Kit for the preparation of Technetium Tc99 Gluceptate

R11/91

Diagnostic - for Intravenous Use

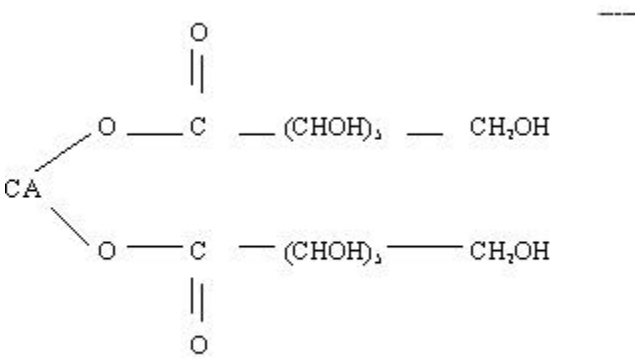
DESCRIPTION

The kit consists of reaction vials which contain the sterile non-pyrogenic, non-radioactive ingredients necessary to produce Technetium Tc 99m Gluceptate Injection (Technetium-99mTc D-glycero-D-gulo-heptonate complex) for diagnostic use by intravenous injection.

Each 10 mL reaction vial contains 50 mg of gluceptate calcium complexed with 0.7 mg (minimum) stannous chloride dihydrate (maximum total tin expressed as stannous chloride dihydrate 1.1 mg) in lyophilized form under an atmosphere of nitrogen. The pH is adjusted to 6.9 to 7.1 with HCl or NaOH prior to lyophilization. The addition of sodium pertechnetate Tc 99m sterile solution produces a rapid labeling which is essentially quantitative. 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.

The structural formula of gluceptate calcium is:



PHYSICAL CHARACTERISTICS

Technetium Tc 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	Mean %/Disintegration	Energy (keV)
Gamma-2	89.07	140.5

EXTERNAL RADIATION

The specific gamma ray constant for Tc 99m is 0.78 R/mCi-hr at 1 cm. The half value layer is 0.017 cm of lead. To facilitate control of the radiation exposure from millicurie amounts of this radionuclide, the use of 0.25 cm of lead with attenuate the radiation emitted by a factor of about 1,000. A range of values for the relative attenuation of the radiation resulting from the interposition of various thicknesses of lead is shown in Table 2.

Table 2 Radiation Attenuation by Lead Shielding

Shield Thickness (Pb) cm	Coefficient of Attenuation
0.017	0.5
0.08	10^{-1}
0.16	10^{-2}
0.25	10^{-3}
0.33	10^{-4}

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: Tc 99m, half-life 6.02 hours

Hours	Fraction Remaining	Hours	Fraction Remaining
0*	1.000	5	0.562
1	0.891	6	0.501
2	0.794	8	0.398
3	0.708	10	0.316
4	0.631	12	0.251

*Calibration Time

CLINICAL PHARMACOLOGY

When injected intravenously, Technetium Tc 99m Gluceptate is rapidly cleared from the blood. The blood clearance curve is triexponential 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 urinary excretion of the radiopharmaceutical are delayed.

Up to 15% of the injected dose is retained in the kidneys. The renal retention is greater in the cortex than in the medulla. The radiopharmaceutical may be bound to the proximal convoluted tubules, which are located primarily in the renal cortex.

Technetium Tc 99m Gluceptate tends to accumulate in intracranial lesions that are associated with excessive neovascularity or an altered blood-brain barrier. The drug does not accumulate in the choroid plexus or salivary glands.

INDICATIONS AND USAGE

Technetium Tc 99m Gluceptate may be used to image kidney and brain, and to assess renal and brain perfusion.

CONTRAINDICATIONS

None known at present.

PRECAUTIONS

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

The components of the kit are sterile and non-pyrogenic. It is essential to follow directions carefully and to adhere to strict aseptic procedures during preparation.

Contents of the reaction vial are intended only for use in the preparation of Technetium Tc 99m Gluceptate Injection and are NOT to be administered directly to the patient.

Radiopharmaceuticals should be used only by physicians who are qualified by training and experience 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.

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 clinical personnel.

The technetium Tc 99m labeling reactions involved depend on maintaining the stannous ion in the reduced state. Hence, sodium pertechnetate Tc 99m containing oxidants should not be employed.

To minimize the radiation dose to the bladder, the patient should be encouraged to increase his fluid intake, and to void when the examination 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 when imaging is restricted to the early period after injection should be borne in mind.

The preparation contains no bacteriostatic preservative. Technetium Tc 99m Gluceptate should be stored at 2^0C to 8^0C and discarded 6 hours after reconstitution. The solution should not be used if it is cloudy.

Carcinogenesis, Mutagenesis, Impairment of Fertility

No long term animal studies have been performed to evaluate carcinogenic or mutagenic potential or whether Technetium Tc 99m Gluceptate affects fertility in males or females.

