**SINOGRAFIN- diatrizoate meglumine and iodipamide meglumine injection, solution**
**BRACCO DIAGNOSTICS INC**

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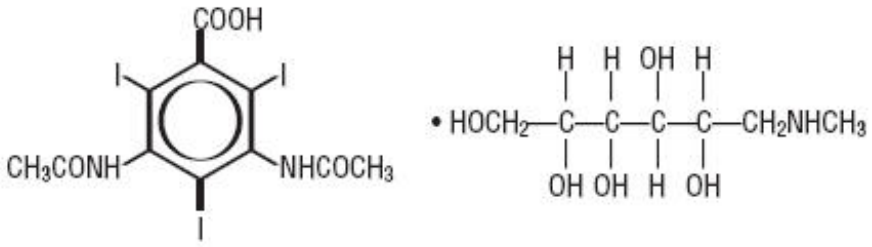
**SINOGRAFIN®**
**Diatrizoate Meglumine and**
**Iodipamide Meglumine Injection**

## DESCRIPTION

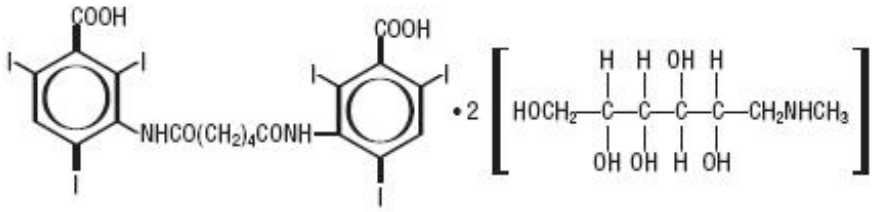
Sinografin (Diatrizoate Meglumine and Iodipamide Meglumine Injection) is a sterile, nonpyrogenic, essentially colorless to pale yellow, aqueous radiopaque contrast medium for intrauterine instillation. Each mL provides 527 mg diatrizoate meglumine and 268 mg iodipamide meglumine with 3.2 mg sodium citrate as a buffer, and 0.4 mg edetate disodium; pH has been adjusted to 7.0 to 7.8 with meglumine and diatrizoic acid. Each mL contains approximately 0.91 mg (0.04 mEq) sodium and 380 mg organically bound iodine. At the time of manufacture, the air in the container is replaced with nitrogen.

Diatrizoate meglumine is designated chemically as 1-deoxy-1-( methylamino)-D-glucitoI 3,5-diacetamido-2,4,6- triiodobenzoate (salt); iodipamide meglumine is 1-deoxy-1- (methylamino)-D-glucitoI 3,3´-(adipoyldiimino)bis[2,4,6- triiodobenzoate] (2:1) (salt). Structural formulas:




diatrizoate meglumine $C_{11}H_9I_3N_2O_4$• $C_7H_{17}NO_5$ MW 809.13

Organically Bound Iodine: 47.1% CAS-131-49-7




iodipamide meglumine $C_{20}H_{14}I_6N_2O_6$• $2C_7H_{17}NO_5$ MW 1530.20

Organically Bound Iodine: 49.8% CAS-3521-84-4

## CLINICAL PHARMACOLOGY

The most important characteristic of contrast media is the iodine content. The relatively high atomic weight of iodine contributes sufficient radiodensity for radiographic contrast of the uterus and uterine tubes with surrounding tissues.

Diagnostic intrauterine radiopaque agents have few known pharmacological effects. Most of the

medium within the uterine cavity is discharged immediately upon termination of the procedure. Any medium retained in the uterine cavity is completely absorbed within one hour, unless there is an obstruction and large hydrosalpinx, in which case absorption is generally complete within 24 hours. Any medium spilled into the peritoneal cavity is absorbed within 20 to 60 minutes and excreted by both the hepatic and renal systems.

## INDICATIONS AND USAGE

Sinografin (Diatrizoate Meglumine and Iodipamide Meglumine Injection) is indicated for use in hysterosalpingography.

## CONTRAINDICATIONS

Hysterosalpingographic agents are contraindicated in pregnant women and those suspected of being pregnant. Hysterosalpingography should not be performed during the menstrual period nor when infection of the external genitalia or genital tract is present. The procedure should not be attempted within 30 days following curettage or conization or within six months following the termination of pregnancy.

