TECHNETIUM Tc 99m TSC Kit for the Preparation of Technetium Tc 99m Sulfur Colloid

Diagnostic For Intravenous And Oral Use

DESCRIPTION: Technetium Tc 99m TSC Kit for the Preparation of Technetium Tc 99m Sulfur Colloid is a multidose reaclton vial with a Syringe A and a Syringe B which contain the sterile, non-pyrogenic, non-radioactive ingredients necessary to produce Technetium Tc 99m Sulfur Colloid Injection for diagnosis use by intravenous injection or oral administration.

Each 10 mL multidose reaction vial contains, in lyophilized form 2.0 mg sodium thiosulfate anhydrous, 2.3 mg edetate disodium and 18.1 mg gelatin; a Syringe A with 1.5 mL of 0.148 N hydrochloric acid solution and a Syringe B with 1.5 mL aqueous solution of 38.8 mg sodium biphosphate anhydrous and 11.1 mg sodium hydroxide.

When a solution of sterile and non-pyrogenic Sodium Pertechnetate Tc 99m Injection in isotonic saline is mixed with these components, following the instructions provided with the kit**,** Technetium Tc 99m SulfurColloid Injection is formed. The product so derived is intended for intravenous injection or oral administration. The precise structure of Technetium Tc 99m Sulfur Colloid 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. Principal Radiation Emission Data

Radiation	Mean % 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 0.78R/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. Pnysical Decay Chart: Tc 99m, half-life 6.02 hours

Hours	Fraction Remaining	Hours	Fraction Remaining
O*	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	0.563	12	0.251
6	0.501		

*Calibration time

CLINICAL PHARMACOLOGY: Following intravenous administration, Technetium Tc 99m Sulfur Colloid Injection is rapidly cleared by the reticuloendothelial system from the blood with a nominal clearance half-life of approximately 2 1/2 minutes. Uptake of the radioactive colloid by organs of the reticuloendothelial system is dependent upon both their relative blood flow rates and the functional capacity of the phagocytic cells**.** In the average patient 80 to 90% of the injected colloidal particles are phagocytized by the Kupffer celts of the liver, 5 to 10% by the spleen and the balance by the bone marrow.

Following administration of Technetium Tc 99m Sulfur Colloid by intraperitoneal injection, the radiopharmaceutical mixes with the peritoneal fluid. Clearance from the peritoneal cavity varies from insignificant, which may occur with complete shunt blockage, to very rapid clearance with subsequent transfer into the systemic circulation when the shunt is patent.

Serial images should be obtained of both the shunt and liver (target organ). However, an adequate evaluation of the difference between total blockage of the shunt and partial blockage may not be feasible in all cases.

INDICATIONS AND USAGE: Technetium Tc 99m Sulfur Colloid Injection is used in adults and children as an agent for imaging areas of functioning reticuloendothelial cells in the liver, spleen and bone marrow.

It is used orally in adults and children for esophageal transit studies, gastroesophageal reflux scintigraphy, and for the detection of pulmonary aspiration of gastric contents.

Technetium Tc 99m Sulfur Colloid may be used in adults as an imaging agent to aid in the evaluation of peritoneo-venous (LeVeen) shunt patency.

CONTRAINDICATIONS: None known.

WARNINGS: Although rare, deaths have occurred following intravenously administered gelatin stabilized Technetium Tc 99m Sulfur Colloid. Advanced cardiopulmonary life support systems should be readily available where and when the drug is administered.

PRECAUTIONS:

General

The contents of the two syringes, one syringe containing the appropriate acidic solution and the second syringe containing the appropriate buffer solution, are intended only for use in the preparation of the Technetium Tc 99m Sulfur Colloid Injection and are NOT to be directly administered to the patient.

Sodium Pertechnetate Tc 99m Injection containing oxidants should not be used to reconstitute this kit.

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

The contents of the kit are sterile and non-pyrogenic. It is essential to follow the directions carefully and to adhere strictly to aseptic procedures during preparation. This preparation contains no bacteriostatic preservative.

The stability of the colloidal preparation may be decreased in the presence of polyvalent cations, thus resulting in the agglomeration of the individual colloidal particles. These larger particles are likely to be trapped by the pulmonary capillary bed following intravenous injection.

Sodium Pertechnetate Tc 99m Injection containing more than 10 micrograms per milliliter of aluminum ion should not be used to formulate the Technetium Tc 99m Sulfur Colloid Injection.

Technetium Tc 99m Sulfur Colloid Injection is physically unstable, and the particles will settle with time. Failure to agitate the vial adequately before use may result in non-uniform distribution of radioactivity. Because of the increasing probability of agglomeration with aging, it is recommended that a vial of the prepared finished drug should not be used more than six hours from the time of formulation.

The components of Technetium Tc 99m TSC 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.

As in the use of any other radioactive material, care should be taken to minimize radiation exposure to patient 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 Sulfur Colloid Injection affects fertility in males or females. Mutagenesis studies have not been conducted.

Pregnancy Category C

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

ADVERSE REACTIONS: The following adverse reactions have been reported associated with the use of Technetium Tc 99m Sulfur Colloid Injection: cardiopulmonary arrest, seizures, anaphylactic shock, hypotension, dyspnea, abdominal pain, fever, chills, broncho-spasm, nausea, vomiting, perspiration, redness, urticaria, numbness, dizziness and burning at the injection site.

Several deaths and cases of lung and soft tissue uptake other than RES have been reported in association with the use of Technetium Tc 99m Sulfur Colloid Injection (see WARNINGS**).**

The size and physical-chemical properties of the sulfurcolloid particles formed from the components of the kit may determine the biodistribution of the colloid and its uptake by the RE system. Diseases affecting the RE system may also alter the expected uptake pattern.

DOSAGE AND ADMINISTRATION: Shielding should be utilized when preparing Technetium Tc 99m Sulfur Colloid Injection.

Liver-Spleen Scanning and Bone Marrow Imaging:

In average ADULT (70 kg) patients:

The suggested dose range used for liver/spleen images is 37 to 296 megabecquerels (1 to 8 millicuries) and for bone marrow images is 111 to 444 megabecquerels (3 to 12 millicuries) of Technetium Tc 99m Sulfur Colloid Injection.

In PEDIATRIC patients:

The suggested intravenous doses employed for various diagnostic indications are as follows:

Liver/spleen imaging: The dose range is 0.56 to 2.78 megabecquerels (15 to 75 microcuries) per kilogram of body weight with a usual dose of 1.85 megabecquerels (50 microcuries) per kg body weight, except in newborn in whom the administered dose should be 7.4 to 18.5 megabecquerels (200 to 500 microcuries). A minimum dose of 7.4 megabecquerels (200 microcuries) should be employed for this procedure.

Bone marrow imaging: The dose range is 1.11 to 5.55 megabecquerels (30 to 150 microcuries) per kilogram of body weight. A minimum dose of 22.2 megabecquerels (600 microcuries) is suggested for this procedure. (See Table 5).

Gastroesophageal and Pulmonary Aspiration:

In the average ADULT (70 kg) patients:

The suggested oral dose range is 5.55-11.1 megabecquerels (150-300 microcuries) for gastroesophageal studies. The suggested oral dose range for pulmonary aspiration studies is 11.I-18.5 megabecquerels (300-500 microcuries).

In PEDIATR1C patients:

The suggested oral dose range in infants and children is 3.7-11.1 megabecquerels (100-300 microcuries) for gastro esophageal and pulmonary aspiration studies.

The drug should be incorporated into a milk feeding when administered orally. Equally good results may be obtained by intubating the stomach and directly instilling the material into the stomach, followed by a dextrose or milk meal. This latter method avoids the introduction of radiation into the esophagus, thus, any tracer appearing there must be due to reflux.

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.
Peritoneo-venous (LeVeen) Shunt Patency Evaluation:

The suggested intraperitoneal dosage range used in the average patient (70 kg) for peritoneo-venous (LeVeen) shunt patency evaluation is 37 to 111 megabecquerels (1 to 3 millicunes). Adequate measures should be taken to assure uniform mixing with peritoneal fluid. Serial images of both the shunt and target organ should be obtained and correlated with other clinical findings. Alternately, the drug may be administered by percutaneous transtubal injection. The suggested percutaneous transtubal (efferent limb) dosage range for the average patient (70 kg) is 12 to 37 megabecquerels (0.3 to 1 0 millicurie) in a volume not to exceed 0.5 mL.

Transperitoneal absorption of Sulfur Colloid may occur, but it occurs slowly. Therefore, the most definitive scintigraphic evaluation of shunt patency will be obtained if there is visualization of both the shunt itself and the liver and/or spleen within the first three hours post intraperitoneal injection.

RADIATION DOSIMETRY: The estimated absorbed radiation doses[2] to an average ADULT patient (70 kg) from an intravenous injection of a maximum dose of 296 megabecquerels (8 millicuries) of Technetium Tc 99m Sulfur Colloid Injection are shown in Table 4.

