PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

DRAXIMAGE® GLUCEPTATE

Powder for solution, 25 mg calcium gluceptate per vial, for intravenous injection

Kit for the preparation of Technetium (^{99m}Tc) Gluceptate Injection and

Stannous Gluceptate Injection

Diagnostic Radiopharmaceutical Kit

ATC V09BA02

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TABLE OF CONTENTS

Sections or subsections that are not applicable at the time of authorization are not listed

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

Draximage® Gluceptate [kit for the preparation of Technetium (^{99m}Tc) Gluceptate Injection], after radiolabeling with Tc-99m, is a radioactive diagnostic agent that may be used to perform kidney and brain imaging, and to assess renal and brain perfusion.

Stannous Gluceptate Injection may be used in conjunction with Technetium (^{99m}Tc) Sodium Pertechnetate Injection for cardiac blood pool imaging.

1.1 Pediatrics

Pediatrics (< 18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

1.2 Geriatrics

Geriatrics (≥ 65 years of age): No formal studies with technetium (^{99m}Tc) gluceptate in patients ≥ 65 years were performed to determine whether they respond differently from a younger population.

2 CONTRAINDICATIONS

Technetium (^{99m}Tc) Gluceptate Injection is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, *see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.*

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Draximage® Gluceptate [kit for the preparatrion of Technetium (^{99m}Tc) Gluceptate Injection] should be used only by those health professionals who are appropriately qualified in the use of radioactive prescribed substances in or on humans (see *12 SPECIAL HANDLING INSTRUCTIONS).*

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

Using proper shielding, the prepared technetium (^{99m}Tc) gluceptate should be inspected for particulate matter and discoloration prior to administration. Do not use if the solution contains particulate matter or is not a clear solution.

4.2 Recommended Dose and Dosage Adjustment

Brain and Kidney Imaging

The recommended dose range for intravenous administration of Technetium (^{99m}Tc) Gluceptate 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 gluceptate Complex should be reconstituted with 3.0 mL of sterile, pyrogen-free saline without preservative. A dose of 0.03 mL/kg (16 mcg Sn/kg) of body weight (Table 1) is injected intravenously 10 to 30 minutes before intravenous administration of 555 to 925 MBq (15 to 25 mCi) of Technetium (^{99m}Tc) Sodium Pertechnetate Injection. Therefore, for a 100 kg patient, the entire 3.0 mL is used. For patients weighing less, the exact dose of Stannous Gluceptate 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).

Table 1- Dose in mL of Stannous Gluceptate Injection by Body Weight

Body (kg)	Weight (lb)	Dose (mL)	Body (kg)	Weight (lb)	Dose (mL)
10	22	0.30	60	132	1.80
15	33	0.45	65	143	1.95
20	44	0.60	70	154	2.10
25	55	0.75	75	165	2.25
30	66	0.90	80	176	2.40
35	77	1.05	85	187	2.55
40	88	1.20	90	198	2.70
45	99	1.35	95	209	2.85
50	110	1.50	100	220	3.00
55	121	1.65			

The patient dose of Technetium (^{99m}Tc) Sodium Pertechnetate Injection should be measured and verified with a suitable dose calibrator immediately prior to administration. The dose calibrator must be calibrated and comply with international standards. Withdrawals for administration must be made aseptically.

Special populations

Renal impairment: Draximage Gluceptate has not been studied in patients with renal impairment.

Hepatic impairment: Draximage Gluceptate has not been studied in patients with hepatic impairment.

Pediatrics (below 18 years): The safety and efficacy of Draximage Gluceptate in pediatric patients below 18 years have not been established. Health Canada has not authorized an indication for pediatric use.

Geriatric patients (65 years of age or above): No formal studies with Draximage Gluceptate in patients ≥ 65 years were performed.

