CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number 074629

Trade Name Iopamidol Injection 41%, 61%, 76%

Generic Name Iopamidol Injection 41%, 61%, 76%

Sponsor Elkins-Sinn

ANDA 74-629

NOV 6 1996

Elkins-Sinn
Attention: Frances M. Cacchio
2 Esterbrook Lane
Cherry Hill, NJ 08003-4099

Dear Madam:

This is in reference to your abbreviated new drug application dated February 17, 1995, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Iopamidol Injection USP, 41%, 61%, and 76% (Vials).

Reference is also made to your amendments dated April 24, 1996 and July 3, 1996.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved. The Division of Bioequivalence has determined your Iopamidol Injection USP, 41%, 61% and 76% to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Isovue-200 (41%), Isovue-300 (61%), and Isovue-370 (76%), respectively, of Bracco Diagnostics, Inc.).

Under 21 CFR 314.70, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

We request that you submit, in duplicate, any proposed advertising or promotional copy which you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-240). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-240) with a completed Form FD-2253 at the time of their initial use.

Sincerely yours,

D. L. Sporn 11/6/96

Douglas L. Sporn
Director
Office of Generic Drugs
Center for Drug and Evaluation and Reseach

1. CHEMISTRY REVIEW NO 3

2. ANDA 74-629

3. NAME AND ADDRESS OF APPLICANT
Elkins-Sinn, Inc.
Attention: Frances M. Cacchio
2 Esterbrook Lane
Cherry Hill, NJ 08003-4099

6. PROPRIETARY NAME N/A

7. NONPROPRIETARY NAME Iopamidol Injection, USP

10. PHARMACOLOGICAL CATEGORY
Imaging Agent

11. Rx or OTC
Rx

13. DOSAGE FORM
Injection (solution)

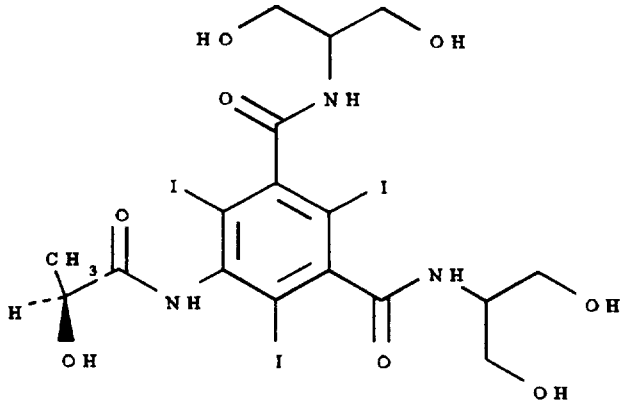
14. POTENCY
41, 61 & 76%

15. CHEMICAL NAME AND STRUCTURE

$C_{17}H_{22}I_3N_3O_8$ M.W. = 777.09

(S)-*N*,*N*'-bis[2-Hydroxy-1-(hydroxymethyl)ethyl]-2,4,6-triiodo-5-lactamido-isophthalamide.

CAS [60166-93-0]



18. CONCLUSIONS AND RECOMMENDATIONS
Recommend: APPROVAL.

19. REVIEWER: J. L. Smith DATE COMPLETED: May 1, 1996

cc: ANDA 74-629
DUP Jacket
Division File

Endorsements:

HFD-623/J.Smith/ JL Smith 5/28/96
HFD-623/V.Sayeed/ Vilayat A. Sayeed 5/29/96
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F/T by:

AUG 23 1995

Iopamidol Injection
41%, 61% and 76% vials
NDA #74-629
Reviewer: J. Lee
74629W.295

Elkins-Sinn, Inc.
Cherry Hill, N. Jersey
Submission date:
February 17, 1995

Review of a Request for Waiver

The company has submitted an application (first generic) for the following strengths of iopamidol injection (a radiopaque diagnostic agent):

41% - 200 ml vial

61% - 50 ml, 100 ml and 150 ml fill in a 200 ml vial

76% 50 ml, 100 ml, 150 ml fill in a 200 ml vial and a 200 ml vial

The waiver of bioavailability requirements for the proposed generic drug product is being requested under 21 CFR 320.22 (b)(1) based on the following considerations submitted by the sponsor:

1. The test product is virtually identical to the brand product marketed by Squibb Diagnostics, Isovue® (NDA #18-735).

2. The drug is administered intravascularly, as is the brand product.

The sponsor has supplied quantitative/qualitative formulations for their own test product as described below; the formulation of the brand product is taken from the package insert.

	Iopamidol/ml			Isovue/ml		
	41%	61%	76%	(-200)	(-300)	(-370)
Iopamidol (mg)	408	612	755	408	612	755
Tromethamine (mg)						
Edetate Ca Na_2 (mg)						
Water for Injection						

Both formulations are adjusted, if needed, to pH 6.5 - 7.5 with HCl.

Recommendation:

1. The Division of Bioequivalence agrees that the information submitted by Elkins-Sinn, Inc. demonstrates that iopamidol injection 41%, 61% and 76% falls under 21 CFR 320.22 (b)(1) of Bioavailability/Bioequivalence Regulations. The Division of

Bioequivalence recommends that the waiver of an in-vivo bioavailability study be granted. Elkins-Sinn's iopamidol injection 41%, 61% and 76% is deemed bioequivalent to Isovue® -200, -300 and -370, respectively, manufactured by Squibb Diagnostics.

J. Lee 7/24/95

J. Lee
Division of Bioequivalence
Review Branch II

RD INITIALED RPATNAIK
FT INITIALED RPATNAIK

Concur: _____ Date: 8/23/95

Keith Chan, Ph.D.
Director, Division of Bioequivalence

JLee/jl/07-24-95

cc: NDA #74-629 (original, duplicate), HFD-630, HFD-600 (Hare), HFD-655 (Lee, Patnaik), HFD-130 (JAllen), HFD-344 (Vish), Drug File, Division File

SECTION IV

COMPARISON BETWEEN GENERIC DRUG AND REFERENCE LISTED DRUG

	Reference Listed Drug	Generic Drug Provided for in this ANDA
	Isovue®	Iopamidol Injection, USP
Conditions of Use:	For angiography throughout the cardiovascular system, including cerebral and peripheral arteriography, coronary arteriography and ventriculography, pediatric angiocardiography, selective visceral arteriography and aortography, peripheral venography (phlebography), and adult and pediatric intravenous excretory urography and intravenous adult and pediatric contrast enhancement of computed tomographic (CECT) head and body imaging.	For angiography throughout the cardiovascular system, including cerebral and peripheral arteriography, coronary arteriography and ventriculography, pediatric angiocardiography, selective visceral arteriography and aortography, peripheral venography (phlebography), and adult and pediatric intravenous excretory urography and intravenous adult and pediatric contrast enhancement of computed tomographic (CECT) head and body imaging.
Active Ingredient:	Iopamidol	Iopamidol, USP
Inactive Ingredients:	Tromethamine Edetate Calcium Disodium Water for Injection Hydrochloric Acid (pH adjustment)	Tromethamine, USP Edetate Calcium Disodium, USP Water for Injection, USP Hydrochloric Acid, NF (pH adjustment)
Route of Administration:	Intravascular	Intravascular
Dosage Form:	Injectable, Solution	Injectable, Solution
Strengths:	41%, 61%, 76%	41%, 61%, 76%

SECTION VII

COMPONENTS AND COMPOSITION STATEMENTS

A statement of the composition of the drug product:

Iopamidol Injection, USP
41%
200 mL Vial

	Per mL
Iopamidol, USP	408 mg
Tromethamine, USP	
Edetate Calcium Disodium, USP	
Water for Injection, USP	

Hydrochloric Acid, NF 1:10 added, if needed for pH adjustment

SECTION VII

COMPONENTS AND COMPOSITION STATEMENTS

A statement of the composition of the drug product:

Iopamidol Injection, USP
61%
50 mL Vial
100 mL Vial
150 mL/200 mL Vial

	Per mL
Iopamidol, USP	612 mg
Tromethamine, USP	
Edetate Calcium Disodium, USP	
Water for Injection, USP	

Hydrochloric Acid, NF 1:10 added, if needed for pH adjustment

SECTION VII

COMPONENTS AND COMPOSITION STATEMENTS

A statement of the composition of the drug product:

Iopamidol Injection, USP
76%
50 mL Vial
100 mL Vial
150 mL/200 mL Vial
200 mL Vial

	Per mL
Iopamidol, USP	755 mg
Tromethamine, USP	
Edetate Calcium Disodium, USP	
Water for Injection, USP	

Hydrochloric Acid, NF 1:10 added, if needed for pH adjustment

J-2474 ESI ELKINS-SINN

IOPAMIDOL

INJECTION, USP

NOT FOR INTRATHECAL USE

Iopamidol Injection 41%, 61% and 76% are NOT FOR INTRATHECAL USE. See INDICATIONS AND USAGE and DOSAGE AND ADMINISTRATION sections for further details on proper use.

DIAGNOSTIC

NONIONIC RADIOPAQUE CONTRAST MEDIA

For Angiography Throughout the Cardiovascular System, Including Cerebral and Peripheral Arteriography, Coronary Arteriography and Ventriculography, Pediatric Angiocardiography, Selective Visceral Arteriography and Aortography, Peripheral Venography (Phlebography), and Adult and Pediatric Intravenous Excretory Urography and Intravenous Adult and Pediatric Contrast Enhancement of Computed Tomographic (CECT) Head and Body Imaging

DESCRIPTION

Iopamidol Injection, USP formulations are stable, aqueous, sterile and nonpyrogenic solutions for intravascular administration.

