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 Pentetate Injection are shown in Table 4.

Table 4. Estimated Absorbed Radiation Doses and Effective Dose Equivalent Technetium Tc 99m Pentetate

Target Organ	mGy/740 MBq	rads/20 mCi
Kidneys	4.3	0.4
Urinary Bladder Wall	53.3	5.4
Testes	2.8	0.3
Ovaries	4.1	0.4
Effective Dose Equivalent	**5.9 mSv**	**0.6 rem**

Doses calculated using the model in MIRD Dose Estimate Report No. 12 (Journal Nuclear Medicine 24:503–505, 1984)

Radiation Doses to Hospital Personnel

The typical total body exposure to a person administering a maximum dose of 740 megabecquerels (20 mCi) of Technetium Tc 99m to a patient is about 0.02 mR.[3]

[3]Barrall RC, Smith SI: Personnel radiation exposure and protection from 99m Tc radiations. In **Biophysical Aspects of the Medical Use of Technetium 99m,** Kereiakes JG, Corey KR, eds, American Association of Physicists in Medicine, Monograph No 1, 1976, p77

HOW SUPPLIED

The AN-DTPA® Kit for the Preparation of Technetium Tc 99m Pentetate Injection is supplied as a set of either 5 or 30 sterile, non-pyrogenic and capped 10mL vials. Each nitrogen-flushed vial contains in lyophilized form 20.6 mg pentetate calcium trisodium, 0.15 mg minimum stannous tin as stannous chloride dihydrate and 0.30 mg maximum total tin as stannous chloride dihydrate. The pH is adjusted to 3.9-4.1 with NaOH and/or HCl prior to lyophilization. Included in each 5-vial kit are one package insert and 10 radiation labels. Included in each 30-vial kit are one package insert and 60 radiation labels. Store the kit as packaged at 15-30° C.

Directions for Use

Technetium Tc 99m Pentetate Injection is prepared from AN-DTPA® by the following aseptic procedure:

1. Waterproof gloves should be worn during the preparation procedure. Remove the flip-off plastic cap from the AN-DTPA® vial and swab the top of the vial closure with alcohol to sterilize the surface.
2. Complete the radiation label and affix to the vial. Place the vial in an appropriate lead-capped radiation shield labeled and identified.
3. With a sterile shielded syringe, aseptically obtain 1-8 mL of a suitable, oxidant-free, sterile and non-pyrogenic Sodium Pertechnetate Tc 99m Injection containing from 0.11-5.92 gigabecquerels (3-160 millicuries). Aseptically add the Sodium Pertechnetate Tc 99m Injection to the vial.
4. Swirl the contents of the vial for about one minute, or until the contents are completely dissolved, and let stand for 1-2 minutes.
5. Record time and date of preparation.
6. The radiochemical purity of the prepared radiopharmaceutical should be checked prior to patient administration.
7. Visually examine the vial contents to ascertain that it is free of particulates and discoloration prior to injection.
8. Withdrawals for administration must be made aseptically using a sterile shielded syringe. Since the vials contain nitrogen to prevent oxidation of the complex, the vials should not be vented. If repeated withdrawals are made from a vial, the replacement of contents with air should be minimized.
9. The finished preparation should be discarded after six (6) hours, or, if used solely for the estimation of glomerular filtration rate, after one (1) hour. Store the reconstituted vial at 15-30° C.
10. The patient dose should be measured by a suitable radioactivity calibration system immediately prior to administration.

NDC # 45567-0010-1 for 5 vial kits

NDC # 45567-0010-2 for 30 vial kits

This reagent kit for preparation of a radiopharmaceutical is approved for use by persons licensed pursuant to Section 120.533, Code of Massachusetts Regulation 105, or under equivalent license of the U.S. Nuclear Regulatory Commission of an Agreement State.

Manufactured by
CIS-US, INC.
5 DeAngelo Drive
Bedford, MA 01730

Jun 2003
RM 2A-001

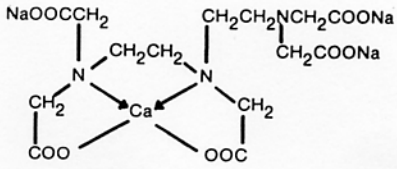
AN-DTPA®
Kit for the Preparation of Technetium Tc 99m Pentetate Injection Diagnostic For Intravenous Use

DESCRIPTION

AN-DTPA® Kit for the Preparation of Technetium Tc 99m Pentetate Injection is a multidose reaction vial which contains 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 20.6 mg pentetate calcium trisodium, 0.15 mg minimum stannous tin as stannous chloride dihydrate and 0.30 mg maximum total tin as stannous chloride dihydrate in lyophilized form and sealed under nitrogen. The pH is adjusted to 3.9-4.1 with sodium hydroxide and/or hydrochloric acid prior to lyophilization. No bacteriostatic preservative is present.

