

FEB 24 1998

Abbott Laboratories
Attention: Thomas Willer, Ph.D.
200 Abbott Park Road, D-389, AP30
Abbott Park, Illinois 60064-3537

Dear Sir:

This is in reference to your abbreviated new drug application dated November 14, 1996, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Iopamidol-250, Iopamidol-300, and Iopamidol-370 (Iopamidol Injection USP, 51%, 61% and 76%, respectively, packaged in plastic syringes).

Reference is also made to your amendments dated, August 15, 1997, September 12, 1997 and February 6, 1998.

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, 51%, 61% and 76% to be bioequivalent and, therefore, therapeutically equivalent to the listed drug [Isovue[®]-250, Isovue[®]-300, and Isovue[®]-370, 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,


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

2-24-98

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 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 iohalamate 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 angiocardiology 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.

Studies with solutions from flexible plastic containers have not been performed to evaluate carcinogenic potential, mutagenic potential or effects on fertility.

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 g I/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.

Caution should be exercised when solutions from flexible plastic containers are administered to a nursing mother.

Pediatric Use

Safety and effectiveness in pediatric patients have been established in pediatric angiocardiology, 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.

Safety and effectiveness of solutions from flexible plastic containers in pediatric patients have not been well established.

ADVERSE REACTIONS

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

In angiocardiology (597 patients), the adverse reactions with an estimated incidence of one percent or higher are: hot flashes 3.4%; angina pectoris 3.0%; flushing 1.8%; bradycardia 1.3%; hypotension 1.0%; hives 1.0%.

In a clinical trial with 76 pediatric patients undergoing angiocardiology, 2 adverse reactions (2.6%) both remotely attributed to the contrast media were reported. Both patients were less than 2 years of age, both had cyanotic heart disease with underlying right ventricular abnormalities and abnormal pulmonary circulation. In one patient pre-existing cyanosis was transiently intensified following contrast media administration. In the second patient pre-existing decreased peripheral perfusion was intensified for 24 hours following the examination. (See PRECAUTIONS section 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 2,246 patients.

System	Adverse Reactions 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

Adverse Reactions (cont'd)

System	Estimated Overall Incidence	
	>1%	≤1%
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 *angiography*, 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 pre-existing 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, cardio-pulmonary 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 percent 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 percent) to 1 in 10,000 patients (0.01 percent). 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 (0.005 percent) patients.

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.
- 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, discard the container, do not use.

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.

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.

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-300 (Iopamidol Injection, 300 mg I/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-300 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-300 have been administered during peripheral arteriography.

Peripheral Venography (Phlebography)

Iopamidol-200 (Iopamidol Injection, 200 mg I/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 250 mL.

Selective Visceral Arteriography and Aortography

Iopamidol-370 (Iopamidol Injection, 370 mg I/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-370 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-370 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-250 (Iopamidol Injection, 250 mg I/mL) or Iopamidol-300 may be used. The usual adult dose for Iopamidol-250 is 50 to 100 mL and for Iopamidol-300 is 50 mL administered by rapid intravenous injection.

Pediatric Excretory Urography

Iopamidol-250 or Iopamidol-300 may be used. The dosage recommended for use in pediatric patients for excretory urography is 1.2 mL/kg to 3.6 mL/kg for Iopamidol-250 and 1 mL/kg to 3 mL/kg for Iopamidol-300. It should not be necessary to exceed a total dose of 30 g I.

Computed Tomography

Iopamidol Injection 250 or Iopamidol Injection 300 may be used.

CECT of the Head: The suggested dose for Iopamidol Injection 250 is 130 to 240 mL, and for Iopamidol 300 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 250 is 130 to 240 mL, and for Iopamidol Injection 300 is 100 to 200 mL administered by rapid intravenous infusion, or bolus injection.

Equivalent doses of Iopamidol Injection 370, 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-250 or Iopamidol-300 may be used. The dosage recommended for use in pediatric patients for contrast enhanced computed tomography is 1.2 mL/kg to 3.6 mL/kg for Iopamidol-250 and 1 mL/kg to 3 mL/kg for Iopamidol-300. It should not be necessary to exceed a total dose of 30 g I.

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.

HOW SUPPLIED

Iopamidol Injection, USP is supplied in single-dose flexible plastic containers as follows:

- | | | |
|-----------|--------------|--|
| List 7529 | Ten - 50 mL | Iopamidol-200 (Iopamidol Injection, USP 41%) |
| List 7529 | Ten - 100 mL | Iopamidol-200 (Iopamidol Injection, USP 41%) |
| List 7529 | Ten - 200 mL | Iopamidol-200 (Iopamidol Injection, USP 41%) |
| List 7530 | Ten - 50 mL | Iopamidol-250 (Iopamidol Injection, USP 51%) |
| List 7530 | Ten - 100 mL | Iopamidol-250 (Iopamidol Injection, USP 51%) |
| List 7530 | Ten - 150 mL | Iopamidol-250 (Iopamidol Injection, USP 51%) |
| List 7530 | Ten - 200 mL | Iopamidol-250 (Iopamidol Injection, USP 51%) |
| List 7531 | Ten - 50 mL | Iopamidol-300 (Iopamidol Injection, USP 61%) |
| List 7531 | Ten - 75 mL | Iopamidol-300 (Iopamidol Injection, USP 61%) |
| List 7531 | Ten - 100 mL | Iopamidol-300 (Iopamidol Injection, USP 61%) |
| List 7531 | Ten - 150 mL | Iopamidol-300 (Iopamidol Injection, USP 61%) |
| List 7533 | Ten - 50 mL | Iopamidol-370 (Iopamidol Injection, USP 76%) |
| List 7533 | Ten - 75 mL | Iopamidol-370 (Iopamidol Injection, USP 76%) |
| List 7533 | Ten - 100 mL | Iopamidol-370 (Iopamidol Injection, USP 76%) |
| List 7533 | Ten - 125 mL | Iopamidol-370 (Iopamidol Injection, USP 76%) |
| List 7533 | Ten - 150 mL | Iopamidol-370 (Iopamidol Injection, USP 76%) |
| List 7533 | Ten - 175 mL | Iopamidol-370 (Iopamidol Injection, USP 76%) |
| List 7533 | Ten - 200 mL | Iopamidol-370 (Iopamidol Injection, USP 76%) |

Iopamidol Injection, USP is supplied in a single-dose teardrop vial as follows:

List 7532 Ten Plastic - 30 mL Iopamidol-300 (Iopamidol Injection, USP 61%)

Iopamidol Injection, USP is supplied in a single-dose ANSVR™ Syringe (LifeShield® Unit of Use Syringe with male luer lock) as follows:

- | | |
|-----------|--|
| List 8117 | Ten - 30 mL Iopamidol-250 (Iopamidol Injection, USP 51%) |
| List 8117 | Ten - 50 mL Iopamidol-250 (Iopamidol Injection, USP 51%) |
| List 8118 | Ten - 30 mL Iopamidol-300 (Iopamidol Injection, USP 61%) |
| List 8118 | Ten - 50 mL Iopamidol-300 (Iopamidol Injection, USP 61%) |
| List 8119 | Ten - 30 mL Iopamidol-370 (Iopamidol Injection, USP 76%) |
| List 8119 | Ten - 50 mL Iopamidol-370 (Iopamidol Injection, USP 76%) |

Discard unused portion. Check for the presence of particulate matter before use.

