

NDA 009-321; CHOLOGRAFIN® MEGLUMINE (Iodipamide Meglumine Injection USP 52%)
[CHOLOGRAFIN_PI_\(CL64904\) CLEAN_Rev MAR-2017](#)



Bracco Diagnostics

CL64904 - 000000

CHOLOGRAFIN® MEGLUMINE
Iodipamide Meglumine Injection USP 52%

NOT FOR INTRATHECAL USE

FOR INTRAVENOUS USE ONLY

DESCRIPTION

Cholografin Meglumine (Iodipamide Meglumine Injection 52%) is a radiopaque contrast agent for rapid intravenous cholangiography and cholecystography supplied as a sterile, aqueous solution. Each mL provides 520 mg iodipamide meglumine; at manufacture, 3.2 mg sodium citrate buffer and 0.4 mg edetate disodium sequestering agent are added per mL. The pH has been adjusted between 6.5 and 7.7 with meglumine and iodipamide. *Each mL of solution also contains approximately 0.91 mg (0.039 mEq) sodium [18.2 mg/20 mL] and 257 mg organically bound iodine (5.2 g/20 mL).* At the time of manufacture, the air in the container is replaced by nitrogen.

The appearance of the solution may vary from essentially colorless to light amber. Solutions which have become substantially darker, however, should not be used.

CLINICAL PHARMACOLOGY

Following intravenous administration of Cholografin Meglumine, iodipamide is carried to the liver where it is rapidly secreted. The contrast medium appears in the bile within 10 to 15 minutes after injection, thus permitting visualization of the hepatic and common bile ducts, even in cholecystectomized patients. The biliary ducts are readily visualized within about 25 minutes after administration, except in patients with impaired liver function. The gallbladder begins to fill within an hour after injection; maximum filling is reached after two to two and one-half hours. The contrast medium is finally eliminated in the feces without passing through the enterohepatic circulation, except for approximately 10 percent of the intravenously administered dose which is excreted through the kidneys.

The LD₅₀ for intravenous administration of a 52% iodipamide meglumine solution in mice is 6.2 ± 0.3 mL/kg (equivalent to 3224 ± 156 mg iodipamide meglumine/kg).

INDICATIONS AND USAGE

Cholografin Meglumine is indicated for intravenous cholangiography and cholecystography as follows: (a) visualization of the gallbladder and biliary ducts in the differential diagnosis of acute abdominal conditions, (b) visualization of the biliary ducts, especially in patients with symptoms after cholecystectomy, and (c) visualization of the gallbladder in patients unable to take oral contrast media or to absorb contrast media from the gastrointestinal tract.

CONTRAINDICATIONS

Cholografin is contraindicated for use in intrathecal procedures.

Iodipamide meglumine is contraindicated in patients with a hypersensitivity to salts of iodipamide or who exhibit sensitivity reactions to the test dose. It is also contraindicated in patients with concomitant severe impairment of renal and liver function.

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.

The possibility exists for inadvertent administration into the intrathecal space during epidural administrations. Therefore, epidural administration procedures, such as pain management catheter placement, should not be performed with use of this product.

General

Administration of radiopaque materials to patients known or suspected to have 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.

Contrast media have been shown to promote the phenomenon of sickling in individuals who are homozygous for sickle cell disease when the material is injected intravenously or intra-arterially.

Since iodine-containing contrast agents may alter the results of thyroid function tests, such tests, if indicated, should be performed prior to the administration of this preparation.

A history of sensitivity to iodine *per se* or to other contrast agents is not an absolute contraindication to the use of iodipamide meglumine, but calls for extreme caution in administration.

Severe Cutaneous Adverse Reactions: Severe cutaneous adverse reactions (SCAR) may develop from 1 hour to several weeks after intravascular contrast agent administration. These reactions include Stevens-Johnson syndrome and toxic epidermal necrolysis (SJS/TEN), acute generalized exanthematous pustulosis (AGEP) and drug reaction with eosinophilia and systemic symptoms (DRESS). Reaction severity may increase and time to onset may decrease with repeat administration of contrast agent; prophylactic medications may not prevent or mitigate severe cutaneous adverse reactions. Avoid administering Cholografin to patients with a history of a severe cutaneous adverse reaction to Cholografin.

