

Ioversol Injection

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

Change to read:

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[▲] (IRA 1-May-2021) 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[▲] (IRA 1-May-2021)

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▲ (IRA 1-May-2021) 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°

▲ (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 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▲ (IRA 1-May-2021) 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▲ (IRA 1-May-2021)	0.15
Ioversol related compound B	▲2.1▲ (IRA 1-May-2021)	1.5

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

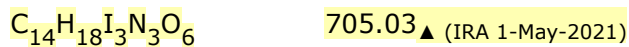
- **PACKAGING AND STORAGE:** Preserve in single-dose containers, preferably of Type I glass, protected from light.
- **LABELING:** Label containers of Injection intended for intravascular injection to direct the user to discard any unused portion remaining in the container.

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.

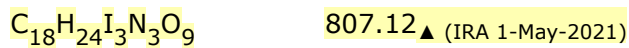


[USP Ioversol RS](#)

▲ (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.



Page Information:

Not Applicable

Current DocID:

© 2021 The United States Pharmacopeial Convention *All Rights Reserved.*