The active agent is a Technetium Tc 99m complex of pentetate calcium trisodium. The chemical names and structure for pentetate calcium trisodium are: (1) Calciate (3-), [N,N-bis[2-[bis(carboxymethyl)amino]ethyl]glycinato(5-)]-,trisodium;(2)Trisodium [N,N-bis[2-[bis(carboxymethyl)amino]ethyl]glycinato(5-)]-calciate(3-).



When a solution of sterile, non-pyrogenic, oxidant-free isotonic Sodium Pertechnetate Tc 99m Injection is added to the vial, Technetium Tc 99m Pentetate Injection is formed. The product so derived is intended for intravenous injection within 6 hours of the time of reconstitution. The precise structure of Technetium Tc 99m Pentetate Injection is not known at this time.

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 Percent Per Disintegration	Mean Energy (keV)
Gamma-2	89.07	140.5

[1]Kocher DC: Radioactive decay data tables. ***DOE/TIC-11026:*** 108, 1981

External Radiation

The specific gamma ray constant for Tc 99m is 0.78 R/millicurie-hr at 1 cm. The first half-value layer is 0.017 cm of lead (Pb). A range of values for the relative attenuation of the radiation emitted by this radionuclide that results from interposition of various thicknesses of Pb is shown in Table 2. For example, the use of a 0.25 cm thickness of Pb will attenuate the radiation emitted by a factor of about 1,000.

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	7	0.447
1	0.891	8	0.398
2	0.794	9	0.355
3	0.708	10	0.316
4	0.631	11	0.282
5	0.562	12	0.251
6	0.501		

*Calibration time

CLINICAL PHARMACOLOGY

Following its intravenous administration, Technetium Tc 99m Pentetate Injection rapidly distributes itself throughout the extracellular fluid space from which it is promptly cleared from the body 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 Injection represent the vascular pool within the kidney. Subsequent images of the kidneys represent radioactivity which is in the urine of both the collecting system and the renal pelvis.

Technetium Tc 99m Pentetate Injection tends to accumulate in intracranial 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

None known.

WARNINGS

None.

PRECAUTIONS

General

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 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 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.

The Technetium Tc 99m labeling reactions involved in preparing the agent depend on maintaining the stannous ion in the reduced state. Hence, Sodium Pertechnetate Tc 99m Injection containing oxidants should not be employed.

To minimize radiation dose to the bladder, the patients should be encouraged to drink fluids and to void immediately after the examination and as often thereafter as possible for the next 4-6 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 develop fully, and the possibility of missing certain lesions when imaging is restricted to the early period after injection should be borne in mind.

Technetium Tc 99m Pentetate Injection should be formulated within six (6) hours prior to clinical use for brain and kidney imaging, and for assessing renal perfusion. For estimating glomerular filtration rates, Technetium Tc 99m Pentetate Injection should be used within one (1) hour after formulation. The preparation contains no bacteriostatic preservative and should be stored at 15-30° C.

High background counts, poor images and erroneous clearance results have been observed with use of kits exceeding expiration time, owing to inadequate labeling.

AN-DTPA® contains no preservative.

Vials are sealed under nitrogen: air or oxygen is harmful to the contents of the vials and the vials should not be vented.

The components of the AN-DTPA® are supplied sterile and non-pyrogenic. Aseptic procedures normally employed in making additions and withdrawals for sterile, non-pyrogenic containers should be used during addition of the pertechnetate solution and the withdrawal of doses for patient administration.

No special handling is required for the non-radioactive drug product.

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.

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

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 and females. Mutagenesis 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 feeding should be substituted for breast feeding.

GERIATRIC USE

Clinical studies of AN-DTPA® did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

Pyrogenic and allergic reactions to Technetium Tc 99m Pentetate Injection preparations have been reported in the literature.

DOSAGE AND ADMINISTRATION

Shielding should be utilized when preparing Technetium Tc 99m Pentetate Injection.

The suggested dose range of Technetium Tc 99m Pentetate Injection for intravenous administration, after reconstitution with oxidant-free Sodium Pertechnetate Tc 99m Injection to be administered to the average adult patient (70 kg) is:

Kidney imaging and glomerular filtration rate estimation	111 - 185 megabecquerels (3-5 mCi)
Brain imaging or assessment of renal perfusion	370 - 740 megabecquerels (10-20 mCi)

Safety and effectiveness have not been established for doses of the drug containing more than 25 mg of pentetate calcium trisodium and 0.275 mg stannous chloride complexed with 740 megbequerels (20 millicuries) of Technetium Tc 99m.

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 whenever solution and container permit. The solution should not be used if cloudy, discolored, or found to contain particulate matter.