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Draft Guidance on Azacitidine

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Additional Comments: The proposed drug product should be qualitatively (Q1)\(^1\) and quantitatively (Q2)\(^2\) the same as the Reference Listed Drug (RLD). Bioequivalence may be established based on comparative in vitro testing of three batches, if available, of both the test product and designated Reference Standard (RS) product.

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

1. **Physicochemical Characteristics.** Evidence that test and RS products have comparable physicochemical properties, 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 be submitted. These data are supportive, and formal statistical testing is not applicable.
3. **In Vitro Drug Release.** Acceptable comparative in vitro drug release of azacitidine from the test and RS formulations. It is recommended that the developed in vitro drug release method to support bioequivalence be based on USP Apparatus 4 (flow-through cell) and be appropriately designed to measure the rapid solubility of the product.
4. **Particle Size Distribution.** Particle size distribution should be compared using the population bioequivalence (PBE) statistical procedure (95% upper confidence bound) based on D\(_{50}\) and SPAN [i.e., (D\(_{90}\)-D\(_{10}\))/D\(_{50}\)]. Refer to the product-specific *Guidance on Budesonide* inhalation suspension for additional information regarding PBE.

**Waiver request of in vivo testing:** Not applicable

**Dissolution test method and sampling times:** Not applicable.

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\(^1\) Q1 (Qualitative sameness) means that the test product uses the same inactive ingredient(s) as the RLD product.

\(^2\) Q2 (Quantitative sameness) means that concentrations of the inactive ingredient(s) used in the test product are within ±5% of those used in the RLD product.