Pregnancy Category C

Animal reproduction and teratogenicity studies have not been conducted with Technetium Tc 99m Gluceptate. It is also not know whether Technetium Tc 99m Gluceptate can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. There have been no studies in pregnant women. Technetium Tc 99m Gluceptate should be given to a pregnant woman only if clearly needed.

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.

Nursing Mothers

Technetium Tc 99m is excreted in human milk during lactation. Therefore, formula feedings should be substituted for breast feedings.

Pediatric Use

Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Allergic dermatologic manifestations have been reported infrequently.

DOSAGE AND ADMINISTRATION

The suggested dose range of intravenous administration in the average adult patient (70 kg), after reconstitution with oxidant-free sodium pertechnetate Tc 99m, is:

Renal imaging studies:
370 - 555 MBq (10-15 mCi)
Brain imaging studies:
555 - 740 MBq (15-20 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.

To minimize the radiation dose to the bladder, the patient should be encouraged to increase his fluid intake, and to void when the examination is completed and as often thereafter as possible for the next 4 to 6 hours.

The patient dose should be measured by a suitable radioactivity calibration system immediately prior to administration.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. The solution should not be used if it is cloudy.

Radiation Dosimetry

The estimated absorbed radiation doses[2] to an average adult patient (70 kg) from an intravenous injection of a maximum dose of 740 megabecquerels (20 millicuries) of Technetium Tc 99m Gluceptate are shown in Table 4.

Table 4 Radiation Doses

Tissue	Absorbed Radiation Dose	
	mGy/740 MBq	rads/20mCi
Total Body	2.0	0.2
Renal cornices	48.0	4.8
Kidneys	34.0	3.4
Liver	2.4	0.24
Bladder Wall		
2 hour void	24.0	2.4
4.8 hour void	56.0	5.6
Ovaries		
2 hour void	2.6	0.26
4.8 hour void	4.0	0.4
Testes		
2 hour void	1.6	0.16
4.8 hour void	2.6	0.26

HOW SUPPLIED

TechneScan® Gluceptate
Technetium Tc 99m gluceptate kit
Product No. 086

Available in kits containing 5 reaction vials, each vial containing in lyophilized form, sterile and non-pyrogenic:

Gluceptate Calcium	50 mg
Stannous Chloride Dihydrate (minimum)	0.7 mg
(maximum total tin expressed as stannous chloride dihydrate	1.1 mg)

The pH is adjusted to 6.9 to 7.1 with HCl or NaOH prior to lyophilization. The vials are sealed under an atmosphere of nitrogen.

Radioassay information tags with radiation warning symbol and a package insert are supplied in each carton.

STORAGE

Store kit at or below room temperature (2^0C to 30^0C). After labeling with Technetium Tc 99m, store solution at 2^0C to 8^0C and use within 6 hours.

DIRECTIONS FOR USE

NOTE: Use aseptic procedures throughout and take precautions to minimize radiation exposure by use of suitable shielding. Use waterproof gloves during the following preparation procedure.

To prepare Technetium Tc 99m Gluceptate:

1. Remove the protective disc from a reaction vial and swab the closure with either an alcohol swab or a suitable bacteriostatic agent.

2. Place the reaction vial in a suitable lead vial shield (minimum wall thickness 1/8 inch) which has a fitted lead cap. Obtain 2 to 10 mL of sterile, non-pyrogenic sodium pertechnetate Tc 99m, using a shielded syringe. The recommended maximum amount of Technetium Tc 99m to be added to a reaction vial is 11.1 gigabecquerels (300 mCi). Sodium pertechnetate Tc 99m solutions containing an oxidizing agent are not suitable for use.

3. Using a shielded syringe, add the sodium pertechnetate Tc 99m solution to the reaction vial aseptically.

4. Place the lead cap on the vial shield and agitate the shielded reaction vial until the contents are completely dissolved. To ensure maximum tagging, allow the preparation to stand for 15 minutes after mixing. Using proper shielding, the vial should be visually inspected to ensure that the solution is clear and free of particulate matter before proceeding.

5. Assay the product in a suitable calibrator, record the radioassay information on the tag with radiation warning symbol, and attach it to the reaction vial.

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

7. The finished preparation should be refrigerated at 2^0C to 8^0C when not in use and discarded after 6 hours. It should also be retained during its life in a lead vial shield with the lead cap in place.

This reagent kit is approved by the U.S. Nuclear Regulatory Commission for distribution to persons licensed to use byproduct material identified in ξ35.200 of 10 CFR Part 35, to persons who have a similar authorization issued by an Agreement State, and, outside the United States, to persons authorized by the appropriate authority.

[1] Kocher, David C., "Radioactive Decay Data Tables", DOE/TIC-11026, 108 (1981)

[2] Method of Calculation "S" , Absorbed Dose per Unit Cumulated Activity for Selected Radionuclides ad Organs, MIRD Pamphlet No. 11 (1975).

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