SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE -MEDICINAL PRODUCT

MON.TEK $^{99}Mo/^{99m}Tc$ GENERATOR, 5-50 GBq radionuclide generator

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient:
Mother nuclide:
Sodium Molybdate ($Na^{99}MoO_4$) 5-50 GBq / Generator
(Mo-99 radioactivity at calibration date)

Daughter nuclide:
Sodium (^{99m}Tc) pertechnetate (Obtained from $^{99}Mo/^{99m}$ Tc generator system.)

MON.TEK $^{99}Mo/^{99m}Tc$ GENERATOR contains ^{99}Mo isotope adsorbed on a chromatographic column. ^{99m}Tc isotope produced from decay of ^{99}Mo, decays with the emission of gamma radiation with a mean energy of 140 keV and a half-life of 6,02 hours to technetium-99 which, in view of its long half-life of 2.13×10^5 years can be regarded as quasi stable.

Sterile sodium ^{99m}Tc pertechnetate solution is obtained by elution from $^{99}Mo/^{99m}$ Tc generator.

The quantity of sodium pertechnetate (^{99m}Tc) that may be eluted from the generator at any one time is dependent on the quantity of sodium (^{99}Mo) molybdate present, the volume of eluate obtained and the elapsed time since the previous elution.

Excipients:
Sodium chloride: 9 mg/mL
Sodium hydroxide: q.s. to adjust pH.

See section 6.1 for a full list of excipients

3. PHARMACEUTICAL FORM

Radionuclide generator.
Clear, colorless solution for injection is obtained from generator system.

4. CLINICAL PARTICULARS

4.1 -Indications

This medicinal product is for diagnostic use only.

The eluate from the generator (Sodium Pertechnetate ^{99m}Tc) may be used as a reagent for labelling of various carrier compounds supplied as kits or administered directly *in-vivo.*

When administered intravenously, the sterile sodium pertechnetate (^{99m}Tc) solution is used as a diagnostic aid for the following, in children and adults:

a) Thyroid scintigraphy: direct imaging and measurement of thyroid uptake to give information on the size, position, nodularity and function of the gland in thyroid disease.
b) Salivary gland scintigraphy: to assess salivary gland function and duct patency.
c) Location of ectopic gastric mucosa: Meckel's diverticulum
d) Cerebral scintigraphy: to identify breaches in the blood-brain barrier caused by tumour, infarction, haemorrhage and oedema, when no other methods are available.
e) Cardiac and vascular scintigraphy
f) Gastrointestinal bleeding scintigraphy
g) Organ perfusion scintigraphy

Following instillation of sterile sodium pertechnetate (^{99m}Tc) solution into the eye:

h) Lacrimal duct scintigraphy: to assess patency of tear ducts

4.2 Posology and method of administration

RADIOPHARMACEUTICALS SHOULD BE ADMINISTERED ONLY BY NUCLEAR MEDICINE PHYSICIANS IN NUCLEAR MEDICINE CENTERS.

Posology and administration method

The average dosages recommended for the main applications on adults and old patients are given below:

- Thyroid scintigraphy: 18.5-80 MBq (0.5 -2.16 mCi)
  Scintigraphy performed 20 minutes after intravenous injection.

- Salivary gland scintigraphy: 37-185 MBq (1-5 mCi)
  Scintigraphy performed immediately after intravenous injection and at regular intervals up to 15 minutes.

- Ectopic gastric mucosa localization (Meckel's diverticulum scintigraphy): 400 MBq (10.8 mCi)
  Scintigraphy performed immediately after intravenous injection and at regular intervals up to 30 minutes.

- Cerebral scintigraphy: 370-740 MBq (10-20 mCi)
  Rapid sequential images are taken immediately within the 1-2 minutes after intravenous administration and static images 1 to 4 hours later. Thyroid and choroid plexus should be blocked to avoid non-specific Technetium-99m uptake.

- Cardiac and vascular scintigraphy: 740 - 925 MBq (-20- 25 mCi)
  Red cells are labelled in-vivo or in-vitro by pretreating with a reducing agent. Dynamic images are taken in the first minute after intravenous administration, followed by regular

images over 30 minutes.

- Gastrointestinal bleeding scintigraphy: 740-925 MBq (-20-25 mCi)
  Red cells are labelled in-vivo or in-vitro by pretreating with a reducing agent. Dynamic images are taken in the first minute after intravenous administration, followed by regular images at appropriate intervals for up to 24 hours.

- Organ perfusion scintigraphy: 518-777 MBq (14-21 mCi)

- Lachrymal duct scintigraphy: 2-4 MBq (-0.05-0.11mCi) for each eye
  Drops are instilled into the eye and dynamic images are taken over 2 minutes, followed by static images at appropriate intervals over 20 minutes.

Method of administration
Sodium (^{99m}Tc) pertechnetate is normally administered intravenously or by dropping into the eyes at activities which vary widely according to the clinical information required and the equipment employed. Pre-treatment of patients with thyroid blocking agents or reducing agents may be necessary for certain indications.

Radiopharmaceutical agents should be used only by qualified personnel with the appropriate government authorisations for the use and manipulations of radionuclides.

For patient preparation, see section 4.4.

For instructions on preparation of radiopharmaceuticals, see section 6.6 and 12.

Additional information on special populations

Renal/hepatic impairment
There is not safety and efficiency studies on patients with renal and liver failure.
Careful consideration of the activity to be administered is required since the product may remain in the body for a longer time in these patients and thus an increased radiation exposure is possible.

Pediatric Population
The use in children and adolescents has to be considered carefully, based upon clinical needs and assessing the risk/benefit ratio in this patient group.

