

PRODUCT
INFORMATION

Gentech®

Molybdenum [⁹⁹Mo]/Technetium [^{99m}Tc] Sterile Generator

For the Production of Sodium Pertechnetate [^{99m}Tc] Injection (fission BP)

Description

The ANSTO Health Generator provides a means of obtaining a sterile, isotonic, additive and pyrogen free solution of Sodium Pertechnetate [^{99m}Tc Injection (fission) BP. The generator contains fission-product molybdenum-99 (⁹⁹Mo) from which ^{99m}Tc is separated by elution into evacuated vials.

The generator consists of a sealed glass vessel containing aluminium oxide. The ⁹⁹Mo is firmly bound to the alumina and as a result, the eluted ^{99m}Tc contains negligible amounts of ⁹⁹Mo. Over the life of the generator, an elution will provide a yield of approximately 90% of the theoretical amount of [^{99m}Tc] available from the ⁹⁹Mo contained within the generator vessel.

Physical Characteristics

Technetium-99m, with a physical half-life of 6 hours, decays by isomeric transition to ⁹⁹Tc. Photons associated with this transition which are useful for detection and imaging studies are listed in Table 1.

Table 1

Principal Radiation	Mean % per Disintegration	Mean Energy (keV)
Gamma-2	89.1	140.5

Reference: "D A Weber, K F Eckerman, LT Dillman and JC Ryman.MIRD: Radionuclide and Decay Schemes." The Society of Nuclear Medicine Inc., New York, 1989.

External Radiation

The specific gamma ray constant for ^{99m}Tc is 0.19mGy per MBq·h⁻¹ at 1cm. The first half value thickness of lead for ^{99m}Tc is 0.2mm. Attenuation by lead is given in the following table.

Table 2

Shield Thicknesses mm Pb	Coefficient of Attenuation (approx.)
0.2	0.5
0.95	10 ⁻¹
1.8	10 ⁻²
2.7	10 ⁻³
3.6	10 ⁻⁴

Elution Behaviour

Molybdenum-99, with a half-life of 2.75 days, decays to ^{99m}Tc. The physical decay characteristics of ⁹⁹Mo are such that 87.5% of its disintegrations form ^{99m}Tc. The activity of ^{99m}Tc available for elution from the generator will depend upon the time interval from

the last elution but reaches a maximum approximately 23 hours after the previous elution which is equivalent to 87.6 percent of the ⁹⁹Mo activity at that time. Table 3 shows the ^{99m}Tc activity for a given growth period following complete elution, relative to the ⁹⁹Mo activity contained in the generator at the end of the growth period.

Table 3

Growth Periods (hours)	^{99m} Tc: ⁹⁹ Mo
1	0.096
2	0.182
4	0.329
8	0.546
24	0.885
48	0.957

Table 4

Physical Decay Chart ⁹⁹Mo

Days	Fraction Remaining	Days	Fraction Remaining
0	1.000	8	0.133
1	0.777	9	0.103
2	0.604	10	0.080
3	0.469	11	0.063
4	0.365	12	0.049
5	0.284	13	0.038
6	0.220	14	0.030
7	0.171		

Table 5

Physical Decay Chart ^{99m}Tc

Days	Fraction Remaining	Days	Fraction Remaining
0	1.000	5	0.562
1	0.891	6	0.501
2	0.794	7	0.447
3	0.708	8	0.398
4	0.631		

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Pharmacology

No pharmacological activity has been observed in the range of doses administered for diagnostic purposes.

Pharmacokinetic Properties

The pertechnetate ion has similar biological distribution to iodide and perchlorate ions, concentrating temporarily in salivary glands, choroid plexus, stomach (gastric mucosa) and in the thyroid gland, from which it is released unchanged. The pertechnetate ion also tends to concentrate in areas with increased vascularisation or with abnormal vascular permeability, particularly when pre-treatment with blocking agents inhibits uptake in glandular structures.

Technetium - 99m is selectively excluded from the cerebrospinal fluid. Following intravenous administration, pertechnetate [^{99m}Tc] is distributed throughout the vascular system from which it is cleared by three main mechanisms:

- rapid removal, depending on the diffusion equilibrium with interstitial fluid;
- intermediate rate of removal, depending on the concentration of the pertechnetate in glandular tissue, mainly thyroid, salivary and gastric fundus glands which have an ionic pump mechanism;
- slow removal, by glomerular filtration by the kidneys, dependent on rate of urinary excretion.

Plasma clearance has a half-life of approximately 3 hours.

Excretion during the first 24 hours following administration is mainly urinary (~25%) with faecal excretion occurring over the next 48 hours. Approximately 50% of the administration activity is excreted within the first 50 hours.