Each mL of Iopamidol Injection, USP 41% contains iopamidol 408 mg, tromethamine 1 mg and edetate calcium disodium 0.26 mg. The solution contains approximately 0.029 mg (0.001 mEq) sodium and 200 mg organically bound iodine per mL.

Each mL of Iopamidol Injection, USP 61% contains iopamidol 612 mg, tromethamine 1 mg and edetate calcium disodium 0.39 mg. The solution contains approximately 0.043 mg (0.002 mEq) sodium and 300 mg organically bound iodine per mL.

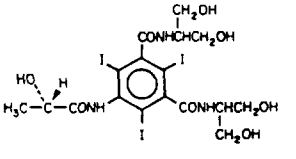
Each mL of Iopamidol Injection, USP 76% contains iopamidol 755 mg, tromethamine 1 mg and edetate calcium disodium 0.48 mg. The solution contains approximately 0.053 mg (0.002 mEq) sodium and 370 mg organically bound iodine per mL.

The pH of Iopamidol Injection, USP contrast media has been adjusted to 6.5-7.5 with hydrochloric acid. Pertinent physicochemical data are noted below. Iopamidol Injection, USP is hypertonic as compared to plasma and cerebrospinal fluid (approximately 285 and 301 mOsm/kg water, respectively).

	IOPAMIDOL		
Parameter	**41%**	**61%**	**76%**
Concentration (mgI/mL)	200	300	370
Osmolality at 37°C (mOsm/kg water)	413	616	796
Viscosity (cP) at 37°C	2.0	4.7	9.4
at 20°C	3.3	8.8	20.9
Specific Gravity at 37°C	1.216	1.328	1.405

Iopamidol is a practically odorless, white to off-white powder. It is very soluble in water; sparingly soluble in methanol; practically insoluble in alcohol and in chloroform.

The chemical name of iopamidol is (*S*)-*N*,*N'*-bis[2-Hydroxy-1-(hydroxymethyl)ethyl]-2,4,6-triiodo-5-lactamidoisophthalamide. The structural formula is:



$C_{17}H_{22}I_3N_3O_8$ Organically Bound Iodine: 49% MW 777.09

CLINICAL PHARMACOLOGY

Intravascular injection of a radiopaque diagnostic agent opacifies those vessels in the path of flow of the contrast medium, permitting radiographic visualization of the internal structures of the human body until significant hemodilution occurs.

Following intravascular injection, radiopaque diagnostic agents are immediately diluted in the circulating plasma. Calculations of apparent volume of distribution at steady-state indicate that iopamidol is distributed between the circulating blood volume and other extracellular fluid; there appears to be no significant deposition of iopamidol in tissues. Uniform distribution of iopamidol in extracellular fluid is reflected by its demonstrated utility in contrast enhancement of computed tomographic imaging of the head and body following intravenous administration.

The pharmacokinetics of intravenously administered iopamidol in normal subjects conform to an open two-compartment model with first order elimination (a rapid alpha phase for drug distribution and a slow beta phase for drug elimination). The elimination serum or plasma half-life is approximately two hours; the half-life is not dose dependent. No significant metabolism, deiodination or biotransformation occurs.

Iopamidol is excreted mainly through the kidneys following intravascular administration. In patients with impaired renal function, the elimination half-life is prolonged dependent upon the degree of impairment. In the absence of renal dysfunction, the cumulative urinary excretion for iopamidol, expressed as a percentage of administered intravenous dose, is approximately 35 to 40 percent at 60 minutes, 80 to 90 percent at 8 hours and 90 percent or more in the 72- to 96-hour period after administration. In normal subjects, approximately one percent or less of the administered dose appears in cumulative 72- to 96-hour fecal specimens.

Iopamidol Injection may be visualized in the renal parenchyma within 30-60 seconds following rapid intravenous administration. Opacification of the calyces and pelves in patients with normal renal function becomes apparent within 1 to 3 minutes, with optimum contrast occurring between 5 and 15 minutes. In patients with renal impairment, contrast visualization may be delayed.

Iopamidol displays little tendency to bind to serum or plasma proteins.

No evidence of *in vivo* complement activation has been found in normal subjects.

Animal studies indicate that iopamidol does not cross the blood-brain barrier to any significant extent following intravascular administration.

Iopamidol Injection enhances computed tomographic brain imaging through augmentation of radiographic efficiency. The degree of enhancement of visualization of tissue density is directly related to the iodine content in an administered dose; peak iodine blood levels occur immediately following rapid injection of the dose. These levels fall rapidly within five to ten minutes. This can be accounted for by the dilution in the vascular and extracellular fluid compartments which causes an initial sharp fall in plasma concentration. Equilibration with the extracellular compartments is reached in about ten minutes; thereafter, the fall becomes exponential. Maximum contrast enhancement frequently occurs after peak blood iodine levels are reached. The delay in maximum contrast enhancement can range from five to forty minutes depending on the peak iodine levels achieved and the cell type of the lesion. This lag suggests that radiographic contrast enhancement is at least in part

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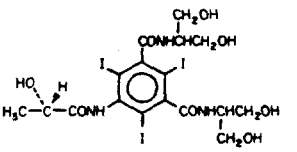

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In CECT head imaging, Iopamidol Injection does not accumulate in normal brain tissue due to the presence of the "blood-brain" barrier. The increase in x-ray absorption in normal brain is due to the presence of contrast agent within the blood pool. A break in the blood-brain barrier such as occurs in malignant tumors of the brain allows the accumulation of the contrast medium within the interstitial tissue of the tumor. Adjacent normal brain tissue does not contain the contrast medium.

In nonneural tissues (during computed tomography of the body), iopamidol diffuses rapidly from the vascular into the extravascular space. Increase in x-ray absorption is related to blood flow, concentration of the contrast medium and extraction of the contrast medium by interstitial tissue of tumors since no barrier exists. Contrast enhancement is thus due to the relative differences in extravascular diffusion between normal and abnormal tissue, quite different from that in the brain.

The pharmacokinetics of iopamidol in both normal and abnormal tissue have been shown to be variable. Contrast enhancement appears to be greatest soon after administration of the contrast medium, and following intraarterial rather than intravenous administration. Thus, greatest enhancement can be detected by a series of consecutive two- to three-second scans performed just after injection (within 30 to 90 seconds), i.e., dynamic computed tomographic imaging.

INDICATIONS AND USAGE

Iopamidol Injection is indicated for angiography throughout the cardiovascular system, including cerebral and peripheral arteriography, coronary arteriography and ventriculography, pediatric angiocardiography, selective visceral arteriography and aortography, peripheral venography (phlebography), and adult and pediatric intravenous excretory urography and intravenous adult and pediatric contrast enhancement of computed tomographic (CECT) head and body imaging (see below).

CECT HEAD IMAGING

Iopamidol Injection may be used to refine diagnostic precision in areas of the brain which may not otherwise have been satisfactorily visualized.

TUMORS

Iopamidol Injection may be useful to investigate the presence and extent of certain malignancies such as: gliomas including malignant gliomas, glioblastomas, astrocytomas, oligodendrogliomas and gangliomas, ependymomas, medulloblastomas, meningiomas, neuromas, pinealomas, pituitary adenomas, craniopharyngiomas, germinomas and metastatic lesions. The usefulness of contrast enhancement for the investigation of the retrobulbar space and in cases of low grade or infiltrative glioma has not been demonstrated.

In calcified lesions, there is less likelihood of enhancement. Following therapy, tumors may show decreased or no enhancement.

The opacification of the inferior vermis following contrast media administration has resulted in false-positive diagnosis in a number of otherwise normal studies.

NONNEOPLASTIC CONDITIONS

Iopamidol Injection may be beneficial in the image enhancement of nonneoplastic lesions. Cerebral infarctions of recent onset may be better visualized with contrast enhancement, while some infarctions are obscured if contrast media are used. The use of iodinated contrast media results in contrast enhancement in about 60 percent of cerebral infarctions studied from one to four weeks from the onset of symptoms.

Sites of active infection may also be enhanced following contrast media administration.

Arteriovenous malformations and aneurysms will show contrast enhancement. For these vascular lesions, the enhancement is probably dependent on the iodine content of the circulating blood pool.

Hematomas and intraparenchymal bleeders seldom demonstrate any contrast enhancement. However, in cases of intraparenchymal clot, for which there is no obvious clinical explanation, contrast media administration may be helpful in ruling out the possibility of associated arteriovenous malformation.

CECT BODY IMAGING

Iopamidol Injection may be used for enhancement of computed tomographic images for detection and evaluation of lesions in the liver, pancreas, kidneys, aorta, mediastinum, abdominal cavity, pelvis and retroperitoneal space.

Enhancement of computed tomography with Iopamidol Injection may be of benefit in establishing diagnoses of certain lesions in these sites with greater assurance than is possible with CT alone, and in supplying additional features of the lesions (e.g., hepatic abscess delineation prior to percutaneous drainage). In other cases, the contrast agent may allow visualization of lesions not seen with CT alone (e.g., tumor extension), or may help to define suspicious lesions seen with unenhanced CT (e.g., pancreatic cyst).

Contrast enhancement appears to be greatest within 60 to 90 seconds after bolus administration of contrast agent. Therefore, utilization of a continuous scanning technique ("dynamic CT scanning") may improve enhancement and diagnostic assessment of tumor and other lesions such as an abscess, occasionally revealing unsuspected or more extensive disease. For example, a cyst may be distinguished from a vascularized solid lesion when precontrast and enhanced scans are compared; the nonperfused mass shows unchanged x-ray absorption (CT number). A vascularized lesion is characterized by an increase in CT number in the few minutes after a bolus of intravascular contrast agent; it may be malignant, benign or normal tissue, but would probably not be a cyst, hematoma or other nonvascular lesion.

