Drug Class Review Monograph – GPI Class 16 – Anti-infective Agents, Miscellaneous

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

Background:
Anti-infective agents are drugs that can either kill an infectious agent or inhibit it from spreading. Anti-infective agents include:

- **Ketolides –** bind to the bacterial 50S ribosomal subunit and inhibit RNA-dependent protein synthesis. They exhibit concentration-dependent killing (bacteriostatic at low concentrations and bactericidal at high concentrations).
- **Lincosamides** (lincomycin derivatives) **–** inhibit the synthesis of bacterial proteins that are essential to survive. Lincomycin derivatives are reserved for treatment of infections due to susceptible strains of pneumococci, staphylococci, and streptococci.
- **Oxazolidinones –** inhibit protein synthesis by binding to the P site at the ribosomal 50S subunit.
- **Antiprotozoals** – destroy protozoa or inhibit their growth and ability to reproduce.

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 patients with healthcare-associated ventriculitis and meningitis who have experienced anaphylaxis to beta-lactam antimicrobial agents and in whom meropenem is contraindicated, aztreonam or ciprofloxacin is recommended for gram-negative coverage (strong, low).
    - For treatment of infection caused by methicillin-resistant S. aureus, vancomycin is recommended as first-line therapy (strong, moderate), with consideration for an alternative antimicrobial agent if the vancomycin minimal inhibitory concentration (MIC) is ≥1 μg/mL (strong, moderate).
    - For treatment of patients with healthcare-associated ventriculitis and meningitis caused by staphylococci in whom beta-lactam agents or vancomycin cannot be used, linezolid (strong, low), daptomycin (strong, low), or trimethoprim-sulfamethoxazole (strong, low) is recommended, with selection of a specific agent based on in vitro susceptibility testing.
    - 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).
    - For treatment of infection caused by extended-spectrum beta-lactamase–producing gram-negative bacilli, meropenem should be used if this isolate demonstrates in vitro susceptibility (strong, moderate).

- For treatment of infection caused by Acinetobacter species, meropenem is recommended (strong, moderate); for strains that demonstrate carbapenem resistance, colistimethate sodium or polymyxin B (either agent administered by the intravenous and intraventricular routes) is recommended (strong, moderate).

Newly approved drugs:
- None identified

Newly approved formulations:
- None identified

Newly approved generics:
- None identified

Discontinued drugs:
- None identified

FDA Safety Alerts/black box warnings:
- None identified

Pipeline alerts:
Agents pending FDA approval include:
- Carbavance (meropenem/vaborbactam): treatment of complicated urinary tract infections, including acute pyelonephritis; PDUFA: 08/21/2017.
- Solosec (secnidazole): treatment of bacterial vaginosis; PDUFA: 09/17/2017.

References:

1. Weller FW. Antiprotozoal therapies. Leder K. (Ed), UpToDate. Waltham MA. Accessed April 2016.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2017. URL: http://www.clinicalpharmacology-ip.com/. Accessed May 2017.
3. 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
4. Envolve Pharmacy Solutions internal pipeline database. Accessed May 2017.
5. US Food and Drug Administration. WWW.FDA.GOV. Accessed May 2017.