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Kit for the Preparation of
Technetium Tc 99m Pentetate Injection

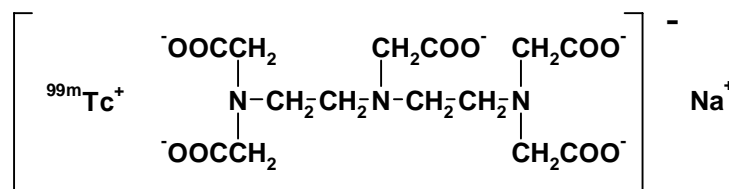
DIAGNOSTIC - For Intravenous Use

DESCRIPTION

Each kit consists of reaction vials which contain the sterile, non-pyrogenic, non-radioactive ingredients necessary to produce Technetium Tc 99m Pentetate Injection for diagnostic use by intravenous injection.

Each 10 mL reaction vial contains 20 mg of pentetic acid, 5 mg of p-aminobenzoic acid, 3.73 mg of calcium chloride dihydrate, and not less than 0.25 mg stannous chloride dihydrate and not more than 0.385 mg total tin expressed as stannous chloride dihydrate in lyophilized form under an atmosphere of nitrogen. The pH is adjusted with HCl or NaOH prior to lyophilization so that the pH range of the reconstituted radiopharmaceutical is 6.5 to 7.5. Addition of sterile, non-pyrogenic, and oxidant-free sodium pertechnetate Tc 99m solution produces a rapid labeling which is essentially quantitative and which remains stable *in vitro* throughout the 12 hour life of the preparation. No bacteriostatic preservative is present.

The structure of the technetium labeled form is:



Its chemical name is:

Technetate (1-)^{99m}Tc,[N,N-bis[2-[bis(carboxymethyl)amino]ethyl]-glycinato(5-)]-, sodium.

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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

<i>Radiation</i>	<i>Mean % / Disintegration</i>	<i>Energy (keV)</i>
Gamma-2	89.07	140.5

External Radiation

The specific gamma ray constant for Technetium-99m is 0.78 R/mCi-hr at 1 cm. The first 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 a 0.25 cm thickness of lead will 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

<i>Shield Thickness (Pb) cm</i>	<i>Coefficient of Attenuation</i>
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: Technetium-99m, Half Life 6.02 Hours

<i>Hours</i>	<i>Fraction Remaining</i>	<i>Hours</i>	<i>Fraction Remaining</i>
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

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

CLINICAL PHARMACOLOGY

Following its intravenous administration, technetium Tc 99m pentetate rapidly distributes itself throughout the extracellular fluid space from which it is promptly cleared from the body. The mechanism of excretion from the body is by glomerular filtration. There should be little or no binding of the chelate by the renal parenchyma. A variable percentage of the technetium Tc 99m pentetate binds to the serum proteins; this ranges from 3.7% following a single injection to approximately 10% if the material is continuously infused. Although the chelate gives useful information on the glomerular filtration rate, the variable percent which is protein bound leads to a measured clearance rate which is lower than that determined by inulin clearance.

The images of the kidneys obtained in the first few minutes after administration of technetium Tc 99m pentetate represent the vascular pool within the kidney. Subsequent images of the kidneys represent radioactivity which is in the urine of both the collection system and the renal pelvis.

Technetium Tc 99m pentetate tends to accumulate in intra-cranial lesions with excessive neovascularity or an altered blood-brain barrier. It does not accumulate in the choroid plexus.

INDICATIONS AND USAGE

Technetium Tc 99m Pentetate Injection may be used to perform kidney imaging, brain imaging, to assess renal perfusion, and to estimate glomerular filtration rate.

CONTRAINDICATIONS

Hypersensitivity to any component of this product.

WARNINGS

None.

PRECAUTIONS

General

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

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

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 develop fully, and the possibility of missing certain lesions when imaging is restricted to the early period after injection should be borne in mind.

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

The preparation contains no bacteriostatic preservative. Technetium Tc 99m Pentetate Injection should be stored at or below room temperature (2°C — 25°C) and discarded 12 hours after reconstitution. The solution should not be used if it is cloudy.

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 the sodium pertechnetate Tc 99m solution and the withdrawal of doses for patient administration.

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

Technetium Tc 99m Pentetate Injection as well as other radioactive drugs must be handled with care, and appropriate safety measures should be taken to minimize radiation exposure to the patients consistent with proper patient management, and to minimize radiation exposure to clinical personnel.

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.

Carcinogenesis, Mutagenesis, Impairment of Fertility

No long term animal studies have been performed to evaluate carcinogenic potential or whether Technetium Tc 99m Pentetate Injection affects fertility in males or females. Mutagenicity studies have not been conducted.

Pregnancy Category C

Animal reproduction and teratogenicity studies have not been conducted with Technetium Tc 99m Pentetate Injection. It is also not known whether Technetium Tc 99m Pentetate Injection 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 Pentetate Injection 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.

Paediatric Use

Safety and effectiveness in paediatric patients have not been established.

ADVERSE REACTIONS

Pyrogenic and allergic reactions to technetium Tc 99m pentetate preparations have been reported in the literature.