## PRECAUTIONS

### General

Diagnostic procedures which involve the use of radiopaque diagnostic 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.

In patients having or suspected of having carcinoma of the uterus and/or uterine tubes, the possible dispersion of carcinogenic cells during hysterosalpingography should be borne in mind.

The possibility of a reaction should always be considered. 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. 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 (see **ADVERSE REACTIONS**, and **PRECAUTIONS, Information for the Patient**).

### Information for the Patient

Patients receiving diagnostic agents for intrauterine radiography should be given the following information:

1. This drug has been prescribed to perform an X-ray study of the uterus and uterine tubes.
2. Patients should be questioned regarding a recent history (within 30 days) of curettage or conization, pregnancy or a recent history (within six months) of termination of pregnancy, and a history of allergy to iodine, any foods, or X-ray dyes.
3. Patients should consult the physician if, at some future date, any thyroid tests are planned. The iodine in this agent may interfere with some thyroid tests.
4. This drug may cause adverse reactions (see **ADVERSE REACTIONS**) in some patients but most reactions are mild and pass quickly.

### Drug/Laboratory Test Interactions

### Thyroid Function Tests

Because a small amount of this medium may be absorbed, thyroid function tests such as protein bound

iodine (PBI) and radioactive iodine uptake, if indicated, generally should be performed prior to instillation. However, thyroid function can be evaluated after use of any iodinated contrast agents by using $T^3$ resin uptake or free thyroxine assays.

**Pregnancy**

See **CONTRAINDICATIONS**.

**Nursing Mothers**

Diatrizoate meglumine and iodipamide meglumine administered intravascularly has been found to be excreted in breast milk.

Because small amounts of these agents may be absorbed following intrauterine instillation, caution should be exercised when any diagnostic intrauterine radiopaque agent is administered to a nursing woman.

**Pediatric Use**

Safety and effectiveness of hysterosalpingography has not been established in pediatric patients.

## ADVERSE REACTIONS

Sudden onset of bradycardia, hypotension, cardiac arrest and death have rarely been reported. Hypersensitivity reactions, which include sweating, flushing, pruritus, urticaria, skin rashes, arthralgia, respiratory distress, and circulatory collapse have occurred. Dizziness, syncope, hypotension, chills, fever, nausea, vomiting, and abdominal pain and tenderness are occasionally seen following instillation of the contrast medium.

It should be kept in mind that the serious or anaphylactoid reactions that may occur with intravascular administration of radiopaque contrast agents are theoretically possible following administration by other routes.

## DOSAGE AND ADMINISTRATION

As a convenience to the physician, the following guidelines which have proven satisfactory are provided (see**PRECAUTIONS, General**). Patients should be counseled prior to radiographic examination (see**PRECAUTIONS, Information for the Patient**).

**Preparation of the patient:** Hysterosalpingography should be performed three to five days after the cessation of the patient’s menstrual period as a precautionary measure. An enema and vaginal douche one hour before the examination are helpful, but not essential. The patient should empty her bladder before the examination. Since the procedure is remarkably free of pain when Sinografin (Diatrizoate Meglumine and Iodipamide Meglumine Injection) is used, the use of a narcotic or anesthesia is unnecessary.

**Dosage:** 3 to 4 mL of Sinografin, administered in fractional doses of approximately 1 mL, are usually adequate to visualize the uterus; an additional 3 to 4 mL will demonstrate the tubes. Total doses varying from 1.5 to 10 mL have been employed with satisfactory results.

**Administration:** The patient is placed in the lithotomy position and the vulva is cleansed with a suitable antiseptic solution. A Graves-type vaginal speculum is introduced, the cervix is exposed, and the vaginal vault is sponged with antiseptic solution.

A tenaculum is placed on the cervical lip, usually the anterior lip. A sterile sound may be passed to determine the position of the uterus and the direction of the cervical canal, and, when necessary, the cervical canal may be dilated. (Sounding the uterine cavity and dilatation of the canal are not usually

required when a flexible cannula tip is used.)

