Diatrizoate Meglumine and Diatrizoate Sodium Solution

Type of Posting	Notice of Intent to Revise
Posting Date	26-Mar-2021
Targeted Official Date	To Be Determined, Revision Bulletin
Expert Committee	Small Molecules 4

In accordance with the Rules and Procedures of the Council of Experts and the Pending Monograph Guideline, this is to provide notice that the Small Molecules 4 Expert Committee intends to revise the Diatrizoate Meglumine and Diatrizoate Sodium Solution monograph. Additionally, minor editorial changes have been made to update the monograph to current *USP* style.

Based on the supporting documentation received from a manufacturer awaiting FDA approval, the Expert Committee proposes to revise the drug product description in the *Definition* to add "It can also be a solution of Diatrizoate Meglumine and Diatrizoate Sodium in Purified Water." in the Diatrizoate Meglumine and Diatrizoate Sodium Solution monograph.

The proposed revision is contingent on FDA approval of a product that meets the proposed monograph specifications. The proposed revision will be published as a Revision Bulletin and an official date will be assigned to coincide as closely as possible with the FDA approval of the associated product.

See below for additional information about the proposed text.[1]

Should you have any questions, please contact Gerald J. Hsu, Senior Scientific Liaison (240-221-2097 or gdh@usp.org).

[1] This text is not the official version of a *USP–NF* monograph and may not reflect the full and accurate contents of the currently official monograph. Please refer to the current edition of the *USP–NF* for official text.

USP provides this text to indicate changes that we anticipate will be made official once the product subject to this proposed revision under the Pending Monograph Program receives FDA approval. Once FDA approval is granted for the associated revision request, a Revision Bulletin will be posted that will include the changes indicated herein, as well as any changes indicated in the product's final approval, combined with the text of the monograph as effective on the date of approval. Any revisions made to a monograph under the Pending Monograph Program that are posted without prior publication for comment in the *Pharmacopeial Forum* must also meet the requirements outlined in the USP Guideline on Use of Accelerated Processes for Revisions to the *USP–NF*.

Notice of Intent to Revise
Official: To Be Determined

Diatrizoate Meglumine and Diatrizoate Sodium Solution

Change to read:

DEFINITION

Diatrizoate Meglumine and Diatrizoate Sodium Solution is a solution of Diatrizoic Acid in Purified Water prepared with the aid of Meglumine and Sodium Hydroxide.

▲It can also be a solution of Diatrizoate Meglumine and Diatrizoate Sodium in Purified Water.▲ (TBD)

It contains NLT 95.0% and NMT 105.0% 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, Edetate Disodium, and flavoring agents.

IDENTIFICATION

- **A. Thin-Layer Chromatographic Identification Test ⟨201⟩**

  Diluent: Sodium hydroxide in methanol (0.8 in 1000)

  Standard solution: 1 mg/mL of USP Diatrizoic Acid RS in *Diluent*

  Sample solution: 1 mg/mL from a volume of Solution, in *Diluent*

  Developing solvent system: Methanol, chloroform, and ammonium hydroxide (10:20:2)

  Analysis

  Samples: *Sample solution* and *Standard solution*

  Locate the spots using short-wavelength UV light.

  Acceptance criteria: Meets the requirements

- **B.**

  Sample solution: Nominally 500 mg of diatrizoate meglumine and diatrizoate sodium from a volume of Solution

  Analysis: Evaporate the *Sample solution* to dryness and heat the residue so obtained in a crucible.

  Acceptance criteria: Violet vapors are evolved.

ASSAY

- **Diatrizoate Meglumine**

  Sample stock solution: 6 mg/mL of diatrizoate meglumine and diatrizoate sodium prepared as follows. Pipet a volume of Solution equivalent to 1.5 g of diatrizoate meglumine and diatrizoate sodium to a 250-mL volumetric flask, and dilute with water to volume.

  Sample solution: Pipet 10 mL of the *Sample stock solution* into a glass-stoppered, 250-mL flask. Add 4 mL of 2 N sulfuric acid and 20 mL of sodium metaperiodate solution (1 in 200). Insert the stopper, and set aside in the dark for 1 h. Add 50 mL of water, mix, and add 10 mL of potassium iodide TS. Insert the stopper quickly and mix by swirling for 20 s.

  Titrimetric system

  Mode: Direct titration

  Titrant: 0.1 N sodium thiosulfate VS

  Endpoint detection: Visual

  Analysis: Immediately titrate the *Sample solution* with *Titrant*, using 3 mL of starch TS. Perform a blank determination, and make any necessary correction. Each milliliter of 0.1 N sodium thiosulfate is equivalent to 10.11 mg of diatrizoate meglumine ($C_{11}H_9I_3N_2O_4 \cdot C_7H_{17}NO_5$).

  Acceptance criteria: 95.0%–105.0%

- **Iodine**

  Sample stock solution: 0.08 g/mL of the total of diatrizoate meglumine and diatrizoate prepared as follows. Transfer an accurately measured volume of Solution, equivalent to 4 g of the total of diatrizoate meglumine and diatrizoate sodium, to a 50-mL volumetric flask, and dilute with water to volume, and mix.

  Sample solution: Pipet 5 mL of *Sample stock 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 h. 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.

  Titrimetric system

  Mode: Direct titration

  Titrant: 0.05 N silver nitrate VS

  Endpoint detection: Visual

  Analysis: Titrate the *Sample solution* with *Titrant* until the yellow precipitate just turns green. Each milliliter of 0.05 N silver nitrate is equivalent to 6.345 mg of iodine (I).

  Acceptance criteria: 95.0%–105.0%

SPECIFIC TESTS

- **pH** ⟨791⟩**:** 6.0–7.6
- **Iodine and Iodide**

  Solution A: Sodium nitrite solution (1 in 50)

  Standard stock solution: Potassium iodide solution (1 in 4000)

  Standard solution: Combine 2.0 mL of *Standard stock solution* and 22 mL of water in a stoppered 50-mL centrifuge tube.

  Sample solution: Dilute a volume of Solution, equivalent to 2 g of diatrizoate meglumine and diatrizoate sodium, with water to 24 mL in a stoppered 50-mL centrifuge tube. Shake to promote dissolution.

  Analysis

  Samples: *Standard solution* and *Sample solution*

  To each of the *Samples*, 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 *Solution A*, shake, and centrifuge.

  Acceptance criteria: Any red color in the toluene layer of the *Sample solution* is not darker than the toluene layer of the *Standard solution*.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers.
- **Labeling:** Label the container to indicate that the contents are not intended for parenteral use.
- **USP Reference Standards** ⟨11⟩

  USP Diatrizoic Acid RS

Page Information:

Not Applicable

Current DocID: