinase-producing staphylococci), but do not have clinically useful activity against enterococci, Listeria, oxacillin-resistant staphylococci, or penicillin-resistant pneumococci
- Second generation: somewhat less active against certain gram-positive cocci than the first generation agents but are more active against certain gram-negative bacilli
- Third generation: stable to the common beta-lactamases of gram-negative bacilli, and highly active against Enterobacteriaceae (E. coli, Proteus mirabilis, indole-positive Proteus, Klebsiella, Enterobacter, Serratia, Citrobacter), Neisseria, and H. influenzae. They are the therapy of choice for gram-negative meningitis due to susceptible Enterobacteriaceae
- Fourth generation: better penetration through the outer membrane of gram-negative bacteria and lower affinity than the third generation cephalosporins for certain chromosomal beta-lactamases of gram-negative bacilli
- Fifth generation: improved gram-positive activity, higher affinity for PBP2a in oxacillin-resistant staphylococci, and activity against MRSA, as well as vancomycin-intermediate Staphylococcus aureus (VISA) and hetero-VISA

New treatment guideline recommendations:

- 2017 Infectious Diseases Society of America's Clinical Practice Guidelines for Healthcare-Associated Ventriculitis and Meningitis.
    - Vancomycin plus an anti-pseudomonal beta-lactam (such as cefepime, ceftazidime, or meropenem) is recommended as empiric therapy for healthcare-associated ventriculitis and meningitis; the choice of empiric beta-lactam agent should be based on local in vitro susceptibility patterns (strong, low).
    - For treatment of infection caused by Pseudomonas species, the recommended therapy is cefepime, ceftazidime, or meropenem (strong, moderate); recommended alternative antimicrobial agents are aztreonam or a fluoroquinolone with in vitro activity (strong, moderate).

Newly approved drugs:

- None identified

Newly approved formulations:

- Non identified

Newly approved generics:

- Approved 02/06/2017: Suprax (cefixime) 500 mg/mL oral suspension; currently available.

Discontinued drugs:

- None identified

FDA Safety Alerts/black box warnings:

- None identified

Pipeline alerts:

Agents pending FDA approval include:

- None identified

References:

1. Calderwood SB. Cephalosporins. Hooper DC, Bloom A. (Ed), UpToDate. Waltham MA. Accessed May 2017.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2016. URL: http://www.clinicalpharmacology-ip.com/. Updated April 2016.
3. Food and Drug Administration. www.fda.gov. Accessed May 2017.
4. Envolve Pharmacy Solutions internal pipeline database. Accessed May 2017.
5. Tunkel AR, Hasbun R, Bhimraj A, et al; 2017 Infectious Diseases Society of America's Clinical Practice Guidelines for Healthcare-Associated Ventriculitis and Meningitis. Clin Infect Dis 2017; 64 (6): e34-e65. doi: 10.1093/cid/ciw861