

the quantity of  $C_{18}H_{24}I_3N_3O_8$  in the portion of Iopromide taken by the formula:

$$C(r_u / r_s)$$

in which  $C$  is the concentration, in mg per mL, of USP Iopromide RS in the *Standard preparation*; and  $r_u$  and  $r_s$  are the sums of the peak responses for Iopromide  $E1$ -isomer, Iopromide  $E2$ -isomer, Iopromide  $Z1$ -isomer, and Iopromide  $Z2$ -isomer in the chromatograms obtained from the *Assay preparation* and the *Standard preparation*, respectively.

## Iopromide Injection

» Iopromide Injection is a sterile solution of Iopromide in Water for Injection. It contains not less than 94.0 per cent and not more than 105.0 percent of the labeled amount of Iopromide ( $C_{18}H_{24}I_3N_3O_8$ ). It may contain small amounts of suitable buffers and of Edetate Calcium Disodium as a stabilizer. It contains no antimicrobial agents.

**Packaging and storage**—Preserve in single-dose glass Containers for Injections as described under *Injections* (1), and protect from light. Store at controlled room temperature.

**Labeling**—Label Injection to state that it is not to be used if it contains particulate matter and that after use any unused portion remaining in the container is to be discarded. It is labeled also to state that it is not for intrathecal use.

### USP Reference standards (11)—

USP Endotoxin RS

USP Iopromide RS

USP Iopromide Related Compound A RS

USP Iopromide Related Compound B RS

5-(Acetylamino)- $N,N'$ -bis(2,3-dihydroxypropyl)-2,4,6-triiodo- $N$ -methyl-1,3-benzenedicarboxamide.

### Identification—

**A:** Evaporate 3 mL of Injection to dryness, and heat the residue so obtained in a crucible in a hood: violet vapors are evolved.

**B:** The  $R_f$  value of the principal spot in the chromatogram obtained from the *Test solution*, developed with the *Basic eluant*, in the test for *Ordinary impurities* corresponds to that obtained from the *Standard solution* similarly tested.

**Bacterial endotoxins** (85)—It contains not more than 1.25 USP Endotoxin Units per mL of Injection.

**pH** (791): between 6.5 and 8.0.

**Free iodine**—Transfer a volume of Injection, equivalent to 2 g of Iopromide, to a 50-mL centrifuge tube. Dilute with water to 24 mL. Add 2 mL of toluene and 2 mL of diluted sulfuric acid solution, and shake: the toluene layer shows no red color.

**Limit of free iodide**—Transfer 10.0 mL of Injection and 50 mL of water to a 150-mL titration vessel, and titrate with 0.001 N silver nitrate VS using a silver or platinum electrode in combination with a reference electrode, determining the endpoint potentiometrically. Each mL of 0.001 N silver nitrate is equivalent to 126.9  $\mu$ g of I. The limit is 80  $\mu$ g of iodide per g of Iopromide, based on the labeled content of Iopromide.

**Limit of free aromatic amine**—Proceed as directed in the test for *Limit of free aromatic amine* under *Iopromide*, except to prepare the *Test solution* as follows. Transfer an accurately measured volume of Injection, equivalent to about 500 mg of

Iopromide, to a 25-mL volumetric flask, dilute with water to 20 mL, and mix. Calculate the per centage of free aromatic amine based on the labeled amount of Iopromide in the Injection taken by the formula:

$$10(W_s / CV)(A_u / A_s)$$

in which  $W_s$  is the quantity, in mg, of USP Iopromide Related Compound A RS taken to prepare the *Standard solution*;  $C$  is the labeled concentration, in mg per mL, of Iopromide in the Injection used to prepare the *Test solution*;  $V$  is the volume, in mL, of Injection to prepare the *Test solution*; and  $A_u$  and  $A_s$  are the absorbances of the *Test solution* and the *Standard solution*, respectively: not more than 0.2% is found.

**Limit of  $N$ -acetyl compound** (Iopromide related compound B)—Using the chromatogram of the *Assay preparation* obtained in the *Assay*, calculate the per centage of  $N$ -acetyl compound in the Iopromide in the Injection taken by the formula:

$$(W_B / C)[(A_{Y1} + A_{Y2}) / (R_{Y1} + R_{Y2})]$$

in which  $W_B$  is the quantity, in mg, of USP Iopromide Related Compound B RS taken to prepare the *Related compound B standard solution*;  $C$  is the concentration, in mg of Iopromide per mL, in the *Assay preparation* based on the labeled amount and the extent of dilution;  $A_{Y1}$  and  $A_{Y2}$  are the peak responses for Iopromide related compound B  $Y1$ - and  $Y2$ -isomers, respectively, from the *Assay preparation*; and  $R_{Y1}$  and  $R_{Y2}$  are the peak responses for Iopromide related compound B  $Y1$ - and  $Y2$ -isomers, respectively, from the *Related compound B standard solution*: not more than 1.5% is found.

