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Diatrizoate Meglumine and Diatrizoate Sodium Injection

» Diatrizoate Meglumine and Diatrizoate Sodium Injection is a sterile solution of Diatrizoate Meglumine and Diatrizoate Sodium in Water for Injection, or a sterile solution of Diatrizoic Acid in Water for Injection prepared with the aid of Sodium Hydroxide and Meglumine. It contains not less than 95.0 percent and not more than 105.0 percent of the labeled amounts of diatrizoate meglumine ($C_{11}H_9I_3N_2O_4 \cdot C_7H_{17}NO_5$) and of iodine (I). It may contain small amounts of suitable buffers and of Edetate Calcium Disodium or Edetate Disodium as a stabilizer. Diatrizoate Meglumine and Diatrizoate Sodium Injection intended for intravascular use contains no antimicrobial agents.

Packaging and storage—Preserve either in single-dose containers, preferably of Type I or Type III glass, protected from light or, where intended for administration with a pressure injector through a suitable transfer connection, in similar glass 500-mL or 1000-mL bottles, protected from light.

Labeling—Label containers of Injection intended for intravascular injection, where packaged in single-dose containers, to direct the user to discard any unused portion remaining in the container or, where packaged in bulk bottles to state, "Bulk Container—only for sterile filling of pressure injectors," to state that it contains no antimicrobial preservatives, and to direct the user to discard any unused portion remaining in the container after 6 hours. Indicate also in the labeling of bulk bottles that a pressure injector is to be charged with a dose just prior to administration of the Injection. Label containers of Injection intended for other than intravascular injection to show that the contents are not intended for intravascular injection.

USP Reference standards ⟨11⟩—
USP Diatrizoic Acid RS
USP Diatrizoic Acid Related Compound A RS

5-Acetamido-3-amino-2,4,6-triiodobenzoic acid.
$C_9H_7I_3N_2O_3$ 571.88

Identification—

A: Dilute a volume of Injection, if necessary, with a 0.8 in 1000 solution of sodium hydroxide in methanol to obtain a test solution having a concentration of 1 mg per mL. The test solution responds to the *Thin-layer Chromatographic Identification Test ⟨201⟩*, the Standard solution being prepared at a concentration of 1 mg of USP Diatrizoic Acid RS per mL in a 0.8 in 1000 solution of sodium hydroxide in methanol, the solvent mixture being a mixture of chloroform, methanol, and ammonium hydroxide (20:10:2), and short-wavelength UV light being used to locate the spots.

B: Evaporate a volume of Injection, equivalent to about 500 mg of diatrizoate meglumine and diatrizoate sodium, to dryness, and heat the residue so obtained in a suitable crucible: violet vapors are evolved.

Bacterial Endotoxins Test ⟨85⟩ —It contains not more than 1.8 USP Endotoxin Units per mL for Injections containing less than 60% of diatrizoate meglumine, and not more than 3.6 USP Endotoxin Units for Injections containing 60% or more of diatrizoate meglumine.

pH ⟨791⟩: between 6.0 and 7.7.

Free aromatic amine—Transfer an accurately measured volume of Injection, equivalent to about 1 g of diatrizoate meglumine and diatrizoate sodium, to a 50-mL volumetric flask. Dilute with water to 5 mL, and add 10 mL of 0.1 N sodium hydroxide. To a second 50-mL volumetric flask transfer 4 mL of water, 10 mL of 0.1 N sodium hydroxide, and 1.0 mL of a Standard solution prepared by dissolving a suitable quantity of USP Diatrizoic Acid Related Compound A RS in 0.1 N sodium hydroxide. Use 0.2 mL of 0.1 N sodium hydroxide for each 5.0 mg of Standard, and dilute with water to obtain a known concentration of 500 µg per mL. Proceed as directed in the test for *Free aromatic amine* under *Diatrizoate Meglumine*, beginning with "To a third 50-mL volumetric flask add 5 mL of water".

Iodine and iodide—Transfer an accurately measured volume of Injection, equivalent to about 2.0 g of the total of diatrizoate meglumine and diatrizoate sodium, to a 50-mL centrifuge tube provided with a stopper. Dilute with water to 24 mL. Add 5 mL of toluene and 5 mL of 2 N sulfuric acid, shake, and centrifuge: the toluene layer shows no red color. Add 1 mL of sodium nitrite solution (1 in 50), shake, and centrifuge: any red color in the toluene layer is not darker than that obtained when a volume of potassium iodide solution (1 in 4000), containing a quantity of iodide corresponding to 0.02% of the weight of diatrizoate meglumine and diatrizoate sodium in the volume of Injection taken is diluted with water to 24 mL and substituted for the solution under test (0.02% of iodide).

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

Assay for diatrizoate meglumine—Pipet 5 mL of Injection into a 10-mL volumetric flask, add water to volume, and mix. Determine the angular rotation (see *Optical Rotation ⟨781⟩*) of the diluted Injection, using a 100-mm tube. Calculate the content, in mg per mL, of $C_{11}H_9I_3N_2O_4 \cdot C_7H_{17}NO_5$ in the Injection by the formula:

$$2000a/6.01$$

in which *a* is the observed angular rotation, in degrees, corrected for the blank, and the factor 6.01 is the specific rotation, in degrees, of diatrizoate meglumine.

Assay for iodine—Transfer an accurately measured volume of Injection, equivalent to about 4 g of the total of diatrizoate meglumine and diatrizoate sodium, to a 50-mL volumetric flask, dilute with water to volume, and mix. Pipet 5 mL of this solution into a glass-stoppered, 125-mL conical flask, add 30 mL of 1.25 N sodium hydroxide and 500 mg of powdered zinc, connect the flask to a reflux condenser, and reflux the mixture for 1 hour. Cool the flask to room temperature, rinse the condenser with 20 mL of water, disconnect the flask from the condenser, and filter the mixture. Rinse the flask and filter thoroughly, adding the rinsings to the filtrate. Add 5 mL of glacial acetic acid and 1 mL of tetrabromophenolphthalein ethyl ester TS, and titrate with 0.05 N silver nitrate VS until the yellow precipitate just turns green. Each mL of 0.05 N silver nitrate is equivalent to 6.345 mg of iodine.

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

Topic/Question	Contact	Expert Committee
DIATRIZOATE MEGLUMINE AND DIATRIZOATE SODIUM INJECTION	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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