Protect from light. It is recommended that the product be stored at 15° to 25°C (59° to 77°F). Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. Protect from freezing.

Caution: Federal (USA) law prohibits dispensing without prescription.



(01) 1 030074 811915 4

Single-dose unit. Discard unused portion. Usual Dosage: See Insert. Store at 15° to 25°C (59° to 77°F). Do not freeze. Use only if solution is clear and colorless to pale yellow. Check for presence of particulate matter before use. Caution: Federal (USA) law prohibits dispensing without prescription.

IOPAMIDOL-370
IOPAMIDOL Injection, USP 76%
NOT FOR INTRATHECAL USE
37% Organically Bound Iodine

OP EN

Lifeshield®
with male luer lock adapter

Unit of Use Syringe

Ansys™

Protect from light.
Retain in carton until time of use.

For Intravascular Use.

37% Organically Bound Iodine

NOT FOR INTRATHECAL USE

IOPAMIDOL-370
IOPAMIDOL Injection, USP 76%

50 mL NDC 0074-8119-15

▶ PUSH AND PULL TO OPEN

50 mL NDC 0074-8119-15
IOPAMIDOL-370
IOPAMIDOL Injection, USP 76%
NOT FOR INTRATHECAL USE
37% Organically Bound Iodine

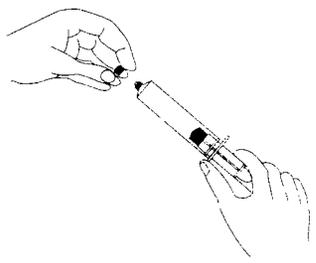
Each mL of sterile, nonpyrogenic, aqueous solution provides 755 mg iopamidol with 1 mg tromethamine and 0.48 mg edetate calcium disodium. May contain hydrochloric acid for pH adjustment. pH is 7.0 (6.5 to 7.5). Each mL contains approximately 0.053 mg (0.002 mEq) sodium and 370 mg organically bound iodine.

IOPAMIDOL-370
IOPAMIDOL Injection, USP 76%
NOT FOR INTRATHECAL USE
37% Organically Bound Iodine

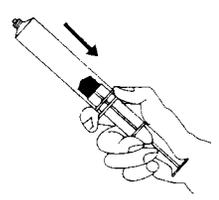
OP EN

USE ASEPTIC TECHNIQUE

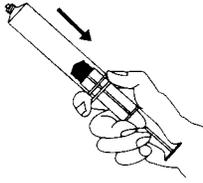
1. Remove luer cover.



2. Pull the barrel down until air is expelled from the syringe.



2. Pull the barrel down until air is expelled from the syringe.



Each mL of sterile, nonpyrogenic, aqueous solution provides 755 mg Iopamidol with 1 mg tromethamine and 0.48 mg edetate calcium sodium. May contain hydrochloric acid for pH adjustment. pH is 0.165 to 7.5. Each mL contains approximately 0.053 mg (0.002 mEq) sodium and 370 mg organically bound iodine.

Protect from light.
Retain in carton until time of use.

AnsyTM

Unit of Use Syringe

LifeShield[®]
with male luer lock adapter

Single-dose
Store at 15°
is clear and
particulate f
Caution: F
prescription

IOPAMIDOL-370
IOPAMIDOL Injection, USP 76%

NOT FOR INTRATHECAL USE

37% Organically Bound Iodine



RAO5614-2/R2-8/97
©Abbott 1997 Printed in USA

Abbott Laboratories
North Chicago, IL 60064, USA



OP EN

◀ **PUSH AND PULL TO OPEN** ▶

OP EN

50 mL NDC 0074-8119-15
IOPAMIDOL-370
IOPAMIDOL Injection, USP 76%
NOT FOR INTRATHECAL USE
37% Organically Bound Iodine

IOPAMIDOL-370



IOPAMIDOL-370

IOPAMIDOL Injection, USP 76%

NOT FOR INTRATHECAL USE

37% Organically Bound Iodine
For Intravascular Use.

Protect from light. Retain in carton until time of use. RAO5613-2/R2-8/97



(01) 0 030074 811915 7

Each mL of sterile, nonpyrogenic, aqueous solution provides 755 mg iopamidol with 1 mg tromethamine and 0.48 mg edetate calcium disodium. May contain hydrochloric acid for pH adjustment. pH is 7.0 (6.5 to 7.5). Each mL contains approximately 0.053 mg (0.002 mEq) sodium and 370 mg organically bound iodine. Check for presence of particulate matter before use. Discard unused portion. Caution: Federal (USA) law prohibits dispensing without prescription. Abbott Laboratories, North Chicago, IL 60064, USA

37% Organically Bound Iodine

NOT FOR INTRATHECAL USE

IOPAMIDOL Injection, USP 76%

IOPAMIDOL-370

NDC 0074-8119-03

30 mL

PUSH AND PULL TO OPEN

30 mL

NDC 0074-8119-03

IOPAMIDOL-370

IOPAMIDOL Injection, USP 76%

NOT FOR INTRATHECAL USE

37% Organically Bound Iodine

For Intravascular Use.

Protect from light.

Retain in carton until time of use.

Ansys™

Unit of Use Syringe

Lifeshield® with male luer lock adapter

APPROVED

Single-dose unit. Discard unused portion. Usual Dosage: See Insert. Store at 15° to 25°C (59° to 77°F). Do not freeze. Use only if solution is clear and colorless to pale yellow. Check for presence of particulate matter before use. Caution: Federal (USA) law prohibits dispensing without prescription.

