PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

CYSTO-CONRAY® II

Iothalamate Meglumine Injection USP
17.2 % w/v
Solution

Ionic Iodinated Radiographic Contrast Medium for Instillation of the Urinary tract.

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PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Non-medicinal Ingredients
Instillation of urinary tract	Solution for instillation / 17.2% w/v	Edetate Calcium Disodium USP, Meglumine USP, Monobasic Sodium phosphate USP. *For a complete listing see Dosage Forms, Composition and Packaging section.*

INDICATIONS AND CLINICAL USE

Cysto-Conray II is indicated for use in retrograde cystography and cystourethrography.
Geriatrics (> *65* years of age):
No data available.

CONTRAINDICATIONS

CYSTO-CONRAY II is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation or component of the container. For a complete listing, see the Dosage Forms, Composition and Packaging section of the product monograph.

In patients with a known hypersensitivity to salts of iothalamic acid, the use of this preparation is contraindicated as intravasation may lead to hypersensitivity reactions and anaphylactic shock. However, a history of sensitivity to iodine per se or to other contrast media is not an absolute contraindication to the use of Cysto-Conray II, but calls for extreme caution in administration.

Obstruction and acute or severe infection of the urinary tract are generally regarded as contraindications to instrumentation and to the retrograde instillation of contrast material; do not inject by intravascular, subcutaneous or intramuscular routes.

WARNINGS AND PRECAUTIONS

WARNINGS

A history of allergy, bronchial asthma, sensitivity to other iodine-containing compounds or a previous reaction to a contrast agent warrant special attention and may predict the likelihood of an allergic reaction.

Severe irritation of the urinary tract and hemorrhagic cystitis may occur following prolonged exposure to contrast media. It is imperative that the urinary bladder be emptied at the completion of the diagnostic procedures.

Thyroid dysfunction

Cysto-Conray II, like all other iodinated contrast media, may induce changes in thyroid function in some patients. Transient hyperthyroidism or hypothyroidism has been reported following iodinated contrast media administration to adult and pediatric patients. Decreased levels of thyroxine (T4) and triiodothyronine (T3) and increased level of TSH were reported after exposure to ICM in infants, especially preterm infants, which remained for up to a few weeks or even more than a month (see ADVERSE REACTIONS). Some patients were treated for hypothyroidism (see PRECAUTIONS – Special populations – Pediatrics - Infants).

PRECAUTIONS

Diagnostic procedures which involve the use of radiopaque contrast media should be carried out under the direction of appropriately trained personnel. Appropriate facilities should be available for coping with emergencies which may arise.

For sensitivity testing, 0.1 mL of the contrast media may be injected intradermally. The patient should be observed for local and general hypersensitivity reaction for 15-30 minutes.

Sensitivity testing cannot be relied upon to predict severe reactions.

An impending reaction is often indicated by apprehension, respiratory difficulty, faintness, sneezing, itching, vomiting or urticaria. In some instances, reactions to the test dose may be delayed.

Endocrine and Metabolism

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

Special Populations

Pregnant Women:
The safe use of this preparation during pregnancy has not been established. Exposures of the abdomen and pelvis to radiation during pregnancy, especially in the first trimester, should be avoided, unless in the judgement of the physician the expected benefits to the mother outweigh the risk to the developing fetus.

Nursing Women:
Where an assessment of the risk to benefit ratio suggests the use of this product in nursing women, formula feeding should be substituted for breast feeding.

Pediatrics:
Infants : Decreased levels of thyroxine (T4) and triiodothyronine (T3) and increased level of TSH were reported after exposure to ICM in infants, especially preterm infants, which remained for up to a few weeks or more than a month (see ADVERSE REACTIONS). Hypothyroidism in infants may be harmful for growth and development, including mental development and may require treatment. Thyroid function in infants exposed to ICM should therefore be evaluated and monitored until thyroid function is normalized.