The activity to be administered to children and adolescents is less than the dosage administered to adults and it is calculated by using the following formula:

$$\text{Pediatric dosage} = \frac{\text{Adult dose} \times \text{Weight of child (kg)}}{70 \text{ kg}}$$

Furthermore, the dose for children is calculated by EANM as a fraction of adult dose and it is informed by EU. According to these references, ^{99m}Tc-Pertechnetate activity dosage to be applied to children can be calculated easily.

Table showing the fractions of adult dosage to be used for the dosages that will be calculated for children

3 Kg	=	0.1	22 Kg	=	0.50	42 Kg	=	0.78
4 Kg	=	0.14	24 Kg	=	0.53	44 Kg	=	0.80
6 Kg	=	0.19	26 Kg	=	0.56	46 Kg	=	0.82
8 Kg	=	0.23	28 Kg	=	0.58	48 Kg	=	0.85
10 Kg	=	0.27	30 Kg	=	0.62	50 Kg	=	0.88
12 Kg	=	0.32	32 Kg	=	0.65	52-54 Kg	=	0.90
14 Kg	=	0.36	34 Kg	=	0.68	56-58 Kg	=	0.92
16 Kg	=	0.40	36 Kg	=	0.71	60-62 Kg	=	0.96
18 Kg	=	0.44	38 Kg	=	0.73	64-66 Kg	=	0.98
20 Kg	=	0.46	40 Kg	=	0.76	68 Kg	=	0.99

(Pediatric Task Group, EANM)

The minimum activity doses required to obtain images of adequate quality for children younger than 1 year are 20 MBq for direct application, 10 MBq for thyroid scintigraphy, and 80 MBq for red blood cell labeling.

Geriatric population
The adult dosage is applied.

4.3 Contraindications
It is contraindicated in the patients who have hypersensitivity to the active substance or to any of the excipients.

If sodium pertechnetate (^{99m}Tc) solution is used for labeling a kit for radiopharmaceutical preparation, information on contraindications should be sought in the SmPC and PIL of the kit for radiopharmaceutical preparation.

4.4 Special warnings and precautions for use

RADIOPHARMACEUTICALS SHOULD BE ADMINISTERED ONLY BY NUCLEAR MEDICINE PHYSICIANS IN NUCLEAR MEDICINE CENTERS.

Sodium pertechnetate solution that is derived from MON.TEK ^{99}Mo / ^{99m}Tc GENERATOR is radioactive. Therefore, vial containing the solution must be kept in a suitable lead shield.

Patient dose preparation and application must be performed using aseptic techniques.

Adequate shield must be available to avoid unnecessary radiation exposure to patients, staff and other people.

Potential for hypersensitivity or anaphylactic reactions
If hypersensitivity or anaphylactic reactions occur, the administration of the medicinal product must be discontinued immediately and intravenous treatment initiated, if necessary. To enable immediate action in emergencies, the necessary medicinal products and equipment such as endotracheal tube and ventilator must be immediately available.

Individual benefit/risk justification
For each patient, radiation exposure must be justifiable by the likely benefit. The activity administered should be in every case as low as reasonably achievable to obtain the required diagnostic information.

Renal impairment
Careful consideration of the benefit risk ratio in these patients is required since an increased radiation exposure is possible.

Paediatric population
For information on the use in paediatric population, see section 4.2.

Careful consideration of the indication is required since the effective dose per MBq is higher than in adults (see section12).

The use in children and adolescents has to be considered carefully, based upon clinical needs and assessing the risk/benefit ratio in this patient group. Thyroid blocking is of special importance when performing cerebral scintigraphy in the paediatric population.

Patient preparation
Pre-treatment of patients with thyroid-blocking medicinal products may be necessary for certain indications.
The patient should be well hydrated before the start of the examination and urged to void as often as possible during the first hours after the examination in order to reduce radiation.

Before the application of Sodium [^{99m}Tc] pertechnetate solution for scintigraphy of Meckel's diverticulum the patient should keep an empty stomach for 3 to 4 hours to reduce intestinal peristalsis.

In thyroid gland scintigraphy, salivary gland scintigraphy or location of ectopic gastric mucosa concomitant application of Sodium perchlorate is associated with reduced uptake of radioactivity in glandular tissue.

In cerebral scintigraphy there is also an uptake of Sodium Pertechnetate [^{99m}Tc] in the plexus choroideus that may be misinterpreted as misfunction of the blood-brain barrier (false-positive finding). To reduce the likelihood of misinterpretation and to reduce radiation exposure pretreatment with Perchlorate is recommended as Perchlorate reduces uptake of Sodium Pertechnetate [^{99m}Tc] to the plexus choroideus.

In Shunt scintigraphy blocking of the thyroid gland to reduce radiation exposure is also necessary as with shunts with normal passability complete activity reaches the peritoneal cavity where it is absorbed and systemically distributed.

After *in vivo* labelling of erythrocytes using stannous ions for reduction Sodium Pertechnetate (^{99m}Tc) is primarily built into erythrocytes, therefore Meckel scintigraphy should be performed before or some days after *in vivo* labelling of erythrocytes.

If sodium pertechnetate (^{99m}Tc) solution is used for labelling a kit, information should be sought in the SmPC and PIL of the specific kit.

Specific warnings

Each ml of Sodium pertechnetate (^{99m}Tc) solution obtained from MON.TEK ^{99}Mo / ^{99m}Tc GENERATOR contains sodium less than 1 mmol (23 mg); in other words actually "it is sodium-free".

When sodium pertechnetate (^{99m}Tc) solution is used for labelling of a kit, the determination of the overall sodium content must take into account the sodium derived from the eluate and the kit. Please refer to the package leaflet of the kit for information on sodium content.

Paravasal injection should be avoided.

For precautions with respect to environmental hazard, see section 6.6.

4.5 Interaction with other medicinal products and other forms of interaction

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 (^{99m}Tc) pertechnetate.