When selective uptake of pertechnetate [^{99m}Tc] in glandular structures is inhibited by the pre-administration of blocking agents, excretion follows the same pathways but there is a higher rate of renal clearance.

When pertechnetate [^{99m}Tc] is administered in association with pretreatment with reducing agents such as stannous/medronate which cause a "stannous leading" of red blood cells, up to approximately 95% of the administered activity is taken up by the red blood cells where it becomes bound within the cells. Any unbound pertechnetate [^{99m}Tc] is cleared by the kidneys. Radioactivity in the plasma normally constitutes less than 5% of the intravascular activity.

The fate of technetium-99m follows that of the labelled erythrocyte themselves and the activity is cleared very slowly. A small level of elution of activity from the circulating red cells is thought to occur.

Sodium pertechnetate injection may be reacted with a range of reagents (cold kits) to provide diagnostic agents for the imaging of specific organs.

Indications

Sodium pertechnetate [^{99m}Tc] is used for scintigraphy, principally of the brain and thyroid. It can also be used to prepare various technetium-99m labelled injections for selective organ imaging especially of the liver, lung, bone and kidney.

Contraindications

Since Sodium Pertechnetate [^{99m}Tc] is excreted through the kidneys and the gastrointestinal tract, its use in patients suffering obstructive pathology may give rise to a higher level of radiation exposure.

Precautions

General

Radiopharmaceuticals should be used only by physicians who are qualified by specific training in the safe use and handling of radionuclides produced by a nuclear reactor or particle accelerator and whose experience and training have been approved by the appropriate government agency authorised to license the use of radionuclides.

Care should be taken to minimise radiation exposure to patients consistent with proper patient management. As with other radioactive drugs, Sodium Pertechnetate [^{99m}Tc] must be handled

with care and appropriate safety measures should be used to minimise radiation exposure to clinical personnel.

Disposal of all radioactive wastes should be carried out in accordance with the NHMRC "Code of Practice for the Disposal of Radioactive Wastes by the User" 1985.

Use with caution in the following circumstances

Because the pertechnetate ion is concentrated in the thyroid gland, choroid plexus and salivary glands, a blocking dose of up to 1 gram of reagent grade potassium perchlorate in a suitable base of capsule may be given orally prior to the administration of Sodium pertechnetate [^{99m}Tc] injection for brain scanning.

Patients who have had scans performed on them in the previous 6 weeks with agents containing tin may show distribution artefacts and/or poor quality images in a subsequent Sodium pertechnetate [^{99m}Tc] brain scan as a result of uptake of pertechnetate by the red blood cells. The physician should give special consideration in such cases to an alternative agent, eg. ^{99m}Tc -DTPA.

Check the following before use

Verification of the dose to be administered and patient identification is necessary prior to administration. Parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration whenever solution or container permits.

At the time of administration the solution should be crystal clear and should not be used if it is cloudy or if it contains particulate matter.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Adequate reproduction studies have not been performed in animals to determine whether this drug affects fertility in males or females, has teratogenic potential, or has other adverse effects on the foetus.

Use in Pregnancy

Direct administration of 800 MBq Sodium pertechnetate [^{99m}Tc] to a patient results in an absorbed dose to the uterus of 6.5 mGy. Following pretreatment of patients with a blocking agent, administration of 800 MBq Sodium pertechnetate [^{99m}Tc] results in an absorbed dose to the uterus of 5.3 mGy.

Administration of 925 MBq ^{99m}Tc -labelled red blood cells results in an absorbed dose to the uterus of 4.3 mGy. Doses above 0.5 mGy should be regarded as a potential risk to the foetus.

Use in Lactation

As a general rule breast-feeding should not be undertaken when a patient is administered radioactive material.

If the administration is considered necessary, breast-feeding should be interrupted and the expressed feeds discarded.

Breast-feeding can be restarted when the activity level in the milk will not result in a radiation dose to the child greater than 1 mSv.

Paediatric Use

Safety and effectiveness in children have not been established.

Interactions with other drugs

Drug interactions have been reported in brain scintigraphy where there can be increased uptake of [^{99m}Tc] pertechnetate in the walls of cerebral ventricles as a result of methotrexate induced ventriculitis.

In abdominal imaging, drugs such as atropine, isoprenaline and analgesics can result in a delay in gastric emptying and redistribution of pertechnetate.