PRECAUTIONS

Diagnostic procedures which involve the use of radiopaque contrast agents 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 situations which may arise as a result of the procedure, as well as for emergency treatment of severe reactions to the contrast agent itself.

After intravascular administration of a radiopaque agent, competent personnel and emergency facilities should be available for at least 30 to 60 minutes, since severe delayed reactions have been known to occur.

These severe, life-threatening reactions suggest hypersensitivity to the radiopaque agent, which has prompted the use of several pretesting methods, none of which can be relied upon to predict severe reactions. Many authorities question the value of any pretest. A history of bronchial asthma or allergy, a family history of allergy, or a previous reaction to a contrast agent warrant special attention. Such a history, by suggesting histamine sensitivity and a consequent proneness to reactions, may be more accurate than pretesting in predicting the likelihood of a reaction, although not necessarily the severity or type of reaction in the individual case.

The sensitivity test most often performed is the slow injection of 0.5 to 1.0 mL of the radiopaque medium, administered intravenously, prior to injection of the full diagnostic dose. It should be noted that the absence of a reaction to the test dose does not preclude the possibility of a reaction to the full diagnostic dose. If the test dose causes an untoward response of any kind, the necessity for continuing with the examination should be carefully reevaluated and, if it is deemed essential, the examination should be conducted with all possible caution. In rare instances reactions to the test dose itself may be extremely severe; therefore, close observation of the patient, and facilities for emergency treatment, appear indicated.

Caution should be exercised with the use of radiopaque media in severely debilitated patients and in those with marked hypertension. The possibility of thrombosis should be borne in mind when intravenous techniques are employed.

Contrast agents may interfere with some chemical determinations made on urine specimens; therefore, urine should be collected before administration of the contrast media or two or more days afterwards.

Some clinicians feel it may be advisable to have a continuous intravenous infusion running prior to and during administration of the drug.

The admixture of Benadryl® (Diphenhydramine Hydrochloride Injection) with Cholografin Meglumine (Iodipamide Meglumine Injection USP 52%) may cause a precipitate which may form in the syringe or tubing. If antihistamines are administered concomitantly, they should not be mixed with the contrast agent but administered at another site.

Usage in Pregnancy

The safety of iodipamide meglumine for use during pregnancy has not been established; therefore, it should be used in pregnant patients, only when, in the judgment of the physician, its use is deemed essential to the welfare of the patient.

ADVERSE REACTIONS

Local reactions at the site of injection are not observed, unless excessive amounts are extravasated during injection. After too rapid administration, mild transient symptoms such as restlessness, sensations of warmth, sneezing, perspiration, salivation, flushing, pressure in the upper abdomen, dizziness, nausea, vomiting, chills, fever, headache, pallor and tremors may occur. These symptoms disappear when the injection has been completed. Rarely, swollen eyelids, laryngospasm, respiratory difficulties, hypotension, cardiac reactions and cyanosis have been reported. Hypersensitivity reactions may occur. In rare instances, despite the most careful sensitivity testing, anaphylactoid reactions may occur.

Renal function tests may be altered and renal failure may occur.

Thyroid function tests indicative of hypothyroidism or transient thyroid suppression have been uncommonly reported following iodinated contrast media administration to adult and pediatric patients, including infants. Some patients were treated for hypothyroidism.

Skin and Subcutaneous Tissue Disorders: Reactions range from mild (e.g. rash, erythema, pruritus, urticaria and skin discoloration) to severe: [e.g. Stevens-Johnson syndrome and toxic epidermal necrolysis (SJS/TEN), acute generalized exanthematous pustulosis (AGEP) and drug reaction with eosinophilia and systemic symptoms (DRESS)].

DOSAGE AND ADMINISTRATION

Cholografin Meglumine (Iodipamide Meglumine Injection USP 52%) is for intravenous use only.