Because unenhanced scanning may provide adequate diagnostic information in the individual patient, the decision to employ contrast enhancement, which may be associated with risk and increased radiation exposure, should be based upon a careful evaluation of clinical, other radiological and unenhanced CT findings.

CONTRAINDICATIONS

None.

WARNINGS

Severe Adverse Events—Inadvertent Intrathecal Administration

Serious adverse reactions have been reported due to the inadvertent intrathecal administration of iodinated contrast media that are not indicated for intrathecal use. These serious adverse reactions include: death, convulsions, cerebral hemorrhage, coma, paralysis, arachnoiditis, acute renal failure, cardiac arrest, seizures, rhabdomyolysis, hyperthermia and brain edema. Special attention must be given to insure that this drug product is not inadvertently administered intrathecally.

Nonionic iodinated contrast media inhibit blood coagulation, *in vitro*, less than ionic contrast media. Clotting has been reported when blood remains in contact with syringes containing nonionic contrast media.

Serious, rarely fatal, thromboembolic events causing myocardial infarction and stroke have been reported during angiographic procedures with both ionic and nonionic contrast media. Therefore, meticulous intravascular administration technique is necessary, particularly during angiographic procedures, to minimize thromboembolic events. Numerous factors, including length of procedure, catheter and syringe material, underlying disease state and concomitant medications may contribute to the development of thromboembolic events. For these reasons, meticulous angiographic techniques are recommended including close attention to guidewire and catheter manipulation, use of manifold systems and/or three-way stopcocks, frequent catheter flushing with heparinized saline solutions, and minimizing the length of the procedure. The use of plastic syringes in place of glass syringes has been reported to decrease, but not eliminate, the likelihood of *in vitro* clotting.

Caution must be exercised in patients with severely impaired renal function, those with combined renal and hepatic disease, or anuria, particularly when larger doses are administered.

Radiopaque diagnostic contrast agents are potentially hazardous in patients with multiple myeloma or other paraproteinemia, particularly in those with therapeutically resistant anuria. Myeloma occurs most commonly in persons over age 40. Although neither the contrast agent nor dehydration has been proved separately to be the cause of anuria in myelomatous patients, it has been speculated that the combination of both may be causative. The risk in myelomatous patients is not a contraindication; however, special precautions are required.

Contrast media may promote sickling in individuals who are homozygous for sickle cell disease when injected intravenously or intraarterially.

Administration of radiopaque materials to patients known or suspected of having pheochromocytoma should be performed with extreme caution. If, in the opinion of the physician, the possible benefits of such procedures outweigh the considered risks, the procedures may be performed; however, the amount of radiopaque medium injected should be kept to an absolute minimum. The blood pressure should be assessed throughout the procedure and measures for treatment of a hypertensive crisis should be available. These patients should be monitored very closely during contrast enhanced procedures.

Reports of thyroid storm following the use of iodinated radiopaque diagnostic agents in patients with hyperthyroidism or with an autonomously functioning thyroid nodule suggest that this additional risk be evaluated in such patients before use of any contrast medium.

PRECAUTIONS

GENERAL

Diagnostic procedures which involve the use of any radiopaque agent should be carried out under the direction of personnel with the prerequisite training and with a thorough knowledge of the particular procedure to be performed. Appropriate facilities should be available for coping with any complication of the procedure, as well as for emergency treatment of severe reaction to the contrast agent itself. After parenteral administration of a radiopaque agent, competent personnel and emergency facilities should be available for at least 30 to 60 minutes since severe delayed reactions may occur.

Preparatory dehydration is dangerous and may contribute to acute renal failure in patients with advanced vascular disease, diabetic patients and in susceptible nondiabetic patients (often elderly with preexisting renal disease). *Patients should be well hydrated prior to and following iopamidol administration.*

The possibility of a reaction, including serious, life-threatening, fatal, anaphylactoid or cardiovascular reactions, should always be considered (see ADVERSE REACTIONS). Patients at increased risk include those with a history of a previous reaction to a contrast medium, patients with a known sensitivity to iodine per se, and patients with a known clinical hypersensitivity (bronchial asthma, hay fever and food allergies). The occurrence of severe idiosyncratic reactions has prompted the use of several pretesting methods. However, pretesting cannot be relied upon to predict severe reactions and may itself be hazardous for the patient. It is suggested that a thorough medical history with emphasis on allergy and hypersensitivity, prior to the injection of any contrast medium, may be more accurate than pretesting in predicting potential adverse reactions. A positive history of allergies or hypersensitivity does not arbitrarily contraindicate the use of a contrast agent where a diagnostic procedure is thought essential, but caution should be exercised. Premedication with antihistamines or corticosteroids to avoid or minimize possible allergic reactions in such patients should be considered. Recent

revealing unsuspected or more extensive disease. For example, a cyst may be distinguished from a vascularized solid lesion when precontrast and enhanced scans are compared; the nonperfused mass shows unchanged x-ray absorption (CT number). A vascularized lesion is characterized by an increase in CT number in the few minutes after a bolus of intravascular contrast agent; it may be malignant, benign or normal tissue, but would probably not be a cyst, hematoma or other nonvascular lesion.

Because unenhanced scanning may provide adequate diagnostic information in the individual patient, the decision to employ contrast enhancement, which may be associated with risk and increased radiation exposure, should be based upon a careful evaluation of clinical, other radiological and unenhanced CT findings.

CONTRAINDICATIONS

None.

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Serious, rarely fatal, thromboembolic events causing myocardial infarction and stroke have been reported during angiographic procedures with both ionic and nonionic contrast media. Therefore, meticulous intravascular administration technique is necessary, particularly during angiographic procedures, to minimize thromboembolic events. Numerous factors, including length of procedure, catheter and syringe material, underlying disease state and concomitant medications may contribute to the development of thromboembolic events. For these reasons, meticulous angiographic techniques are recommended including close attention to guidewire and catheter manipulation, use of manifold systems and/or three-way stopcocks, frequent catheter flushing with heparinized saline solutions, and minimizing the length of the procedure. The use of plastic syringes in place of glass syringes has been reported to decrease, but not eliminate, the likelihood of *in vitro* clotting.

Caution must be exercised in patients with severely impaired renal function, those with combined renal and hepatic disease, or anuria, particularly when larger doses are administered.

Radiopaque diagnostic contrast agents are potentially hazardous in patients with multiple myeloma or other paraproteinemia, particularly in those with therapeutically resistant anuria. Myeloma occurs most commonly in persons over age 40. Although neither the contrast agent nor dehydration has been proved separately to be the cause of anuria in myelomatous patients, it has been speculated that the combination of both may be causative. The risk in myelomatous patients is not a contraindication; however, special precautions are required.

Contrast media may promote sickling in individuals who are homozygous for sickle cell disease when injected intravenously or intraarterially.

Administration of radiopaque materials to patients known or suspected of having pheochromocytoma should be performed with extreme caution. If, in the opinion of the physician, the possible benefits of such procedures outweigh the considered risks, the procedures may be performed; however, the amount of radiopaque medium injected should be kept to an absolute minimum. The blood pressure should be assessed throughout the procedure and measures for treatment of a hypertensive crisis should be available. These patients should be monitored very closely during contrast enhanced procedures.

Reports of thyroid storm following the use of iodinated radiopaque diagnostic agents in patients with hyperthyroidism or with an autonomously functioning thyroid nodule suggest that this additional risk be evaluated in such patients before use of any contrast medium.

PRECAUTIONS

GENERAL

Diagnostic procedures which involve the use of any radiopaque agent should be carried out under the direction of personnel with the prerequisite training and with a thorough knowledge of the particular procedure to be performed. Appropriate facilities should be available for coping with any complication of the procedure, as well as for emergency treatment of severe reaction to the contrast agent itself. After parenteral administration of a radiopaque agent, competent personnel and emergency facilities should be available for at least 30 to 60 minutes since severe delayed reactions may occur.

Preparatory dehydration is dangerous and may contribute to acute renal failure in patients with advanced vascular disease, diabetic patients and in susceptible nondiabetic patients (often elderly with preexisting renal disease). *Patients should be well hydrated prior to and following iopamidol administration.*

The possibility of a reaction, including serious, life-threatening, fatal, anaphylactoid or cardiovascular reactions, should always be considered (see ADVERSE REACTIONS). Patients at increased risk include those with a history of a previous reaction to a contrast medium, patients with a known sensitivity to iodine per se, and patients with a known clinical hypersensitivity (bronchial asthma, hay fever and food allergies). The occurrence of severe idiosyncratic reactions has prompted the use of several pretesting methods. However, pretesting cannot be relied upon to predict severe reactions and may itself be hazardous for the patient. It is suggested that a thorough medical history with emphasis on allergy and hypersensitivity, prior to the injection of any contrast medium, may be more accurate than pretesting in predicting potential adverse reactions. A positive history of allergies or hypersensitivity does not arbitrarily contraindicate the use of a contrast agent where a diagnostic procedure is thought essential, but caution should be exercised. Premedication with antihistamines or corticosterioids to avoid or minimize possible allergic reactions in such patients should be considered. Recent reports indicate that such pretreatment does not prevent serious life-threatening reactions, but may reduce both their incidence and severity.

General anesthesia may be indicated in the performance of some procedures in selected patients; however, a higher incidence of adverse reactions has been reported with radiopaque media in anesthetized patients, which may be attributable to the inability of the patient to identify untoward symptoms, or to the hypotensive effect of anesthesia which can reduce cardiac output and increase the duration of exposure to the contrast agent.