Thyroid hormones, iodine, iodide, perchlorate, thiocyanate, aluminium containing antacids, sulfonamides and products containing stannous (II) ions, may lead to increased concentrations of Sodium (^{99m}Tc) Pertechnetate in the vascular space, in the case of stannous (II) ions and sulfonamides the concentration of Sodium (^{99m}Tc) Pertechnetate in red blood cells may be increased, and there may be decreased accumulation in plasma and cerebral lesions. Such medicines should be discontinued several days before the procedure.

Iodine containing radiologic contrast media and perchlorate may decrease uptake of ^{99m}Tc-pertechnetate to digestive mucous. Barium sulphate absorbs most of gamma radiation of the tracer. Scintigraphy of Meckel's diverticulum should therefore be performed at the earliest 2 - 3 days after application of these substances.
Laxatives may increase transport of ^{99m}Tc-pertechnetate from the stomach and the intestines and should not be taken before performing scintigraphy of Meckel's diverticulum.

The possible types of interactions following intravenous administration of a ^{99m}Tc labelled pharmaceutical preparation will be dependent on the specific compound being used. Such information can be found in the SmPC of the kit used for radiopharmaceutical preparation.

Sodium pertechnetate administration does not indicate any interaction with any food and beverage.

The most important incompatibilities:
Sodium(^{99m}Tc) pertechnetate solution or technetium-99m labelled preparations must not be mixed or administered together with other medicinal products or components. After nuclear medicine intervention using stannous (II) labelling kits, a waiting time of at least 8 days is advised, otherwise the effect may be undesired labelling of the red blood cells.

Additional information on special populations:
No interaction study performed.

Pediatric Population:
No interaction study performed.

4.6 Pregnancy and lactation

General recommendation
Pregnancy category: C

Women of childbearing potential / Contraception
Information on effect of sodium pertechnetate (^{99m}Tc) administration to pregnant women is insufficient.

The studies conducted to animals are insufficient in terms of effects on pregnancy/ and-or/ embryonic/ fetal growth/ and-or/ natal/ and-or/ post-natal growth. (See section 5.3) Risk for humans is not known.

MON.TEK ^{99}Mo /^{99m}Tc GENERATOR should not be applied in pregnancy (except for the cases where the benefits to be provided in the event of application may cover the potential damage to arise).

When it is necessary to apply the radioactive product on women that have the potential of being pregnant, it should definitely be inquired whether she is pregnant or not. A woman who has missed a menstruation period should be assumed to be pregnant unless otherwise evidenced. Application of ionizing radiation on pregnant women brings radiation dosages to fetus as well. Therefore, the minimum dosage required for optimum imaging should be applied where necessary. Alternative techniques which do not involve ionising radiation should be considered.

Pregnancy
Technetium-99m (as free pertechnetate) has been shown to cross the placental barrier.

Radionuclide procedures carried out on pregnant women also involve radiation doses to the foetus. MON.TEK ^{99}Mo / ^{99m}Tc GENERATOR should not be used during pregnancy, unless likely benefit exceeds the risk incurred by the mother and the foetus.

Direct administration of 800 MBq sodium (^{99m}Tc) pertechnetate 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 (^{99m}Tc) pertechnetate results in an absorbed dose to the uterus of 5.3 mGy. Administration of 925 MBq technetium-99m 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. When ^{99m}Tc pertechnetate administration is required, pregnancy status of the woman should be definitely inquired before application.

Lactation
Before administering a radioactive medicinal product to a woman who is breast feeding, consideration should be given as to whether the investigation could be reasonably delayed until the mother has ceased breastfeeding, and as to whether the most appropriate choice of radiopharmaceuticals has been made.
If MON.TEK ^{99}Mo / ^{99m}Tc GENERATOR application to a women at lactation is considered necessary, breast-feeding should be interrupted for 12 hours post administration and the expressed feeds discarded. Breasting should be resumed only when the radiation dosage in the mother milk is below 1 mSv.

Close contact with infants should be restricted during this period.

Fertility
Effect of sodium pertechnetate on fertility ability is unknown. However, if it is required to apply ^{99m}Tc pertechnetate, radiation dose to be administered will be the minimum amount required to get the clinical information (ALARA principle).

Following direct administration of 800 MBq sodium pertechnetate (^{99m}Tc) on patient, the dose absorbed at uterus is 6.5 mGy. If blocking drugs are administered to the patient prior to application, the dosage absorbed at uterus as a result of application of 800 MBq sodium pertechnetate is 5.3 mGy. As a result of labelling the red blood cells with 925 MBq ^{99m}Tc, the dose absorbed at uterus is 4.3 mGy. Over the dose of 0.5 mGy is assumed as potential risk for fetus. If it is necessary to apply ^{99m}Tc pertechnetate, information must be obtained about the pregnancy of patient before administration.

4.7 Effects on ability to drive and use machines
No studies on the effects of Sodium pertechnetate (^{99m}Tc) administration on the ability to drive and use machines have been performed.

4.8 Undesirable effects
Summary of the safety profile
Information on adverse reactions is available from spontaneous reporting. The reported reaction types are anaphylactoid reactions, vegetative reactions, as well as different kinds of injection site reactions.

Sodium pertechnetate (^{99m}Tc) obtained from MON.TEK ^{99}Mo / ^{99m}Tc GENERATOR is used for radioactive labeling of a variety of compounds. These medicinal products generally have a higher potential for adverse reactions than ^{99m}Tc, and therefore the reported adverse reactions are rather related to the labelled compounds than to ^{99m}Tc.

The possible types of adverse reactions following intravenous administration of ^{99m}Tc -labelled pharmaceutical preparation will be dependent on the specific compound being used. Such information can be found in the SmPC of the kit used for radiopharmaceutical preparation.

The frequencies of undesirable effects are defined as follows:
Very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000) and not known (cannot be estimated from the available data)

Although frequencies are unknown, reported adverse reactions upon intravenous application of Sodium pertechnetate (^{99m}Tc) is given below.