ADVERSE REACTIONS

General
Irritation of the bladder or ureter, common to some degree to all contrast media administered for retrograde urographic procedures, may occasionally occur. Hemorrhagic cystitis may result. As with all contrast media, intravasation may lead to hypersensitivity reactions such as a sense of warmth, flushing, sneezing, sweating, chills, fever, urticaria, laryngeal edema, bronchospasm, hypertension, hypotension, cardiac arrhythmias, cardiac arrest and anaphylactic shock.

Post-Market Adverse Drug Reactions:

Endocrine disorders: 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

TREATMENT OF ADVERSE REACTIONS TO CONTRAST MEDIA

Contrast media should be administered only by physicians thoroughly familiar with the emergency treatment of all adverse reactions to contrast media. The assistance of other trained personnel such as cardiologists, internists and anesthetists is required in the management of severe reactions.

A guideline for the treatment of adverse reactions is presented below. This outline is not intended to be a complete manual on the treatment of adverse reactions to contrast media or on cardiopulmonary resuscitation. The physician should refer to the appropriate texts on the subject.

It is also realized that institutions or individual practitioners will already have appropriate systems in effect and that circumstances may dictate the use of additional or different measures.

For minor allergic reactions: (if considered necessary). The intravenous (i.v.) or intramuscular administration of an antihistaminic such as Diphenhydramine HCl (Benadryl) 25-50 mg is generally sufficient (contraindicated in epileptics). The resulting drowsiness makes it imperative to ensure that out-patients do not drive or go home unaccompanied.

Major or life-threatening reactions: A major reaction may be manifested by signs and symptoms of cardiovascular collapse, severe respiratory difficulty and nervous system dysfunction. Convulsions, coma and cardio-respiratory arrest may ensue.

The following measures should be considered:

1. Start emergency therapy immediately, carefully monitoring vital signs.

2. Have emergency resuscitation team summoned - do not leave patient unattended.

3. Ensure patient airway - guard against aspiration.

4. Commence artificial respiration if patient is not breathing.

5. Administer oxygen if necessary.

6. Start external cardiac massage in the event of cardiac arrest.

7. Establish route for i.v. medication by starting infusion of appropriate solution (5% Dextrose in water).

8. Judiciously administer specific drug therapy as indicated by the type and severity of the reaction. Careful monitoring is mandatory to detect adverse reactions of all drugs administered:

- Soluble Hydrocortisone 500-1000 mg i.v. for all acute allergic anaphylactic reactions.

- Adrenaline 1:1000 solution (in the presence of anoxia it may cause ventricular fibrillation):

  - 0.2-0.4 mL subcutaneously for severe allergic reactions

  - in extreme emergency 0.1 mL per minute, appropriately diluted, may be given intravenously until desired effect is obtained. Do not exceed 0.4 mL.

  - in case of cardiac arrest 0.1-0.2 mL, appropriately diluted may be given intracardially.

In Hypotension (carefully monitoring blood pressure):

- Phenylephrine HCl (Neo-Synephrine) 0.1-0.5 mg appropriately diluted slowly i.v. or by slow infusion

OR

- Levarterenol Bitartrate (Levophed) 4 mL of 0.2% solution in 1000 mL of 5% Dextrose by slow drip infusion.

- Sodium bicarbonate 5%; 50 mL i.v. every 10 minutes as needed to combat post-arrest acidosis.

- Atropine 0.4-0.6 mg i.v. to increase heart rate in sinus bradycardia. May reverse 2nd or 3rd degree block.

To control convulsions:

- Pentobarbital Sodium (Nembutal) 50 mg in fractional doses slowly i.v. (contraindicated if cyanosis is present)

OR

- Diazepam (Valium) 5-10 mg slowly i.v. titrating the dose to the response of the patient.

9. Defibrillation, administration of antiarrhythmics and additional emergency measures and drugs may be required.

10. Transfer patient to intensive care unit when feasible for further monitoring and treatment.

DOSAGE AND ADMINISTRATION

Patient Preparation: Unless contraindicated, an appropriate laxative is given the night before the examination. The bladder should be emptied before the contrast agent is instilled.