Table 4. Estimated ADULT Absorbed Radiation Dose
Technetium 99m, mGy/296 MBq (rads/8 mCi) Intravenous Dose

Diffuse Parenchymal Disease

Target Organ	Normal Liver	Early Intermediate	Intermediate Advanced
Liver	27	17	13
	(2.7)	(1.7)	(1.3)
Spleen	17	22	34
	(1.7)	(2.2)	(3.4)
Bone Marrow	2.2	3.6	6.3
	(0.22)	(0.36)	(0.63)
Testes	0.088	0.17	0.26
	(0.0088)	(0.017)	(0.026)
Ovanes	0.45	0.65	0.96
	(0.045)	(0.065)	(0.096)
Total Body	1.5	1.5	1.4
	(0.15)	(0.15)	(0.14)

[2]Modified from Summary of Current Radiation Dose Estimates to Humans with Various Liver Conditions from 99m Tc-Sulfur Colloid, MIRD Dose Estimate Report No. 3, *J Nucl Med* 16:108A-108B, 1975

PEDIATRIC RADIATION DOSES: In PEDIATRIC patients, the radiation absorbed doses, using the maximum recommended doses for liver/ spleen imaging [2.78 megabecquerels (75 microcuries) per kilogram of body weight] and for bone marrow imaging [5.55 megabecquerels (150 microcuries) per kilogram of body weight}, except in the newborn where the doses used for calculating the radiation absorbed dose estimates are 18.5 megabecquerels (500 microcuries) for liver/spleen imaging and 22.2 megabecquerels (600 microcuries) for bone marrow imaging, are shown in Table 5.

Table 5. Estimated PEDIATRIC Absorbed Radiation Dose Technetium Tc 99m Sulfur Colloid Intravenous Injection

Age	**Newborn**		**1 year**		**5 years**		**10 years**		**18 years**	
Weight (kg)	3.5		12.1		20.3		33.5		55.0	
Maximum Recommended Dose										
megabecquerels	18.5a	22.2b	33.3a	67.3b	55.5a	114.7b	92.5a	186.1b	151.7a	307.1b
(millicuries)	(0.5)a	(0.6)b	(0.9)a	(1.82)b	(1.5)a	(3.1)b	(2.5)a	(5.03)b	(4.1)a	(83)b
Absorbed Dose mGy/max dose (rads/max dose)										
Total Body	0.6	0.71	0.86	1.73	0.99	2.09	1.07	2.16	0.9	1.83
	(0.06)a	(0.071)	(0.086)	(0.173)	(0.099)	(0.209)	(0.107)	(0.216)	(0.09)	(0.183)
Uver	16	19	12.6	25.5	12.3	25.4	16.7	33.2	20.1	40.7
	(1.6)	(1.9)	(1.26)	(2.55)	(1.23)	(2.54)	(1.67)	(3.32)	(2.01)	(4.07)
Spleen	14	17	10.8	21.8	9.75	20.2	12.2	24.7	13.5	27.4
	(1.4)	(1.7)	(1.08)	(2.18)	(0.975)	(2.02)	(1.22)	(2.47)	(1.35)	(2.74)
Red Marrow	2.9	3.5	1.62	32.8	1.65	34.1	2.03	4.07	1.48	2.99
	(0.29)	(0.35)	(0.162)	(3.28)	(0.165)	(3.41)	(0.203)	(0.407)	(0.148)	(0.299)
Ovaries	0.7	0.81	0.58	1.17	0.57	1.08	0.4	0.81	0.34	0.69
	(0.07)	(0.081)	(0.058)	(0.1l7)	(0.057)	(0.108)	(0.04)	(0.081)	(0.034)	(0.069)
Testes	0.2	0.71	0.19	0.38	0.2	0.4	0.35	0.70	0.09	0.18
	(0.02)	(0.071)	(0.019)	(0.038)	(0.02)	(0.04)	(0.035)	(0.070)	(0.009)	(0.018)

a. Liver/Spleen Imaging Dose (See DOSAGE AND ADMINISTRATION)
b. Bone Marrow Imaging Dose (See DOSAGE AND ADMINISTRATION)

Assumptions: (from Table 5)

1. Used the biologic data of MIRD Dose Estimate Report No. 3*, J Nucl Med* 16: 108A **-** 108B**,** 1975
2. Used the Age-dependent "S" values of Henrichs et al, Berlin, 1980**,** except for the 1-year old. The 1-year old "S" values were taken from preliminary phantom work of the Metabolism and Dosimetry Group at ORNL**.**

Table 6. Adult Radiation Dose from Oral Administration of 18.5 MBq (500 µCi) of Technetium Tc 99m Sulfur Colloid in mGy (mrad)

Target Organ	**Assumed Residence Time (hr.)**	**Absorbed Dose (mGy/18.5 MBq)**	**(mrad/500 µCi)**
Total Body	-	0.09	9
Stomach Wall	1.5	0.70	70
Small Intestine	4	1.3	130
Upper Large Intestine Wall	13	2.4	240
Lower Large Intestine Wall	24	1.65	165
Ovaries	-	0.48	48
Testes	-	0.025	2.5

Table 6. (Continued) RADIATION DOSES TO HOSPITAL PERSONNEL

Technician	Preparation Of Drug*	Administered Drug
Target	µSv/7.4 GBq (millirem/400 mCi)	µSv/148 MBq (millirem/8 mCi)
Extremity Dose	230 (23)	20 (2)
Whole Body Dose	10 (1)	1 (0.1)

*Using shielded vial and syringe.