Even though the osmolality of iopamidol is low compared to diatrizoate- or iothalamate-based ionic agents of comparable iodine concentration, the potential transitory increase in the circulatory osmotic load in patients with congestive heart failure requires caution during injection. These patients should be observed for several hours following the procedure to detect delayed hemodynamic disturbances.

In angiographic procedures, the possibility of dislodging plaques or damaging or perforating the vessel wall should be borne in mind during catheter manipulations and contrast medium injection. Test injections to ensure proper catheter placement are suggested.

Selective coronary arteriography should be performed only in selected patients and those in whom the expected benefits outweigh the procedural risk. The inherent risks of *angiocardiography* in patients with chronic pulmonary emphysema must be weighed against the necessity for performing this procedure. *Angiography* should be avoided whenever possible in patients with homocystinuria, because of the risk of inducing thrombosis and embolism. See also PRECAUTIONS-Pediatric Use.

In addition to the general precautions previously described, special care is required when venography is performed in patients with suspected thrombosis, phlebitis, severe ischemic disease, local infection or a totally obstructed venous system.

Extreme caution during injection of contrast media is necessary to avoid extravasation, and fluoroscopy is recommended. This is especially important in patients with severe arterial or venous disease.

INFORMATION FOR PATIENTS

Patients receiving injectable radiopaque diagnostic agents should be instructed to:

1. Inform your physician if you are pregnant.
2. Inform your physician if you are diabetic or if you have multiple myeloma, pheochromocytoma, homozygous sickle cell disease, or known thyroid disorder (See WARNINGS).
3. Inform your physician if you are allergic to any drugs, food or if you had any reactions to previous injections of substances used for x-ray procedures (see PRECAUTIONS-General).
4. Inform your physician about any other medications you are currently taking, including nonprescription drugs, before you have this procedure.

DRUG INTERACTIONS

Renal toxicity has been reported in a few patients with liver dysfunction who were given oral cholecystographic agents followed by intravascular contrast agents. Administration of intravascular agents should therefore be postponed in any patient with a known or suspected hepatic or biliary disorder who has recently received a cholecystographic contrast agent.

Other drugs should not be admixed with iopamidol.

DRUG/LABORATORY TEST INTERACTIONS

The results of PBI and radioactive iodine uptake studies, which depend on iodine estimations, will not accurately reflect thyroid function for up to 16 days following administration of iodinated contrast media. However, thyroid function tests not depending on iodine estimations, e.g., T3 resin uptake and total or free thyroxine (T4) assays are not affected.

Any test which might be affected by contrast media should be performed prior to administration of the contrast medium.

LABORATORY TEST FINDINGS

In vitro studies with animal blood showed that many radiopaque contrast agents, including iopamidol, produced a slight depression of plasma coagulation factors including prothrombin time, partial thromboplastin time and fibrinogen, as well as a slight tendency to cause platelet and/or red blood cell aggregation (see PRECAUTIONS-General).

Transitory changes may occur in red cell and leucocyte counts, serum calcium, serum creatinine, serum glutamic oxalacetic transaminase (SGOT) and uric acid in urine; transient albuminuria may occur.

These findings have not been associated with clinical manifestations.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY

Long-term studies in animals have not been performed to evaluate carcinogenic potential. No evidence of genetic toxicity was obtained in *in vitro* tests.

PREGNANCY

Teratogenic Effects—Pregnancy Category B. Reproduction studies have been performed in rats and rabbits at doses up to 2.7 and 1.4 times the maximum recommended human dose (1.48 gI/kg in a 50 kg individual), respectively, and have revealed no evidence of impaired fertility or harm to the fetus due to iopamidol. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

NURSING MOTHERS

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when iopamidol is administered to a nursing woman.

PEDIATRIC USE

Safety and effectiveness in pediatric patients have been established in pediatric angiocardiography, computed tomography (head and body) and excretory urography. Pediatric patients at higher risk of experiencing adverse events during contrast medium administration may include those having asthma, a sensitivity to medication and/or allergens, cyanotic heart disease, congestive heart failure, a serum creatinine greater than 1.5 mg/dL or those less than 12 months of age.

ADVERSE REACTIONS

Adverse reactions following the use of iopamidol are usually mild to moderate, self-limited and transient.

In angiocardiography (597 patients), the adverse reactions with an estimated incidence of one percent or higher are: hot flashes 3.4%; angina pectoris 3%; flushing 1.8%; bradycardia 1.3%; hypotension 1%; hives 1%.

In a clinical trial with 76 pediatric patients undergoing angiocardiography, two adverse reactions (2.6%) both remotely attributed to the contrast media were reported. Both patients were less than two years of age; both had cyanotic heart disease with underlying right ventricular abnormalities and abnormal pulmonary circulation. In one patient, preexisting cyanosis was transiently intensified following contrast media administration. In the second patient preexisting decreased peripheral perfusion was intensified for 24 hours following the examination. (See PRECAUTIONS for information on high risk nature of these patients).

Intravascular injection of contrast media is frequently associated with the sensation of warmth and pain, especially in peripheral arteriography and venography; pain and warmth are less frequent and less severe with Iopamidol Injection than with diatrizoate meglumine and diatrizoate sodium injection.

The following table of incidence of reactions is based on clinical studies with Iopamidol Injection in about 2246 patients.

ADVERSE REACTIONS

System	Estimated Overall Incidence >1%	≤1%
Cardiovascular	none	tachycardia, hypotension, hypertension, myocardial ischemia, circulatory collapse, S-T segment depression, bigeminy, extrasystoles, ventricular fibrillation, angina pectoris, bradycardia, transient ischemic attack, thrombophlebitis
Nervous	pain (2.8%), burning sensation (1.4%)	vasovagal reaction, tingling in arms, grimace, faintness
Digestive	nausea (1.2%)	vomiting, anorexia
Respiratory	none	throat constriction, dyspnea, pulmonary edema
Skin and Appendages	none	rash, urticaria, pruritus, flushing
Body as a Whole	hot flashes (1.5%)	headache, fever, chills, excessive sweating, back spasm
Special Senses	warmth (1.1%)	taste alterations, nasal congestion, visual disturbances
Urogenital	none	urinary retention

Regardless of the contrast agent employed, the overall estimated incidence of serious adverse reactions is higher with *coronary arteriography* than with other procedures. Cardiac decompensation, serious arrhythmias or myocardial ischemia or infarction have been reported with Iopamidol Injection and may occur during *coronary arteriography and left ventriculography*. Following coronary and ventricular injections, certain electrocardiographic changes (increased QTc, increased R-R, T-wave amplitude) and certain hemodynamic changes (decreased systolic pressure) occurred less frequently with Iopamidol Injection than with diatrizoate meglumine and diatrizoate sodium injection; increased LVEDP occurred less frequently after ventricular iopamidol injections.

In *aortography*, the risks of procedures also include injury to the aorta and neighboring organs, pleural puncture, renal damage including infarction and acute tubular necrosis with oliguria and anuria, accidental selective filling of the right renal artery during the translumbar procedure in the presence of preexisting renal disease, retroperitoneal hemorrhage from the translumbar approach and spinal cord injury and pathology associated with the syndrome of transverse myelitis.

The following adverse reactions have been reported for iopamidol:

Cardiovascular—arrhythmia, arterial spasms, flushing, vasodilation, chest pain, cardiopulmonary arrest

Nervous—confusion, paresthesia, dizziness, convulsions, paralysis, coma

Respiratory—increased cough, sneezing, asthma, apnea, laryngeal edema, chest tightness, rhinitis

Skin and Appendages—injection site pain usually due to extravasation and/or erythematous swelling, pallor,

6

...however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

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Respiratory	none	throat constriction, dyspnea, pulmonary edema
Skin and Appendages	none	rash, urticaria, pruritus, flushing
Body as a Whole	hot flashes (1.5%)	headache, fever, chills, excessive sweating, back spasm
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Cardiovascular—arrhythmia, arterial spasms, flushing, vasodilation, chest pain, cardiopulmonary arrest

Nervous—confusion, paresthesia, dizziness, convulsions, paralysis, coma

Respiratory—increased cough, sneezing, asthma, apnea, laryngeal edema, chest tightness, rhinitis

Skin and Appendages—injection site pain usually due to extravasation and/or erythematous swelling, pallor, periorbital edema, facial edema

Urogenital—pain, hematuria

Special Senses—watery, itchy eyes; lacrimation; conjunctivitis

Musculoskeletal—muscle spasm, involuntary leg movement

Body as a Whole—tremors, malaise, anaphylactoid reaction (characterized by cardiovascular, respiratory and cutaneous symptoms), pain

Digestive—severe retching and choking, abdominal cramps

Some of these may occur as a consequence of the procedure. Other reactions may also occur with the use of any contrast agent as a consequence of the procedural hazard; these include hemorrhage or pseudoaneurysms at the puncture site, brachial plexus palsy following axillary artery injections, chest pain, myocardial infarction and transient changes in hepatorenal chemistry tests. Arterial thrombosis, displacement of arterial plaques, venous thrombosis, dissection of the coronary vessels and transient sinus arrest are rare complications.

GENERAL ADVERSE REACTIONS TO CONTRAST MEDIA

Reactions known to occur with parenteral administration of iodinated ionic contrast agents (see the listing below) are possible with any nonionic agent. Approximately 95% of adverse reactions accompanying the use of other water-soluble intravascularly administered contrast agents are mild to moderate in degree. However, life-threatening reactions and fatalities, mostly of cardiovascular origin, have occurred. Reported incidences of

death from the administration of other iodinated contrast media range from 6.6 per 1 million (0.00066%) to 1 in 10,000 patients (0.01%). Most deaths occur during injection or 5 to 10 minutes later, the main feature being cardiac arrest with cardiovascular disease as the main aggravating factor. Isolated reports of hypotensive collapse and shock are found in the literature. The incidence of shock is estimated to be 1 out of 20,000 patients (0.005%).