IOPAMIDOL-370

IOPAMIDOL Injection, USP 76%

NOT FOR INTRATHECAL USE

37% Organically Bound Iodine



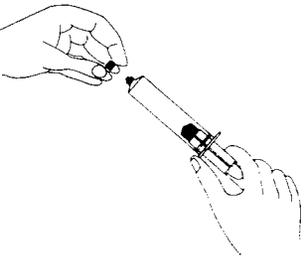
37% Organically Bound Iodine

IOPAMIDOL-370 IOPAMIDOL Injection, USP 76% NOT FOR INTRATHECAL USE

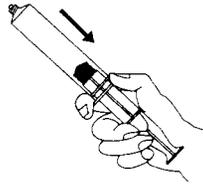
Each mL of sterile, nonpyrogenic, aqueous solution provides 755 mg iopamidol with 1 mg tromethamine and 0.48 mg edetate calcium disodium. May contain hydrochloric acid for pH adjustment. pH is 7.0 (6.5 to 7.5). Each mL contains approximately 0.053 mg (0.002 mEq) sodium and 370 mg organically bound iodine.

USE ASEPTIC TECHNIQUE

1. Remove luer cover.



2. Pull the barrel down until air is expelled from the syringe.



RAO5612-2/R2-8/97 ©Abbott 1997 Printed in USA Abbott Laboratories North Chicago, IL 60064, USA

OP EN

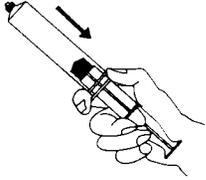
PUSH AND PULL TO OPEN

OP EN

30 mL

NDC 0074-8119-03

2. Pull the barrel down until air is expelled from the syringe.



sterile, nonpyrogenic, aqueous solution
54 mg Iopamidol with 1 mg tromethamine and
0.5 mg calcium disodium. May contain
sulfuric acid for pH adjustment. pH is 7.0 (6.5
to 7.5). Each mL contains approximately 0.053 mg
of sodium and 370 mg organically bound

time of use.

Ansys™

Unit of Use Syringe

LifeShield®
with male luer lock
adapter

IOPAMIDOL-37

IOPAMIDOL Injection, USP 76

NOT FOR INTRATHECAL USE

37% Organically Bound Iodine



RAO5612-2/R2-8/97

©Abbott 1997

Printed in USA

Abbott Laboratories
North Chicago, IL 60064, USA

OP EN

◀ PUSH AND PULL TO OPEN ▶

OP EN

30 mL

NDC 0074-8119-03

IOPAMIDOL-370

IOPAMIDOL Injection, USP 76%

NOT FOR INTRATHECAL USE

37% Organically Bound Iodine

25% Organically Bound Iodine

NOT FOR INTRATHECAL USE

IOPAMIDOL Injection, USP 51%
IOPAMIDOL-250

30 mL NDC 0074-8117-03

OP EN

PUSH AND PULL TO OPEN

30 mL NDC 0074-8117-03

IOPAMIDOL-250

IOPAMIDOL Injection, USP 51%

NOT FOR INTRATHECAL USE

25% Organically Bound Iodine

For Intravascular Use.

Protect from light.

Retain in carton until
time of use.

Ansyrtm

Unit of Use Syringe

LifeShield®
with male luer lock
adapter

IOPAMIDOL-250
IOPAMIDOL Injection, USP 51%
NOT FOR INTRATHECAL USE
25% Organically Bound Iodine

Each mL of sterile, nonpyrogenic, aqueous solution provides 510 mg iopamidol with 1 mg tromethamine and 0.33 mg edetate calcium disodium. May contain hydrochloric acid for pH adjustment. pH is 7.0 (6.5 to 7.5). Each mL contains approximately 0.036 mg (0.002 mEq) sodium and 250 mg organically bound iodine.

OP EN

Single-dose unit. Discard unused portion. Usual Dosage: See Insert. Store at 15° to 25°C (59° to 77°F). Do not freeze. Use only if solution is clear and colorless to pale yellow. Check for presence of particulate matter before use.
Caution: Federal (USA) law prohibits dispensing without prescription.

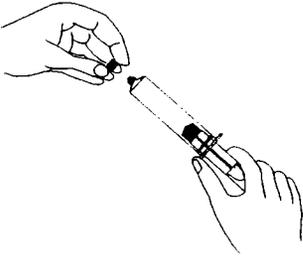
IOPAMIDOL-250
IOPAMIDOL Injection, USP 51%

NOT FOR INTRATHECAL USE

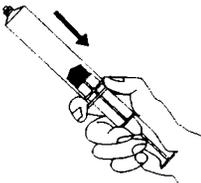
25% Organically Bound Iodine

USE ASEPTIC TECHNIQUE

1. Remove luer cover.



2. Pull the barrel down until air is expelled from the syringe.



24 1998

APPROVED



(01) 1 030074 811703 7

RAO5635-2/R2-9/97

©Abbott 1997

Printed in USA

Abbott Laboratories
North Chicago, IL 60064, USA

OP EN

PUSH AND PULL TO OPEN

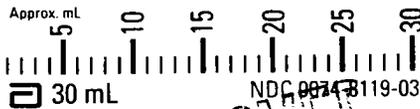
OP EN

30 mL

NDC 0074-8117-03

2 1008

IOPAMIDOL-370



NDC 0074-8119-03

IOPAMIDOL-370

IOPAMIDOL Injection, USP 76%

NOT FOR INTRATHECAL USE

37% Organically Bound Iodine
For Intravascular Use.

Protect from light. Retain in carton until time of use.

Abbott Labs., N. Chicago, IL 60064, USA RAO5611-2/R2-8/97



(01) 0 030074 811903 4

Each mL of sterile, nonpyrogenic, aqueous solution provides 755 mg iopamidol with 1 mg tromethamine and 0.48 mg edetate calcium disodium. May contain hydrochloric acid for pH adjustment, pH is 7.0 (6.5 to 7.5). Each mL contains approximately 0.053 mg (0.002 mEq) sodium and 370 mg organically bound iodine. Check for presence of particulate matter before use. Discard unused portion. Caution: Federal (USA) law prohibits dispensing without prescription.



30% Organically Bound Iodine

IOPAMIDOL-300
IOPAMIDOL Injection, USP 61%
NOT FOR INTRATHECAL USE

Single-dose unit. Discard unused portion. Usual Dosage: See Insert. Store at 15° to 25°C (59° to 77°F). Do not freeze. Use only if solution is clear and colorless to pale yellow. Check for presence of particulate matter before use.
Caution: Federal (USA) law prohibits dispensing without prescription.

OPEN

IOPAMIDOL-300
IOPAMIDOL Injection, USP 61%
NOT FOR INTRATHECAL USE
50 mL
NDC 0074-8118-15

PUSH AND PULL TO OPEN

IOPAMIDOL-300
IOPAMIDOL Injection, USP 61%
NOT FOR INTRATHECAL USE
50 mL
NDC 0074-8118-15

30% Organically Bound Iodine

For Intravascular Use.

Protect from light.
Retain in carton until
time of use.

