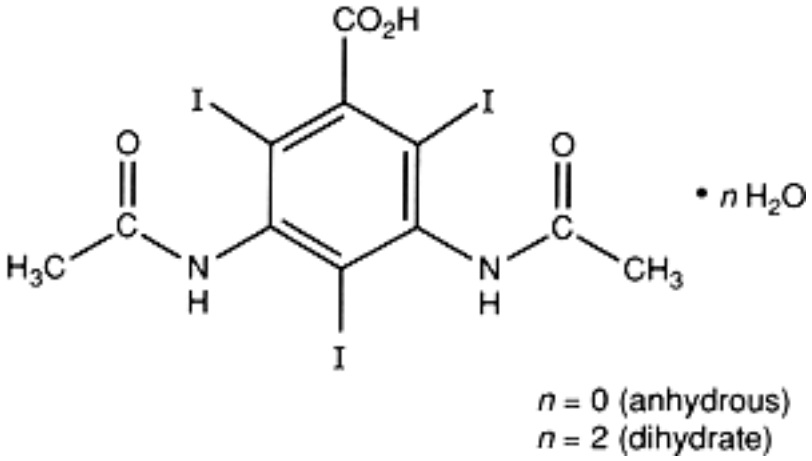
Amidotrizoic acid (Acidum amidotrizoicum)

Amidotrizoic acid, anhydrous

Amidotrizoic acid, dihydrate



$C_{11}H_9I_3N_2O_4$ (anhydrous)

$C_{11}H_9I_3N_2O_4,2H_2O$ (dihydrate)

Relative molecular mass. 613.9 (anhydrous); 649.9 (dihydrate).

Chemical name. 3,5-Diacetamido-2,4,6-triiodobenzoic acid; 3,5-bis(acetylamino)-2,4,6-triiodobenzoic acid; CAS Reg. No. 117-96-4 (anhydrous).

3,5-Diacetamido-2,4,6-triiodobenzoic acid dihydrate; 3,5-bis(acetylamino)-2,4,6-triiodobenzoic acid dihydrate; CAS Reg. No. 50978-11-5 (dihydrate).

Other name. Diatrizoic acid.

Description. A white or almost white, crystalline powder; odourless.

Solubility. Very slightly soluble in water and ethanol (~750 g/l) TS; soluble in dimethylformamide R; sparingly soluble in methanol R; practically insoluble in ether R; dissolves in solutions of alkali hydroxides.

Category. Used in the preparation of meglumine amidotrizoate as a radiocontrast medium.

Storage. Amidotrizoic acid should be kept in a well-closed container, protected from light.

Labelling. The designation on the container of amidotrizoic acid should state whether the substance is the dihydrate or the anhydrous form.

Requirements

Amidotrizoic acid contains not less than **98.0%** and not more than the equivalent of **102.0%** of $C_{11}H_9I_3N_2O_4$, calculated with reference to the dried substance.

Identity tests

• Either test A alone or tests B, C, and D may be applied.

A. Carry out the examination as described under 1.7 Spectrophotometry in the infrared region. Previously dry the dihydrate of amidotrizoic acid at 105 °C for 4 hours. The infrared absorption spectrum is concordant with the spectrum obtained from amidotrizoic acid RS or with the *reference spectrum* of amidotrizoic acid.

B. Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography, using silica gel R4 as the coating substance and a mixture of 20 volumes of chloroform R, 10 volumes of methanol R, and 2 volumes of ammonia (~260 g/l) TS as the mobile phase. Apply separately to the plate 10 µl of each of two solutions in a mixture of 0.8 g of sodium hydroxide R dissolved in 1000 mL of methanol R containing (A) 1 mg of Amidotrizoic acid per mL and (B) 1 mg of amidotrizoic acid RS per mL. After removing the plate from the chromatographic chamber, allow it to dry in air, and examine the chromatogram in ultraviolet light (254 nm).

The principal spot obtained with solution A corresponds in position, appearance, and intensity with that obtained with solution B.