A sterile syringe containing the Sinografin is attached by Luer-Lok to a uterine cannula. The two-way cannula valve is opened and all air bubbles in the cannula and syringe are expressed. About 1.5 to 2 mL of Sinografin (Diatrizoate Meglumine and Iodipamide Meglumine Injection) are required to fill the cannula. (If preferred, a tubal insufflator under controlled pressure with a salpingogram attachment may be used instead of the syringe.)

The cannula tip is inserted into the cervical canal so that the adjustable rubber acorn obturator fits snugly at the external os. Careful placement of the cannula is important to avoid trauma and pain. Squeezing the trigger of the cannula to provide simultaneous traction on the tenaculum and forward pressure on the cannula should give a nonleaking cervical seal. Sinografin flows freely so that only gentle pressure on the plunger is necessary; however, the medium should be used as promptly as possible following withdrawal into the syringe. The syringe should be rinsed as soon after the procedure as possible to prevent freezing of the plunger.

The connection at the external os is checked for leakage. If the acorn obturator is inadequate, an inflatable balloon-obturator may be used to seal the cervical canal. When the equipment has been positioned satisfactorily, the tenaculum and cannula may be fixed in position until the procedure is terminated.

**Radiography:** A scout film may be made before the medium is administered. After the initial fractional injection, a film should be made using a Bucky diaphragm. After each successive injection of 1 mL, a film is taken, developed immediately, and inspected in the dark room before the next fractional dose of Sinografin (Diatrizoate Meglumine and Iodipamide Meglumine Injection) is given, until the procedure is completed. Further injection and subsequent films can be made as required using posterior-anterior or oblique angles.

Clinical experience indicates that tubal patency, if present, will be demonstrable at the time of the injection and delayed films have not been required.

### General

Diatrizoate Meglumine and Iodipamide Meglumine Injection should be inspected visually for particulate matter and discoloration prior to instillation whenever solution and container permit. The solution may vary in color from essentially colorless to pale yellow. Solutions which may have become substantially darker should not be used.

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 solution is clear. If cloudiness persists, the preparation should not be used. Allow the solution to cool to body temperature before administering.

## HOW SUPPLIED

### Sinografin (Diatrizoate Meglumine and Iodipamide Meglumine Injection)

Packages of ten single-dose 10 mL vials (NDC 0270-0523-30).

### Storage

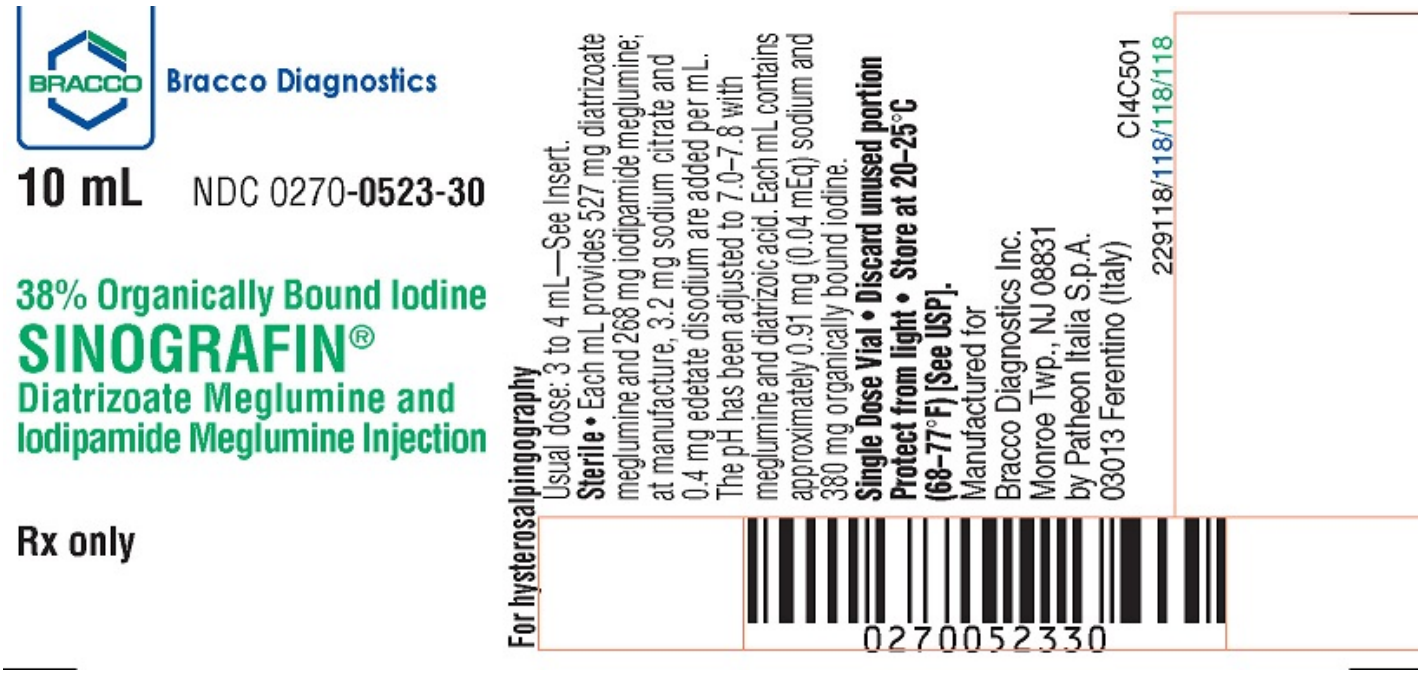
Store at 20-25°C (68-77°F) [See USP]. Protect from light.

