Interim Revision Announcement
Official: May 1, 2021

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.

$C_{14}H_{18}I_3N_3O_6$ 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)

Page Information:

Not Applicable

Current DocID: