



**BRACCO DIAGNOSTICS™**

**Multi-Dose**

**TECHNEPLEX®**

**Kit for the Preparation of Technetium Tc 99m Pentetate Injection**

**DIAGNOSTIC-FOR INTRAVENOUS USE**

### **DESCRIPTION**

Each kit contains sterile, pyrogen-free, non-radioactive ingredients necessary to produce technetium Tc 99m pentetate injection for diagnostic use by intravenous injection.

Each 10 mL reaction vial contains, in lyophilized form and under nitrogen atmosphere, 5 mg of pentetate pentasodium, and 0.17 mg (minimum) stannous chloride (maximum stannous and stannic chloride 0.275 mg). The pH is adjusted to 4.0 to 7.5 with hydrochloric acid and sodium hydroxide prior to lyophilization. The addition of sterile, pyrogen-free and oxidant-free sodium pertechnetate Tc 99m injection produces technetium Tc 99m pentetate injection, which contains no bacteriostatic preservative.

The chemical names for Technetium Tc 99m Pentetate Injection are: 1. Technetate (1-)<sup>99m</sup>Tc,[N,N-bis{2-(carboxy-methyl)amino}ethyl]glycinato(5-)-, sodium; and 2. Sodium [N,N-bis[2-[bis(carboxymethyl)amino]ethyl] glycinato(5-)]-technetate(1-)-<sup>99m</sup>Tc.

### **PHYSICAL CHARACTERISTICS**

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

**TABLE 1.**

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

<sup>1</sup>Kocher, David C., 'Radioactive Decay Data Tables', DOE/TIC-11026, 108, 1981

### External Radiation

The specific gamma ray constant for Technetium Tc 99m is 0.78 R/hr-mCi at 1 cm. The first half-value layer is 0.017 cm of Pb. A range of values for the relative attenuation of the radiation emitted by this radionuclide that results from the 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 <sup>-1</sup>
0.16	10 <sup>-2</sup>
0.25	10 <sup>-3</sup>
0.33	10 <sup>-*</sup>

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

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 Injection binds to serum proteins; this ranges from 3.7% following the 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 glomerular filtration rate which is lower than the glomerular filtration rate as determined by inulin clearances.

Since Technetium Tc 99m Pentetate Injection is excreted by glomerular filtration, the images of the kidneys obtained in the first few minutes after 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. The chelate 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 contents of this kit are not radioactive. However, after Sodium Pertechnetate Tc 99m Injection is added, adequate shielding of the final preparation must be maintained.

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

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

Literature reports indicate that the target to nontarget 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 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 4-6 hours.

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 optimal results, this time should be minimized. Intervals longer than one hour should be the exception.

Technetium Tc 99m Pentetate Injection for use in estimating glomerular filtration rate should be formulated within one (1) hour prior to clinical use.

The components of the kit are supplied sterile and pyrogen-free. Aseptic procedures normally employed in making additions and withdrawals from sterile, pyrogen-free containers should be used during the addition of the pertechnetate 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 may thus adversely affect the quality of the radiopharmaceutical. Hence, sodium pertechnetate Tc 99m 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 used to minimize external radiation exposure to clinical personnel. Also, care should be taken to minimize radiation exposure to patients consistent with proper patient management.

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.

High background counts, poor images and erroneous clearance results have been observed with use of kits exceeding expiration time, owing to inadequate labeling. The vials should not be used after the expiration date shown on the label.

### **Carcinogenesis, Mutagenesis, Impairment of Fertility**

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

### **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 reproduction 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, in 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**

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

### **DOSAGE AND ADMINISTRATION**

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

Kidney imaging and glomerular filtration rate estimation:

111 MBq to 185 MBq (3 to 5 mCi).

Brain imaging or assessment of renal perfusion:

370 MBq to 740 MBq (10 to 20 mCi).

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

Parenteral drug products should be inspected for particulate matter and discoloration prior to administration, whenever solution and container permit.

### **RADIATION DOSIMETRY**

The estimated absorbed radiation doses<sup>2</sup> to an average 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.**

Organ	Absorbed Radiation Doses <sup>2</sup>	
	mGy/740 MBq	rads/20 mCi
Kidneys	18.0	1.8
Whole body	1.2	0.12
Bladder Wall		
2-hr. void	23.0	2.3
4.8-hr. void	54.0	5.4
Testes		
2-hr. void	1.5	0.15
4.8-hr. void	2.1	0.21
Ovaries		
2-hr. void	2.2	0.22
4.8-hr. void	3.1	0.31

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

The typical total exposure to a person administering a maximum dose of 740 MBq (20mCi) of Technetium Tc 99m to a patient is about 0.20u,Sv (0.02 mrem).<sup>3</sup>

<sup>3</sup>Barrall RC, Smith SI: Personnel radiation exposure and protection from 99m Tc radiations.

In: Kereiakes, JG, Corey KR, Eds., "Biophysical Aspects of the Medical Use of Technetium 99m. Amer Assoc of Phys in Med Monograph 1:77, 1976.

## HOW SUPPLIED

### Kit Contents

10 STERILE REACTION VIALS each 10 mL vial containing, in lyophilized form and under nitrogen atmosphere, 5 mg of pentetate pentasodium, and 0.17 mg (minimum) stannous chloride (maximum stannous and stannic chloride 0.275 mg). Hydrochloric acid and sodium hydroxide have been added for pH adjustment prior to lyophilization.

10 PRESSURE-SENSITIVE LABELS for final preparation of technetium Tc 99m pentetate injection.

1 PACKAGE INSERT

NDC 0270-3877-00

### Storage

Store kit contents and final preparation at room temperature.

### Preparation

The following instructions must be carefully followed for optimum preparation of Technetium Tc 99m Pentetate Injection.

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

1. Remove the central metal disc from the reaction vial and aseptically swab the top of the vial closure with alcohol.
2. Place the vial in a properly labeled and identified radiation shield. With an appropriately shielded syringe, aseptically obtain 2-8 mL of sterile, pyrogen-free sodium pertechnetate Tc 99m injection. Sodium pertechnetate Tc 99m solutions containing an oxidizing agent are not suitable for use.
3. Aseptically add the Sodium Pertechnetate Tc 99m Injection to the vial.
4. Swirl the contents of the vial for one minute and let stand 1-2 minutes. 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 pressure-sensitive label and affix it to the vial.
6. Withdrawals for administration should be made aseptically using a shielded, 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 from a vial, the replacement of contents with air should be minimized.
7. Do not use more than one (1) hour after preparation for use in estimating glomerular filtration rate.
8. Do not use more than six (6) hours after preparation for imaging and assessing renal perfusion.

Note: It is recommended that with proper shielding and equipment, the final formulation be tested for radio-chemical purity. If radiochemical purity is not adequate, discard the finished drug.

### Disposal

The residual materials may be discarded in ordinary trash provided the vials and syringes read no greater than background with an appropriate low-range survey meter. All identifying labels should be destroyed before discarding.

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.

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