Immune system disorder
Frequency unknown: Anaphylactoid reactions (e.g. dyspnoea, coma, urticaria, erythema, rash, pruritus, oedema at various location e.g. face oedema)

Nervous system disorders
Frequency unknown: Vasovagal reactions (e.g. syncope, tachycardia, bradycardia, dizziness, headache, vision blurred, flushing)

Gastrointestinal disorders
Frequency unknown: Vomiting, nausea, diarrhoea

General disorders and administration site conditions
Frequency unknown: Injection site reactions due to extravasation (e.g. cellulitis, pain, erythema, swelling)

Unspecific systemic reactions and gastrointestinal disorders are rather considered to be related to the examinational setting than to technetium (^{99m}Tc), especially in anxious patients.
Injection site reactions are related to extravasation of the radioactive material during the injection and may range from local swelling up to cellulitis.

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose is 10.4 mSv when the maximal recommended activity of 800 MBq is administered these adverse reactions are expected to occur with a low probability.

For most diagnostic investigations using a nuclear medicine procedure, the effective dose is less than 20 mSv. Higher doses may be justified in some clinical circumstances.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

4.9 Overdose
No overdose event has been reported.

In the event of the administration of a radiation overdose with sodium (^{99m}Tc) pertechnetate, the absorbed dose should be reduced where possible by increasing the elimination of the radionuclide from the body. Measures to reduce possible harmful effects include frequent voiding of urine and promotion of diuresis and faecal excretion.

Very little supportive treatment can be undertaken in the event of an overdose of Technetium-99m labelled red blood cells since elimination is dependent on the normal haemolytic process.

The uptake in the thyroid, salivary glands and the gastric mucosa can be significantly reduced when sodium perchlorate is given immediately after an accidentally high dose of sodium pertechnetate (^{99m}Tc) was administered.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Diagnostic Radiopharmaceuticals
ATC Code: V09FX01

No pharmacodynamic effect is expected when applied at normal dosage limits.

5.2 Pharmacokinetic characteristics

General properties

Distribution

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. ^{99m}Tc 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 tissues, 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.

Biotransformation

Technetium is discharged directly from the body without noticeable metabolisation.

Elimination

Excretion during the first 24 hours following administration is mainly urinary (approximately 25 %) with faecal excretion occurring over the next 48 hours. Approximately 50 % of the administered 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 pre-treatment with reducing agents such as stannous/medronate which cause a "stannous loading" 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 the technetium-99m follows that of the labelled erythrocytes themselves and the activity is cleared very slowly. A small level of elution of activity from the circulating red cells is thought to occur.

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

Linearity/ Non-Linear Case
Effect of Technetium-99m does not have a linear relation with dosage.

5.3 Preclinical safety data

There is no information about acute, sub-acute and chronic toxicity at single dosage or repeated dosages. The quantity of ^{99m}Tc sodium pertechnetate to be applied for diagnostic purpose is very low and any adverse reaction apart from allergic reactions has not been reported.

Fertility Toxicity
Penetration of sodium pertechnetate to placenta following intravenous application has been studied on rats. If perchlorate is not applied before the application, more than 60% of the dosage of ^{99m}Tc applied in pregnancy is found in uterus. The studies have been completed during pregnancy of the pregnant rats and change in weight of offspring during pregnancy and lactation and only during lactation and falling hair and change in sterility have been observed.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Excipients used in Generator:
Aluminium oxide
Molybdenum trioxide
0.9 % Sodium chloride solution
Sodium hydroxide
Hydrochloric acid
Hydrogen peroxide

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products, except with sodium chloride 9 mg/ml (0.9%) solution for injection.

6.3 Shelf life

The shelf life for generator is 21 days following the date of production and 15 days following the date of calibration.

^{99m}Tc sodium pertechnetate solution is suitable for use for 12 hours as from the date and time of labeling.

The shelf life after labelling with the kit should be determined according to the shorter one by taking the shelf life of labelling product into account.

6.4 Special precautions for storage

MON.TEK ^{99}Mo / ^{99m}Tc GENERATOR must be stored at room temperature below 25 ºC in the original package and lead shield which is specifically designed and must not be frozen.

Eluate derived elution must be stored at room temperature below 25 °C.

6.5 Nature and content of container

Primary packaging:
Ph. Eur. Type I colourless glass column,
Ph. Eur. Type I bromobutyl stopper and
Aluminum cap, and
Stainless steel needle set

Secondary packaging:
Lead shield

Content of a generator set:
One ^{99}Mo/^{99m}Tc radionuclide generator in a special packaging,
Sterile %0.9 NaCl solution 10 ml or 5 ml (5 vial per each) in cardboard box packages,
10 sterile evacuated vial in a cardboard box,
10 vial label for technetium pertechnetate solution (^{99m}Tc),
10 lead shield label,
10 isopropyl alcohol tissues %70,
Package Leaflet and Product Information Manual.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the local competent official organisation.

Radiopharmaceuticals should be prepared in a manner which satisfies both radiation safety and pharmaceutical quality requirements.

The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spill of urine, vomiting etc. Radiation protection precautions in accordance with national regulations must therefore be taken.

Since generator and used evacuated vials have radioactive characteristics, any unused product or waste material should be disposed of in accordance with local requirements for radioactive material.

Any unused product or waste material should be disposed of in accordance with local requirements. Contaminated material must be disposed of as radioactive waste via an authorized route.

Normal safety precautions for handling radioactive materials should be observed. After use, all materials associated with the preparation and administration of radiopharmaceuticals, including any unused product and its container, should be decontaminated or treated as radioactive waste and disposed of in accordance with the conditions specified by the local competent authority. Contaminated material must be disposed of as radioactive waste via an authorized route.