Adverse reactions to injectable contrast media fall into two categories: chemotoxic reactions and idiosyncratic reactions. Chemotoxic reactions result from the physico-chemical properties of the contrast medium, the dose and the speed of injection. All hemodynamic disturbances and injuries to organs or vessels perfused by the contrast medium are included in this category. Experience with iopamidol suggests there is much less discomfort (e.g., pain and/or warmth) with peripheral arteriography. Fewer changes are noted in ventricular function after ventriculography and coronary arteriography.

Idiosyncratic reactions include all other reactions. They occur more frequently in patients 20 to 40 years old. Idiosyncratic reactions may or may not be dependent on the amount of drug injected, the speed of injection, the mode of injection and the radiographic procedure. Idiosyncratic reactions are subdivided into minor, intermediate and severe. The minor reactions are self-limited and of short duration; the severe reactions are life-threatening and treatment is urgent and mandatory.

The reported incidence of adverse reactions to contrast media in patients with a history of allergy is twice that for the general population. Patients with a history of previous reactions to a contrast medium are three times more susceptible than other patients. However, sensitivity to contrast media does not appear to increase with repeated examinations. Most adverse reactions to intravascular contrast agents appear within one to three minutes after the start of injection, but delayed reactions may occur [see PRECAUTIONS-General].

In addition to the adverse drug reactions reported for iopamidol, the following additional adverse reactions have been reported with the use of other intravascular contrast agents and are possible with the use of any water-soluble iodinated contrast agent:

Cardiovascular—cerebral hematomas, petechiae

Skin and Appendages—skin necrosis

Urogenital—osmotic nephrosis of proximal tubular cells, renal failure, neutropenia

Special Senses—conjunctival chemosis with infection

Hematologic—neutropenia

OVERDOSAGE

Treatment of an overdose of an injectable radiopaque contrast medium is directed toward the support of all vital functions and prompt institution of symptomatic therapy.

DOSAGE AND ADMINISTRATION

GENERAL

It is desirable that solutions of radiopaque diagnostic agents for intravascular use be at body temperature when injected. In the event that crystallization of the medium has occurred, place the vial in hot (60°-100°C) water for about five minutes, then shake gently to obtain a clear solution. Cool to body temperature before use. Discard vial without use if solids persist.

Withdrawal of contrast agents from their containers should be accomplished under aseptic conditions with sterile syringes. Sterile techniques must be used with any intravascular injection and with catheters and guidewires.

Patients should be well hydrated prior to and following Iopamidol Injection administration.

As with all radiopaque contrast agents, only the lowest dose of Iopamidol Injection necessary to obtain adequate visualization should be used. A lower dose reduces the possibility of an adverse reaction. Most procedures do not require use of either a maximum dose or the highest available concentration of Iopamidol Injection; the combination of dose and Iopamidol Injection concentration to be used should be carefully individualized, and factors such as age, body size, size of the vessel and its blood flow rate, anticipated pathology and degree and extent of opacification required, structure(s) or area to be examined, disease processes affecting the patient and equipment and technique to be employed should be considered.

CEREBRAL ARTERIOGRAPHY

Iopamidol Injection 61% (300 mgI/mL) should be used. The usual individual injection by carotid puncture or transfemoral catheterization is 8 to 12 mL, with total multiple doses ranging to 90 mL.

PERIPHERAL ARTERIOGRAPHY

Iopamidol Injection 61% usually provides adequate visualization. For injection into the femoral artery or subclavian artery, 5 to 40 mL may be used; for injection into the aorta for a distal runoff, 25 to 50 mL may be used. Doses up to a total of 250 mL of Iopamidol Injection 61% have been administered during peripheral arteriography.

PERIPHERAL VENOGRAPHY (PHLEBOGRAPHY)

Iopamidol Injection 41% (200 mgI/mL) should be used. The usual dose is 25 to 150 mL per lower extremity. The combined total dose for multiple injections has not exceeded 350 mL.

SELECTED VISCERAL ARTERIOGRAPHY AND AORTOGRAPHY

Iopamidol Injection 76% (370 mgI/mL) should be used. Doses up to 50 mL may be required for injection into the larger vessels such as the aorta or celiac artery; doses up to 10 mL may be required for injection into the renal arteries. Often, lower doses will be sufficient. The combined total dose for multiple injections has not exceeded 225 mL.

PEDIATRIC ANGIOCARDIOGRAPHY

Iopamidol Injection 76% should be used. Pediatric angiocardiography may be performed by injection into a large peripheral vein or by direct catheterization of the heart.

The usual dose range for single injections is provided in the following table:

Single Injection — Usual Dose Range

Age	mL
< 2 years	10-15
2-9 years	15-30
10-18 years	20-50

The usual dose for cumulative injections is provided in the following table:

Cumulative Injections — Usual Dose Range

Age	mL
< 2 years	40
2-4 years	50
5-9 years	100
10-18 years	125

CORONARY ARTERIOGRAPHY AND VENTRICULOGRAPHY

Iopamidol Injection 76% should be used. The usual dose for selective coronary artery injections is 2 to 10 mL. The usual dose for ventriculography, or for nonselective opacification of multiple coronary arteries following injection at the aortic root, is 25 to 50 mL. The total dose for combined procedures has not exceeded 200 mL. EKG monitoring is essential.

EXCRETORY UROGRAPHY

Iopamidol Injection 61% may be used. The usual adult dose for Iopamidol Injection 61% is 50 mL administered by rapid intravenous injection.

PEDIATRIC EXCRETORY UROGRAPHY

Iopamidol Injection 61% may be used. The dosage recommended for use in children for excretory urography is 1 mL/kg to 3 mL/kg for Iopamidol Injection 61%. It should not be necessary to exceed a total dose of 30 gI.

COMPUTED TOMOGRAPHY

Iopamidol Injection 61% may be used.

CECT of the Head—The suggested dose of Iopamidol Injection 61% is 100 to 200 mL by intravenous administration. Imaging may be performed immediately after completion of administration.

CECT of the Body—The usual adult dose range for Iopamidol Injection 61% is 100 to 200 mL administered by rapid intravenous infusion or bolus injection.

Equivalent doses of Iopamidol Injection 76%, based on organically bound iodine content, may also be used. Total dose for either CECT procedure should not exceed 60 grams of iodine.

PEDIATRIC COMPUTED TOMOGRAPHY

Iopamidol Injection 61% may be used. The dosage recommended for use in children for contrast enhanced computed tomography is 1 mL/kg to 3 mL/kg for Iopamidol Injection 61%. It should not be necessary to exceed a total dose of 30 gI.

DRUG INCOMPATIBILITIES

Many radiopaque contrast agents are incompatible *in vitro* with some antihistamines and many other drugs; therefore, no other pharmaceuticals should be admixed with contrast agents.

As with all radiopaque contrast agents, only the lowest [illegible] adequate visualization should be used. A lower dose reduces the possibility of an adverse reaction. Most procedures do not require use of either a maximum dose or the highest available concentration of Iopamidol Injection; the combination of dose and Iopamidol Injection concentration to be used should be carefully individualized, and factors such as age, body size, size of the vessel and its blood flow rate, anticipated pathology and degree and extent of opacification required, structure(s) or area to be examined, disease processes affecting the patient and equipment and technique to be employed should be considered.

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The usual dose for cumulative injections is provided in the following table:

Cumulative Injections — Usual Dose Range

Age	mL
< 2 years	1[illegible]
2-4 years	[illegible]
5-9 years	1[illegible]
10-18 years	12[illegible]

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Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Iopamidol solutions should be used only if clear and within the normal colorless to pale yellow range.

HOW SUPPLIED

Iopamidol Injection, USP 41%
- 200 mL *SINGLE DOSE* Vial packaged in 10s (*NDC* 0641-2474-43)

Iopamidol Injection, USP 61%
- 50 mL *SINGLE DOSE* Vial packaged in 10s (*NDC* 0641-2476-43)
- 100 mL *SINGLE DOSE* Vial packaged in 10s (*NDC* 0641-2477-43)
- 150 mL *SINGLE DOSE* Vial packaged in 10s (*NDC* 0641-2478-43)

Iopamidol Injection, USP 76%
- 50 mL *SINGLE DOSE* Vial packaged in 10s (*NDC* 0641-2481-43)
- 100 mL *SINGLE DOSE* Vial packaged in 10s (*NDC* 0641-2482-43)
- 150 mL *SINGLE DOSE* Vial packaged in 10s (*NDC* 0641-2483-43)
- 200 mL *SINGLE DOSE* Vial packaged in 10s (*NDC* 0641-2484-43)

STORAGE

Store at controlled room temperature 20°-25°C (68°-77°F). *Protect from light.* Discard unused portion.

Caution: Federal law prohibits dispensing without prescription.