Adverse Reactions

The following adverse reactions have been reported following intravenous injection of Sodium pertechnetate [^{99m}Tc]:

Hypersensitivity and Skin	urticaria, pruritus
Cardiovascular	arrhythmia, vasodilation
Body as a whole	facial oedema, coma

Dosage and Administration

Sodium Pertechnetate [^{99m}Tc] injection is administered by intravenous injection. The dosage employed varies for each diagnostic procedure with due allowances being made for patient body weight. The suggested intravenous dose range employed in the average adult (70kg) for the various diagnostic procedures is as follows:

Brain Scan	370-740 MBq (10-20 mCi)
Thyroid Gland Scan	37-185 MBq (1-5 mCi)
Salivary Gland Scan	37-185 MBq (1-5 mCi)
Blood Pool Imaging	370-740 MBq (10-20 mCi)

In order to reduce radiation dose to the bladder the patient should be encouraged to drink fluids and to void as frequently as possible after the administration of the radiopharmaceutical for a period of four to six hours.

Overdosage

In the event of an administration of a radiation overdose with Sodium pertechnetate [^{99m}Tc], increasing the elimination of the radionuclide from the body should reduce the absorbed dose. Measures to reduce possible harmful effects include frequent voiding of urine and promotion of diureses and faecal excretion. Very little treatment can be undertaken in the event of an overdose of [^{99m}Tc] labelled red blood cells since elimination is dependent on the normal haemolytic process.

Radiation Dosimetry

The estimated absorbed radiation doses to an average patient (70kg) from an intravenous injection of a maximum dose of 740 MBq of Sodium Pertechnetate [^{99m}Tc] administered with and without a thyroid blocking agent is shown in Table 6.

Table 6

	Dose (mGy)	
	With Blocking Agent	Without Blocking Agent
Stomach Wall	2.4	21.5
Upper large Intestine	2.8	45.9
Lower large Intestine	3.3	16.3
Ovaries	3.5	7.4
Red Marrow	3.3	4.5
Testes	2.4	2.0
Thyroid	1.6	17.0
Bladder Wall	23.7	14.1
Effective Dose	3.5	8.9

Reference:

ICRP Publication 62 (Nov 1992) Radiation doses to patients from radiopharmaceuticals, Johansson L, Mattsson S, Nosslin B and Leide-Svegborn S. Effective dose to patients from radiopharmaceuticals. Eur J Nucl Med (1992) 19:933-938

How Supplied

The generator is supplied in sizes ranging from 20 to 120 GBq and 370 GBq of ^{99}Mo at 0900 hours Sydney time on the day of calibration.

The generator pack contains the following items for use in its elution:

- (i) 1 Sterile generator.
- (ii) 2 kits each containing 5x5mL or 5x10mL or 5x20mL vials of Sodium Chloride for Injections BP.
- (iii) 2 kits each containing 5 x 30 evacuated vials, 5 sterile needles and 5 sterile mediswabs.
- (iv) Elution vial shield with viewing window supplied with initial order only.

Expiry

The Sodium Pertechnetate [^{99m}Tc] Injection contains no bactericide and should not be used later than 8 hours after elution. The generator has an expiration time of 14 days after the date of calibration (shown on the generator label).

Storage

The generator is designed to operate at normal room temperature (below 30°C). The yield of Sodium Pertechnetate [^{99m}Tc] may be affected if the generator and the 0.9% sodium chloride solution are stored below room temperature.

Disposal of the Generator

The generator (and packaging) should be kept and not disposed of as normal waste within 70 days of the calibration date. Users are encouraged to return their generators to ANSTO Health for recycling. A special set of instructions and labels are included with each generator.

References

- European Commission Committee for Proprietary Medicinal Products Ad hoc group on radiopharmaceuticals Technetium [^{99m}Tc] Generator Dec 1994 111/3143/93-En Final.
- Walker, A.G., Effect of ^{99m}Tc bone scan agent on subsequent brain scans. Ad hoc J. Nucl. Med. 16:579, 1975.
- Richards, P. and O'Brien, M.J., Rapid determination of ^{99}Mo in separated ^{99m}Tc . J. Nucl. Med., 10:517, 1969.

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ANSTO Health is a commercial enterprise of the Australian Nuclear Science and Technology Organisation (ANSTO), which is located at Lucas Heights, in Sydney, NSW.

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Gentech[®] Directions for Use

Molybdenum [⁹⁹Mo] / Technetium
 [^{99m}Tc] Sterile Generator

The Gentech[®] generator is delivered with 0.9% Sodium Chloride injection BP (saline) vials, evacuated elution vials, sterile swabs and needles. The generators are sterile and pyrogen free when they leave ANSTO Health. Observe aseptic technique during the use of the Gentech[®] generator.

