Stannous DISIDA Kit for the preparation of Technetium Tc-99m Disofenin Injection

Product Package Insert

Calgary Radiopharmaceutical Centre
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NAME

Stannous DISIDA Kit
Technetium Tc-99m Disofenin Injection

PHARMACOLOGICAL CLASSIFICATION

Radiodiagnostic agent

DESCRIPTION

Stannous DISIDA (di-isopropyl-IDA) Kit is supplied as a frozen solution.

Each vial of Stannous DISIDA Kit contains 20 mg of di-isopropyl-IDA and 0.3 mg of stannous chloride dihydrate in 1.0 mL.

When reconstituted with Technetium Tc-99m sodium pertechnetate in saline, each mL of Technetium Tc-99m Disofenin Injection contains a complex composed of:

Technetium Tc-99m	0.65-1.3	GBq
Di-isopropyl-IDA	5.0-10.0	mg
Stannous chloride dihydrate	75-150	μg
L-ascorbic acid	25-50	μg
Sodium chloride	0.9	%

The addition of Technetium Tc-99m sodium pertechnetate in sterile saline provides Technetium Tc-99m Disofenin Injection as a sterile, non-pyrogenic solution for intravenous administration.

ACTION

Upon intravenous administration, Technetium Tc-99m Disofenin Injection is rapidly cleared from the blood via the hepatobiliary system with 8% of the administered dose remaining in blood 30 minutes post-injection. The clearance rate is dependent on hepatocyte function and biliary patency. Typically, hepatic duct visualization occurs within 10 - 15 minutes; in patients with normal hepatobiliary function, gallbladder and intestinal visualization occurs by 60 minutes post-injection. Approximately 9% is excreted in the urine after two hours; up to 30% of the dose is excreted in 24 hours. Technetium Tc-99m Disofenin Injection effectively competes with serum bilirubin levels between 15-30 mg/dL (250-500 μmoles/L).

INDICATIONS

Technetium Tc-99m Disofenin Injection is indicated as an adjunct for the diagnosis of hepatobiliary disease. It has been useful in the detection of biliary leaks and fistulae, as well as the demonstration of altered biliary/GI tract anatomy. In addition, Technetium Tc-99m Disofenin Injection has been useful in the diagnosis of acute cholecystitis with or without cholelithiasis, and of chronic cholelithiasis with cystic duct obstruction.

WARNINGS

As with any radiopharmaceutical, this product should not be administered to pregnant patients unless the potential benefit outweighs the possible risks. Ideally, examinations using radiopharmaceuticals, especially those elective in nature, of a woman of childbearing capability should be performed during the first few (10) days following menses. Nursing mothers should substitute formula feeding for 48 hours since Technetium Tc-99m Disofenin Injection may be excreted in the milk.

This product should only be used by qualified physicians who have been licenced by the appropriate agency to use and administer radiopharmaceuticals.

The contents of the kit are not radioactive. However, after Technetium Tc-99m sodium pertechnetate is added, adequate shielding of the final preparation must be maintained.

PRECAUTIONS

The contents of the vial are sterile and non-pyrogenic. It is essential for the user to employ aseptic procedures during reconstitution and withdrawals for administration.

Adequate shielding must be maintained to minimize radiation exposure to personnel and patients.

Since Technetium Tc-99m Disofenin Injection does not contain a bacteriostatic agent and to maintain radiochemical stability, storage at 4°C is advised. Do not freeze.

ADVERSE REACTIONS

No side effects specifically attributable to Technetium Tc-99m Disofenin Injection have been reported to date.

TOXICOLOGY

Safety of Stannous DISIDA Kits has been evaluated in rodents. After five intravenous injections of 200 mg/kg of nonradioactive, reconstituted complex into six mice at 2 to 4 day intervals, no evidence of acute toxicity was observed. Histological examinations of tissue did not reveal any morphological changes due to drug toxicity (1).

