Penicillin Drugs

1. What is Penicillin?

Penicillin is defined as a group of natural or semi-synthetic antibiotics derived from fungi strains of the genus *Penicillium.* Generally, all penicillin share a three-carbon, one-nitrogen, and four-member cyclic amide structure, known as the beta-lactam ring.

2. What are the Penicillin drugs?

The Manual of Clinical Microbiology, 9th edition, identifies penicillin drugs as follows:

Natural Penicillins:

- Benzylpenicillin* (commonly known as penicillin G)
- Benzylpenicilloyl-polylysine (BPP)
- Phenoxymethyl penicillin* (commonly known as penicillin V)

Semi-synthetic Penicillins:

- Methicillin
- Nafcillin
- Cloxacillin*
- Dicloxacillin*
- Ampicillin*
- Amoxicillin*
- Bacampicillin
- Pivampicillin
- Carbenicillin
- Ticarcillin*
- Azlocillin
- Mezlocillin
- Piperacillin
- Hetacillin*

*Penicillins approved for veterinary use

Please be aware that penicillin trade names may vary by region and country. Manufacturers, including repackers, are responsible for knowing whether their drug is penicillin. FDA's "Approved Drug Products with Therapeutic Equivalence Evaluations" (Orange Book) or Drugs@FDA, both of which are located at FDA's website, enable searching by trade name (i.e., proprietary name) and by active ingredient name (i.e., generic or non-proprietary name).

3. Is cross-contamination a concern with penicillin drugs?

Yes, penicillin can be a sensitizing agent that triggers a hypersensitive exaggerated allergic immune response in some people. Differences in the chemically substituted 6-aminopenicillanic acid side chain can generate allergic reactions ranging from skin rashes to life-threatening anaphylaxis.

4. Are there special manufacturing requirements for Penicillin drugs?

Yes, all penicillin finished pharmaceutical manufacturers, including repackers, are required by the CGMP regulations to establish a comprehensive control strategy designed to prevent cross-contamination of other drugs with penicillin. These requirements include:

- 21 CFR 211.42(d): Separation of facility and equipment
- 21 CFR 211.46(d): Separate air handling systems (HVAC)
- 21 CFR 211.176: Test for traces of penicillin where possible exposure exits.

Penicillin Active Pharmaceutical Ingredients (APIs) are also required to be manufactured under CGMPs in accordance with Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act. FDA has published internationally harmonized guidance on the manufacture of APIs; see International Conference on Harmonization (ICH) Q7A *Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients*. Chapter 4, section 4.4 of this guidance describes actions API manufacturers, including those who manufacture or package APIs or penicillin intermediates, are to follow to ensure such material is contained and does not contaminate other drugs.

References:

1. Yao, Joseph D. C., and Robert C. Moellering, Jr. "Antibacterial Agents." Manual of Clinical Microbiology. 9th ed. Washington D.C., ASM, 2007

2. FDA CGMP regulations (21 C.F.R. Parts 210-211)
http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm095412.htm

3. The Federal Food, Drug, & Cosmetic Act 501(a)(2)(B)
http://www.fda.gov/RegulatoryInformation/Legislation/
FederalFoodDrugandCosmeticActFDCAct/default.htm

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