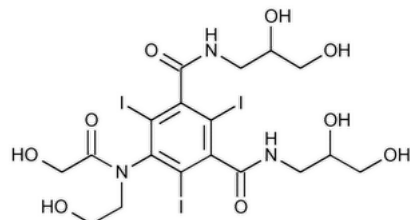


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Ioversol

Change to read:



$C_{18}H_{24}I_3N_3O_9$ ▲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 CAS RN®: 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

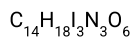
• **PACKAGING AND STORAGE:** Preserve in well-closed containers. Store at 25°, excursions permitted between 15° and 30°.

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.



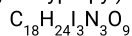
705.03 ▲ (IRA 1-May-2021)

[USP loversol RS](#)

▲ ▲ (IRA 1-May-2021)

[USP loversol 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.



807.12 ▲ (IRA 1-May-2021)

Auxiliary Information - Please [check for your question in the FAQs](#) before contacting USP.

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

Chromatographic Database Information: [Chromatographic Database](#)

Most Recently Appeared In:

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