Directions For Use

Preparation of the Patient: For best results, the usual preliminary measures for cholecystography are recommended, particularly in cholecystectomized patients, i.e., a low residue diet on the day before examination and administration of castor oil the night before or neostigmine at the time of examination to dispel excess intestinal gas. Cholecystography is preferably carried out in the morning with the patient fasting.

Patient Counseling Information: Advise patients to inform their physician if they develop a rash after receiving Cholografin.

Dose: The usual adult dose is 20 mL. For infants and children, the suggested dose is 0.3 to 0.6 mL/kg of body weight; the dosage for infants and children should not exceed 20 mL.

Note: The dose should not be repeated for 24 hours.

Administration: After warming to body temperature, Cholografin Meglumine should be given by slow intravenous injection, following the usual precautions of intravenous administration. *It is important that the preparation be injected slowly over a period of 10 minutes.* Use of a narrow bore hypodermic needle will ensure a slow rate of injection. During the injection, the patient should be watched for untoward reactions such as a feeling of warmth, flushing and occasionally nausea. Nausea indicates that the injection rate is too rapid.

Radiography: A scout film should be exposed routinely before the intravenous injection is made.

Position of the Patient: With the patient prone and the right side elevated, radiographs are made in the posterior-anterior projection. Some radiologists prefer the supine position with the left side elevated. Serial 10-minute exposures should be started 10 minutes after the injection is made and

continued until optimal visualization of the *biliary* ducts is obtained. Wet films should be examined immediately by the radiologist. In some cases a 15-degree rotation or the upright position may prove helpful. Depending on the situation revealed by the roentgenograms in which the duct is first seen, the position of the subject should be changed to displace the shadow of the common bile duct from that of the spine. Tomography is a useful technique for enhancing bile duct visualization after administration of the radiopaque medium.

Examination of the *gallbladder* should be started about two hours after administration. The standard positions in routine examination of the gallbladder should be used unless otherwise indicated. There is no need for the patient to remain quiet awaiting the time for the gallbladder film to be exposed. Moderate activity on the part of the patient will, in most cases, preclude “stratification” of the contrast agent in the gallbladder. If the contrast medium should stratify in the gallbladder, decubitus as well as upright films should be obtained. Additional exposures may be made after the ingestion of a fatty meal.

If visualization is not achieved after two and one-half hours, the patient should be returned for a 24-hour film, whenever possible. Occasionally, delayed opacification of the gallbladder will occur in 24 hours.

In infants and children, gallbladder visualization may be expected to occur 30 minutes to four hours after administration.

Note: In the presence of liver disease (BSP retention greater than 30 to 40 percent), the contrast medium is not excreted efficiently by the liver and visualization is usually not achieved. Visualization is rarely achieved in the presence of a serum bilirubin of 3.0 mg per 100 mL if the elevated bilirubin level is due to mechanical obstruction or hepatocellular damage. In the presence of severe liver damage, the contrast agent is excreted by the kidneys.

Interpretation: When intravenous cholecystography and cholangiography are used as an aid in the differential diagnosis of acute abdominal conditions, visualization of the gallbladder is considered strong evidence against a diagnosis of acute cholecystitis, while nonvisualization of the gallbladder two and one-half hours after administration with visualization of the bile ducts is considered strong evidence in favor of a diagnosis of acute cholecystitis (if the bile ducts are only faintly visualized, gallbladder films four hours after administration may occasionally show visualization of the gallbladder). When neither the bile ducts nor the gallbladder is visualized, the study provides no definitive information with regard to determining the presence or absence of acute cholecystitis.

HOW SUPPLIED

Cholografin Meglumine (Iodipamide Meglumine Injection USP 52%) is available in single dose vials of 20 mL (NDC 0270-0265-20).

Storage

Protect from light; store at 20 -25°C (68-77°F) [See USP]; avoid excessive heat.

In the event that crystallization occurs, the solution may be clarified by placing the vial in hot water and shaking gently for several minutes or until the solids redissolve. If cloudiness persists, discard the preparation. Allow the solution to cool to body temperature before administering.

Cholografin is a registered trademark of Bracco Diagnostics Inc.

Rx only

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