After decay of radioactivity there are no special precautions for waste disposal.

7. MARKETING AUTHORISATION HOLDER

Curium Nükleer Tıp A.Ş.TÜBİTAK MAM Teknoparkı
41470 Gebze Kocaeli TURKEY
Tel: +90 262 648 02 00
Fax: +90 262 646 40 39

8. MARKETING AUTHORISATION NUMBER

223/48

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF AUTHORIZATION

Date of first authorisation: 05.02.2010
Date of last renewal: 15.02.2017

10. DATE OF REVISION OF THE TEXT

06/2025

11. DOSIMETRY

Technetium (^{99m}Tc) is produced by means of a (^{99}Mo/^{99m}Tc) generator and decays with the emission of gamma radiation with a mean energy of 140 keV and a half-life of 6.02 hours to technetium (^{99}Tc) which, in view of its long half-life of 2.13 x 10^5 years can be regarded as quasi stable.

The data listed below are from ICRP (International Commission of Radiological Protection, Radiation Dose to Patients from Radiopharmaceuticals, Pergamon Press, 1998) Publication 80

(i) Without pre-treatment with blocking agent:

Organ	Absorbed dose per unit activity administered (mGy/MBq)				
	Adult	15 Year	10 Year	5 Year	1 Year
Adrenals	0.0037	0.0047	0.0072	0.011	0.019
Bladder wall	0.018	0.023	0.030	0.033	0.060
Bone surfaces	0.0054	0.0066	0.0097	0.014	0.026
Brain	0.0020	0.0025	0.0041	0.0066	0.012
Breast	0.0018	0.0023	0.0034	0.0056	0.011
Gallbladder	0.0074	0.0099	0.016	0.023	0.035
GI tract					
Stomach wall	0.026	0.034	0.048	0.078	0.16
Small intestine	0.016	0.020	0.031	0.047	0.082
Large intestine	0.042	0.054	0.088	0.14	0.27
ULI wall	0.057	0.073	0.12	0.20	0.38
LLI wall	0.021	0.028	0.045	0.072	0.13
Heart	0.0031	0.0040	0.0061	0.0092	0.017
Kidneys	0.0050	0.0060	0.0087	0.013	0.021
Liver	0.0038	0.0048	0.0081	0.013	0.022
Lungs	0.0026	0.0034	0.0051	0.0079	0.014
Muscles	0.0032	0.0040	0.0060	0.0090	0.016
Oesophagus	0.0024	0.0032	0.0047	0.0075	0.014
Ovaries	0.010	0.013	0.018	0.026	0.045
Pancreas	0.0056	0.0073	0.011	0.016	0.027
Red marrow	0.0036	0.0045	0.0066	0.0090	0.015
Salivary glands	0.0093	0.012	0.017	0.024	0.039
Skin	0.0018	0.0022	0.0035	0.0056	0.010
Spleen	0.0043	0.0054	0.0081	0.012	0.021
Testes	0.0028	0.0037	0.0058	0.0087	0.016
Thymus	0.0024	0.0032	0.0047	0.0075	0.014
Thyroid	0.022	0.036	0.055	0.12	0.22
Uterus	0.0081	0.010	0.015	0.022	0.037
Other tissues	0.0035	0.0043	0.0064	0.0096	0.017
Effective dose (mSv/MBq)	0.013	0.017	0.026	0.042	0.079

(ii) With pre-treatment with blocking agent:

Organ	**Absorbed dose per unit activity administered (mGy/MBq)**				
	Adult	**15 Year**	**10 Year**	**5 Year**	**1 Year**

Adrenals	0.0029	0.0037	0.0056	0.0086	0.016
Bladder wall	0.030	0.038	0.048	0.050	0.091
Bone surfaces	0.0044	0.0054	0.0081	0.012	0.022
Brain	0.0020	0.0026	0.0042	0.0071	0.012
Breast	0.0017	0.0022	0.0032	0.0052	0.010
Gallbladder	0.0030	0.0042	0.0070	0.010	0.013
GI tract					
Stomach wall	0.0027	0.0036	0.0059	0.0086	0.015
Small intestine	0.0035	0.0044	0.0067	0.010	0.018
Large intestine	0.0036	0.0048	0.0071	0.010	0.018
ULI wall	0.0032	0.0043	0.0064	0.010	0.017
LLI wall	0.0042	0.0054	0.0081	0.011	0.019
Heart	0.0027	0.0034	0.0052	0.0081	0.014
Kidneys	0.0044	0.0054	0.0077	0.011	0.019
Liver	0.0026	0.0034	0.0053	0.0082	0.015
Lungs	0.0023	0.0031	0.0046	0.0074	0.013
Muscles	0.0025	0.0031	0.0047	0.0072	0.013
Oesophagus	0.0024	0.0031	0.0046	0.0075	0.014
Ovaries	0.0043	0.0054	0.0078	0.011	0.019
Pancreas	0.0030	0.0039	0.0059	0.0093	0.016
Red marrow	0.0025	0.0032	0.0049	0.0072	0.013
Skin	0.0016	0.0020	0.0032	0.0052	0.0097
Spleen	0.0026	0.0034	0.0054	0.0083	0.015
Testes	0.0030	0.0040	0.0060	0.0087	0.016
Thymus	0.0024	0.0031	0.0046	0.0075	0.014
Thyroid	0.0024	0.0031	0.0050	0.0084	0.015
Uterus	0.0060	0.0073	0.011	0.014	0.023
Other tissues	0.0025	0.0031	0.0048	0.0073	0.013
Effective dose (mSv/MBq)	**0.0042**	**0.0054**	**0.0077**	**0.011**	**0.019**

The effective dose equivalent resulting from an administered activity of 800 MBq sodium pertechnetate (^{99m}Tc) is 10.4 mSv. Following pretreatment of patients with a blocking agent, administration of 800 MBq sodium (^{99m}Tc) pertechnetate results in an effective dose equivalent of 4.24 mSv

(iii) The radiation dose absorbed by the lens of the eye following administration of sodium (^{99m}Tc) pertechnetate for lacrimal duct scintigraphy is estimated to be 0.038 mGy/MBq. This results in an effective dose equivalent of less than 0.01 mSv for an administered activity of 4 MBq.