Ansyrr™

Unit of Use Syringe

Lifeshield®
with male luer lock
adapter

Each mL of sterile, nonpyrogenic, aqueous solution provides 612 mg iopamidol with 1 mg tromethamine and 0.39 mg edetate calcium disodium. May contain hydrochloric acid for pH adjustment. pH is 7.0 (6.5 to 7.5). Each mL contains approximately 0.043 mg (0.002 mEq) sodium and 300 mg organically bound iodine.

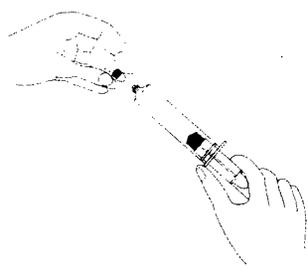
IOPAMIDOL-300
IOPAMIDOL Injection, USP 61%
NOT FOR INTRATHECAL USE

30% Organically Bound Iodine

OPEN

USE ASEPTIC TECHNIQUE

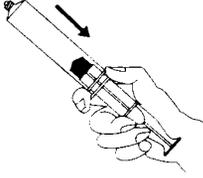
1. Remove luer cover.



2. Pull the barrel down until air is expelled from the syringe.



2. Pull the barrel down until air is expelled from the syringe.



Each mL of sterile, nonpyrogenic, aqueous solution provides 612 mg Iopamidol with 1 mg tromethamine and 0.39 mg edetate calcium disodium. May contain hydrochloric acid for pH adjustment. pH is 5.0 (6.5 to 7.5). Each mL contains approximately 0.043 mg (0.002 mEq) sodium and 300 mg organically bound iodine.

Protect from light.
Retain in carton until time of use.

Ansys™

Unit of Use Syringe

LifeShield®
with male luer lock adapter

Single-dose
Store at 15°
is clear an
particulate
Caution: I
prescription

IOPAMIDOL-300
IOPAMIDOL Injection, USP 61%
NOT FOR INTRATHECAL USE

30% Organically Bound Iodine



RAO5610-2/R2-8/97
©Abbott 1997 Printed in USA

Abbott Laboratories
North Chicago, IL 60064, USA

OP EN

◀ PUSH AND PULL TO OPEN ▶

OP EN

50 mL NDC 0074-8118-15
IOPAMIDOL-300
IOPAMIDOL Injection, USP 61%
NOT FOR INTRATHECAL USE
30% Organically Bound Iodine

IOPAMIDOL-300



IOPAMIDOL-300

IOPAMIDOL Injection, USP 61%

NOT FOR INTRATHECAL USE

**30% Organically Bound Iodine
For Intravascular Use.**

Protect from light. Retain in carton until time of use.

RAO5609-2/R2-8/97



(01) 0 030074 811815 0

Each mL of sterile, nonpyrogenic, aqueous solution provides 612 mg iopamidol with 1 mg tromethamine and 0.39 mg edelate calcium disodium. May contain hydrochloric acid for pH adjustment, pH is 7.0 (6.5 to 7.5). Each mL contains approximately 0.043 mg (0.002 mEq) sodium and 300 mg organically bound iodine. Check for presence of particulate matter before use. Discard unused portion. Caution: Federal (USA) law prohibits dispensing without prescription.
Abbott Laboratories, North Chicago, IL 60064, USA

30% Organically Bound Iodine

NOT FOR INTRATHECAL USE

IOPAMIDOL Injection, USP 61%

30 mL NDC 0074-8118-03

▶ PUSH AND PULL TO OPEN ◀

30 mL NDC 0074-8118-03

IOPAMIDOL-300

IOPAMIDOL Injection, USP 61%

NOT FOR INTRATHECAL USE

30% Organically Bound Iodine

For Intravascular Use.

Protect from light.

Retain in carton until time of use.

Ansys™

Unit of Use Syringe

Lifeshield® with male luer lock adapter

OP EN

Single-dose unit. Discard unused portion. Usual Dosage: See Insert. Store at 15° to 25°C (59° to 77°F). Do not freeze. Use only if solution is clear and colorless to pale yellow. Check for presence of particulate matter before use. Caution: Federal (USA) law prohibits dispensing without prescription.

IOPAMIDOL-300 IOPAMIDOL Injection, USP 61%

NOT FOR INTRATHECAL USE

30% Organically Bound Iodine

OP EN



IOPAMIDOL-300

IOPAMIDOL Injection, USP 61%

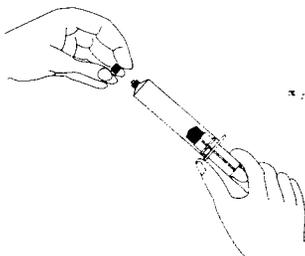
NOT FOR INTRATHECAL USE

30% Organically Bound Iodine

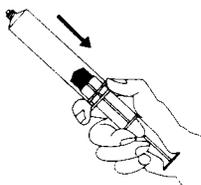
Each mL of sterile, nonpyrogenic, aqueous solution provides 612 mg iopamidol with 1 mg tromethamine and 0.39 mg edetate calcium disodium. May contain hydrochloric acid for pH adjustment. pH is 7.0 (6.5 to 7.5). Each mL contains approximately 0.043 mg (0.002 mEq) sodium and 300 mg organically bound iodine.

USE ASEPTIC TECHNIQUE

1. Remove luer cover.



2. Pull the barrel down until air is expelled from the syringe.



APPROVED



OP EN

▶ PUSH AND PULL TO OPEN ◀

30 mL NDC 0074-8118-03

IOPAMIDOL-300

OP EN



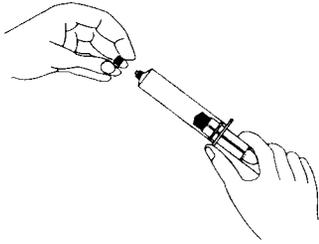
(01) 1 030074 811803 4

RAO5609-2/R2-8/97 ©Abbott 1997 Printed in USA

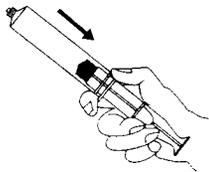
Abbott Laboratories North Chicago, IL 60064, USA

USE ASEPTIC TECHNIQUE

1. Remove luer cover.



2. Pull the barrel down until air is expelled from the syringe.



30% Organically Bound Iodine

NOT FOR INTRATHECAL USE

IOPAMIDOL-300
IOPAMIDOL Injection, USP 61%

Each mL of sterile, nonpyrogenic, aqueous solution provides 612 mg Iopamidol with 1 mg tromethamine and 0.39 mg edetate calcium disodium. May contain hydrochloric acid for pH adjustment. pH is 7.0 (6.5 to 7.5). Each mL contains approximately 0.043 mg (0.002 mEq) sodium and 300 mg organically bound iodine.