Table 7. Adult Radiation Dose from Intraperitoneal Administration of 111 MBq (3 mCi) of Technetium Tc 99m Sulfur Colloid in mGy (rad)

Target Organ	**Shunt Patency (Open)**		**Shunt Patency (Closed)**	
	mGy	**rads**	**mGy**	**rads**
Liver	10.2	1.02	1.68	0.168
Ovaries & Testes	0.036 to 0.18	0.0036 to 0.018	1.68	0.168
Organs in the Peritoneal Cavity	--	--	1.68	0.168
Total Body	0.54	0.054	0.57	0.057

Assumptions:
Calculations for the absorbed radiation dose are based upon an effective half-time of 3 hours for the open shunt and 6.02 hours for the closed shunt and an even distribution of the radiopharmaceutical in the peritoneal cavity with no biological clearance.

HOW SUPPLIED: TSC is supplied as a 5-kit package. Five complete and separate kits are included in each package. All components of each kit are sterile and non-pyrogenic. Each kit consists of a 10 mL multidose reaction vial containing, in lyophilized form, 2.0 mg sodium thiosulfate anhydrous, 2.3 mg edetate disodium and 18.1 mg gelatin; a Syringe A with1.5 mL 0.148 N hydrochloric acid solution and a Syringe B with 1.5 mL aqueous solution of 38.8 mg sodium biphosphate anhydrous and 11.1 mg sodium hydroxide. Included in each kit are one string label and two sterile needles. Included in each 5 kit package are one package insert and 10 radiation labels. Store the kit as packaged at 15-30°C.

Directions for Use
TechnetiumTc 99m Sulfur Colloid Injection is prepared from TSC by the following aseptic procedure:

1. Waterproof gloves should be worn during the preparation procedure. Remove the dark brown flip-off plastic cap from the TSC 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. With a sterile shielded syringe, aseptically obtain 1-3 mL of a suitable, oxidant-free, sterile and non-pyrogenic Sodium Pertechnetate Tc 99m Injection, each milliliter containing a maximum activity of 18.5 gigabecquerels (500 millicuries). Do not use Sodium Pertechnetate Tc 99m Injection if it contains foreign matter or more than 10 micrograms/mL of aluminum (Sodium Pertechnetate Tc 99m Injection containing more than a total of 10 micrograms/mL of aluminum may produce a flocculent precipitate and since such a precipitate may localize in the lung, preparations containing precipitates should not be used).
3. Aseptically add the Sodium Pertechnetate Tc 99m Injection to the vial.
4. Place a lead cover on the vial shield and dissolve the reagent by gentle swirling.
5. Attach a sterile needle to a Syringe A and aseptically inject its entire contents into the reaction vial and swirl again.
6. Transfer the reaction vial from vial shield and place in a vigorously boiling water bath (water bath should be shielded with 1/8" to 1/4" lead) deep enough to cover the entire liquid contents of the vial. Keep the vial in the water bath for five minutes.
7. Remove the reaction vial from the water bath and place in the lead shield and allow to cool for three minutes. Swab the via! closure again with an antiseptic.
8. Attach a sterile needle to Syringe B and aseptically inject the entire contents into the reaction vial and swirl again.
9. Record time and date of preparation.
10. The radiochemical purity of the prepared radiopharmaceutical should be checked prior to patient administration.
11. Allow the preparation to cool to body temperature before use. Maintain adequate shielding of the radioactive colloid preparation at all times.
12. Where appropriate, dilute the preparation with sterile Sodium Chloride Injection to bring the dosage to within the recommended range.
13. The patient dose should be measured by a suitable radioactivity calibration system immediately prior to administration.
14. Aseptically withdraw material with a sterile shielded syringe for use within six (6) hours of preparation. For optimum results this time should be minimized. The vial contains no bacteriostatic preservative. Store the reconstituted vial at 15-30° C. Discard vial six (6) hours after reconstitution.

This radiopharmaceutical is approved by the U.S. Nuclear Regulatory Commission for distribution to persons licensed pursuant to Sections 35.14and 35.100 of 10 CFR Part 35 (superseded), or Section 35.200 of 10 CFR Part 35, effective April 1**,** 1987, or under equivalent licenses issued by an Agreement State**.**

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