The specified radiation exposure is only applicable if all organs accumulating sodium (^{99m}Tc) pertechnetate will function normally. Hyper/hypofunction (e.g. of the thyroid, gastric mucosa or kidney) and extended processes with impairment to the blood-brain-barrier or renal elimination disorders, may result in changes to the radiation exposure, locally even in strong increases of it.

External radiation exposure

The surface dose rates and the accumulated dose depends on many factors. Measurements on the location and during work are critical and should be practised for more precise and instructive determination of overall radiation dose to the staff.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

As with any pharmaceutical product, if at any time in the preparation of this product the integrity of this vial is compromised it should not be used.

MON.TEK ^{99}Mo/^{99m}Tc GENERATOR can be eluted at any time, however the quantity of ^{99m}Tc obtained from eluate depends on the time between the last elution and the first elution.

^{99m}Tc sodium pertechnetate eluate obtained after elution must be stored in lead shield. At these conditions, the eluate is suitable for use for 12 hours at the temperatures below 25 ºC as from the date and time of elution. Any unused product or waste material should be disposed of in accordance with local requirements for radioactive material.

Method of preparation

Radiopharmaceuticals should be prepared by the user in a manner which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken complying with the requirements of Good Pharmaceutical Manufacturing Practice for radiopharmaceuticals.

MON.TEK ^{99}Mo/^{99m}Tc GENERATOR Use (Elution) Instruction:

Safe handling

Consideration should be given to the safe lifting and carrying of the generators. Local manual handling operations regulations should be observed in order to reduce the risk of injury caused by manual handling activities.

Elution instructions

The facilities used for elutions should comply with the appropriate regulations for safe radiological handling. Strict aseptic techniques should be used during the elution of the generator to ensure sterility of the generator eluate.

To avoid unsatisfactory performance it is important to adhere to the following sequence of elution steps.

To elute the generator a vial of sodium chloride solution is placed onto the inlet needle. Elution of Sodium Pertechnetate (^{99m}Tc) Injection, is achieved by placing a sterile evacuated vial onto the elution port.

First elution

Please perform the elution procedure as described below to obtain sterile, isotonic ^{99m}Tc pertechnetate solution from generator. The generator elution process is illustrated in Figure 1 as a guide for the elution processes.

1. The vials containing MON.TEK $^{99}Mo/^{99m}Tc$ GENERATOR and NaCl 0.9 % and the evacuated vials are prepared under aseptic conditions and pertechnetate solution that you will obtain from generator will be sterile, non-pyrogenic and isotonic.
2. Observe the aseptic working rules during elution process for safety of product and your safety.
3. Put on mask and sterile disposable gloves before starting the process.
4. Remove the generator and accompanying accessories from their packaging. Place MON.TEK $^{99}Mo/^{99m}Tc$ GENERATOR behind the lead shield inside LAF. **Do not remove** needle protector vial until you are ready to carry out the first elution.
5. Take the bottle which contains intended volume of NaCl 0.9 % solution for injection.
6. Wipe the rubber plugs of the vacuum vials and 0.9% NaCl solution vials with 70% isopropyl alcohol.
7. Remove the cover of generator and remove the vials that protect the needles (Figure 1, Position A).
8. Place the NaCl %0.9 solution vial as shown in the figure (Figure 1, Position A).
9. Select an evacuated elution vial and swab the elution vial closure using a supplied swab containing 70% isopropyl alcohol and allow drying. Prior to placing the elution vial inside the elution vial shield ensures that the vial contact surfaces of the shield have been swabbed using the swab containing 70% isopropyl alcohol provided and allow drying. Then, place elution vial inside the elution vial shield.
10. Place the prepared shield containing elution vial on the needle as shown in the figure (Figure 1, Position B). Please be sure that the needle hole of the elution vial shield fit the plunger. The plunger is an irremovable spring system. It is used for protection purposes for the needle. Otherwise needle may be damaged or broken. Push down to ensure that elution vial shield is locked with the plunger and the vial is fully located on the elution needle.
11. Elution from generator starts when elution vial shield is pushed to the bottom of the inlet and pertechnetate solution is obtained in evacuated vial. Air bubbles might form in the vial containing NaCl 0.9 % solution for injection and also the solution level in this vial will decrease.
12. After all, NaCl 0.9 % solution for injection moved, allow at least 3 minutes for the elution to proceed to completion. **Do not remove either the NaCl 0.9 % solution for injection vial or elution vial before the elution is complete.**
13. After completion of elution, pull elution vial shield vertically. A resistance may be felt before elution vial shield is detached from the plunger, keep pulling the elution vial shield vertically to overcome the resistance and remove it from the plunger. Put the label containing the elution activity, solution volume and elution time on the lead shield.
14. Leave the empty NaCl 0.9 % solution for injection vial in place until the next elution to preserve sterility.

Subsequent elution

Repeat steps from 1 to 14, using a newly sanitised NaCl 0.9 % solution for injection vial of the required volume and an elution vial.

^{99m}Tc sodium pertechnetate is taken from generator at appropriate quantity according to the

process and administered to patients through venous injection or dropping on eye and scintigraphy is performed.

Patient dosage is calculated using the factors given Table 3 and Table 4 and radioactivity value is measured before application to the patient.

As in all preparations to be applied parentally, check the ^{99m}Tc sodium pertechnetate solution physically before application to patient. Do not apply discolored or solution containing particles to patient.