**Isomer distribution**—Using the chromatogram of the *Assay preparation* obtained in the *Assay*, calculate the per centage of Iopromide isomers in the Iopromide in the Injection taken by the formula:

$$100(r_i) / (r_{E1} + r_{E2} + r_{Z1} + r_{Z2})$$

in which  $r_i$  is the peak response of each individual Iopromide isomer; and  $r_{E1}$ ,  $r_{E2}$ ,  $r_{Z1}$ , and  $r_{Z2}$  are the peak responses for the Iopromide  $E1$ -,  $E2$ -,  $Z1$ -, and  $Z2$ -isomers, respectively, from the *Assay preparation*: between 8.0% and 12.0% of the  $E1$ -isomer, between 9.0% and 14.0% of the  $E2$ -isomer, between 32.0% and 40.0% of the  $Z1$ -isomer, and between 38.0% and 46.0% of the  $Z2$ -isomer are found.

**Other requirements**—It meets the requirements under *Injections* (1), and meets the requirements for *Ordinary impurities* and *Heavy metals* under *Iopromide*.

### Assay—

*Diluent*, *Mobile phase*, *Standard preparation*, *Related compound B standard solution*, and *Chromatographic system*—Proceed as directed in the *Assay* under *Iopromide*.

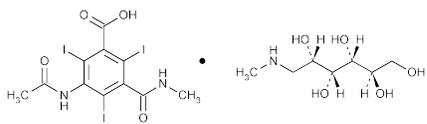
*Assay preparation*—Dilute an accurately measured volume of Injection, quantitatively and stepwise, with *Diluent* to obtain a solution having a final nominal concentration of 1.9 mg of Iopromide per mL.

*Procedure*—Proceed as directed in the *Assay* under *Iopromide*. Calculate the quantity, in mg, of Iopromide ( $C_{18}H_{24}I_3N_3O_8$ ) in each mL of the Injection taken by the formula:

$$(CL/D)(r_u / r_s)$$

in which  $C$  is the concentration, in mg per mL, of USP Iopromide RS in the *Standard preparation*;  $L$  is the labeled quantity, in mg, of Iopromide in each mL of Injection;  $D$  is the concentration, in mg per mL, of Iopromide in the *Assay preparation*, based on the volume of Injection taken and the extent of dilution; and the other factors are as defined therein.

## Iothalamate Meglumine Injection



$C_{11}H_9I_3N_2O_4 \cdot C_7H_{17}NO_5$  809.13

Benzoic acid, 3-(acetylamino)-2,4,6-triiodo-5-[(methylamino)carbonyl]-, compd. with 1-deoxy-1-(methylamino)-D-glucitol (1:1).

1-Deoxy-1-(methylamino)-D-glucitol 5-acetamido-2,4,6-triiodo-N-methylisophthalamate (salt) [13087-53-1].

» Iothalamate Meglumine Injection is a sterile solution of Iothalamic Acid in Water for Injection, prepared with the aid of Meglumine. It contains not less than 95.0 per cent and not more than 105.0 percent of the labeled amount of iothalamate meglumine ( $C_{11}H_9I_3N_2O_4 \cdot C_7H_{17}NO_5$ ). It may contain small amounts of suitable buffers and of Edetate Calcium Disodium or Edetate Disodium as a stabilizer. Iothalamate Meglumine Injection intended for intravascular use contains no antimicrobial agents.

**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. Label containers of Injection intended for other than intravascular injection to show that the contents are not intended for intravascular injection.

**USP Reference standards** (11)—

USP 5-Amino-2,4,6-triiodo-N-methylisophthalamate RS  
 $C_9H_7I_3N_2O_3$  571.88

USP Endotoxin RS

USP Iothalamic Acid RS

**Identification**—Dilute 3 mL of Injection with water to 100 mL, add an excess of 3 N hydrochloric acid, and filter. Wash the precipitated iothalamate acid on the filter with four 10-mL portions of water, and dry at 105° for 4 hours: the dried iothalamate acid responds to the following tests.

**A:** The IR absorption spectrum of a 0.5% potassium bromide dispersion of the dried acid exhibits maxima only at the same wavelengths as that of a similar preparation of USP Iothalamic Acid RS.