First Elution

1. Remove the Gentech[®] generator and its accessories from the transport packaging. Install in the Gentech[®] Garage or the user shielding.
2. Lift the Gentech[®] handle. Rotate the cover until the yellow saline spike cover and elution outlet filter are exposed. Push the handle down to lock the lid in the operating position.
3. Remove the flip off seal from the saline vial (5 or 10ml). The minimum elution volume is 5ml. For elution volume between 5 and 10ml, aseptically remove the unwanted saline from the vial with a hypodermic sterile needle and discard.
4. Place a Gentech[®] saline vial into the **new** Gentech[®] saline vial holder, provided in the foam insert of the transport packaging with every generator. Swab the exposed part of the saline vial's silicon septum with a sterile swab provided.
Ensure to allow to dry.
5. Remove the yellow protective cap from the Gentech[®] saline spike.
6. Align the lugs of the Gentech[®] saline vial holder with the grooves in the saline port of the Gentech[®] generator and push down firmly. When the vial is fully depressed, turn clockwise in the direction of the arrows to engage the vial on the saline spike and lock the saline vial holder in place.
7. Remove the white plastic lid from the elution vial shield. Unscrew the metal top. Remove the red flip-off seal from a 30ml evacuated elution vial. Place the decapped vial in the elution vial shield and screw on the metal cap to hold the vial in place. Swab the top of the evacuated elution vial shield and the exposed part of the septum of the evacuated elution vial, with a sterile swab provided. **Ensure to allow to dry.**
8. Grip the red protective cap (male luer closure), turn it anti-clockwise through 90° and remove from the outlet filter. With the sterile needle cover in place, attach a sterile needle (screw clockwise). **Caution, do not over-tighten.** Remove the sterile needle cover.
9. Invert the prepared elution vial shield onto the sterile needle. Lower the evacuated elution vial shield until the evacuated elution vial is fully penetrated by the sterile needle. **Allow at least 3 minutes to complete the elution.**
10. Observe the emptying of the saline vial and the filling of the evacuated elution vial, indicated by the sight and sound of air bubbles in the elution vial.
11. Visibly check the saline vial is empty, and through the elution vial shield window, that the elution occurred. If the elution did not occur, repeat steps 3 and 4 and 6 to 10 with fresh saline and evacuated elution vials.
12. Remove the elution vial shield from the sterile needle. Cover the elution vial shield with the white plastic lid.
13. Place the needle cover back on to the sterile needle and leave it in place until the next elution. (Replace with a fresh sterile needle before each elution).

14. **Do not remove the saline vial assembly until the next elution.**
15. Record the appropriate information on the elution vial in accordance with your facility procedures, such as date, time and the contents being radioactive.
16. Assay the contents of the vial for its ^{99m}Tc content using a previously calibrated ^{99m}Tc dose calibrator (or other suitable measuring instrument). Record the results.
17. Perform a gamma spectroscopy test to determine the extent of ⁹⁹Mo breakthrough. The method described by *Richards and O'Brien may be used.

Subsequent Elutions

1. Remove the used saline vial (by twisting anti-clockwise) then repeat steps 3, 4, and 6, 7.
2. Remove the used elution needle (by twisting anti-clockwise) and replace with a fresh sterile needle.
3. Repeat steps 9 through to 17.

Troubleshooting tips when the generator is not eluting

1. Check that the elution needle is not loose (see step 8).
2. Try another evacuated elution vial.
3. If you inadvertently removed the elution vial before it finished eluting, the column will have become wet and will need to be dried.
 Attach a fresh evacuated elution vial, but do **not** replace the saline vial unless it still contains some saline. In this case, replace it with an empty saline vial. This will allow air and not saline, to pass through and this will dry off the column.
 This process using an empty saline vial and a new evacuated elution vial, can be repeated to ensure the column is dry.
4. Call ANSTO Health on 1800 251 572 or email health@ansto.gov.au

To prevent damaging the spike

Ensure:

1. To use the new Gentech[®] saline vial holder, provided with every new generator in the foam insert of the packaging of every new Gentech[®] generator.
2. The protective flip off seal is removed from the saline vial.
3. The lid of the Gentech[®] generator garage is fully open, to allow clear access to the Gentech[®] generator.
4. The yellow protective cap is removed from the saline spike.
5. The saline vial is placed on the spike vertically and not at an angle.
6. Following swabbing of the silicon septum of the saline vial, **ensure to allow to dry.**

Reference

*Richards, P. and O'Brien, M.J., Rapid determination of ⁹⁹Mo in separated ^{99m}Tc. J. Nucl. Med., 10:517, 1969.

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