Elution activity and yield of technetium-99m

MON.TEK ^{99}Mo/^{99m}Tc GENERATOR is calibrated in terms of the amount of molybdenum loaded on the column. The available technetium-99m at any time depends on the time before or after reference (due to the decay of ^{99}Mo), the time elapsed since the previous elution (due to "growth" of ^{99m}Tc) and on the decay characteristics of ^{99}Mo (86.2 % of all decay yields ^{99m}Tc). Factors listed in Tables 1 - 3 may be used to calculate the available ^{99m}Tc activity using the following method.

First, multiply the stated reference activity by the appropriate factor from Table 1 (which allows for decay of ^{99}Mo). Then multiply the product by the appropriate factor from Table 3 (which allows for the growth of ^{99m}Tc and for decay characteristics of ^{99}Mo) or if you elute once you may use Table 4 directly if you elute the generator once a day. You may use Table 2 (which allows for decay of ^{99m}Tc) to calculate the eluate activity at any time.

The actual yield of ^{99m}Tc will vary slightly due to variation in elution efficiency from generator to generator. It should typically be not less than 90% of the available ^{99m}Tc activity.

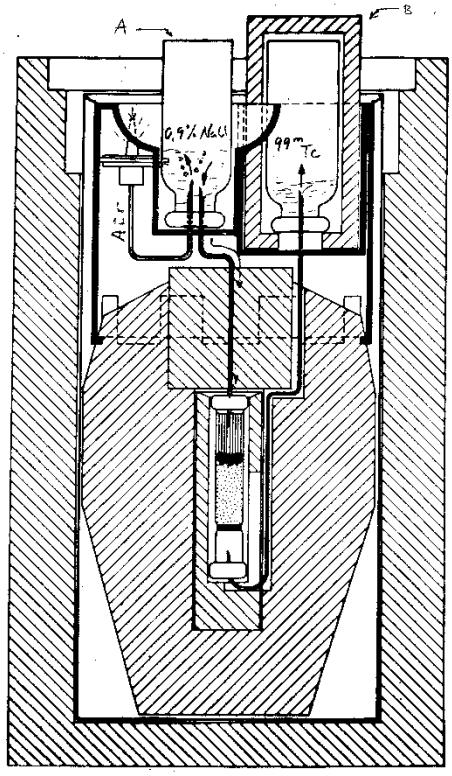


Figure 1: MON.TEK $^{99}Mo/^{99m}Tc$ GENERATOR elution diagram

Table 1: ^{99}Mo Decay table (^{99}Mo half-life 66 hour)

t (h)	0	1	2	3	4	5	6	7	8	9
0	1.0000	0.9896	0.9792	0.9690	0.9589	0.9488	0.9389	0.9291	0.9194	0.9098
10	0.9003	0.8909	0.8816	0.8724	0.8633	0.8542	0.8453	0.8365	0.8278	0.8191
20	0.8105	0.8021	0.7937	0.7854	0.7772	0.7691	0.7610	0.7531	0.7452	0.7374
30	0.7297	0.7221	0.7146	0.7071	0.6997	0.6924	0.6852	0.6780	0.6709	0.6639
40	0.6570	0.6501	0.6433	0.6366	0.6300	0.6234	0.6169	0.6104	0.6040	0.5977
50	0.5915	0.5853	0.5792	0.5731	0.5672	0.5612	0.5554	0.5496	0.5438	0.5381
60	0.5325	0.5270	0.5215	0.5160	0.5106	0.5053	0.5000	0.4948	0.4896	0.4845
70	0.4794	0.4744	0.4695	0.4646	0.4597	0.4549	0.4502	0.4454	0.4408	0.4362
80	0.4316	0.4271	0.4227	0.4182	0.4139	0.4096	0.4053	0.4010	0.3968	0.3927
90	0.3886	0.3845	0.3805	0.3765	0.3726	0.3687	0.3649	0.3611	0.3573	0.3536
100	0.3499	0.3462	0.3426	0.3390	0.3355	0.3320	0.3285	0.3251	0.3217	0.3183

Table 2: ^{99m}Tc Decay table (^{99m}Tc half-life 6,02 hour)

Min / H	0	6	12	18	24	30	36	42	48	54
0	1.0000	0.9885	0.9772	0.9660	0.9549	0.9439	0.9331	0.9224	0.9118	0.9014
1	0.8910	0.8808	0.8707	0.8607	0.8508	0.8411	0.8314	0.8219	0.8124	0.8031
2	0.7939	0.7848	0.7758	0.7669	0.7581	0.7494	0.7408	0.7323	0.7239	0.7156
3	0.7074	0.6993	0.6913	0.6833	0.6755	0.6677	0.6601	0.6525	0.6450	0.6376
4	0.6303	0.6231	0.6159	0.6089	0.6019	0.5950	0.5881	0.5814	0.5747	0.5681
5	0.5616	0.5552	0.5488	0.5425	0.5363	0.5301	0.5240	0.5180	0.5121	0.5062
6	0.5004	0.4947	0.4890	0.4834	0.4778	0.4723	0.4669	0.4616	0.4563	0.4510
7	0.4459	0.4408	0.4357	0.4307	0.4258	0.4209	0.4160	0.4113	0.4066	0.4019
8	0.3973	0.3927	0.3882	0.3838	0.3794	0.3750	0.3707	0.3664	0.3622	0.3581
9	0.3540	0.3499	0.3459	0.3419	0.3380	0.3341	0.3303	0.3265	0.3228	0.3191
10	0.3154	0.3118	0.3882	0.3047	0.3012	0.2977	0.2943	0.2909	0.2876	0.2843
11	0.2810	0.2778	0.2746	0.2715	0.2684	0.2653	0.2622	0.2592	0.2562	0.2533
12	0.2504	0.2475	0.2447	0.2419	0.2391	0.2364	0.2337	0.2310	0.2283	0.2557