**B:** Heat about 500 mg of the dried acid in a suitable crucible: violet vapors are evolved.

**Bacterial endotoxins** (85)—It contains not more than 0.9 USP Endotoxin Unit per mL.

**pH** (791): between 6.5 and 7.7.

**Free aromatic amine**—Dilute a suitable volume of Injection with water to yield a solution containing 100 mg of iothalamate meglumine per mL. Proceed as directed in the test for *Free aromatic amine* under *Iothalamic Acid*, beginning with "Pipet 5 mL of this solution into a 50-mL volumetric flask."

**Iodine and iodide**—Dilute a volume of Injection, equivalent to 2 g of iothalamate meglumine, with 20 mL of water in a 50-mL beaker, add 5 mL of 2 N sulfuric acid, stir, and filter into a glass-stoppered, 50-mL cylinder. Proceed as directed for *Procedure in the test for Iodine and iodide* under *Iothalamic Acid*, beginning with "To the filtrate add 5 mL of toluene."

**Heavy metals** (231)—In a 50-mL color-comparison tube, mix a volume of Injection, equivalent to 1.0 g of iothalamate meglumine, with 5 mL of 1 N sodium hydroxide, dilute with water to 40 mL, and mix. Using this as the *Test preparation*,

proceed as directed in the test for *Heavy metals* under *Diatrizoate Meglumine*: the limit is 0.002%.

**Meglumine content**—Proceed as directed in the test for *Meglumine content* under *Diatrizoate Meglumine Injection*. The meglumine content is not less than 22.9% and not more than 25.3% of the labeled amount of iothalamate meglumine.

**Other requirements**—It meets the requirements under *Injections* (1).

**Assay**—Pipet a volume of Injection, equivalent to about 4 g of iothalamate meglumine, into a 250-mL volumetric flask, dilute with water to volume, and mix. Pipet 25 mL of this solution into a glass-stoppered, 125-mL conical flask, add 12 mL of 5 N sodium hydroxide and 1 g of powdered zinc, connect the flask to a reflux condenser, and reflux for 30 minutes. Cool to room temperature, rinse the condenser with 20 mL of water, disconnect the flask from the condenser, and filter the mixture. Rinse the filter and the flask thoroughly, adding the rinsings to the filtrate. Add 40 mL of 2 N sulfuric acid, and titrate immediately with 0.05 N silver nitrate VS, determining the endpoint potentiometrically, using silver-calomel electrodes and an agar-potassium nitrate salt bridge. Each mL of 0.05 N silver nitrate is equivalent to 13.49 mg of  $C_{11}H_9I_3N_2O_4 \cdot C_7H_{17}NO_5$ .

## Iothalamate Meglumine and Iothalamate Sodium Injection

» Iothalamate Meglumine and Iothalamate Sodium Injection is a sterile solution of Iothalamic Acid in Water for Injection, prepared with the aid of Meglumine and Sodium Hydroxide. It contains not less than 95.0 per cent and not more than 105.0 percent of the labeled amounts of iothalamate meglumine ( $C_{11}H_9I_3N_2O_4 \cdot C_7H_{17}NO_5$ ) and iothalamate sodium ( $C_{11}H_8I_3N_2NaO_4$ ). It may contain small amounts of suitable buffers and of Edetate Calcium Disodium or Edetate Disodium as a stabilizer. Iothalamate Meglumine and Iothalamate Sodium Injection intended for intravascular use contains no antimicrobial agents.

**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. Label containers of Injection intended for other than intravascular injection to show that the contents are not intended for intravascular injection.

**USP Reference standards** (11)—

USP 5-Amino-2,4,6-triiodo-N-methylisophthalamate RS  
 $C_9H_7I_3N_2O_3$  571.88

USP Endotoxin RS

USP Iothalamic Acid RS

**Identification**—Dilute 3 mL of Injection with water to 100 mL, add an excess of 3 N hydrochloric acid, mix, and filter. Wash the precipitate of iothalamate acid so obtained with four 10-mL portions of water, and dry at 105° for 4 hours: the dried iothalamate acid so obtained responds to the following tests.

**A:** The IR absorption spectrum of a potassium bromide dispersion of it exhibits maxima only at the same wavelengths as that of a similar preparation of USP Iothalamic Acid RS.

**B:** Heat about 500 mg in a suitable crucible: violet vapors are evolved.

**Bacterial endotoxins** (85)—It contains not more than 3.35 USP Endotoxin Units per mL.