Radiographic Technique: The radiographic procedure normally employed for cystography, cystourethrography should be employed. A preliminary radiograph is recommended before the contrast agent is administered.

Administration: Sterile catheterization is essential. Cysto-Conray II may be introduced by gravity flow using an appropriate venoclysis set or by syringe. Excessive pressure should be avoided with any method of administration.

Usual adult dosage: The desired concentration will vary depending on the patient's size and age and also with the technique and equipment used. Sufficient volume of contrast medium is administered to adequately fill the urinary bladder. The volume of solution required will vary depending upon the individual patient. Adults usually require a volume in the range of 200-400 mL.

Usual pediatric dosage: Children require a volume in proportion to their body size. The usual dose ranges from 30 to 300 mL.

Until further experience has been gained, the use of Cysto-Conray II for retrograde pyelography in children is not recommended.

OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre immediately.

ACTION AND CLINICAL PHARMACOLOGY

Retrograde instillation opacifies selected segments of the urinary tract, permitting fluoroscopic and radiographic visualization of structures such as the urethra, bladder, ureters and pelvico-

calyceal system.

STORAGE AND STABILITY

Store between 15-30°C. Protect from light and freezing. Discard unused portion within 8 hours.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Cysto-Conray II is a sterile aqueous solution containing 17.2% w/v of the meglumine salt of 5-acetamido-2,4,6-triiodo-N-methylisophthalamic acid. Each milliliter of Cysto-Conray II contains 172 mg of iothalamate meglumine, equivalent to 81 mg (8.1% w/v) of organically bound iodine. Each milliliter of Cysto-Conray II contains 0.110 mg edetate calcium disodium as a stabilizer and 0.115 mg of sodium biphosphate as a buffer. Cysto-Conray II is hypertonic under conditions of use and is supplied in containers from which the air has been displaced by nitrogen.

Available in single dose bottles of 250 mL.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

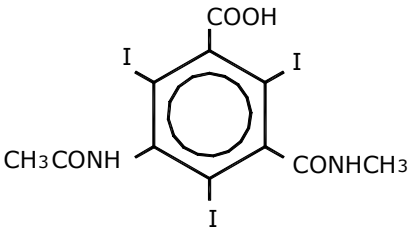
Drug Substance

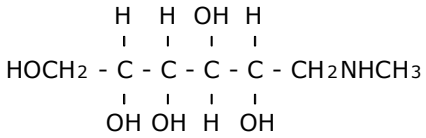
Proper name: Iothalamate Meglumine Injection USP, 17.2 % w/v

Chemical name: Meglumine salt of 5-acetamido-2,4,6-triiodo-N-methylisophthalamic acid

Molecular formula and molecular mass: $C_7H_{17}NO_5C_{11}H_9I_3N_2O_4$, 809.13

Structural formula:





Physicochemical properties: Cysto-Conray II is relatively thermostable and may be autoclaved without harmful effects. As is the case with all iodinated contrast media, Cysto-Conray II is somewhat sensitive to light and must be protected from strong daylight or direct exposure to the sun. Store between 15ºC and 30ºC and do not freeze

DETAILED PHARMACOLOGY

See ACTION AND CLINICAL PHARMACOLOGY in PART I of the Product Monograph.

PATIENT MEDICATION INFORMATION

CYSTO-CONRAY® II
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17.2 % w/v

Read this carefully before you start taking Cysto-Conray II and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about Cysto-Conray II.

What is Cysto-Conray II used for?
Cysto-Conray II:

- is for diagnostic use only and is used to help identify an illness.
- makes contrast in the bladder and the urinary tract for certain X-rays procedures.
- is used in children and adults.

How does Cysto-Conray II work?
Cysto-Conray II is administered through the bladder. Cysto-Conray II creates contrast in your bladder and urinary tract that makes it easier for your doctor to make a diagnosis.