4.3 Reconstitution

Technetium (^{99m}Tc) Gluceptate Injection for Brain and Kidney Imaging

Reaction vials containing the sterile, non-pyrogenic, lyophilized powder are reconstituted with 2 to 10 mL of sterile non-pyrogenic technetium (^{99m}Tc) sodium pertechnetate to prepare Technetium (^{99m}Tc) Gluceptate Injection for intravenous administration. The recommended maximum amount of technetium (^{99m}Tc) (at the time of elution) to be added to a reaction vial is 11.1 GBq (300 mCi) (see *11 STORAGE, STABLITY AND DISPOSAL).*

Stannous Gluceptate 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 Gluceptate Injection for cardiac blood pool imaging and administered 10 to 30 minutes before injecting Technetium (^{99m}Tc) Sodium Pertechnetate Injection. See *11 STORAGE, STABLITY AND DISPOSAL.*

4.4 Administration

After reconsitiution, Technetium (^{99m}Tc) Gluceptate solution or Stannous Gluceptate should be administered by slow intravenous injection, in order to avoid local extravasation resulting in inadvertent radiation exposure to the patient and imaging artifacts.

The total radioactivity in the syringe should be verified with a dose calibrator immediately before and after Technetium (^{99m}Tc) Gluceptate solution administration to the patient. The dose calibrator must be calibrated and comply with international standards.

See *4.7 Instructions for Preparation and Use* for the preparation of Technetium (^{99m}Tc) Gluceptate Injection or Stannous Gluceptate Injection.

Visually inspect the (^{99m}Tc) labelled Technetium (^{99m}Tc) Gluceptate Injection or Stannous Gluceptate Injection after reconstitution for particulate matter prior to administration. Do not use or administer if there is evidence of foreign matter or the solution is not clear.

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 preparation contains no bacteriostatic preservative. The solution should not be used if it is cloudy.

4.6 Image Acquisition and Interpretation

Brain and Kidneys Imaging

Dynamic brain perfusion studies may be performed immediately after injection. Depending on the indication, these may be followed by delayed static imaging one to several hours after injection for brain studies. During imaging, the head should be fixed close to the collimator.

The absence of significant accumulation of technetium (^{99m}Tc) gluceptate in brain parenchyma except for low background radioactivity indicates an intact blood-brain barrier (BBB). Literature evidence indicates 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.

For renal imaging, serial images are to be taken of both kidneys 5-30 minutes post-injection with the use of a gamma camera with a low energy parallel hole collimator. Static images are obtained 3-4 hours post-injection. Early images will reveal renal parenchyma without radioactivity while later images depicting the whole renal structure.

Cardiac Blood Pool Imaging

Stannous Gluceptate 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 Technetium (^{99m}Tc) Sodium Pertechnetate Injection within one week after a cardiac blood pool imaging procedure will re-label some of the red blood cells. Therefore, if an imaging procedure using Technetium (^{99m}Tc) Sodium Pertechnetate Injection is anticipated, this examination should be carried out prior to the use of Stannous Gluceptate Injection or not less than one week after the administration of the drug.

4.7 Instructions for Preparation and Use

General

- Use aseptic techniques, radiation shielding, and wear waterproof gloves throughout the entire prepration procedure.
- Before reconstituting a vial, it should be inspected for cracks and/or a melted plug or any other indication that the integrity of the vacuum seal has been lost.

- The components of the kit are supplied sterile and non-pyrogenic. Aseptic procedures normally employed in making additions and withdrawals from sterile, non-pyrogenic containers should be used during the addition of a technetrium (^{99m}Tc) sodium pertechnetate solution and the withdrawal of doses for patient administration.

To prepare Technetium (^{99m}Tc) Gluceptate Injection:

a) Remove the protective disc from a reaction vial and swab the closure with an alcohol swab.

b) Place the vial in a suitable radiation shield. Obtain 2 to 10 mL of Technetium (^{99m}Tc) Sodium Pertechnetate Injection using a shielded syringe. The recommended maximum amount of technetium (^{99m}Tc) to be added to a reaction vial is 11.1 GBq (300 mCi). Technetium (^{99m}Tc) sodium pertechnetate containing an oxidizing agent is not suitable for use.

c) Add the Technetium (^{99m}Tc) Sodium Pertechnetate Injection to the reaction vial aseptically.

d) Agitate the shielded vial until the contents are completely dissolved. Using proper shielding, the vial should be visually inspected and not used if there is evidence of particulate or foreign matter. To ensure maximum radiolabeling, allow the preparation to stand at room temperature (15 ºC to 30 ºC) for 15 minutes after mixing.