Manufactured by **ELKINS-SINN, Cherry Hill, NJ 08003-4099**
A division of A. H. Robins Company

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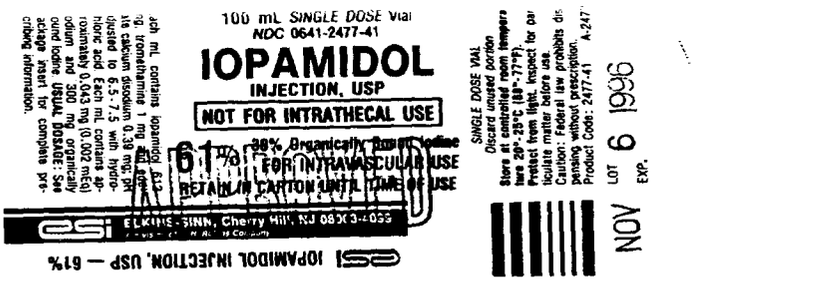
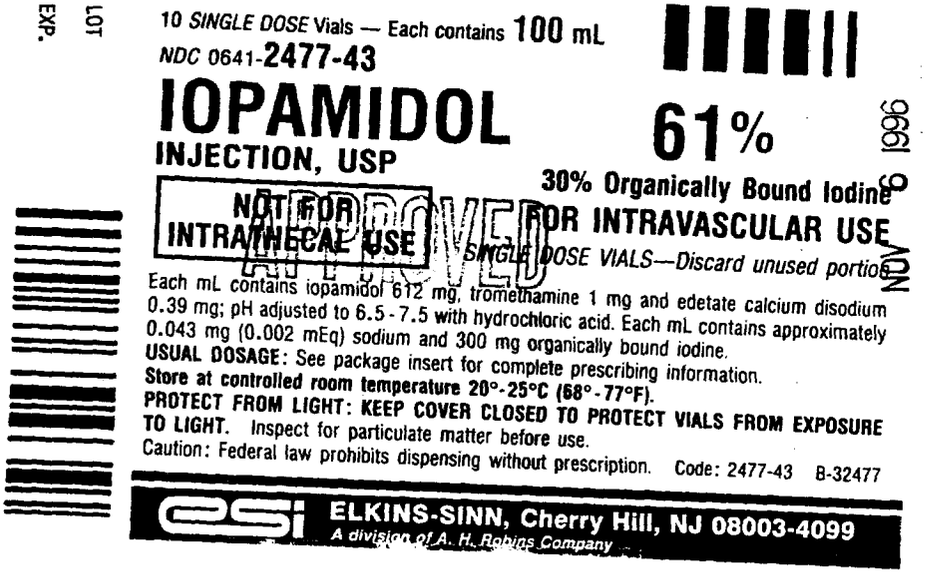
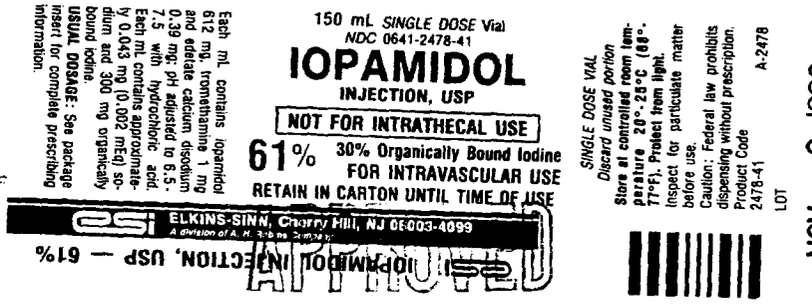
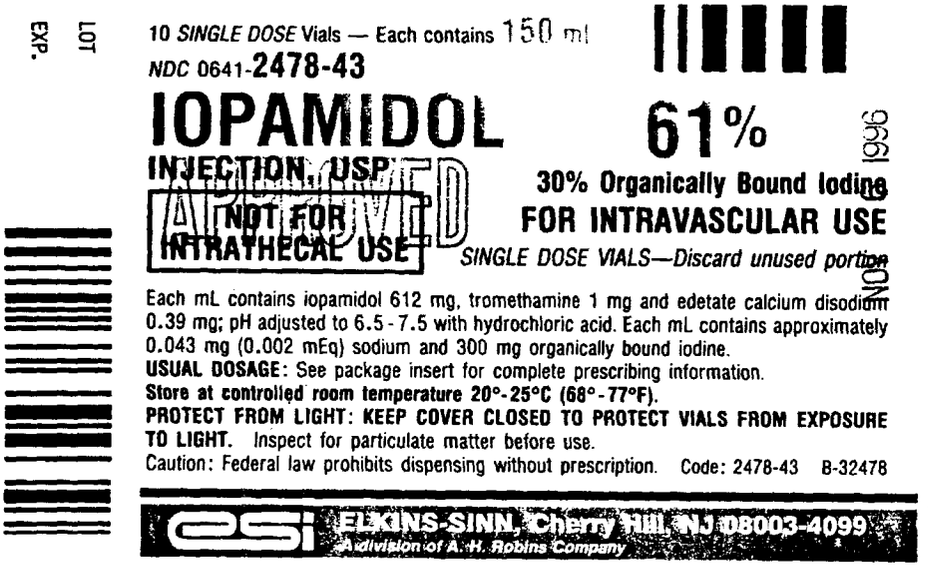
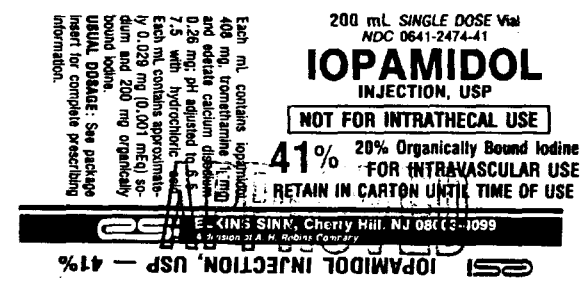
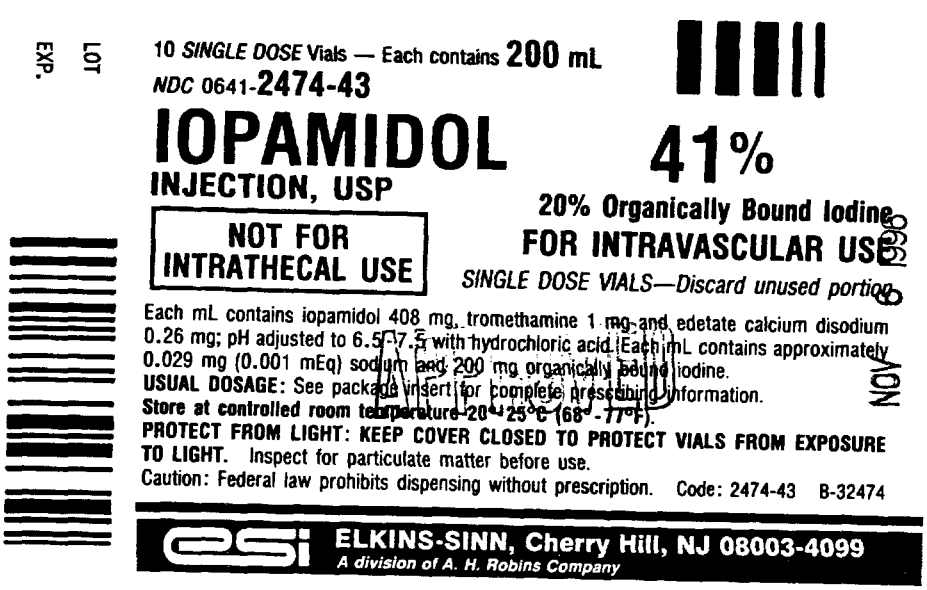

100 mL SINGLE DOSE Vial
NDC 0641-2477-41
IOPAMIDOL
INJECTION, USP
NOT FOR INTRATHECAL USE
61%
30% Organically Bound Iodine
FOR INTRAVASCULAR USE
RETAIN IN CARTON UNTIL TIME OF USE
ELKINS-SINN, Cherry Hill, NJ 08003-4099
IOPAMIDOL INJECTION, USP — 61%
SINGLE DOSE VIAL
Discard unused portion
LOT
EXP.
NOV 6 1996

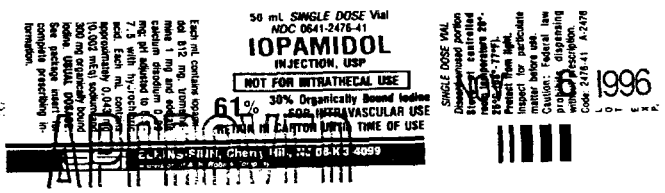

10 SINGLE DOSE Vials — Each contains 100 mL
NDC 0641-2477-43
IOPAMIDOL
INJECTION, USP
61%
30% Organically Bound Iodine
FOR INTRAVASCULAR USE
NOT FOR INTRATHECAL USE
APPROVED
SINGLE DOSE VIALS—Discard unused portion
Each mL contains iopamidol 612 mg, tromethamine 1 mg and edetate calcium disodium 0.39 mg; pH adjusted to 6.5 - 7.5 with hydrochloric acid. Each mL contains approximately 0.043 mg (0.002 mEq) sodium and 300 mg organically bound iodine.
USUAL DOSAGE: See package insert for complete prescribing information.
Store at controlled room temperature 20°-25°C (68°-77°F).
PROTECT FROM LIGHT: KEEP COVER CLOSED TO PROTECT VIALS FROM EXPOSURE TO LIGHT. Inspect for particulate matter before use.
Caution: Federal law prohibits dispensing without prescription. Code: 2477-43 B-32477
ELKINS-SINN, Cherry Hill, NJ 08003-4099
A division of A. H. Robins Company
LOT
EXP.
NOV 6 1996

