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Draft Guidance on Pegulicianine Acetate

December 2025

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Active Ingredient:	Pegulicianine acetate
Dosage Form:	Powder
Route:	Intravenous
Strength:	EQ 40 mg Base/vial
Recommended Studies:	Comparative characterization studies to support active ingredient sameness and request for waiver of in vivo bioequivalence study requirements

Comparative characterization studies to support active ingredient sameness:

Pegulicianine acetate is a fluorescent imaging drug that consists of a fluorescence quencher moiety connected to a 20 kDa polyethylene glycol (PEG) and a Cy5 fluorophore via a GGRK peptide linker.[1] Demonstration of active ingredient sameness requires comparative characterization of the test active ingredient and the active ingredient in the reference listed drug (RLD). To assess active ingredient sameness, characterization should be performed on a minimum of three batches of the test active ingredient and the active ingredient extracted from three batches of the RLD. The active ingredient sameness can be established by demonstrating equivalence in chemical composition and physicochemical properties of the active ingredient.

[1] Whitley MJ, et. Al. A mouse-human phase 1 co-clinical trial of a protease-activated fluorescent probe for imaging cancer, *Sci Transl Med*. 2016, 8(320):320ra4. doi:10.1126/scitranslmed.aad0293.

Comparative characterization of the test active ingredient and the active ingredient in the RLD should be conducted using properly validated analytical methods which may include but not be limited to the following:

a. Spectral analysis: mass spectrometry (MS), nuclear magnetic resonance (NMR) spectroscopy, Fourier transform infrared (FTIR) spectroscopy, ultraviolet/visible (UV/Vis) absorbance and fluorescence spectroscopy
b. Molecular weight determination by size exclusion chromatography coupled with multi-angle light scattering (SEC-MALS)
c. Amino acid analysis and peptide sequence analysis
d. Liquid chromatography
e. Optical purity by specific rotation
f. Elemental analysis

Request for waiver of in vivo bioequivalence study requirements:

To qualify for a waiver from the requirement for submission of evidence of in vivo bioequivalence on the basis that bioequivalence is self-evident under 21 CFR 320.22(b)(1), a generic pegulicianine acetate intravenous powder product should be qualitatively (Q1)[2] and quantitatively (Q2)[3] the same as the RLD.

An applicant may seek approval of a drug product intended for parenteral use that differs from the RLD in preservative, buffer, or antioxidant provided that the applicant identifies and characterizes the differences and provides information demonstrating that the differences do not affect the safety or efficacy of the test product.[4]

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[2] Q1 (Qualitative sameness) means that the test product uses the same inactive ingredient(s) as the RLD.
[3] 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.
[4] 21 CFR 314.94(a)(9)(iii).