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DRAX IMAGE[®]**GLUCEPTATE****Kit for the Preparation of Technetium Tc 99m****Glucеptate Injection (Brain and Kidney Imaging Agent) or Stannous Glucеptate Injection (Cardiac Blood Pool Imaging Agent)****DIAGNOSTIC – For Intravenous Use DESCRIPTION**

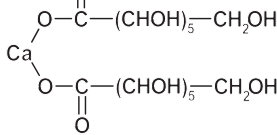
The kit consists of reaction vials which contain the sterile, non-pyrogenic, non-radioactive ingredients necessary to produce either Technetium Tc 99m Glucеptate Injection for diagnostic use in kidney and brain imaging or Stannous Glucеptate Injection for diagnostic use in cardiac blood pool imaging. Both diagnostic products are administered by intravenous injection.

Each 10 mL reaction vial contains 25 mg calcium glucеptate¹ complexed with 3 mg of stannous chloride dihydrate in lyophilized form under an atmosphere of nitrogen. The pH has been adjusted with sodium hydroxide and/or hydrochloric acid.

Technetium Tc 99m Glucеptate Injection for Brain and Kidney Imaging

The addition of Sodium Pertechnetate Tc 99m Injection to produce Technetium Tc 99m Glucеptate Injection results in the rapid labeling of calcium glucеptate which is essentially quantitative and which remains stable throughout the useful life of the preparation. No bacteriostatic preservative is present.

The precise structure of the reaction vial complex or of its technetium labeled form is not known at this time.

**Calcium Glucеptate**

^{*} Registered Trademark of DRAXIS Specialty Pharmaceuticals Inc.

¹ USP/USAN term for glucoheptonate

Blood Pool Imaging

The estimated absorbed radiation dose⁴ to various organs of an average patient (70 kg) from an intravenous injection of a maximum dose of 925 MBq (25 mCi) of Sodium Pertechnetate Tc 99m Injection thirty minutes after the intravenous administration of Stannous Glucеptate Injection are shown in Table 5.

Organ	rad/25 mCi (10 ⁻² Gy/925 MBq)
Blood	1.375
Urinary bladder wall	2.750
Ovaries	0.525
Testes	0.375
Whole body	0.375

DOSAGE AND ADMINISTRATION**Brain and Kidney Imaging**

The recommended dose range for intravenous administration of Technetium Tc 99m Glucеptate Injection in the average adult patient (70 kg) is:

Renal imaging studies: 370 to 555 MBq (10 to 15 mCi)

Brain imaging studies: 555 to 740 MBq (15 to 20 mCi)

Dynamic kidney or brain perfusion studies may be performed immediately after injection. Depending on the indication, these may be followed by delayed static imaging one-half to several hours after injection for renal studies, and one to several hours after injection for brain studies.

Cardiac Blood Pool Imaging

Stannous Glucеptate Complex should be reconstituted with 3.0 mL of sterile, pyrogen-free saline without preservative. A dose of 0.03 mL/kg (16 µg Sn/kg) of body weight (Table 6) is injected intravenously 10 to 30 minutes before intravenous administration of 555 to 925 MBq (15 to 25 mCi) of Sodium Pertechnetate Tc 99m Injection. Therefore, for a 100 kg patient, the entire 3.0 mL is used. For patients weighing less, the exact dose of Stannous Glucеptate Injection may be determined by using the body weight in **kilograms** as a percentage to calculate the volume required, e.g., for a 70 kg patient, 2.1 mL is required (70 % x 3.0 mL = 2.1 mL).

Stannous Glucеptate Injection for Cardiac Blood Pool Imaging

The contents of the kit may be reconstituted with sterile, non-pyrogenic preservative-free normal saline to form Stannous Glucеptate Injection for cardiac blood pool imaging and administered 10 to 30 minutes before injecting Sodium Pertechnetate Tc 99m Injection.