e) Assay the product in a suitable dose calibrator, record the radioassay information on the label with a radiation warning symbol, and apply it to the vial shield.

f) The radiochemical purity of the finished preparation should be checked prior to patient administration. The radiochemical purity should not be less than 90%.

g) Withdrawals for administration must be made aseptically using a sterile syringe and needle. Since the vials contain nitrogen to prevent oxidation of the complex, the vials should not be vented. If repeated withdrawals are made, minimize the replacement of the contents with room air.

h) The finished preparation should be stored at 2 ºC to 8 ºC when not in use and discarded after 8 hours.

Stannous Gluceptate Injection for Blood Pool Imaging

To prepare Stannous Gluceptate Injection:

a) Remove the protective disc from a reaction vial and swab the closure with an alcohol swab.

b) Add 3.0 mL of sterile, non-pyrogenic, preservative-free normal saline to the reaction vial aseptically.

c) Agitate the vial until the contents are completely dissolved. The vial should be visually inspected and not used if there is evidence of particulate or foreign matter.

d) Withdrawals for administration must be made aseptically using a sterile syringe and needle. Since the vials contain nitrogen to prevent oxidation of the complex, the vials should not be vented. If repeated withdrawals are made, minimize the replacement of the contents with room air.

e) The finished preparation should be stored at 2 ºC to 8 ºC when not in use and discarded after 8 hours.

The technetium (^{99m}Tc) sodium pertechnetate eluate should be less than 2 hours old and should be obtained from a generator which has been eluted within the last 24 hours.

Specifications and quality control

Perform the quality controls in Table 2 behind a lead glass shield for radioprotection purpose.

Table 2 – Specifications of the Technetium (^{99m}Tc) Gluceptate Injection

Test	Acceptance criteria	Method
Appearance	Clear, free of particulate matter	Visual inspection
pH	6.0 to 8.0	pH indicator strips
Labeling efficiency	Non-complexed technetium-99m species ≤ 10%	Instant thin layer chromatography (ITLC, see details below)

Determine labeling efficiency of Technetium (^{99m}Tc) Gluceptate Injection by performing instant thin layer chromatography (ITLC). The method is used for determining free pertechnetate in a mixture of chelated and reduced technetium.

Perform ITLC using ITLC SG strips and using acetone as mobile phase.

Radiochemical Purity – ITLC method

a) 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.

b) Prepare one chromatography strip (1 x 10 cm) of silica gel impregnated glass fiber sheets (ITLC type SG). Apply one small drop (~ 20 000 cpm) of the radioactive gluceptate solution to the origin at 1.5 cm from one end and dry under a nitrogen jet.

c) 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.

d) 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.

e) The bound and reduced technetium appear at the origin or Rf 0 and the free pertechnetate $^{99m}TcO4^-$ migrates to the front at Rf 0.85 to 1.0.

f) Cut the dried strip 2 cm from the solvent front end. The short piece is the top piece and the long piece is the bottom piece. Measure the pieces in a suitable radioactivity dose calibrator or counter and determine the percentage of free perctechnetate according to the following formula:

$$Percent\ ^{99m}TcO4^- = \frac{Counts\ in\ Radioactivity\ top\ piece}{Counts\ Radioactivity\ bottom\ piece + Radioactivity\ top\ piece} \times 100$$

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

4.8 Radiation Dosimetry

Brain and Kidney Imaging

The estimated absorbed radiation doses 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 (^{99m}Tc) Gluceptate Injection are shown in Table 3.

Table 3 Estimated Radiation Absorbed Dose of Technetium (^{99m}Tc) Gluceptate Injection

Organ	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	

Blood Pool Imaging

The estimated absorbed radiation doses to various organs of an average patient (70 kg) from an intravenous injection of a maximum dose of 925 MBq (25 mCi) of Technetium (^{99m}Tc) Sodium Pertechnetate Injection thirty minutes after the intravenous administration of Stannous Gluceptate Injection are shown in Table 4.

