

Draft Guidance on Clevidipine

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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:	Clevidipine
Dosage Form; Route:	Emulsion; intravenous
Strength:	25 mg/50 mL, 50 mg/100 mL
Recommended Studies:	In vitro studies

I. In vitro option:

To qualify for the in vitro option for this drug product all the following criteria should be met:

- i. The Test and Reference Listed Drug (RLD) formulations are qualitatively¹ and quantitatively² the same (Q1/Q2).
- ii. Acceptable comparative physicochemical characterization of the test and Reference Standard (RS) products. The comparative study should be performed on at least three exhibit batches of both the test and RS products and should include³:

Parameters to measure: Globule size distribution, viscosity, pH, zeta-potential, osmolality, and distribution of clevidipine in the aqueous and oil phase of the formulation.

Bioequivalence based on (95% upper confidence bound): Population bioequivalence (PBE) based on D₅₀ and SPAN (alternatively harmonic intensity weighted average particle diameter and polydispersity index derived from cumulant analysis of the intensity size distribution) for the globule size distribution only (the other parameters do not require PBE analysis). The applicant should provide no fewer than ten data sets from three different batches of both the Test and RS products for PBE analysis. Please refer to the product-specific *Guidance on Budesonide* inhalation suspension for additional information regarding PBE. In addition, the applicant should provide globule size parameters and size distribution histograms upon serial dilution (if applicable) of both the Test and the RS products.

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 the concentrations of the inactive ingredient(s) used in the test product are within $\pm 5\%$ of those used in the RLD product.

³ The manufacturing process for the exhibit batches should be reflective of the manufacturing process to be utilized for commercial batches.

- iii. Acceptable comparative in vitro drug release rate tests from 12 units of each of the Test and RS products.⁴

⁴ Please note that, if determined to be warranted, an in vitro release test (IVRT) method used as part of the quality control specifications may and/or can ultimately be different than the IVRT method developed to support bioequivalence determination, and will be assessed at the time of review of the ANDA.