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Gadoteridol Injection

» Gadoteridol Injection is a sterile solution of Gadoteridol in Water for Injection. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of gadoteridol ($C_{17}H_{29}GdN_4O_7$). It may contain buffers and stabilizers. Gadoteridol Injection intended for intravenous use contains no antimicrobial agents.

Packaging and storage—Preserve in single-dose containers as described in *Packaging and Storage Requirements ⟨659⟩, Injection Packaging*, preferably of Type I glass. Store at controlled room temperature, and protect from light.

Labeling—Label containers of Injection intended for intravenous injection to direct the user to examine the product to ensure that all solids are dissolved, to discard the product if solids persist, and to discard any unused portion remaining in the container.

USP Reference standards ⟨11⟩—

USP Gadoteridol RS

USP Gadoteridol Related Compound A RS

10-(2-hydroxypropyl)-1,4,7,10-tetraazacyclododecane-1,4,7-triaacetic acid.

$C_{17}H_{32}N_4O_7$ 404.46

Identification—

Change to read:

A: ▲*Spectroscopic Identification Tests ⟨197⟩, Ultraviolet-Visible Spectroscopy: 197U*▲ (CN 1-May-2020) —

Solution: 10 mg per mL.

Medium: water.

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay*.

Bacterial Endotoxins Test ⟨85⟩ —It contains not more than 8.3 USP Endotoxin Units per mL of Gadoteridol Injection.

pH ⟨791⟩: between 6.5 and 8.0.

Particulate Matter in Injections ⟨788⟩: meets the requirements for small-volume injections.

Limit of free gadolinium (III)—

Buffer solution, *Mobile phase*, and *Diluent*—Proceed as directed for *Test 1* in the *Chromatographic purity* test under *Gadoteridol*.

Standard solution—Prepare a solution of gadolinium (Gd III) acetate in water to obtain a solution having a known concentration of about 0.4 mg of gadolinium acetate per mL. Transfer 1.0 mL of the solution to a 10-mL volumetric flask, dilute with *Diluent* to volume, and mix. Transfer 1.0 mL of this solution to a small vial, add 3.0 mL of *Diluent*, and mix.

Test solution—Transfer an accurately measured volume of Injection, equivalent to about 150 mg of gadoteridol, to a small vial, dilute with *Diluent* to 5.0 mL, and mix. Immediately place in a bath maintained at about 5°.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a fluorometric detector operating at an excitation wavelength of 275 nm and an emission wavelength of 314 nm and a 4.6-mm × 25-cm column that contains 5-µm packing L1. The flow rate is about 1 mL per minute. Chromatograph the *Standard solution*, and record the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 5.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms for about 1.5 times the retention time of the gadoteridol peak, and measure the peak responses. Calculate the percentage, by weight, of free gadolinium (III) in the volume of Injection taken by the formula:

$$500(157.25/334.38)(C/VP)(r_U/r_S)$$

in which 157.25 and 334.38 are the molecular weights of gadolinium and gadolinium acetate, respectively; C is the concentration, in mg per mL, of gadolinium (Gd III) acetate, calculated on the anhydrous basis, in the *Standard solution; V* is the volume, in mL, of Injection taken for the *Test solution; P* is the labeled potency of gadoteridol, in mg per mL, in the Injection; and r_U and r_S are the peak responses for free gadolinium (III) obtained from the *Test solution* and the *Standard solution*, respectively: not more than 0.02% is found.

Limit of gadoteridol related compound A—

Buffer solution, *Mobile phase*, *Cupric acetate solution*, *Standard stock solution*, *Standard solution*, and *Chromatographic system*—Proceed as directed for the *Limit of gadoteridol related compound A* test under *Gadoteridol*.

Test solution—Transfer an accurately measured volume of Injection, equivalent to about 30 mg of gadoteridol, to a test tube, dilute with chilled *Buffer solution* to 1.0 mL, and mix. Add 1.0 mL of chilled *Cupric acetate solution*, mix on a vortex mixer for about 10 seconds, and immediately inject as directed for *Procedure*.

Procedure—Separately inject equal volumes (about 50 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the percentage of gadoteridol related compound A in the Injection by the formula:

$$0.2(C/VP)(r_U/r_S)$$

in which C is the concentration, in µg per mL, of USP Gadoteridol Related Compound A RS in the *Standard solution*; V is the volume, in mL, of Injection taken for the *Test solution*; P is the labeled potency, in mg per mL, of gadoteridol in the Injection; and r_U and r_S are the peak responses of gadoteridol related compound A in the *Test solution* and the *Standard solution*, respectively: not more than 0.02% is found.

Other requirements—It meets the requirements under *Injections and Implanted Drug Products* ⟨1⟩.

Assay—

Buffer solution, *Mobile phase*, *Standard preparation*, and *Chromatographic system*—Proceed as directed in the *Assay* under *Gadoteridol*.

Assay preparation—Transfer an accurately measured volume of Injection, equivalent to about 150 mg of gadoteridol, to a 250-mL volumetric flask, dilute with *Buffer solution* to volume, and mix.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg per mL, of gadoteridol ($C_{17}H_{29}GdN_4O_7$) in the volume of Injection taken by the formula:

$$250(C/V)(r_U/r_S)$$

in which C is the concentration, in mg per mL, of USP Gadoteridol RS in the *Standard preparation*; V is the volume of Injection taken, in mL; and r_U and r_S are the gadoteridol peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
GADOTERIDOL INJECTION	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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