ACTION**Technetium Tc 99m Glucеptate Injection for Brain and Kidney Imaging**

When injected intravenously, Technetium Tc 99m Glucеptate Injection is rapidly cleared from the blood. The blood clearance curve is tri-exponential with the two faster components accounting for more than 90 % of the injected dose. In patients with normal renal function, less than 15 % of the initial activity remains in the blood after one hour. About 40 % of the injected dose is excreted in the urine in one hour, while about 70 % is excreted in 24 hours. In patients with renal disease, the blood clearance and urine excretion of the radiopharmaceutical are delayed.

Up to 15 % of the injected dose is retained in the kidneys with the remainder being excreted in the urine. The renal retention is greater in the cortex than in the medulla. This may be due to the binding of the radiopharmaceutical to the proximal or distal convoluted tubules, which are primarily located in the renal cortex.

Technetium Tc 99m Glucеptate Injection tends to accumulate in intracranial lesions with excessive neo-vascularity or an altered blood-brain barrier. It does not accumulate in the choroid plexus or salivary glands.

Stannous Glucеptate Injection for Cardiac Blood Pool Imaging

When tin, as stannous glucеptate, is injected intravenously, it is taken up by red blood cells and by an unknown mechanism facilitates the labeling of these cells by technetium-99m when the latter is subsequently administered as Sodium Pertechnetate Tc 99m Injection.

Following *in vivo* red blood cell labeling in both normal volunteers and patients, approximately 89 % of the injected dose of Sodium Pertechnetate Tc 99m Injection remained in the intravascular compartment ten minutes post-injection. The blood clearance curve can be resolved into two exponential components; the first may have been due to the extra-vascular distribution and urinary excretion of ^{99m}Tc sodium pertechnetate, as well as accumulation of damaged red blood cells by the spleen.

About 6 % of the injected dose was excreted in the urine of normal volunteers in 3 hours, and about 28 % was excreted in 24 hours. In five patients with ischemic heart disease however, only about 3 % of the injected dose was excreted in 2 hours, and only about 13 % was excreted in 24 hours.

INDICATIONS AND USAGE

Technetium Tc 99m Glucеptate Injection may be used to perform kidney and brain imaging, and to assess renal and brain perfusion.

Stannous Glucеptate Injection may be used in conjunction with Sodium Pertechnetate Tc 99m Injection for cardiac blood pool imaging.

CONTRAINDICATIONS

Hypersensitivity to this agent.

WARNINGS

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

Radiopharmaceuticals should be used only by or under the control of physicians who are qualified by specific training in the safe use and handling of radionuclides and whose experience and training have been approved by the appropriate government agency authorized to license the use of radionuclides.

Since adequate reproduction studies have not been performed in animals to determine whether this drug affects fertility in males or females, has teratogenic potential, or has other adverse effects on the fetus, this radiopharmaceutical preparation should not be administered to pregnant or nursing women unless it is considered that the benefits to be gained outweigh the potential hazards.

Where an assessment of the risk to benefit ratio suggests use of this product in lactating mothers, nursing should be stopped.

Adequate studies do not exist to support the use of this radiopharmaceutical in pediatric patients. As in pregnancy and lactating mothers, the risk to benefit ratio should be assessed before consideration is given to the use of this product in this age group.

Ideally, examinations using radiopharmaceuticals, especially those elective in nature, of a woman of childbearing capability should be performed during the first few (approximately 10) days following the onset of menses.

PRECAUTIONS

The Stannous Glucеptate Injection kit may be used to prepare Technetium Tc 99m Glucеptate Injection for brain and kidney imaging by addition of Sodium Pertechnetate Tc 99m Injection. However, the contents may also be reconstituted with sterile, non-pyrogenic, preservative-free normal saline to form Stannous Glucеptate Injection for cardiac blood pool imaging and administered intravenously 10 to 30 minutes before injecting Sodium Pertechnetate Tc 99m Injection.

