Contains Nonbinding Recommendations

Draft Guidance on Granisetron

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Injection, extended release; subcutaneous

Recommended Studies: One study

Additional comments: The proposed parenteral drug product should be qualitatively (Q1)[1] and quantitatively (Q2)[2] the same as the Reference Listed Drug (RLD) product. Comparative characterization data on triethylene glycol poly(orthoester) in the drug product from a minimum of three batches of both Test and Reference products should be provided. The three batches of Test product should be manufactured from a minimum of three different batches of drug substance, excipients, and container/closure system. Comparative characterization data should include, but is not limited to:

- Polymer composition, structure, molecular weight (e.g., molecular weight profile, weight average, and number average), polydispersity, viscosity, and glass transition temperature.
- Polymer degradation kinetics, including molecular weight distribution profile of the Test and reference products as a function of time upon incubation in aqueous medium (e.g., pH 7.4 buffer) at a defined temperature (i.e., 25 °C or 37 °C).

The following characterization data should also be submitted for three lots of triethylene glycol poly(orthoester) polymer ingredient:

- Molecular weight (e.g., molecular weight profile, weight average, and number average), polydispersity, viscosity, and glass transition temperature
- Contents of the individual hydrolytic products after complete hydrolysis of triethylene glycol poly(orthoester)

Additional characterization data on the triethylene glycol poly(orthoester) polymer may be requested during the review of the ANDA.

In vivo study:

Type of study: Bioequivalence study with pharmacokinetic (PK) endpoints
Design: Single dose, two-period, two-sequence crossover in vivo study
Strength: 10 mg/0.4 mL

[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.

Subjects: Males and non-pregnant females, general population

Analytes to measure (in appropriate biological fluid): Granisetron in plasma

Bioequivalence based on (90% CI): Granisetron

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 website, 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 the test and reference products. Specifications will be determined upon review of the abbreviated new drug application (ANDA).