PHYSICAL CHARACTERISTICS

Technetium Tc-99m decays by isomeric transition with a physical half-life of 6.02 hours. The principal photon useful for imaging studies is:

Radiation	Gamma-2
Mean % for disintegration	89.07
Mean energy (keV)	140.5

EXTERNAL RADIATION

The specific gamma ray constant for Technetium Tc-99m is 5.4 microcoulombs/kg MBq h (0.78 R/mCi-h) at 1 cm. The first half value layer of lead is 0.017 cm. To facilitate control of the radiation exposure from MBq amounts of this radionuclide, the use of a 0.25 cm thickness of lead will attenuate the radiation emitted by a factor of about 1000.

DOSAGE AND ADMINISTRATION

The suggested dose range for hepatobiliary imaging with Technetium Tc-99m Disofenin Injection is 111 to 185 MBq (3 to 5 mCi). Slow injection is recommended.

RADIATION DOSIMETRY

The estimated absorbed doses to an average person (70 kg) from an intravenous injection of Technetium Tc-99m Disofenin Injection are listed below:

ORGAN	mGy/100 MBq
Gallbladder Wall*	13.5
Bladder Wall	2.4
Small Intestine	5.9
Large Intestine (Wall)	8.1
Liver	1.4
Red Marrow	0.8
Total Body	0.5

* Assuming 80% of radioactivity localizes in liver and 100% is transferred from liver to gallbladder (2).

DIRECTIONS FOR PREPARATION

1. Remove one Stannous DISIDA Kit from the freezer and allow to thaw. Check for clarity and absence of particulate matter.
2. Aseptically add 1 to 3 mL of a solution of Technetium Tc-99m sodium pertechnetate in 0.9% Saline for Injection USP to the kit and mix. The maximum recommended activity is 2.6 GBq.
3. Incubate Technetium Tc99m Disofenin for a minimum of 15 minutes. Shorter incubation periods may result in inadequate labeling.
4. Measure radioactivity content in a dose calibrator. Complete documentation and affix label to shielded container.
5. Radiochemical purity must be checked prior to patient administration.

QUALITY CONTROL

Instant thin layer chromatography is used to determine the levels of Technetium Tc-99m sodium pertechnetate and Technetium Tc-99m colloidal impurities in the product.

Technetium Tc-99m colloid impurity

1. Approximately 1 cm from the bottom of a 1 x 7 cm strip of ITLC-SG chromatography paper, spot a small drop of product, using a 1 mL syringe with a 25 g needle.
2. Allow spot to dry in air.
3. Develop strip with 50% methanol. Allow solvent to run 5 cm from the origin.
4. Cut strip at 1 cm from the origin. Measure the radioactivity contained in each segment using a suitable detector. Technetium Tc-99m Disofenin and Technetium Tc-99m sodium pertechnetate will migrate to the solvent front; Technetium Tc-99m colloid will remain at the origin.
5. Calculate the percent Technetium Tc-99m colloidal impurity using the formula:

$$\frac{\text{total counts at origin}}{\text{total counts in all segments}} \times 100$$

Technetium Tc-99m sodium pertechnetate impurity

1. Approximately 1 cm from the bottom of a 1 x 7 cm strip of ITLC-SA chromatography paper, spot a small drop of product, using a 1 mL syringe with a 25 g needle.
2. Allow spot to dry in air.
3. Develop strip with 30% sodium chloride (saturated sodium chloride solution). Allow solvent to run to run 5 cm from the origin.
4. Cut strip at 4 cm from the origin. Technetium Tc-99m sodium pertechnetate will migrate to the solvent front; Technetium Tc-99m Disofenin and Technetium Tc-99m colloid will remain at the origin.
5. Calculate the percent Technetium Tc-99m sodium pertechnetate impurity using the formula:

$$\frac{\text{total counts at solvent front}}{\text{total count in all segments}} \times 100$$

Calculate the percent purity of the product as follows:

Purity = 100 - (% Tc-99m sodium pertechnetate impurity + % Tc-99m colloidal impurity).

Do not use the product if the purity is less than 90%.

STORAGE CONDITIONS

Stannous DISIDA Kits are kept frozen at -10°C. Technetium Tc-99m Disofenin Injection is stored at 4°C.

EXPIRY

Technetium Tc-99m Disofenin Injection expires 12 hours from preparation.

REFERENCES

1. Technetium-99m Di-Isopropyl-IDA Package Insert, Edmonton Radiopharmaceutical Centre.
2. Hepatolite Package Insert Reprint, NEN Canada, April 1980.