DOSAGE AND ADMINISTRATION

The recommended dose range for intravenous administration, after reconstitution with oxidant-free sodium pertechnetate Tc 99m, to be administered to the average patient (70 kg) is:

Kidney imaging and
glomerular filtration
rate estimation..... 111 to 185 MBq (3 to 5 mCi)

Brain imaging or
assessment of
renal perfusion..... 370 to 740 MBq (10 to 20 mCi)

To minimize the radiation dose to the bladder, the patient should be encouraged to increase 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.

Store finished preparation at 2°C to 25°C in a suitable lead shield.

Parenteral drug products should be inspected for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use if the solution contains particulate matter or is not a clear solution.

RADIATION DOSIMETRY

The estimated absorbed radiation doses² to various organs of an average patient (70 kg) from an intravenous injection of maximum doses of 185 MBq (5 mCi) and 740 MBq (20 mCi) of Technetium Tc 99m Pentetate Injection are shown in Table 4.

Table 4. Estimated Absorbed Radiation Doses

<i>Organs</i>	<i>Kidney Imaging or GFR estimation</i>		<i>Brain Imaging or Assessment of Renal Perfusion</i>	
	<i>mGy/ 185 MBq</i>	<i>rads/ 5 mCi</i>	<i>mGy/ 740 MBq</i>	<i>rads/ 20 mCi</i>
Kidney	4.5	0.45	18.0	1.8
Whole Body	0.3	0.03	1.2	0.12
Bladder Wall				
2.0 hr void	5.75	0.58	23.0	2.3
4.8 hr void	13.5	1.35	54.0	5.4
Testes				
2.0 hr void	0.38	0.04	1.5	0.15
4.8 hr void	0.53	0.05	2.1	0.21
Ovaries				
2.0 hr void	0.55	0.06	2.2	0.22
4.8 hr void	0.78	0.08	3.1	0.31

²Method of calculation: "S" Absorbed Dose per Unit Cumulated Activity for Selected Radionuclides and Organs, MIRDO Pamphlet No. 11 (1975).

HOW SUPPLIED

DRAXIMAGE™ DTPA

Product No. 0330-X60 or 0330-X61

Kit for the preparation of Technetium Tc 99m Pentetate Injection

Available in cartons containing 5 or 30 reaction vials, each reaction vial containing in lyophilized form, sterile and non-pyrogenic:

Pentetic Acid	20 mg
p-Aminobenzoic Acid	5 mg
Calcium Chloride Dihydrate	3.73 mg
Stannous Chloride Dihydrate (minimum)	0.25 mg
(Maximum tin as stannous chloride dihydrate)	0.385 mg)

The pH is adjusted with HCl or NaOH prior to lyophilization so that the pH of the reconstituted radiopharmaceutical is 6.5 to 7.5. The vials are sealed under an atmosphere of nitrogen.

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

STORAGE

Store the unreconstituted reaction vials at or below room temperature (2°C - 25°C). Store the reconstituted reaction vial at or below room temperature (2°C - 25°C) in a suitable lead shield and discard after 12 hours.

DIRECTIONS FOR PREPARATION

NOTE: Use aseptic procedures throughout and take precautions to minimize radiation exposure by use of suitable shielding. Waterproof gloves should be worn during the preparation 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.

To prepare Technetium Tc 99m Pentetate Injection:

1. Remove the protective disc from a reaction vial and swab the rubber septum with an alcohol swab.
2. Place the vial in a suitable lead vial shield which has a minimum wall thickness of 1/8 inch (3 mm) and 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 18.5 gigabecquerels (500 mCi). Sodium pertechnetate Tc 99m solutions containing an oxidizing agent are not suitable for use.
3. Using a shielded syringe, aseptically add the sodium pertechnetate Tc 99m solution to the reaction vial while avoiding the buildup of excessive pressure in the vial. Pressure buildup may be avoided by injecting several milliliters of pertechnetate solution into the reaction vial, then withdrawing several milliliters of nitrogen gas (present to prevent oxidation of the complex) into the syringe. Repeat the procedure as necessary until the entire amount of the pertechnetate solution is added and normal pressure is established within the vial.
4. Place the lead cap on the vial shield and agitate the shielded 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 reaction vial should be visually inspected to ensure that the solution is clear and free of particulate matter before proceeding; if it is not, the radiopharmaceutical should not be used.
5. Assay the product in a suitable calibrator, record the radioassay information on the label with radiation warning symbol, and apply it to the reaction vial.
6. Withdrawals for administration must be made aseptically using a sterile needle and syringe. Since the reaction vials contain nitrogen, the vials should not be vented. If repeated withdrawals are made from the vial, replacement of the contents with air should be minimized.
7. The finished preparation should be stored at or below room temperature (2°C — 25°C) when not in use and discarded after 12 hours. It should be retained during its life in a lead vial shield with the lead cap in place.

NOTE: It is recommended that with proper shielding and equipment, the final formulation be tested for radiochemical purity (percent technetium Tc 99m binding), and each patient dose be visually inspected for foreign matter. If the radiochemical purity is not adequate or foreign matter is observed in the patient dose, it is recommended that the patient dose be discarded.

This reagent kit is approved by the U.S. Nuclear Regulatory Commission for distribution to persons licensed to use byproduct material identified in §35.200 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.

The use of p-aminobenzoic acid in this radiopharmaceutical is licensed under Canadian Patent No. 1,190,473 and foreign counterparts.

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