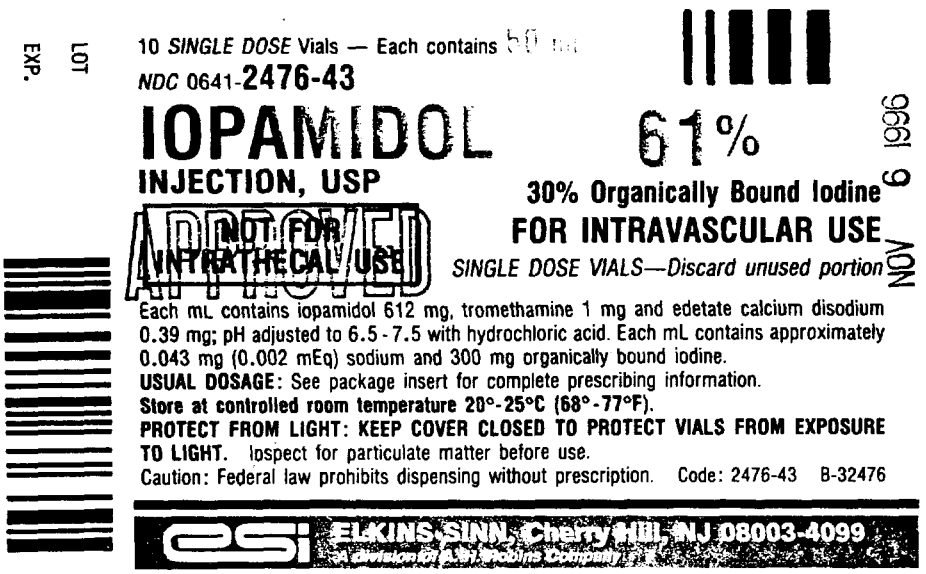

150 mL SINGLE DOSE Vial
NDC 0641-2478-41
IOPAMIDOL
INJECTION, USP
NOT FOR INTRATHECAL USE
61%
30% Organically Bound Iodine
FOR INTRAVASCULAR USE
RETAIN IN CARTON UNTIL TIME OF USE
ELKINS-SINN, Cherry Hill, NJ 08003-4099
IOPAMIDOL INJECTION, USP — 61%
APPROVED
SINGLE DOSE VIAL
Discard unused portion
LOT
EXP.
NOV 6 1996

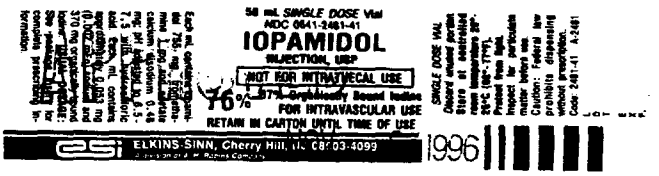

10 SINGLE DOSE Vials — Each contains 150 mL
NDC 0641-2478-43
IOPAMIDOL
INJECTION, USP
61%
30% Organically Bound Iodine
FOR INTRAVASCULAR USE
NOT FOR INTRATHECAL USE
APPROVED
SINGLE DOSE VIALS—Discard unused portion
Each mL contains iopamidol 612 mg, tromethamine 1 mg and edetate calcium disodium 0.39 mg; pH adjusted to 6.5 - 7.5 with hydrochloric acid. Each mL contains approximately 0.043 mg (0.002 mEq) sodium and 300 mg organically bound iodine.
USUAL DOSAGE: See package insert for complete prescribing information.
Store at controlled room temperature 20°-25°C (68°-77°F).
PROTECT FROM LIGHT: KEEP COVER CLOSED TO PROTECT VIALS FROM EXPOSURE TO LIGHT. Inspect for particulate matter before use.
Caution: Federal law prohibits dispensing without prescription. Code: 2478-43 B-32478
ELKINS-SINN, Cherry Hill, NJ 08003-4099
A division of A. H. Robins Company
LOT
EXP.
NOV 6 1996


200 mL SINGLE DOSE Vial
NDC 0641-2474-41
IOPAMIDOL
INJECTION, USP
NOT FOR INTRATHECAL USE
41%
20% Organically Bound Iodine
FOR INTRAVASCULAR USE
RETAIN IN CARTON UNTIL TIME OF USE
ELKINS-SINN, Cherry Hill, NJ 08003-4099
A Division of A. H. Robins Company
IOPAMIDOL INJECTION, USP — 41%
Each mL contains iopamidol 408 mg, tromethamine 1 mg and edetate calcium disodium 0.26 mg; pH adjusted to 6.5-7.5 with hydrochloric acid. Each mL contains approximately 0.029 mg (0.001 mEq) sodium and 200 mg organically bound iodine.
USUAL DOSAGE: See package insert for complete prescribing information.
SINGLE DOSE VIAL
Discard unused portion
Store at controlled room temperature 20°-25°C (68°-77°F). Protect from light.
Inspect for particulate matter before use.
Caution: Federal law prohibits dispensing without prescription.
Product Code
2474-41
A-2474
LOT
EXP.
NOV 6 1996


LOT
EXP.
10 SINGLE DOSE Vials — Each contains 200 mL
NDC 0641-2474-43
IOPAMIDOL
INJECTION, USP
41%
NOT FOR INTRATHECAL USE
20% Organically Bound Iodine
FOR INTRAVASCULAR USE
SINGLE DOSE VIALS—Discard unused portion
Each mL contains iopamidol 408 mg, tromethamine 1 mg and edetate calcium disodium 0.26 mg; pH adjusted to 6.5-7.5 with hydrochloric acid. Each mL contains approximately 0.029 mg (0.001 mEq) sodium and 200 mg organically bound iodine.
USUAL DOSAGE: See package insert for complete prescribing information.
Store at controlled room temperature 20°-25°C (68°-77°F).
PROTECT FROM LIGHT: KEEP COVER CLOSED TO PROTECT VIALS FROM EXPOSURE TO LIGHT. Inspect for particulate matter before use.
Caution: Federal law prohibits dispensing without prescription. Code: 2474-43 B-32474
ELKINS-SINN, Cherry Hill, NJ 08003-4099
A division of A. H. Robins Company
NOV 6 1996


50 mL SINGLE DOSE Vial
NDC 0641-2476-41
IOPAMIDOL
INJECTION, USP
NOT FOR INTRATHECAL USE
61%
30% Organically Bound Iodine
FOR INTRAVASCULAR USE
RETAIN IN CARTON UNTIL TIME OF USE
ELKINS-SINN, Cherry Hill, NJ 08003-4099
A Division of A. H. Robins Company
SINGLE DOSE VIAL
Discard unused portion
Store at controlled room temperature 20°-25°C (68°-77°F). Protect from light.
Inspect for particulate matter before use.
Caution: Federal law prohibits dispensing without prescription.
Code 2476-41 A-2476
LOT
EXP.
NOV 6 1996


LOT
EXP.
10 SINGLE DOSE Vials — Each contains 50 mL
NDC 0641-2476-43
IOPAMIDOL
INJECTION, USP
61%
NOT FOR INTRATHECAL USE
30% Organically Bound Iodine
FOR INTRAVASCULAR USE
SINGLE DOSE VIALS—Discard unused portion
Each mL contains iopamidol 612 mg, tromethamine 1 mg and edetate calcium disodium 0.39 mg; pH adjusted to 6.5-7.5 with hydrochloric acid. Each mL contains approximately 0.043 mg (0.002 mEq) sodium and 300 mg organically bound iodine.
USUAL DOSAGE: See package insert for complete prescribing information.
Store at controlled room temperature 20°-25°C (68°-77°F).
PROTECT FROM LIGHT: KEEP COVER CLOSED TO PROTECT VIALS FROM EXPOSURE TO LIGHT. Inspect for particulate matter before use.
Caution: Federal law prohibits dispensing without prescription. Code: 2476-43 B-32476
ELKINS-SINN, Cherry Hill, NJ 08003-4099
A division of A. H. Robins Company
NOV 6 1996



LOT
EXP.

10 *SINGLE DOSE* Vials — Each contains **50 mL**

NDC 0641-**2481-43**

IOPAMIDOL

INJECTION, USP

76%

37% Organically Bound Iodine

FOR INTRAVASCULAR USE

APPROVED

NOT FOR INTRATHECAL USE

SINGLE DOSE VIALS—Discard unused portion

1996 6 NOV

Each mL contains iopamidol 755 mg, tromethamine 1 mg and edetate calcium disodium 0.48 mg; pH adjusted to 6.5 - 7.5 with hydrochloric acid. Each mL contains approximately 0.053 mg (0.002 mEq) sodium and 370 mg organically bound iodine.

USUAL DOSAGE: See package insert for complete prescribing information.

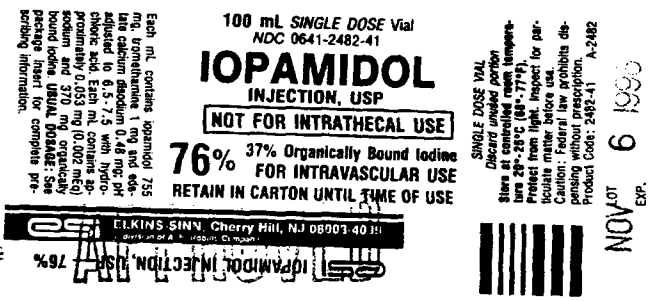
Store at controlled room temperature 20°-25°C (68°-77°F).

PROTECT FROM LIGHT: KEEP COVER CLOSED TO PROTECT VIALS FROM EXPOSURE TO LIGHT. Inspect for particulate matter before use.

Caution: Federal law prohibits dispensing without prescription. Code: 2481-43 B-32481

ELKINS-SINN, Cherry Hill, NJ 08003-4099

A division of A. H. Robins Company



LOT
EXP.