What are the ingredients in Cysto-Conray II?
Medicinal ingredients: Iothalamate Acid.
Non-medicinal ingredients: Edetate Calcium Disodium USP, Meglumine USP, Monobasic Sodium phosphate USP.

Cysto-Conray II comes in the following dosage forms:
250 mL Bottles of Iothalamate Meglumine Injection USP, 17.2% w/v

Do not use Cysto-Conray II if:

- You are hypersensitive to this drug or to any ingredient in the formulation or component of the container.
- You have severe infection of the urinary tract.
- You have a blockage in your urinary tract

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Cysto-Conray II. Talk about any health conditions or problems you may have, including if you:

- have had a previous allergic reaction to a contrast agent or have a history of iodine sensitivity.

- have a history of bronchial asthma.
- have a history of allergies.
- have severe irritation of the urinary tract or blood in your urine.
- have thyroid tests planned. The iodine in Cysto-Conray II may interfere with your thyroid tests.
- are pregnant or could be pregnant. If you need to take Cysto-Conray II during your pregnancy, your doctor will discuss the benefits and risks of giving it to you.
- are breast-feeding. It is not known if Cysto-Conray II is excreted in breast milk. You should bottle feed your baby for at least 24 hours after taking Cysto-Conray II.

Other warnings you should know about:
Thyroid function
Contrast media containing iodine, such as Cysto-Conray II, may change thyroid activity in some patients, both in adults and infants. This may cause:

- Hypothyroidism (i.e. too little thyroid hormones in the blood)
- Or hyperthyroidism (i.e. too much thyroid hormones in the blood)

Thyroid function in infants
Contrast media containing iodine may cause hypothyroidism in infants, especially infants born too soon that:

- Can continue for several weeks to a month after treatment
- Can harm growth and development
- Can harm mental growth
- May require treatment
- Can cause symptoms such as:
    - Fatigue, shortness of breath, low heart rate
    - Reduced appetite, feeling cold, weight gain
    - Muscle stiffness

Contact your doctor if these symptoms happen to you or your infant.

Your doctor may order blood tests for your infant after treatment to follow thyroid hormone levels in the blood.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

How to take Cysto-Conray II:
Cysto-Conray II will always be used in a hospital or similar setting. It will only be administered to you under the supervision of a health professional skilled and experienced in the

particular procedure to be performed.

Usual dose:

- Your doctor will determine the amount of Cysto-Conray II to be used.
- The dose administered will depend on your weight, your age and the procedure.
- You may be given a laxative the night before your examination.
- You will need to empty your bladder before you receive Cysto-Conray II.
- Cysto-Conray II will be injected into your bladder.

Overdose:

If you think you have been given too much Cysto-Conray II, contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

What are possible side effects from using Cysto-Conray II?

These are not all the possible side effects you may feel when taking Cysto-Conray II. If you experience any side effects not listed here, contact your healthcare professional.

Common side effects may include:

- Irritation of the bladder or ureter

Uncommon side effects can include:

- Inflammation and bleeding of the bladder (known as hemorrhagic cystitis)

Serious side effects and what to do about them		
Symptom/ Effect	Talk to your healthcare professional	
	Only if severe	In all cases
UNCOMMON • Severe allergic reaction including symptoms such as: sense of warmth, redness of the skin, sneezing, sweating, chills, fever, skin rash, swelling, high or low blood pressure, heart malfunction. • Lack of a sufficient amount of the thyroid hormone (known as hypothyroidism)		$ $

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects
You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html, for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:
Store at controlled room temperature. Protect from light and freezing. Discard unused portion within 8 hours. Keep out of reach and sight of children.

If you want more information about Cysto-Conray II:

- Talk to your healthcare professional.
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; or by calling 1-844-208-7620.

This leaflet was prepared by Liebel-Flarsheim Company LLC.
This document prepared for health professionals is included with the product or may be obtained by contacting the sponsor, Liebel-Flarsheim Company LLC at 1-844-208-7620.

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