The components of the kit are sterile and non-pyrogenic. It is essential that the user follows the directions carefully and adheres to strict aseptic procedures during preparation.

The ^{99m}Tc labeling reactions involved depend on maintaining the tin (stannous ion) in the reduced state. Hence, ^{99m}Tc sodium pertechnetate containing oxidants should not be employed.

As in the use of any other radioactive material, care should be taken to insure minimal radiation exposure to the patient, consistent with proper patient management, and to insure minimum radiation exposure to occupational workers.

Brain and Kidney Imaging

The patient should be encouraged to drink fluids before and after the examination. To minimize the radiation dose to the bladder, the patient should be encouraged to void when the imaging procedure is completed and as often thereafter as possible for the next 4 to 6 hours.

The image quality may be adversely affected by impaired renal function.

Literature reports indicate that the target to non-target ratio for intracranial lesions may take several hours to fully develop, and the possibility of missing certain lesions by restricting imaging to only the early period after injection should be borne in mind.

Blood Pool Imaging

Stannous Glucеptate Injection should be administered by direct venipuncture. Heparinized catheter systems must be avoided.

When the cardiac blood pool is imaged, the patient's cardiac condition should be stable. Imaging in conjunction with stress-exercise should be conducted under the supervision of an experienced cardiologist in an examination room equipped with an ECG recorder, a defibrillator and standard resuscitation equipment. Similarly, during the scanning procedure of patients with known or suspected myocardial infarction, the required clinical supervision and supportive therapy must be maintained.

Subsequent re-administration of Sodium Pertechnetate Tc 99m Injection within one week after a cardiac blood pool imaging procedure will re-label some of the red blood cells. Therefore, if an

Solid phase: ITLC-SG
Solvent A: 0.9 % sodium chloride (for determination of reduced hydrolyzed technetium)
Solvent B: Acetone (for determination of pertechnetate)

Step 1

Add 1 mL of the required solvent to an 18 mm x 150 mm test tube. Stopper and allow the atmosphere in the tube to equilibrate for 1 minute.

Step 2

Prepare two chromatography strips (1 x 10 cm) of silica gel impregnated glass fiber sheets (ITLC type SG). Pretreat one ITLC-SG strip by applying 2 drops of a saturated solution of glucеptate (or suitable sugar) in water to the origin at 1.5 cm from one end of the strip. Dry the pretreated ITLC-SG strip under a nitrogen jet and apply one small drop of the radioactive glucеptate solution (~20,000 cpm) to the same origin. Immediately develop the chromatogram in a 0.9 % sodium chloride solution.

To the non-treated ITLC-SG strip apply one small drop (~20,000 cpm) of the radioactive glucеptate solution to the origin at 1.5 cm from one end and dry under a nitrogen jet. Develop the non-treated chromatogram in acetone.

For both ITLC-SG strips, allow the solvent front to move 8 cm from the origin. Dry the strips and examine the chromatograms using an appropriate instrument, such as the Berthold TLC Analyser.

In the saline system, the reduced hydrolyzed technetium TcO₂ appears at the origin or Rf 0 and the free and bound technetium TcO₄⁻ migrates to the front at Rf 0.85 to 1.0.

In the acetone system, the bound and reduced hydrolyzed technetium appear at the origin or Rf 0 and the free pertechnetate TcO₄⁻ migrates to the front at Rf 0.85 to 1.0.

Determine the percentage of free pertechnetate TcO₄⁻ on the basis of the level of activity between Rf 0.85 and Rf 1.0 in the acetone system and the percentage of reduced hydrolyzed pertechnetate TcO₂ on the basis of the level of activity at Rf 0 in the saline system.

Step 3

Develop the chromatogram by placing it, with the origin down, in the previously equilibrated test tube. Stopper the test tube. The test tube should be kept upright, ideally in a test tube rack. Development requires about 10 minutes for ITLC-SG strips.