Table 4 - Estimated Absorbed Radiation Doses

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

5 OVERDOSAGE

In the event of the administration of a radiation overdose with Technetium (^{99m}Tc) Gluceptate Injection, if the patient's medical condition allows, the absorbed dose to the patient should be reduced where possible by increasing the elimination of the radionuclide from the body via forced diuresis and frequent bladder voiding. It might be helpful to estimate the effective dose to the patient.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 5– Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intravenous	Kit for the preparation of solution for intravenous injection Vial contains: 25 mg calcium gluceptate and 3 mg stannous chloride dihydrate	Sodium Hydroxide and/or Hydrochloric Acid

The kit consists of reaction vials which contain the sterile, non-pyrogenic, non-radioactive ingredients necessary to produce either Technetium (^{99m}Tc) Gluceptate Injection for diagnostic use in kidney and brain imaging or Stannous Gluceptate 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 of calcium gluceptate complexed with 3 mg of stannous chloride dihydrate in lyophilized form under an atmosphere of nitrogen.

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

Calcium gluceptate	25 mg
Stannous chloride dihydrate	3 mg

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

Labels with radiation warning symbols and a package insert are supplied in each carton.

6.1 Physical Characteristics

Technetium-99m decays by isomeric transition with a physical half-life of 6.02 hours. The principal photon that is useful for detection and imaging studies is listed in Table 6.

Table 6- Principal Radiation Emission Data

Radiation	Mean % per Disintegration	Mean Energy (keV)
Gamma-2	89.07	140.5

6.2 External Radiation

The specific gamma ray constant for technetium-99m is 5.44 $\mu C \cdot kg^{-1} \cdot MBq^{-1} \cdot hr^{-1}$ (0.78 R/mCi-hr) at 1 cm. The half-value layer is 0.2 mm of Pb. To facilitate control of the radiation exposure from millicurie amounts of this radionuclide, the use of 2.5 mm thickness of Pb will attenuate the radiation emitted by a factor of about 1000.

Table 7 - 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 8.

Table 8 - Physical Decay Chart of Technetium-99m, Half-Life: 6.02 Hours

Hours	Fraction Remaining	Hours	Fraction Remaining	Hours	Fraction Remaining
0*	1.000	5	0.562	10	0.316
1	0.891	6	0.501	11	0.282
2	0.794	7	0.447	12	0.251
3	0.708	8	0.398	18	0.126
4	0.631	9	0.355	24	0.063

*Calibration Time

7 WARNINGS AND PRECAUTIONS

Please see 3 SERIOUS WARNINGS AND PRECAUTIONS BOX.

General

The product should be administered under the supervision of a health professional who is experienced in the use of radiopharmaceuticals. Appropriate management of therapy and complications is only possible when adequate diagnostic and treatment facilities are readily available.

The radiopharmaceutical product may be received, used and administered only by authorized persons in designated clinical settings. Its receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licenses of local competent official organizations.

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

The contents of the reaction vial are intended **only** for use in the preparation of Technetium (^{99m}Tc) Gluceptate Injection and are **not** to be administered directly to the patient.

The technetium (^{99m}Tc) labelling reactions involved in preparing the agent depend on maintaining the stannous ion in the reduced state. Any oxidant present in the technetium (^{99m}Tc) sodium pertechnetate solution may thus adversely affect the quality of the radiopharmaceutical. Hence, technetium (^{99m}Tc) sodium pertechnetate solutions containing oxidants should not be employed.

The contents of the kit before preparation are not radioactive. However, after the technetium (^{99m}Tc) sodium pertechnetate is added, adequate shielding of the final preparation must be maintained.

Carcinogenesis and Mutagenesis

No long term animal studies have been performed to evaluate carcinogenic potential of Technetium (^{99m}Tc) Gluceptate Injection. Mutagenesis studies have not been conducted.

Contamination

Proper radiopharmaceutical practices should be used to minimize radioactive contamination. Following administration, a toilet should be used instead of a urinal and the toilet should be flushed several times after use.

Radiation Risk

Technetium (^{99m}Tc) gluceptate contributes to a patient's overall long-term cumulative radiation exposure. Long-term cumulative radiation exposure is associated with an increased risk of cancer. Ensure safe handling and preparation procedures to protect patients and health care workers from unintentional radiation exposure. Encourage patients to drink fluids and bladder void as frequently as possible after intravenous administration.

