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Ioversol Injection

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click www.uspnf.com/rb-ioversol-inj-20241227.

DEFINITION

Ioversol Injection is a sterile solution of Ioversol in Water for Injection. It contains NLT 95.0% and NMT 105.0% of the labeled amount of Ioversol ($C_{18}H_{24}I_3N_3O_9$) and iodine (I). It may contain small amounts of suitable buffers and Edetate Calcium Disodium as a stabilizer. Ioversol

Injection intended for intravascular use contains no antimicrobial agents.

IDENTIFICATION

• **A.** The IR absorption spectrum of a portion of Injection exhibits maxima only at the same wavelengths, when measured using a zinc sulfide cell with a thickness of 0.01–0.2 mm, as that of a similar preparation of [USP Ioversol RS](#).

• **B.**

Analysis: Heat about 1 mL of Injection in a crucible.

Acceptance criteria: Violet vapors are evolved.

ASSAY

• PROCEDURE

Sample solution: Transfer a volume of Injection, nominally equivalent to 500 mg of Ioversol, to a suitable glass-stoppered flask, add 12 mL of 5 N [sodium hydroxide](#), 20 mL of [water](#), and 1 g of powdered [zinc](#). Connect the flask to a reflux condenser, and reflux for 30 min. Cool the flask to room temperature, and 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: 95.0%–105.0% of the labeled amount of Ioversol

IMPURITIES

Change to read:

• ORGANIC IMPURITIES

Mobile phase: [Acetonitrile](#) and [water](#) (0.5: 99.5)

Standard solution: 1.5 µg/mL of [USP Iohexol Related Compound B RS](#) and 15 µg/mL of [USP Ioversol Related Compound B RS](#) in [water](#)

Sample solution: Nominally 1000 µg/mL of Ioversol from Injection diluted with [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°

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 and Ioversol related compound B

Relative standard deviation: NMT 5%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each related compound in the portion of Injection 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](#) or [USP Ioversol Related Compound B RS](#) in the *Standard solution* (µg/mL)

C_U = nominal 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	0.15
Ioversol related compound B	2.1	▲2.0▲ (RB 1-Jan-2025)

SPECIFIC TESTS

- **pH (791):** 6.0–7.4
- **BACTERIAL ENDOTOXINS TEST (85):** NMT 1.4 USP Endotoxin Units/mL of Injection
- **OTHER REQUIREMENTS:** It meets the requirements in [Injections and Implanted Drug Products \(1\)](#).

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in single-dose containers, preferably of Type I glass, protected from light.
- **LABELING:** Label containers of Injection intended for intravascular injection to direct the user to discard any unused portion remaining in the container.

• 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

[USP Ioversol RS](#)

[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

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

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

Chromatographic Database Information: [Chromatographic Database](#)

Most Recently Appeared In:

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