Step 4

When the solvent front has climbed to the top of the strip, remove it with forceps and allow it to dry. The strips can be dried by placing them radioactive side up on a disposable non-porous pad at room temperature.

imaging procedure using Sodium Pertechnetate Tc 99m Injection is anticipated, this examination should be carried out prior to the use of Stannous Glucеptate Injection or not less than one week after the administration of the drug.

ADVERSE REACTIONS

Although adverse reactions have not been reported that are specifically attributable to the use of Technetium Tc 99m Glucеptate Injection, allergic dermatological manifestations (erythema) have been infrequently reported with similar agents.

PHARMACOLOGY**Technetium Tc 99m Glucеptate Injection for Brain and Kidney Imaging**

Intravenous administration of Technetium Tc 99m Glucеptate Injection to rats resulted in rapid clearance of the drug from the blood pool with less than 3% of the injected dose remaining in the circulation at 1 hour post-injection. The kidney retention of the radiopharmaceutical was approximately 12% of the dose, which decreased slowly to less than 8% within 24 hours. A similar pattern was observed in rabbits except that the kidney retention was lower and the blood clearance was slower. About half of the injected dose was excreted in the urine within the first hour post-injection.

Stannous Glucеptate Injection for Cardiac Blood Pool Imaging

In a dose range study, rabbits were injected with doses of Stannous Glucеptate Injection containing between 2.6 and 31.6 µg of tin. The following table indicates the percentage of labeled red blood cells with the increasing dose of tin.

Tin (µg/kg body weight)	% Labeled RBC
2.6	86.3
5.3	93.6
10.5	95.5
15.8	95.3
31.6	96.2

Therefore, a dose of 16 µg of tin per kilogram of body weight is considered optimal for red blood cell labeling.

When *in vivo* red blood cell labeling is performed in rats, not less than 90 % of the injected dose of Sodium Pertechnetate Tc 99m Injection remains in the blood thirty minutes after injection. More than 98 % of the radioactivity in the blood is associated with the red blood cells and there is a minimal loss of the label over a 6-hour period.

Step 5

Method A – Determination of reduced technetium

Cut the dried strip 3 cm from the origin end. The short piece is marked as *Part I* and the long piece is marked as *Part II*. Count the pieces in a suitable counter and determine the percentage of reduced technetium according to the following formula:

$$\text{Percent TcO}_2 = \frac{\text{Counts in Part I}}{\text{Counts Part I + Part II}} \times 100$$

Method B – Determination of pertechnetate

Cut the dried strip 2 cm from the solvent front end. The short piece is marked *Part IV* and the long piece is marked *Part III*. Count the pieces in a suitable counter and determine the percentage of free pertechnetate according to the following formula:

$$\text{Percent TcO}_4^- = \frac{\text{Counts in Part IV}}{\text{Counts Part III + Part IV}} \times 100$$

NOTE: IT IS IMPORTANT TO NOTE THAT THE STRIPS ARE CUT IN DIFFERENT POSITIONS FOR METHODS A AND B.

Step 6

Determine the amount of chelated technetium according to the following formula:

$$\text{Percent chelated Tc} = 100 - \% \text{TcO}_4^- - \% \text{TcO}_2$$

Step 7

Store all waste radioactive strips for 48 hours before disposing of them as non-radioactive waste. Store used chromatographic solvents in a similar fashion.

HOW SUPPLIED

DRAXIMAGE[®] GLUCEPTATE

Kit for the Preparation of Technetium Tc 99m Glucеptate Injection or Stannous Glucеptate Injection

Product No. 500220

The kit consists of 5 vials of stannous glucеptate complex, each vial containing in lyphophilized form under an atmosphere of nitrogen:

Calcium glucеptate	25mg
Stannous chloride dihydrate	3 mg

The pH has been adjusted with sodium hydroxide and/or hydrochloric acid.

TOXICOLOGY

A safety assessment in two rodent and one non-rodent species was made using Stannous Glucеptate Injection reconstituted with saline but without any ^{99m}Tc sodium pertechnetate.