Reproductive Health: Female and Male Potential Fertility

- Studies have not been performed to evaluate whether technetium (^{99m}Tc) gluceptate has an effect on fertility in males or females.

Risk for Image Misinterpretation

- Underlying pathologies such as infection or inflammatory conditions can lead to atypical localization of technetium (^{99m}Tc) gluceptate. For example, increased uptake in areas of inflammation or infection can mimic malignant lesions**.**

- Patient factors, including age and renal function, can influence the biodistribution of the technetium (^{99m}Tc) gluceptate, which can lead to potentially misleading results.

7.1 Special Populations

7.1.1 Pregnant Women:

There are no available data with technetium (^{99m}Tc) gluceptate in pregnant women to inform about drug-related risk of major birth defects, miscarrages, or adverse meternal or fetal outcomes. Animal reproduction studies have not been conducted with technetium (^{99m}Tc) gluceptate. All radiopharmaceuticals, including technetium (^{99m}Tc) gluceptate, have the potential to cause fetal harm.

Ideally, examinations using radiopharmaceuticals, especially those elective in nature of women of childbearing capability, should be performed during the first ten days following the onset of menses, or after ensuring the woman is not pregnant. The benefit of using a diagnostic radiopharmaceutical should be weighed against the possible risk to an embryo or a fetus.

7.1.2 Breastfeeding

There are no available data on the presence of technetium (^{99m}Tc) in human milk, the effect on the breastfed infant, or the effect on milk production. Lactation studies have not been conducted in animals with technetium (^{99m}Tc). Where an assessment of the risk to benefit ratio suggests use of this product in lactating mothers, nursing should be stopped.

7.1.3 Pediatrics

Pediatrics (< 18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

7.1.4 Geriatrics

Geriatrics (> 65 years of age): No formal studies with technetium (^{99m} Tc) gluceptate in patients ≥ 65 years were performed to determine whether the respond differently from younger population.

8 ADVERSE REACTIONS

8.1 Adverse Drug Reaction Overview

Adverse reactions that have been identified during post-approval use of Technetium (^{99m}Tc) Gluceptate Injection are uncommon. Although not specifically associated with technetium (^{99m}Tc) Gluceptate, all adverse reactions are reported sponstanously from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to product exposure.

8.5 Post-Market Adverse Reactions

The following adverse reactions have been rarely during post-approval use of Technetium (^{99m}Tc) Gluceptate Injection. Although not specifically associated with technetium (^{99m}Tc) gluceptate:

- Gastrointestinal disorders: Nausea, Vomiting
- General disorders and administration site conditions: Injection site pain, Discomfort, Feeling hot
- Immune system disorders: Hypersensitivity
- Respiratory, thoracic and mediastinal disorders: Dyspnea
- Skin and subcutaneous tissue disorders: Erythema, Pruritis, Urticaria, allergic dermatitis, Rash/macular
- Vascular disorders: Flushing

9 DRUG INTERACTIONS

9.4 Drug-Drug Interactions

Interactions with other drugs have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Brain Imaging: technetium (^{99m}Tc) gluceptate accumulates in areas with compromised blood-brain barriers or increased neovascularity. This facilitates the detection of intracranial lesions. Importantly, technetium (^{99m}Tc) gluceptate does not accumulate in the choroid plexus or salivary glands, making it useful for specific imaging of brain pathologies.

Renal Imaging: In patients with normal renal function, technetium (^{99m}Tc) gluceptate accumulates in the kidneys, with preferential localization in the renal cortex. The radiopharmaceutical binds to certain renal structures, aiding in the detailed imaging of renal function and structure.

Cardiac Blood Pool Imaging: stannous gluceptate, when combined with technetium (^{99m}Tc) sodium pertechnetate, acts as a reducing agent. This facilitates the binding of technetium (^{99m}Tc) to red blood cells, allowing for detailed imaging of blood flow and volume within the heart chambers. Following in vivo red blood cell labeling in both normal volunteers and patients, approximately 89% of the injected dose of Technetium (^{99m}Tc) Sodium Pertechnetate 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 technetium (^{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 healthy 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.