C. Heat 0.5 g in a suitable crucible; violet vapours are evolved.

D. Use 10 mg; it yields the reaction described for the identification of primary aromatic amines under 2.1 General identification tests, producing a red-violet precipitate.

Heavy metals. Suspend 10 g in 10 mL of water and with stirring add slowly 1.5 mL of sodium hydroxide (~400 g/l) TS. When dissolved, adjust the pH to between 7.0 and 7.5 with sodium hydroxide (~80 g/l) TS or hydrochloric acid (~70 g/l) TS, and dilute with water to 20 mL. Use 2 mL of this solution and determine the heavy metals content as described under 2.2.3 Limit test for heavy metals, Method A; not more than 20 µg/g. (Keep the remaining solution for "Iodine and iodides".)

Halides. Dissolve 2.5 g in a mixture of 20 mL of water and 2.5 mL of ammonia (~100 g/l) TS. Add 20 mL of nitric acid (~130 g/l) TS, dilute with sufficient water to produce 100 mL, allow to stand for 15 minutes with occasional shaking, and filter. Eliminate the first 10 mL of the filtrate and proceed with 25 mL of the filtrate as described under "2.2.1 Limit test for chlorides"; the content of halides, expressed as chlorides, does not exceed 35 µg/g.

Iodine and iodides. Place 4 mL of the solution prepared above for "Heavy metals" in a 50-mL centrifuge tube and add 20 mL of water, 5 mL of toluene R, and 5 mL of sulfuric acid (~100 g/l) TS. Shake and centrifuge; the toluene layer shows no red colour. Add 2 mL of sodium nitrite (10 g/l) TS, shake well, and centrifuge. Similarly prepare a reference solution containing 0.5 mg of potassium iodide R in 22 mL of water. Any red colour in the toluene layer is no darker than that obtained with the reference solution (200 µg I/g).

Sulfated ash. Not more than 1.0 mg/g.

Loss on drying. Dry at 105 °C for 4 hours; anhydrous Amidotrizoic acid loses not more than 10 mg/g and the dihydrate loses not less than 45 mg/g and not more than 70 mg/g.

Primary aromatic amines. Dissolve about 0.2 g, accurately weighed, in a mixture of 5 mL of water and 1 mL of sodium hydroxide (~80 g/l) TS. Add 4 mL of sodium nitrite (10 g/l) TS and 10 mL of hydrochloric acid (1 mol/l) VS, shake, and allow to stand for 2 minutes. Add 5 mL of ammonium sulfamate (25 g/l) TS, shake well, allow to stand for 1 minute, add 0.4 mL of 1-naphthol/ethanol TS and 15 mL of sodium hydroxide (~80 g/l) TS, and dilute with water to 50 mL.

Measure the absorbance at about 485 nm against a solvent cell containing the reagents prepared in a similar manner; the absorbance is not greater than 0.15.

Assay. Place about 0.3 g, accurately weighed, in a 125-mL conical flask and add 30 mL of sodium hydroxide (50 g/l) TS and 0.5 g of zinc R powder. Connect the flask to a reflux condenser and boil for 1 hour. Cool the flask to room temperature, rinse the condenser with 20 mL of water into the flask, and filter the mixture. Rinse the flask and the filter thoroughly and add the rinse liquids to the filtrate. Add 5 mL of glacial acetic acid R and 1 mL of tetrabromophenolphthalein ethyl ester TS and titrate with silver nitrate (0.05 mol/l) VS until the yellow precipitate just changes to green.

Each mL of silver nitrate (0.05 mol/l) VS is equivalent to 10.23 mg of $C_{11}H_9I_3N_2O_4$.

Additional requirement for Amidotrizoic acid for parenteral use

Complies with the monograph for "Parenteral preparations".

Pyrogens. Carry out the test as described under 3.5 Test for pyrogens, injecting, per kg of the rabbit's mass, a solution in sterile water R containing 0.6 g of Amidotrizoic acid in not more than 5 mL.