# Iohexol Injection

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Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Manufacturers are also invited to submit samples of their products to the IPC to ensure that the proposed monograph adequately controls the quality of the product(s) they manufacture. Comments and samples received after the last date will not be considered by the IPC before finalizing the monograph.

**Please send any comments you may have on this draft document to lab.ipc@gov.in, with a copy to Dr. Gaurav Pratap Singh (email: gpsingh.ipc@gov.in) before the last date for comments.**



## Document History and Schedule for the Adoption Process

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| Further follow-up action as required. | |

# Iohexol Injection

Iohexol Injection is a sterile solution of Iohexol in Water for Injection.

Iohexol Injection contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of iohexol, $C_{19}H_{26}I_3N_3O_9$ as organically bound Iodine. It may contain small amounts of suitable buffers and edetate calcium disodium as a stabilizer. Iohexol injection intended for intravascular or intrathecal use contains no antimicrobial agents.

**Usual strengths.** 300 mg I per ml.

## Identification

In the Related substances, the principal peak in the chromatogram obtained with the test solution corresponds to the peaks in the chromatogram obtained with the reference solution.

## Tests

**pH** (2.4.24). 6.8 to 7.7.

**Limit of free iodide**. Not more than 0.02 per cent, based on the content of iohexol.

Transfer a suitable volume of the injection containing 1.5 g of Iohexol to a suitable container, add 20 mL of *water*. Titrate with *0.001 M silver nitrate* determining the end-point potentiometrically (2.4.25) using a silver electrode in combination with an appropriate reference electrode. Carry out a blank titration.

1 ml of *0.001 M silver nitrate* is equivalent to 0.0001269 g of *iodide*.

**Related substances**. Determine by liquid chromatography (2.4.14).

*Test solution*. Dilute a volume of the injection containing 150 mg of Iohexol to 100.0 ml with *water*.

*Reference solution*. A solution containing 0.15 per cent w/v of *iohexol IPRS*, 0.00075 per cent w/v of *iohexol related compound A IPRS* and 0.00069 per cent w/v of *iohexol related compound C IPRS* in *water*.

Chromatographic system
- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Inertsil ODS 3V),
- mobile phase: A. *acetonitrile*,
  B. *water*,
- a gradient programme using the conditions given below,
- flow rate: 1 ml per minute,
- spectrophotometer set at 254 nm,
- injection volume: 10 µl.

| Time (in min.) | Mobile phase A (per cent v/v) | Mobile phase B (per cent v/v) |
|---|---|---|
| 0 | 1 | 99 |
| 65 | 13 | 87 |
| 70 | 1 | 99 |
| 75 | 1 | 99 |

| Name | Relative Retention time |
|---|---|
| Iohexol Related compound A[1] | 0.84 |
| Iohexol endo-isomer | 0.96 |
| Iohexol exo-isomer | 1.0 |
| O-alkylated compounds | 1.1-1.4 |

[1]5-(Acetylamino)-N,N′-bis(2,3-dihydroxypropyl)-2,4,6-triiodo-1,3-benzenedicarboxamide.

Inject the reference solution. The test is not valid unless the resolution between the peaks due to iohexol related compound A and iohexol related compound C is not less than 20.0.

Inject the test solution. The area of any peak due to *o*-alkylated compounds is not more than 0.6 per cent, the area of any other secondary peak is not more than 0.1 per cent and the sum of areas of all the secondary peaks other than *o*-alkylated compounds is not more than 0.3 per cent, calculated by area normalization. Ignore all the peaks with retention time between 0.84 (relative to the endo-isomer of iohexol, which is the 1st main peak) and 1.0.

**Other tests.** Comply with the tests stated under Parenteral Preparations (Injections).

**Bacterial endotoxins** (2.2.3). Not more than 0.2 Endotoxin Unit per 50 mg of iodine.

**Assay.** Transfer a volume of the injection containing 300 mg of iodine to a 250-ml stoppered conical flask, add 25 ml of *1.25 M sodium hydroxide* and 500 mg of *powdered zinc*. Connect the flask to a reflux condenser and reflux the solution for 1 hour. 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 the filter thoroughly with small portions of *water*, adding the rinsing to the filtrate. Add 5 ml of *glacial acetic acid* and titrate with *0.1 M silver nitrate*, determining the end point potentiometrically (2.4.25). Carry out a blank titration.

1 ml of *0.1 M silver nitrate* is equivalent to 0.02737 g of $C_{19}H_{26}I_3N_3O_9$.

**Storage**. Store injection intended for intravascular or intrathecal use in single dose or multiple dose plastic or Type 1 glass containers. Store protected from light, at a temperature not exceeding 30°. Do not freeze.

**Labelling.** Label states to direct the user to discard any unused portion. The labeling states also that it is not to be used if it is discolored or contains a precipitate. Label it also to state its routes of administration. When the specific dose strength is not intended for intrathecal use, label it to indicate “serious injury can occur if given by intrathecal route”.