10.2 Pharmacodynamics

At the chemical concentration used for diagnositic examination, technetium (^{99m}Tc) gluceptate or stannus gluceptate do not have any pharmacodynamics activity.

10.3 Pharmacokinetics

Absorption

Technetium (^{99m}Tc) gluceptate is adminstered intravenously; thus it is immediately and completely bioavailable.

Distribution

After intravenous administration, technetium (^{99m}Tc) gluceptate is rapidly cleared from the blood. The clearance follows a triexponential pattern, with the two faster components accounting for over 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.

Elimination Technetium (^{99m}Tc) gluceptate is predominantly excreted by the kidneys. Approximately 40% of the injected dose is excreted in the urine within the first hour, and about 70% is excreted within 24 hours. The compound shows retention in the kidneys, with up to 15% of the injected dose being retained, particularly in the renal cortex, rather than the medulla.

Renal Retention: Up to 15% of the injected dose is retained in the kidneys, primarily in the renal cortex, providing clear imaging of renal function. Blood and renal clearance are delayed due in the presence of renal impairment. In patients with renal disease, the blood clearance and urine excretion of the radiopharmaceutical are delayed.

Special Populations and Conditions

Hepatic Insufficiency: the effect of hepatic impariment on technetium (^{99m}Tc) gluceptate pharmacokintetics has not been established.

Renal Insufficiency: the effect of renal impariment on technetium (^{99m}Tc) gluceptate pharmacokintetics has not been established. Renal impairment has shown to reduce the uptake of technetium (^{99m}Tc) gluceptate in the kidneys**.**

11 STORAGE, STABILITY AND DISPOSAL

Before reconstitution, vials should be stored at or below room temperature (2 °C to 30 °C).

After reconsitiution, the finished preparation should be stored at 2 ºC to 8 ºC when not in use and discarded after 8 hours.

Do not use the kit beyond the expiry date stamped on the box.

The storage of the radiolabeled product must comply with regulatory requirements for radioactive materials.

This product must not be mixed with medicinal products other than those mentioned in the Instructions for use and handling (see *4.7 Instructions for Preparation and Use).*

12 SPECIAL HANDLING INSTRUCTIONS

After reconsitiution and radiolabeling, Technetium (^{99m}Tc) Gluceptate Injection should be handled with appropriate safety measures to minimize radiation exposure. Waterproof gloves, effective radiation shielding, and other safety measures should be used when preparing and handling technetium (^{99m}Tc) gluceptate solution in order to minimize radiation exposure to occupational workers, clinical personnel, and other persons (see *4.7 Instructions for Preparation and Use).*

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

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

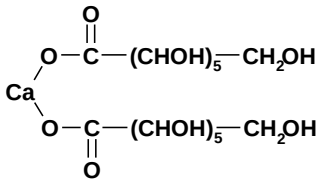
Drug Substance

Proper name: calcium gluceptate (or Calcium Glucoheptonate)

Chemical name: Calcium Gluceptate; Calcium (3R,4S,5R,6R)-2,3,4,5,6,7-hexahydroxyheptanoate

Molecular formula and molecular mass: $C_{14}H_{26}CaO_{16}$, 490.42 g/mol

Structural formula of calcium gluceptate:



Physicochemical properties: White to almost white powder. Free of visible contamination.

Product Characteristics

The kit consists of reaction vials which contain the sterile, non-pyrogenic, non-radioactive ingredients necessary to produce either Technetium (^{99m}Tc) Gluceptate Injection for diagnostic use in kidney and brain imaging or Stannous Gluceptate 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 of calcium gluceptate 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.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

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

The acute intravenous lethal dose (LD50) of Stannous Gluceptate 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 Gluceptate 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).

Carcinogenicity, Genotoxicity, and Reproductive and Developmental Toxicology

No long-term animal studies have been performed to evaluate carcinogenic or mutagenic potential or whether technetium (^{99m}Tc) gluceptate affects fertility in males or females.

As with other radiopharmaceuticals which distribute intracellularly, there may be increased risk of chromosome damage from Auger electrons if nuclear uptake occurs.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Draximage® Gluceptate (Kit for the Preparation of Technetium (^{99m}Tc) Gluceptate solution for injection and Stannous Gluceptate solution for injection)

Read this carefully before you start taking Draximage Gluceptate. 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 Draximage Gluceptate.

