Contains Nonbinding Recommendations

Draft Guidance on Azacitidine

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

Active Ingredient: Azacitidine

Dosage Form; Route: Powder; IV (Infusion), Subcutaneous

Strength: 100 mg/Vial

The proposed drug product should be qualitatively (Q1) and quantitatively (Q2) the same as the corresponding reference listed drug. Bioequivalence may be established based on comparative in vitro testing.

The three criteria to provide in vitro evidence that the test product, when reconstituted as a suspension for subcutaneous administration, demonstrates bioequivalence are:

1. **Physico-chemical Characteristics**. Evidence of equivalence that test and RLD products have the same final physico-chemical characteristics, such as viscosity, osmolality, and pH.
2. **Particle Morphology**. It is recommended that a suitable method for qualitative determination be used to allow observation of particles in the size range in which azacitidine particles are expected to fall. Representative micrographs should also be submitted. These data are supportive, and formal statistical testing is not applicable.
3. **Particle Diameter**. In addition, a suitable method should be used to determine particle diameter. The D10, D50, D90 and span (i.e., (D90–D10)/D50) measurements can be analyzed by using the population bioequivalence (PBE) statistical approach. Refer to the product-specific recommendation for budesonide inhalation suspension for additional information regarding PBE analysis procedures (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM319977.pdf)

The in vitro testing should be performed on ten samples from one lot of the test product and one lot of the reference listed drug.

Waiver request of in-vivo testing: Not applicable

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods web site, available to the public at the following location: http://www.accessdata.fda.gov/scripts/cder/dissolution/. Conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application (ANDA).