Manufactured for
**Bracco Diagnostics Inc.**
Monroe Township,NJ 08831

by Patheon Italia S.p.A.
03013 Ferentino (Italy)

Revised October 2013
CL64C01
255762

Sinografin
Diatrizoate Meglumine and Iodipamide Meglumine Injection




## SINOGRAFIN

diatrizoate meglumine and iodipamide meglumine injection, solution

| Product Information | | | |
|---|---|---|---|
| **Product Type** | HUMAN PRESCRIPTION DRUG | **Item Code (Source)** | NDC:0270-0523 |
| **Route of Administration** | INTRAUTERINE | **DEA Schedule** | |

| Active Ingredient/Active Moiety | | |
|---|---|---|
| **Ingredient Name** | **Basis of Strength** | **Strength** |
| **diatrizoate meglumine** (UNII: 3X9MR4N98U) (diatrizoic acid - UNII:5UVC90J1LK) | diatrizoate meglumine | 527 mg in 1 mL |
| **iodipamide meglumine** (UNII: X064O0Y1A4) (iodipamide - UNII:TKQ858A3VW) | iodipamide meglumine | 268 mg in 1 mL |

| Inactive Ingredients | |
|---|---|
| **Ingredient Name** | **Strength** |
| **sodium citrate** (UNII: 1Q73Q2JULR) | 3.2 mg in 1 mL |
| **edetate disodium** (UNII: 7FLD91C86K) | .4 mg in 1 mL |

| Packaging | | | | |
|---|---|---|---|---|
| # | Item Code | Package Description | Marketing Start | Marketing End |

| # | Item Code | Package Description | Date | Date |
|---|---|---|---|---|
| 1 | NDC:0270-0523-30 | 10 in 1 PACKAGE | | |
| 1 | | 10 mL in 1 VIAL, SINGLE-DOSE; Type 0: Not a Combination Product | | |

## Marketing Information

| Marketing Category | Application Number or Monograph Citation | Marketing Start Date | Marketing End Date |
|---|---|---|---|
| NDA | NDA011324 | 12/02/1958 | |

## Labeler - BRACCO DIAGNOSTICS INC (849234661)

## Registrant - BRACCO DIAGNOSTICS INC (849234661)

## Establishment

| Name | Address | ID/FEI | Business Operations |
|---|---|---|---|
| Patheon Italia S.p.A | | 434078638 | MANUFACTURE(0270-0523) |

## Establishment

| Name | Address | ID/FEI | Business Operations |
|---|---|---|---|
| Justesa Imagen, S.A.U | | 477020325 | API MANUFACTURE(0270-0523) |

## Establishment

| Name | Address | ID/FEI | Business Operations |
|---|---|---|---|
| Interpharma Praha, a.s | | 644354706 | API MANUFACTURE(0270-0523) |

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