10 *SINGLE DOSE* Vials — Each contains **100 mL**

NDC 0641-**2482-43**

IOPAMIDOL

INJECTION, USP

76%

37% Organically Bound Iodine

FOR INTRAVASCULAR USE

APPROVED

NOT FOR INTRATHECAL USE

SINGLE DOSE VIALS—Discard unused portion

NOV 6 1996

Each mL contains iopamidol 755 mg, tromethamine 1 mg and edetate calcium disodium 0.48 mg; pH adjusted to 6.5 - 7.5 with hydrochloric acid. Each mL contains approximately 0.053 mg (0.002 mEq) sodium and 370 mg organically bound iodine.

USUAL DOSAGE: See package insert for complete prescribing information.

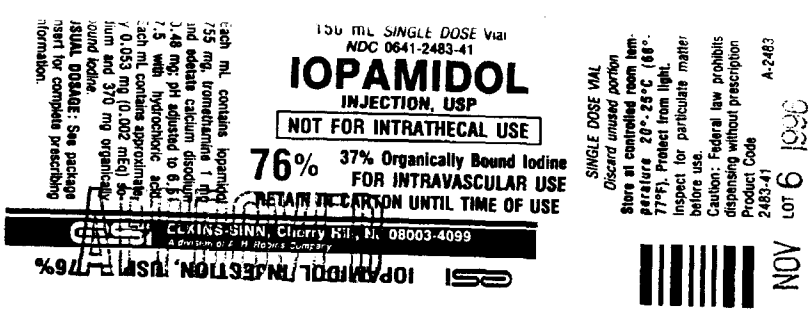
Store at controlled room temperature 20°-25°C (68°-77°F).

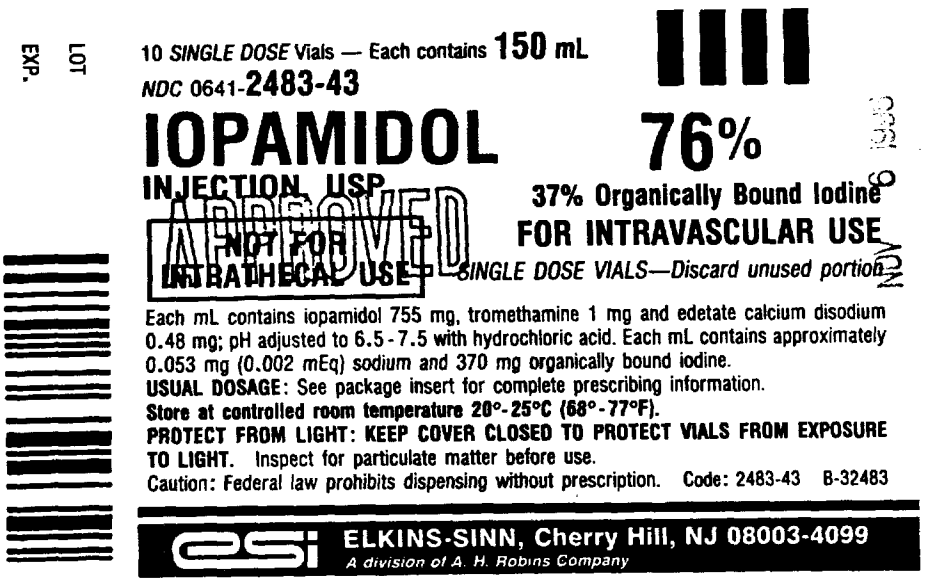
PROTECT FROM LIGHT: KEEP COVER CLOSED TO PROTECT VIALS FROM EXPOSURE TO LIGHT. Inspect for particulate matter before use.

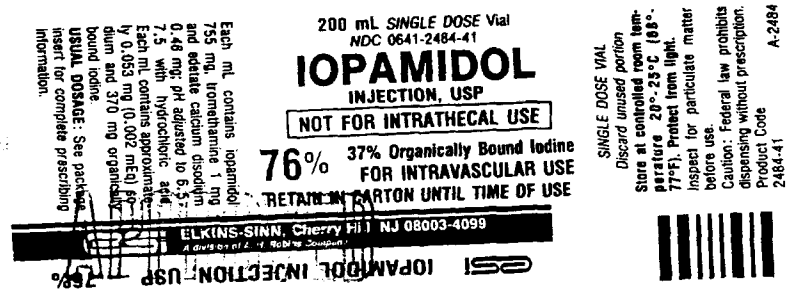
Caution: Federal law prohibits dispensing without prescription. Code: 2482-43 B-32482

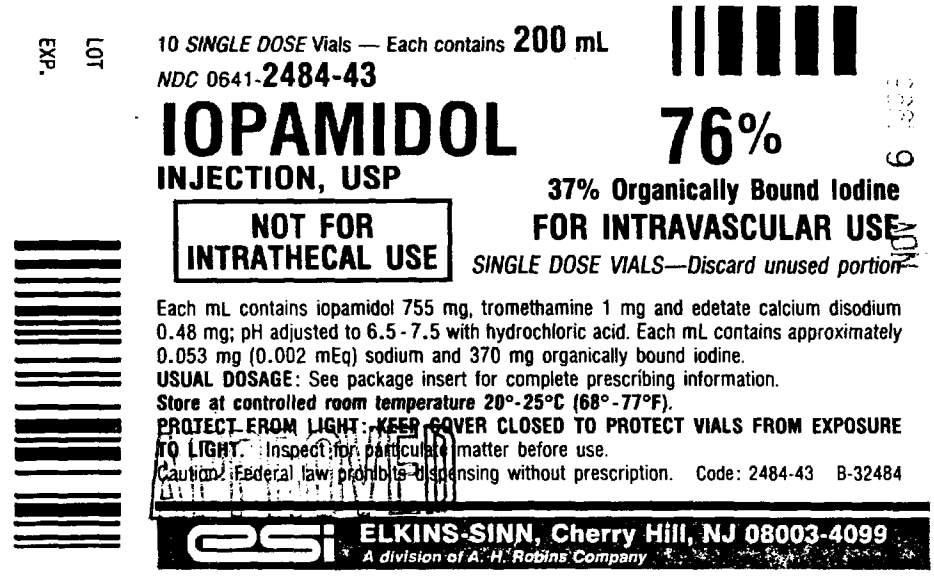
ELKINS-SINN, Cherry Hill, NJ 08003-4099

A division of A. H. Robins Company


150 mL SINGLE DOSE Vial
NDC 0641-2483-41
IOPAMIDOL
INJECTION, USP
NOT FOR INTRATHECAL USE
76%
37% Organically Bound Iodine
FOR INTRAVASCULAR USE
RETAIN IN CARTON UNTIL TIME OF USE
ELKINS-SINN, Cherry Hill, NJ 08003-4099
A division of A. H. Robins Company
SINGLE DOSE VIAL
Discard unused portion
Store at controlled room temperature 20°-25°C (68°-77°F). Protect from light.
Inspect for particulate matter before use.
Caution: Federal law prohibits dispensing without prescription
Product Code 2483-41
A-2483
LOT
EXP.
NOV


10 SINGLE DOSE Vials — Each contains 150 mL
NDC 0641-2483-43
IOPAMIDOL
INJECTION, USP
76%
37% Organically Bound Iodine
FOR INTRAVASCULAR USE
NOT FOR INTRATHECAL USE
SINGLE DOSE VIALS—Discard unused portion
Each mL contains iopamidol 755 mg, tromethamine 1 mg and edetate calcium disodium 0.48 mg; pH adjusted to 6.5-7.5 with hydrochloric acid. Each mL contains approximately 0.053 mg (0.002 mEq) sodium and 370 mg organically bound iodine.
USUAL DOSAGE: See package insert for complete prescribing information.
Store at controlled room temperature 20°-25°C (68°-77°F).
PROTECT FROM LIGHT: KEEP COVER CLOSED TO PROTECT VIALS FROM EXPOSURE TO LIGHT. Inspect for particulate matter before use.
Caution: Federal law prohibits dispensing without prescription. Code: 2483-43 B-32483
ELKINS-SINN, Cherry Hill, NJ 08003-4099
A division of A. H. Robins Company
LOT
EXP.
NOV


200 mL SINGLE DOSE Vial
NDC 0641-2484-41
IOPAMIDOL
INJECTION, USP
NOT FOR INTRATHECAL USE
76%
37% Organically Bound Iodine
FOR INTRAVASCULAR USE
RETAIN IN CARTON UNTIL TIME OF USE
ELKINS-SINN, Cherry Hill, NJ 08003-4099
SINGLE DOSE VIAL
Discard unused portion
Store at controlled room temperature 20°-25°C (68°-77°F). Protect from light.
Inspect for particulate matter before use.
Caution: Federal law prohibits dispensing without prescription.
Product Code 2484-41
A-2484
LOT
EXP.
NOV


10 SINGLE DOSE Vials — Each contains 200 mL
NDC 0641-2484-43
IOPAMIDOL
INJECTION, USP
76%
37% Organically Bound Iodine
FOR INTRAVASCULAR USE
NOT FOR INTRATHECAL USE
SINGLE DOSE VIALS—Discard unused portion
Each mL contains iopamidol 755 mg, tromethamine 1 mg and edetate calcium disodium 0.48 mg; pH adjusted to 6.5-7.5 with hydrochloric acid. Each mL contains approximately 0.053 mg (0.002 mEq) sodium and 370 mg organically bound iodine.
USUAL DOSAGE: See package insert for complete prescribing information.
Store at controlled room temperature 20°-25°C (68°-77°F).
PROTECT FROM LIGHT: KEEP COVER CLOSED TO PROTECT VIALS FROM EXPOSURE TO LIGHT. Inspect for particulate matter before use.
Caution: Federal law prohibits dispensing without prescription. Code: 2484-43 B-32484
ELKINS-SINN, Cherry Hill, NJ 08003-4099
A division of A. H. Robins Company
LOT
EXP.
NOV