IOPAMIDOL-300
IOPAMIDOL Injection, USP 61%

NOT FOR INTRATHECAL USE

30% Organically Bound Iodine

For Intravascular Use.

Protect from light.
Retain in carton until
time of use.

Ansys™

Unit of Use Syringe

Lifeshield®
with male luer lock
adapter

Single-dose unit. Discard unused portion.
Dosage: See insert. Store at 15° to 25°C (5° to 77°F). Do not freeze. Use only if solution is clear and colorless. Check for presence of matter before use.
Caution: Federal (USA) law prohibits without prescription.

IOPAMIDOL-300
IOPAMIDOL Injection, USP 61%

NOT FOR INTRATHECAL USE

30% Organically Bound Iodine

APPROVED



RAO5608-2/R2-8/97
©Abbott 1997 Printed in USA
Abbott Laboratories
North Chicago, IL 60064, USA

OP EN

◀ PUSH AND PULL TO OPEN ▶

OP EN

30 mL NDC 0074-8118-03
IOPAMIDOL-300
IOPAMIDOL Injection, USP 61%
NOT FOR INTRATHECAL USE
30% Organically Bound Iodine

IOPAMIDOL-300



IOPAMIDOL-300

IOPAMIDOL Injection, USP 61%

NOT FOR INTRATHECAL USE

**30% Organically Bound Iodine
For Intravascular Use.**

Protect from light. Retain in carton until time of use.

Abbott Labs, N. Chicago, IL 60064, USA RAO5607-2/R2-8/97



(01) 0 030074 811803 7

Each mL of sterile, nonpyrogenic, aqueous solution provides 612 mg iopamidol with 1 mg tromethamine and 0.39 mg edetate calcium disodium. May contain hydrochloric acid for pH adjustment. pH is 7.0 (6.5 to 7.5). Each mL contains approximately 0.043 mg (0.002 mEq) sodium and 300 mg organically bound iodine. Check for presence of particulate matter before use. Discard unused portion. Caution: Federal (USA) law prohibits dispensing without prescription.



25% Organically Bound Iodine

IOPAMIDOL-250

IOPAMIDOL Injection, USP 51%

NOT FOR INTRATHECAL USE

Single-dose unit. Discard unused portion. Usual Dosage: See insert. Store at 15° to 25°C (59° to 77°F). Do not freeze. Use only if solution is clear and colorless to pale yellow. Check for presence of particulate matter before use. Caution: Federal (USA) law prohibits dispensing without prescription.

Lifeshield®
with male luer lock
adapter

Unit of Use Syringe

Ansys™

Protect from light.
Retain in carton until
time of use.

For Intravascular Use.

25% Organically Bound Iodine

IOPAMIDOL-250

IOPAMIDOL Injection, USP 51%

NOT FOR INTRATHECAL USE

► PUSH AND PULL TO OPEN ◀

50 mL NDC 0074-8117-15

IOPAMIDOL-250
IOPAMIDOL Injection, USP 51%
NOT FOR INTRATHECAL USE

25% Organically Bound Iodine

APPROVED

24 1998

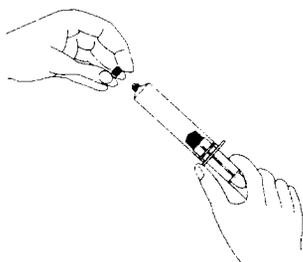
Each mL of sterile, nonpyrogenic, aqueous solution provides 510 mg iopamidol with 1 mg tromethamine and 0.33 mg edetate calcium disodium. May contain hydrochloric acid for pH adjustment. pH is 7.0 (6.5 to 7.5). Each mL contains approximately 0.036 mg (0.002 mEq) sodium and 250 mg organically bound iodine.

IOPAMIDOL-250
IOPAMIDOL Injection, USP 51%
NOT FOR INTRATHECAL USE
25% Organically Bound Iodine

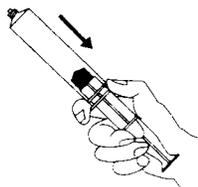
OP EN

USE ASEPTIC TECHNIQUE

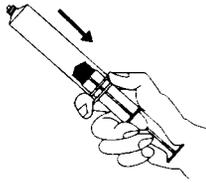
1. Remove luer cover.



2. Pull the barrel down until air is expelled from the syringe.



2. Pull the barrel down until air is expelled from the syringe.



each mL of sterile, nonpyrogenic, aqueous solution provides 510 mg Iopamidol with 1 mg tromethamine and 0.33 mg edetate calcium sodium. May contain hydrochloric acid for pH adjustment. pH is 6.5 to 7.5. Each mL contains approximately 0.036 mg (0.002 mEq) iodine and 250 mg organically bound iodine.

time of use.

AnsyTM

Unit of Use Syringe

LifeShield[®]
with male luer lock
adapter

Single-dose
Store at 15
is clear and
particulate
Caution: I
prescription

IOPAMIDOL-250
IOPAMIDOL Injection, USP 51%
NOT FOR INTRATHECAL USE

25% Organically Bound Iodine

APPROVED

2 4 1998



RAO5606-2/R2-8/97
©Abbott 1997 Printed in USA

Abbott Laboratories
North Chicago, IL 60064, USA

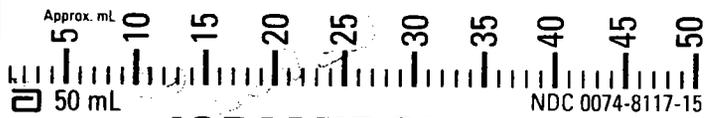
OP EN

◀ PUSH AND PULL TO OPEN ▶

OP EN

50 mL NDC 0074-8117-15
IOPAMIDOL-250
IOPAMIDOL Injection, USP 51%
NOT FOR INTRATHECAL USE
25% Organically Bound Iodine

IOPAMIDOL-250



IOPAMIDOL-250

IOPAMIDOL Injection, USP 51%

NOT FOR INTRATHECAL USE

25% Organically Bound Iodine
For Intravascular Use.

Protect from light. Retain in carton until time of use.

Abbott Laboratories, North Chicago, IL 60064, USA

RAO5605-2/R2-8/97



(01) 0 030074 811715 3

Each mL of sterile, nonpyrogenic, aqueous solution provides 510 mg iopamidol with 1 mg tromethamine and 0.33 mg edetate calcium disodium. May contain hydrochloric acid for pH adjustment. pH is 7.0 (6.5 to 7.5). Each mL contains approximately 0.036 mg (0.002 mEq) sodium and 250 mg organically bound iodine. Check for presence of particulate matter before use. Discard unused portion. Caution: Federal (USA) law prohibits dispensing without prescription.