Table 3: Factors allowing for growth of ^{99m}Tc at various times following the previous elution (^{99m}Tc half-life 6.02 hours)

Hour	**Factor**	**Hour**	**Factor**	**Hour**	**Factor**	**Hour**	**Factor**	**Hour**	**Factor**	**Hour**	**Factor**
1	0.094	9	0.579	17	0.788	25	0.879	33	0.918	41	0.935
2	0.179	10	0.615	18	0.804	26	0.884	34	0.921	42	0.937
3	0.256	11	0.648	19	0.818	27	0.892	35	0.924	43	0.938
4	0.324	12	0.678	20	0.831	28	0.898	36	0.926	44	0.940
5	0.386	13	0.705	21	0.843	29	0.903	37	0.929	45	0.941
6	0.442	14	0.729	22	0.853	30	0.907	38	0.930	46	0.941
7	0.492	15	0.751	23	0.863	31	0.911	39	0.932	47	0.941
8	0.538	16	0.771	24	0.871	32	0.915	40	0.934	48	0.942

Table 4: TABLE of (TC^{99m}) ACTIVITIES OBTAINED FROM MON-TEK $^{99}Mo/^{99m}Tc$ GENERATORS

GÜNLER		MON.TEK 5		MON.TEK 10		MON.TEK 15		MON.TEK 20		MON.TEK 25		MON.TEK 30		MON.TEK 35		MON.TEK 40		MON.TEK 45		MON.TEK 50	
		mCi	MBq	mCi	MBq	mCi	MBq	mCi	MBq	mCi	MBq	mCi	MBq	mCi	MBq	mCi	MBq	mCi	MBq	mCi	MBq
-6	Friday	543	20.091	1.079	39.923	1.631	60.347	2.183	80.771	2.734	101.158	3.286	121.582	3.838	142.006	4.390	162.430	4.950	183.150	5.521	204.277
-5	Saturday	418	15.466	831	30.747	1.256	46.472	1.680	62.160	2.105	77.885	2.530	93.610	2.955	109.335	3.380	125.060	3.812	141.026	4251	157.287
-4	Sunday	322	11.914	640	23.680	967	35.779	1.294	47.878	1.621	59.977	1.948	72.076	2.275	84.175	2.602	96.274	2.935	108.590	3273	121.101
-3	Monday	248	9.176	492	18.204	744	27.528	996	36.852	1.248	46.176	1.500	55.500	1.752	64.824	2.004	74.148	2.260	83.614	2520	93.240
-2	Tuesday	191	7.067	379	14.023	573	21.201	767	28.379	961	35.557	1.155	42.735	1.349	49.913	1.543	57.091	1.740	64.383	1940	71.780
-1	Wednesday	147	5.439	292	10.804	441	16.317	590	21.830	740	27.380	889	32.893	1.038	38.406	1.188	43.956	1.340	49.575	1494	55.278
0	**Thursday**	**113**	**4.181**	**225**	**8.325**	**340**	**12.580**	**455**	**16.835**	**570**	**21.090**	**685**	**25.345**	**800**	**29.600**	**915**	**33.855**	**1.032**	**38.173**	**1150**	**42.550**
+1	Friday	87	3.219	173	6.401	261	9.657	350	12.950	438	16.206	527	19.499	616	22.792	704	26.048	794	29.393	886	32.782
+2	Saturday	67	2.479	133	4.921	201	7.437	269	9.953	337	12.469	406	15.022	474	17.538	542	20.054	612	22.633	682	25.234
+3	Sunday	52	1.924	102	3.774	155	5.735	207	7.659	260	9.620	312	11.544	365	13.505	417	15.429	471	17.427	525	19.425
+4	Monday	40	1.480	79	2.923	119	4.403	159	5.883	200	7.400	240	8.880	281	10.397	321	11.877	363	13.419	404	14.948
+5	Tuesday	31	1.147	60	2.220	92	3.404	123	4.551	154	5.698	185	6.845	216	7.992	247	9.139	279	10.332	311	11.507
+6	Wednesday	24	888	46	1.702	70	2.590	94	3.478	118	4.366	142	5.254	166	6.142	190	7.030	215	7.956	240	8.880
+7	Thursday	18	666	36	1.332	54	1.998	73	2.701	91	3.367	109	4.033	128	4.736	146	5.402	166	6.126	185	6.845
+8	Friday	14	518	27	999	42	1.554	56	2.072	70	2.590	84	3.108	98	3.626	113	4.181	127	4.717	142	5.254
+9	Saturday	11	407	21	777	32	1.184	43	1.591	54	1.998	65	2.405	76	2.812	87	3.219	98	3.632	109	4.033
+10	Sunday	8	296	16	592	24	888	33	1.221	41	1.517	50	1.850	58	2.146	67	2.479	76	2.797	84	3.108
+11	Monday	6	222	12	444	19	703	25	925	32	1.184	38	1.406	45	1.665	51	1.887	58	2.154	65	2.405
+12	Tuesday	5	185	9	333	14	518	19	703	24	888	29	1.073	34	1.258	39	1.443	45	1.658	50	1.850
+13	Wednesday	4	148	7	259	11	407	15	555	19	703	22	814	26	962	30	1.110	35	1.277	38	1.406
+14	Thursday	3	111	5	185	8	296	11	407	14	518	17	629	20	740	23	851	27	983	29	1.073
+15	Friday	2	74	4	148	6	222	9	333	11	407	13	481	15	555	18	666	20	757	22	814

*Elution Activity is the activity obtained from a generator eluted at 8 A.M by at least 5 ml sodium chloride 9 mg/ml (0.9%) solution for injection that is not eluted during 24 hours.

** The activities to be obtained are the 90-110% of the given activity amounts.