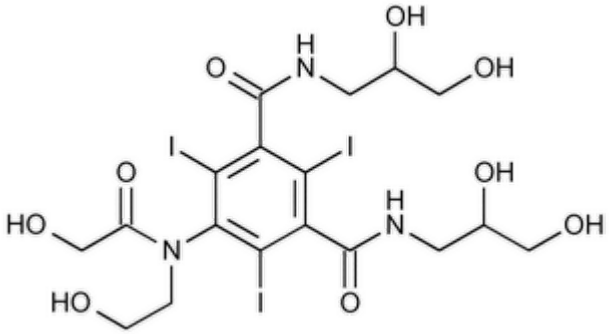
Interim Revision Announcement
Official: May 1, 2021

Ioversol

Change to read:



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$C_{18}H_{24}I_3N_3O_9$ ▲807.12▲ (IRA 1-May-2021)
1,3-Benzenedicarboxamide, *N,N′*-bis(2,3-dihydroxypropyl)-5-[(hydroxyacetyl)(2-hydroxyethyl)amino]-2,4,6-triiodo-;
N,N′-Bis(2,3-dihydroxypropyl)-5-[*N*-(2-hydroxyethyl)glycolamido]-2,4,6-triiodoisophthalamide [87771-40-2]; UNII: N3RIB7X24K.

DEFINITION
Ioversol contains NLT 97.0% and NMT 101.0% of ioversol ($C_{18}H_{24}I_3N_3O_9$), calculated on the anhydrous basis.

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K
- **B.**

Sample: About 500 mg

Analysis: Heat the *Sample* in a crucible.

Acceptance criteria: Violet vapors are evolved.

ASSAY

Change to read:

- **Procedure**

Sample solution: Transfer about 500 mg of Ioversol to a glass-stoppered 125-mL conical flask, add 12 mL of 5 N sodium hydroxide, 20 mL of water, and 1 g of powdered zinc. Connect the conical flask to a reflux condenser, and reflux for 30 min. 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 40 mL of 2 N sulfuric acid, and titrate immediately.

Titrimetric system

Mode: Direct titration

Titrant: 0.05 N silver nitrate VS

Endpoint detection: Potentiometric

Electrode system: Silver–silver chloride double junction reference electrode and silver billet electrode

Analysis

Sample: *Sample solution*

Titrate with the *Titrant* determining the endpoint potentiometrically. Each milliliter of 0.05 N silver nitrate is equivalent to 13.45 mg of ioversol ($C_{18}H_{24}I_3N_3O_9$).

▲**Acceptance criteria:** 97.0%–101.0% on the anhydrous basis▲ (IRA 1-May-2021)

IMPURITIES

● **Residue on Ignition** ⟨281⟩**:** NMT 0.1%

Change to read:

● **Iodine and Iodide**

Standard solution: Transfer 2 mL of 0.25 mg/mL of potassium iodide in water to a 50-mL glass-stoppered cylinder, and add 13 mL of water.

Sample solution: Dissolve 2.0 g of Ioversol in water in a 50-mL glass-stoppered cylinder, and dilute with water to 15 mL.

Analysis: To the 50-mL glass-stoppered cylinders with the *Standard solution* and *Sample solution*, add 5 mL each of diluted sulfuric acid and toluene. Shake vigorously, and allow the layers to separate. The toluene layer shows no red color. Add 1 mL of 20 mg/mL of sodium nitrite solution to both the *Standard solution* and *Sample solution*, and shake.

Acceptance criteria: Any red color in the toluene layer of the *Sample solution* is not darker than that of the *Standard solution* (▲NMT▲ (IRA 1-May-2021) 0.02% of iodide).

Change to read:

● **Organic Impurities**

Mobile phase: Acetonitrile and water (0.5: 99.5)

Standard solution: 1.0 µg/mL of ▲USP Iohexol Related Compound B RS▲ (IRA 1-May-2021) and 5.0 µg/mL of USP Ioversol Related Compound B RS in water

Sample solution: 1000 µg/mL of Ioversol in water

Chromatographic system

(See *Chromatography* ⟨621⟩*, System Suitability*.)

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; packing L7

Temperature: 35 ± 0.5°

▲▲ (IRA 1-May-2021)

Flow rate: 1 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

[Note—See *Table 1* for relative retention times.]

Suitability requirements

Resolution: NLT 2.0 between ▲iohexol related compound B▲ (IRA 1-May-2021) and ioversol related compound B

Relative standard deviation: NMT 5%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each ▲▲ (IRA 1-May-2021) related compound in the portion of Ioversol taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of each related compound from the *Sample solution*

r_S = average peak response of each corresponding related compound from the *Standard solution*

C_S = concentration of ▲USP Iohexol Related Compound B RS▲ (IRA 1-May-2021) or USP Ioversol Related Compound B RS in the *Standard solution* (µg/mL)

C_U = concentration of Ioversol in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Ioversol	1.0	—
▲Iohexol related compound B	1.8▲ (IRA 1-May-2021)	0.10
Ioversol related compound B	▲2.1▲ (IRA 1-May-2021)	0.50

SPECIFIC TESTS

● **WATER DETERMINATION** ⟨921⟩*, Method I*: NMT 5%

ADDITIONAL REQUIREMENTS

● **PACKAGING AND STORAGE:** Preserve in well-closed containers. Store at 25°, excursions permitted between 15° and 30°.

Change to read:

● **USP REFERENCE STANDARDS** ⟨11⟩

▲ USP Iohexol Related Compound B RS

5-Amino-*N*,*N*'-bis(2,3-dihydroxypropyl)-2,4,6-triiodoisophthalamide.

$C_{14}H_{18}I_3N_3O_6$ 705.03▲ (IRA 1-May-2021)

USP Ioversol RS

▲▲ (IRA 1-May-2021)

USP Ioversol Related Compound B RS

▲*N*,*N*'-Bis(2,3-dihydroxypropyl)-5-[{(*N*-(2-hydroxyethyl)amino}-2-oxoethoxy]-2,4,6-triiodoisophthalamide; also known as *N*,*N*'-Bis(2,3-dihydroxypropyl)-5-[(*N*-(2-hydroxyethyl)-carbamoyl)methoxy]-2,4,6-triiodoisophthalamide.

$C_{18}H_{24}I_3N_3O_9$ 807.12▲ (IRA 1-May-2021)

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