Handwritten initials and signature

24 1998

IOPAMIDOL-250



IOPAMIDOL-250

IOPAMIDOL Injection, USP 51%

NOT FOR INTRATHECAL USE

25% Organically Bound Iodine

For Intravascular use.

Protect from light. Retain in carton until time of use.

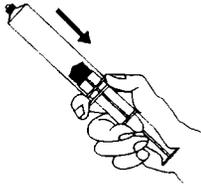
Abbott Labs., N. Chgo., IL 60064, USA RAO5634-2/R2-9/97



(01) 0 030074 811703 0

Each mL of sterile, nonpyrogenic, aqueous solution provides 510 mg iopamidol with 1 mg tromethamine and 0.23 mg edetate calcium disodium. May contain hydrochloric acid for pH adjustment, pH is 7.0 (6.5 to 7.5). Each mL contains approximately 0.036 mg (0.002 mEq) sodium and 250 mg organically bound iodine. Check for presence of particulate matter before use. Discard unused portion. Caution: Federal (USA) law prohibits dispensing without prescription.

2. Pull the barrel down until air is expelled from the syringe.



h mL of sterile, nonpyrogenic, aqueous solution
ides 510 mg Iopamidol with 1 mg tromethamine and
1 mg edetate calcium disodium. May contain
rochloric acid for pH adjustment. pH is 7.0 (6.5 to
02 mEq) sodium and 250 mg organically bound
iodine.

Unit of Use.

Ansys™

Unit of Use Syringe

LifeShield®

with male luer lock
adapter

IOPAMIDOL-250
IOPAMIDOL Injection, USP 51%

NOT FOR INTRATHECAL USE

25% Organically Bound Iodine

24 1998

APPROVED



(01) 1 030074 811703 7

RAO5635-2/R2-9/97

©Abbott 1997

Printed in USA

Abbott Laboratories

North Chicago, IL 60064, USA



OP EN

◀ PUSH AND PULL TO OPEN ▶

OP EN

30 mL

NDC 0074-8117-03

IOPAMIDOL-250

IOPAMIDOL Injection, USP 51%

NOT FOR INTRATHECAL USE

25% Organically Bound Iodine

JUN 5 1997

**Iopamidol
Injection
51%, 61% & 76%
in 30 mL/50 mL Polypropylene Syringe
ANDA #75-005
Reviewer: Lin-Whei Chuang**

**Abbott Laboratories
Abbott Park, IL**

**Submission Date:
November 14, 1996**

Review of a Waiver Request for an Injectable Dosage Form

Iopamidol solution is a radiopaque agent. When injected intravascularly, it opacifies those vessels in the path of flow of the contrast medium, permitting radiographic visualization of the internal structures of human body until significant hemodilution occurs. It is used for angiography throughout the cardiovascular system.

This application was submitted for iopamidol injection, 51%, 61%, and 76% in 30 mL and 50 mL of polypropylene syringe. The firm requests a waiver of the bioavailability/bioequivalence requirement for the test products per 21CFR 320.22(b)(1). The test products are intended for intravascular administration. The listed reference products which are the basis of this submission are Isovue-250^R (iopamidol injection, 51%), Isovue-300^R (iopamidol injection, 61%), and Isovue-370^R (iopamidol injection, 76%), manufactured by Bracco Diagnostics Inc. (Formerly Squibb Diagnostics), approved under NDA #18735 and #20327. (The reference products are in glass containers).

The comparative formulations of the test and reference products are presented below:

Ingredient per mL	Isovue-250 ^R (Bracco)*	Iopamidol inj. 51% (Abbott)*	Isovue-300 ^R (Bracco)**	Iopamidol inj. 61% (Abbott)**	Isovue-370 ^R (Bracco)***	Iopamidol inj. 76% (Abbott)***
Iopamidol	510 mg	510 mg	612 mg	612 mg	755 mg	755 mg
Edetate Calcium Disodium	0.33 mg	0.33 mg	0.39 mg	0.39 mg	0.48 mg	0.48 mg
Tromethamine	1 mg	1 mg	1 mg	1 mg	1 mg	1 mg
Water for Injection	qs to 1 mL	qs to 1 mL	qs to 1 mL	qs to 1 mL	qs to 1 mL	qs to 1 mL

* Equivalent to 250 mg iodine/mL

** Equivalent to 300 mg iodine/mL

*** Equivalent to 370 mg iodine/mL

Comments:

1. The test product is a parenteral solution intended solely for administration by injection (IV).
2. The test products, iopamidol injection 51%, 61%, and 76%, contain the same active and inactive ingredients in the same concentrations as Bracco's Isovue-250^R, Isovue-300^R, and Isovue-370^R, respectively, which were approved under NDA #18735.

Recommendation:

The Division of Bioequivalence agrees that the information submitted by Abbott Laboratories demonstrates that Iopamidol Injection, 51%, 61%, and 76%, fall under 21 CFR Section 320.22 (b)(1) of the Bioavailability/Bioequivalence Regulations. The waiver of in-vivo bioequivalence study for the firm's Iopamidol Injection, 51%, 61% and 76%, is granted. From the bioequivalence point of view, the Division of Bioequivalence deems the test injectable formulations to be bioequivalent to Isovue-250^R, Isovue-300^R, and Isovue-370^R, respectively, manufactured by Bracco Diagnostics Inc..

Lin-Whei Chuang
Division of Bioequivalence
Review Branch I

RD INITIALED YHUANG
FT INITIALED YHUANG.

cc: ANDA 75005 (original, duplicate), Chuang, HFD-652 (Huang), HFD-650 (Director),
Drug File, Division File.

First Draft, LWC, 05/16/97, c:\wpfiles\75005w.n96
Final Pink, LWC, 06/02/97. X:\new\firm\firm\abbott\75005w.n96

11)

DIVISION OF CHEMISTRY I
OFFICE OF GENERIC DRUGS

Microbiologist's Review #1

April 24, 1997

A. 1. ANDA: 75-005

APPLICANT: Abbott Laboratories
Attention: Thomas F. Willer, Ph.D.
One Abbott Park Road
Abbott Park, Illinois 60064-3500

2. PRODUCT NAMES: **Iopamidol Injection USP**

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: Sterile aqueous nonpyrogenic parenteral solutions, contained in single dose polypropylene plastic syringes for intravenous infusion

51% (250 mg Iodine/mL) 50 mL fill in a 50 mL syringe

61% (300 mg Iodine/mL) 30 mL fill in a 50 mL syringe
50 mL fill in a 50 mL syringe

76% (370 mg Iodine/mL) 30 mL fill in a 50 mL syringe
50 mL fill in a 50 mL syringe

4. METHOD(S) OF STERILIZATION

5. PRINCIPLE INDICATIONS: Angiography of the cardiovascular system, including contrast enhancement of computed tomographic brain imaging

6. PHARMACOLOGICAL CATEGORY: Radiopaque diagnostic agent (contrast medium)

B. 1. DATE OF INITIAL SUBMISSION:

November 14, 1996 (Received by OGD on 11/15/96)

- Subject of this Review

2. DATE OF AMENDMENT: N/A; no amendments containing sterility assurance information were submitted by the time of this review

3. RELATED DOCUMENTS:

4. ASSIGNED FOR REVIEW: April 17, 1997

C. REMARKS: The information provided in the submissions was sufficient to determine that the applicant is taking the necessary steps to ensure the sterility of the subject drug products (Iopamidol Injection USP 51%, 61% & 76%).