The acute intravenous lethal dose₅₀ (LD₅₀) of Stannous Glucеptate Injection in Swiss Albino mice is 605 mg/kg body weight, and 440 mg/kg in BBL Sprague-Dawley rats. The signs of acute intoxication in mice were moderate respiratory depression and clonic-tonic convulsions shortly after drug administration. No signs of acute drug intoxication were observed in rats.

A slow intravenous injection of 56 mg Stannous Glucеptate Injection (6 mg stannous chloride dihydrate) per kg body weight in four beagle dogs produced no toxic or gross pathological changes. This dose represents a 200 fold excess over the human dose (0.28 mg/kg).

PHYSICAL CHARACTERISTICS

Technetium-99m decays by isomeric transition with a physical half-life of 6.02 hours.¹ The principal photon that is useful for detection and imaging studies is listed in Table 1.

Table 1

Principal Radiation Emission Data		
Radiation	Means % per Disintegration	Mean Energy (keV)
Gamma 2	89.07	140.5

Table 2

Radiation Attenuation by Lead Shielding		
Shield Thickness (Pb) mm	Coefficient of Attenuation	
0.2	0.5	
0.8	10 ⁻¹	
1.6	10 ⁻²	
2.5	10 ⁻³	
3.3	10 ⁻⁴	
4.5	10 ⁻⁵	

To correct for physical decay of this radionuclide, the fractions that remain at selected intervals after the time of calibration are shown in Table 3.

Table 3

Physical Decay Chart of Technetium-99m Half-Life: 6.02 Hours			
Hours	Fraction Remaining	Hours	Fraction Remaining
0*	1.000	8	0.398
1	0.891	9	0.355
2	0.794	10	0.316
3	0.708	11	0.282
4	0.631	12	0.251
5	0.562	18	0.126
6	0.501	24	0.063

*Calibration Time

RADIATION DOSIMETRY**Brain and Kidney Imaging**

The estimated absorbed radiation doses^{2,3} to various organs of an average adult patient (70 kg) from an intravenous injection of a maximum dose of 740 MBq (20 mCi) of Technetium Tc 99m Glucеptate Injection are shown in Table 4.

Table 4

Estimated Absorbed Radiation Doses		
Tissue	mGy/MBq	rad/mCi
Adrenals	0.0046	0.017
Bladder wall	0.056	0.21
Bone surfaces	0.0026	0.0096
Breast	0.0014	0.0052
GI-tract		
Stomach wall	0.0027	0.010
Small intestine	0.0037	0.014
Large intestine wall (upper)	0.0033	0.012
Large intestine wall (lower)	0.0044	0.016
Kidneys	0.049	0.18
Liver	0.0027	0.010
Lungs	0.0017	0.0063
Ovaries	0.0046	0.017
Pancreas	0.0036	0.013
Red marrow	0.0039	0.014
Spleen	0.0039	0.014
Testes	0.0029	0.011
Thyroid	0.0011	0.0041
Uterus	0.0077	0.029
Other tissue	0.0023	0.0085
Effective dose equivalent (mSv/MBq)	0.0090	

Labels with a radiation warning symbol and directions are supplied with each kit.

STORAGE

Store kit at or below room temperature. Do not use the kit beyond the expiry date stamped on the box.

REFERENCES

- Martin, M.J., Ed. Nuclear Decay Data for Selected Radionuclides, ORNL Report No. 5114, page 24, March 1976.
- Arnold, R.W. et al.: Comparison of ^{99m}Tc Complexes for Renal Imaging. J. Nucl. Med. 16: 357, 1975.
- Radiopharmaceutical Internal Dosimetry Information Center, Oak Ridge Associated Universities, Oak Ridge, TN, Jan 5, 1977.
- Calculated by Mr. Jack L. Coffey, Radiopharmaceutical Internal Dose Information Center, Oak Ridge Associated Universities, Oak Ridge, TN.

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