Serious Warnings and Precautions

- Technetium (^{99m}Tc) Gluceptate Injection should be used only by a healthcare professional who is experienced in the use of radiopharmaceuticals in or on humans.

What is Draximage Gluceptate used for?

Draximage® Gluceptate is a kit for prepration of a radioactive diagnostic product, Technetium (^{99m}Tc) Gluceptate Injection, that can be used for kidney and brain imaging.

Stannous Gluceptate Injection is used for diagnostic imaging of cardiac blood pool.

Both diagnostic products are administered by intravenous injection.

How does Draximage® Gluceptate work?

Technetium (^{99m}Tc) Gluceptate Injection

After injection, the product travels in the blood and binds to kidneys, which results in the ability to image the kidneys.

Brain imaging is achieved when the product accumlates intracranial lesions with increased blood flow or an altered blood-brain barrier.

Stannous Gluceptate Injection

After injection, stannous gluceptateis 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 Technetium (^{99m}Tc) Sodium Pertechnetate Injection.

What are the ingredients in Draximage® Gluceptate?

Medicinal Ingredients: 25 mg Calcium gluceptate

Non-medicinal ingredients: 3 mg Stannous chloride dihydrate, sodium hydroxide/hydrochloric acid.

Draximage® Gluceptate comes in the following dosage forms:

Lyophilized powder in a vial.

Do not use Draximage® Gluceptate if:

- you are allergic (hypersensitive) to any of its ingredients as mentioned above.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you receive Draximage® Gluceptate. Talk about any health conditions or problems you may have, including if you:

- are or think you might be pregnant;
- are breast feeding an infant;

Other warnings you should know about:

Drink plenty of fluids and go to the toilet as much as possible for up to 24 hours after receiving the product, to help reduce radiation exposure.

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

The following may interact with Draximage® Gluceptate:

Interactions with other drugs have not been established

How to take Draximage® Gluceptate:

Draximage® Gluceptate The radioactive product will be given to you by a healthcare professional who is experienced in the use of radiopharmaceuticals. It is administered by intravenous injection.

Usual dose:

Brain and Kidney Imaging

The recommended dose range for intravenous administration of Technetium (^{99m}Tc) Gluceptate 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)

Duration of the procedure

Your nuclear medicine doctor will inform you about the usual duration of the procedure.

Cardiac Blood Pool Imaging

A dose of 0.03 mL/kg (16 mcg Sn/kg) of body weight is injected intravenously 10 to 30 minutes before intravenous administration of 555 to 925 MBq (15 to 25 mCi) of Technetium (^{99m}Tc) Sodium Pertechnetate Injection. Your nuclear medicine doctor will calculate the required dose based on your body weight.

Overdose:

If you think you, or a person you are caring for, have received too much Draximage® Gluceptate, contact your healthcare professional, hospital emergency department or Canadian Nuclear Safety Commission immediately, even if there are no symptoms.

What are possible side effects from using Draximage® Gluceptate?

Possible side effects of Draximage Gluceptate include rare reactions of nausea, vomiting, erythema, allergic dermatitis (allergic skin reaction), rash, pruritus (itching), flushing and dyspnea (difficulty breathing) have been reported following the administration of Technetium (^{99m}Tc) Gluceptate Injection from post-market experience. Rare cases of hypersensitivity have also occurred.

These are not all the possible side effects of **Draximage® Gluceptate**. If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell 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/drug.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:

Before reconstitution, vials should be stored at or below room temperature (2°C to 30°C).

After reconsitiution, the finished preparation should be stored at 2 ºC to 8 ºC when not in use and discarded after 8 hours.

Do not use the kit beyond the expiry date stamped on the box.

Keep out of reach and sight of children.

If you want more information about Draximage® Kit for the Preparation of Technetium (^{99m}Tc) Gluceptate Injection:

- 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; the manufacturer's website https://www.jubilantradiopharma.com or by calling 1-888-633-5343 / 514-630-7080.

This leaflet was prepared by:

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