D. CONCLUSIONS: The submissions are therefore acceptable on the basis of sterility assurance. Specific comments are provided in "E. Review Notes."

12/197
Kenneth H. Muhvich, Ph.D.

HFD-620/initialed by RPatel
drafted by: KHMuhvich, 4/24/97

cc:

Original ANDA 75-005
Field Copy

4/24/97



Hospital Products Division
 Abbott Laboratories
 One Abbott Park Road
 Abbott Park, Illinois 60064-3500

November 14, 1996

CENTER FOR DRUG EVALUATION AND RESEARCH
 DIVISION OF GENERIC DRUGS, HFD #630
 Metro Park North II
 7500 Standish Place, Room 150
 Rockville, Maryland 20855

ATTENTION: Douglas Sporn
 Acting Director

RE: lopamidol Injection, USP, Plastic Syringe

~~505(S)(2)(c)(ii)~~
 12/20/96
 Carol Marie Hill
 Chase
 12/26/96
 RTF

RECEIVED

NOV 15 1996

GENERIC DRUGS

ORIGINAL ABBREVIATED NEW DRUG APPLICATION

Abbott Laboratories hereby submits this original Abbreviated New Drug Application for the subject drug to provide for 50% Dextrose Injection, USP, in a 50 mL polypropylene plastic syringe, in accordance with Section 505(j) of the Federal Food, Drug and Cosmetic Act. The subject drug is an aqueous, terminally sterilized drug product. The dosage form and manufacturing site may be described as follows:

The dosage forms and manufacturing sites may be described as follows:

Abbott List Number	Concentration	Dosage Form*	Manufacturing Facility
8117	lopamidol 51%**	30 mL/50 mL 50 mL/ 50 mL	Rocky Mount, North Carolina
8118	lopamidol 61%***	30 mL/50 mL 50 mL/ 50 mL	Rocky Mount, North Carolina
8119	lopamidol 76%****	30 mL/50 mL 50 mL/ 50 mL	Rocky Mount, North Carolina

- * Polypropylene Plastic Syringe
- ** 250 mg Iodine/ mL
- *** 300 mg Iodine/ mL
- **** 370 mg Iodine/ mL

Abbott Laboratories is filing this ANDA in accordance with guidance furnished by CDER on February 21, 1996 in a meeting with industry trade groups concerning packaging changes for established drug products from glass to plastic primary containers. We include a copy of a letter from Dr. Roger Williams, CDER, to Dr. Thomas Willer, dated September 3, 1996, notifying Abbott that this product should be submitted as an ANDA. See the attachment to this letter.



D. Sporn
Page Two
November 14, 1996

The Agency has determined that the process for submitting currently approved small volume parenteral products in glass containers to be packaged in plastic containers shall be via an abbreviated new drug application.

The subject drug is a prescription drug and not an over-the-counter drug. Abbott Laboratories' Hospital Products Division will manufacture the 50 mL finished dosage form at its currently approved Rocky Mount, North Carolina facility. Please refer to Drug Master File for a full description of this Abbott Laboratories, Hospital Products Division facility.

Please refer to the accompanying Table of Contents for a list of the data supporting this newly prepared submission. These data have been presented in nine volumes consistent with the Office of Generic Drugs Policy and Procedure Guide #30-91, entitled "Organization of an Abbreviated New Drug Application and an Abbreviated Antibiotic Application," dated April 10, 1991.

We also include in Section XXI of this application the "Certification Requirement for All Applications For Approval of a Drug Product" and "Certification Requirement for All Applications For Approval of a Drug Product Concerning Using Services of Disbarred Persons" as required by the Generic Drug Enforcement Act of 1992.

In compliance with 21 CFR 314 covering FDA preapproval inspections of manufacturing sites, Abbott Laboratories has submitted a complete true copy of the CMC section from this application ("designated as the field copy") to the FDA district office (Atlanta, Georgia) with inspection responsibilities for the Abbott Laboratories Hospital Products Division manufacturing site (Rocky Mount, North Carolina) listed in this application. The signed certification follows this letter.

We request twenty-four months expiration dating for this product based on the accelerated stability data enclosed herein. At the request of the Agency, we will provide samples of the bulk drug substance and finished dosage form.

Additionally, we include after this letter a copy "Checklist for completeness and acceptability for filing Abbreviated applications." This is part of Mr. Douglas Sporn's letter to industry, April 8, 1994, as Attachment A. We added an extra column the OGD checklist in which we included the location (volume number and page number) in this ANDA where the specified information can be found. We hope that this aid will permit the Agency to expedite its prereview and acceptance of the ANDA.



D. Sporn
Page Three
November 14, 1996

This is the second in a series of submissions of drug products to be packaged in plastic syringes. These products were summarized in Dr. Williams' letter (September 3, 1996). The first submission was for 50% Dextrose Injection, USP, 50 mL, Plastic Syringe, as a supplement (S-002) to NDA 19-445, *Division Of Metabolism And Endocrine Drug Products*, HFD #510. This supplement was accepted for review on May 30, 1996 and the Agency review is underway now. We have included the full data package for the plastic container in that submission. We also include a full data package of several volumes herein.

We trust that this submission is complete.

Sincerely,

ABBOTT LABORATORIES

A handwritten signature in cursive script that reads "Thomas F. Willer".

Thomas F. Willer, Ph.D.
Manager, Regulatory Affairs
Hospital Products Division
Phone: (847) 937-6845
Fax: (847) 938-7867
Internet: WILLETF@hpdapp01.hpdap.msmail.abbott.com

TFW:tw

g:iopf.tfw/5
Attachments



Hospital Products Division

Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-3537

December 20, 1996

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS, HFD #630
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

ATTENTION: Douglas Sporn
Director

Re: ANDA 75-005 Iopamidol Injection, USP, Plastic Syringe

TELEPHONE AMENDMENT

Abbott Laboratories hereby amends the above-referenced abbreviated new drug application for the subject drug product. We are responding to a telephone request from Ms. Anna Marie Weikel, OGD Consumer Safety Officer, to Dr. Thomas Willer on December 20, 1996, in which an original signature debarment statement be submitted. We include the requested original signature documents in Exhibit I.

Please telephone me at your earliest convenience if you need additional information.

Sincerely,

ABBOTT LABORATORIES

Thomas F. Willer, Ph.D.
Manager, Regulatory Affairs
Hospital Products Division
Phone: (847) 937-6845
Fax: (847) 938-7867
Internet: WILLETF@hpdapp01.hpdap.msmail.abbott.com

TFW:tw

g:12-96f.tfw/253
Attachment

RECEIVED

DEC 23 1996

GENERIC DRUGS



Hospital Products Division

Abbott Laboratories
D-389, Bldg. AP30 -
200 Abbott Park Road
Abbott Park, Illinois 60064-3537

*NAI for
Microbiology
KHMulwich
7/8/97*

January 17, 1997

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS, HFD #630
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

RECEIVED

N/A C

ATTENTION: Douglas Sporn
Director

Re: ANDA 75-005 Iopamidol Injection USP, 51%, 61%, and 76% in Plastic Syringes

Abbott Laboratories hereby amends the above-referenced abbreviated new drug application for the subject drug. We are responding to the Agency's letter dated January 3, 1997 which made the following comment:

COMMENT: "We are refusing to file this ANDA under 21 CFR 314.101(d)(3) for the following reason:

The application is not acceptable for filing without an approved ANDA Suitability Petition, because the approved labeling for the reference listed drug for Iopamidol Injection USP, 51%, ISOVUE-250, does not list your proposed 30 mL container size. Therefore, please withdraw all references to the 30 mL container size for the 51% strength."

RESPONSE: Abbott Laboratories hereby withdraws the 30 mL plastic syringe, 51% concentration from this ANDA. We provide a listing of all references in this ANDA to the 30 mL container, 51% concentration in Exhibit I. We will file an ANDA Suitability Petition in the near future. We trust that this information is sufficient for OGD to accept for filing and commence its ANDA review.

Sincerely,

ABBOTT LABORATORIES

Thomas F. Willer

Thomas F. Willer, Ph.D.
Manager, Regulatory Affairs
Hospital Products Division
Phone: (847) 937-6845
Fax: (847) 938-7867
Internet: WILLETTF@hpdapp01.hpdap.msmail.abbott.com
TFW:tw

RECEIVED

JAN 27 1997

GENERIC DRUGS



Hospital Products Division

Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-3537

September 12, 1997

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS, HFD #630
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

ATTENTION: Douglas Sporn
Director

Re: ANDA 75-005 Iopamidol Injection
MINOR AMENDMENT

Abbott Laboratories hereby amends the above-referenced abbreviated new drug application for the subject drug product. We are responding to the Agency's letter dated July 9, 1997 which contained comments on chemistry and labeling issues. We previously responded to the chemistry questions on August 15, 1997.

RE-INCLUSION OF 30 ML SYRINGE, 51% CONCENTRATION, IN ANDA 75-005

We request the re-inclusion of the 30 mL plastic syringe container for the 51% concentration that we had previously withdrawn from the application on January 17, 1997 per Agency directive. We filed a citizen petition (Docket No. 97P-0073/CP1) to file this container size in an ANDA. The FDA approved this petition on June 10, 1997. We include a copy of the approval letter in Exhibit I. We hereby reactivate all referenced documents in the application pertaining to the 30 mL size container, 51% concentration. The list of these (previously) withdrawn pages is stated in the amendment (see Pages 3-6). We will include the 30 mL presentation in the final printed labeling contained herein.

LABELING RESPONSE

We were initially delayed in responding to the labeling issues in the Agency's July 9, 1997 because Abbott Laboratories recently purchased Sanofi's McPherson, Kansas manufacturing facility and all products (NDAs and ANDAs) manufactured there. Our internal graphics department, studio, and labeling department is processing this massive number of container, carton, and package insert labeling changes as we change all marketed products labeling from Sanofi to Abbott Laboratories. All other labeling changes are being slightly delayed. The Agency made the following labeling comments in its July 7, 1997 letter:

COMMENTS: "Labeling Deficiencies:

1. CONTAINER - 30 mL and 50 mL
 - a. Include the statement "For Intravascular Use".
 - b. Include the statement "Retain in carton until time of use".
 - c. Include the statements "check for presence of particulate matter before use. Discard Unused portion."
 - d. Please include the storage temperature statement, if space permits.

AMENDMENT

AM

RECEIVED

SEP 15 1997

GENERIC



D. Sporn
 Page Two
 August 29, 1997.

2. CARTON - 1's

- a. See the comment (b) under CONTAINER.
- b. Include the statement "Use only if solution is clear and colorless to pale yellow. Check for presence of particulate matter before use."
- c. We encourage you to relocate the statement "For Intravaeular Use" to the main panel.

3. INSERT

- a. TITLE
- b. Replace "Iopamidol Injection 41%, 61% and 76% are NOT ... USE." with "Iopamidol Injection is NOT ... USE".
- c. ADVERSE REACTIONS (Digestive)
 Start a new paragraph with the text "Some of these ... rare complications."
- c. DOSAGE AND ADMINISTRATION (General)
 - i. General
 Add the following as the second sentence of the first paragraph. In the event that crystallization of the medium has occurred, discard the container, do not use.
 - ii. Computed Tomography
 Revise the name of your drug product to read "Iopamidol-xx%" rather than "Iopamidol Injection xx%" to be consistent throughout the DOSAGE AND ADMINISTRATION section.
- d. HOW SUPPLIED
 - i. Delete reference to the 30 mL glass vial container. ✓
 - ii. We acknowledge your withdrawal of 30 mL plastic syringe of Iopamidol-250. Please delete reference to this product." ✓

revised

not true anymore

RESPONSE: We made the requested changes and we provide annotated copies of the changes made to the labeling in Exhibit II. We provide twelve copies of final printed container, carton, and package insert labeling in Exhibit III. Please note our comments about re-including the 30 mL container, 51% concentration, in the application and, hence, in the labeling.

We trust that this submission is complete and that the ANDA may now be approved.

Sincerely,

ABBOTT LABORATORIES

Thomas F. Willer

Thomas F. Willer, Ph.D.
 Assistant Director, Regulatory Affairs
 Hospital Products Division
 Phone: (847) 937-6845
 Fax: (847) 938-7867
 Internet: WILLETF@hpd.abbott.com
 g:8-97f.tfw/96 - Attachment