Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

MONTEK 10-40 GBq radionuclide generator

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Sodium pertechnetate (^{99m}Tc) injection is produced by means of a (^{99}Mo/^{99m}Tc) generator. Technetium (^{99m}Tc) decays with the emission of gamma radiation with a mean energy of 140 keV and a half-life of 6.01 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 radionuclide generator containing the parent isotope ^{99}Mo, adsorbed on a chromatographic column delivers sodium pertechnetate (^{99m}Tc) injection in sterile solution.

The ^{99}Mo on the column is in equilibrium with the formed daughter isotope ^{99m}Tc. The generators are supplied with the following ^{99}Mo activity amounts at activity reference time which deliver the following technetium (^{99m}Tc) amounts, assuming a 100% theoretical elution yield and 24 hours time from previous elution and taking into account that branching ratio of ^{99}Mo is about 87%:

^{99m}Tc activity (Maximal theoretical eluable activity at calibration date, 8 A.M. GMT +3)	8.3	12.6	16.8	21.1	25.3	29.6	33.9	GBq
^{99}Mo activity (at calibration date, 8 A.M. GMT +3)	10	15	20	25	30	35	40	GBq

The technetium (^{99m}Tc) amounts available by a single elution depend on the real yields of the kind of generator used itself declared by manufacturer and approved by NCA.

Excipient(s) with known effect
Each mL of sodium pertechnetate (^{99m}Tc) solution contains 3.54 mg of sodium.

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Radionuclide generator.

Plastic covered cylindrical body and closure, attached to the body with 2 clamps, with a holder on top.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

The eluate from the radionuclide generator (sodium pertechnetate (^{99m}Tc) injection) is indicated for: labelling of various kits for radiopharmaceutical preparation developed and approved for radiolabelling with such solution.

Thyroid scintigraphy: direct imaging and measurement of thyroid uptake to give information on the size, position, nodularity and function of the gland in case of thyroid disease.

Salivary gland scintigraphy: diagnosis of chronic sialadenitis (e.g. (Sjögren's Syndrom) as well as assessment of salivary gland function and duct patency in salivary glands disorders and monitoring of the response to therapeutic interventions (in particular radio iodine therapy).

Location of ectopic gastric mucosa (Meckel's diverticulum).

Lacrimal duct scintigraphy: to assess functional disorders of lacrimation and monitoring of the response to therapeutic interventions

4.2 Posology and method of administration

Posology

If sodium pertechnetate (^{99m}Tc) solution is administered intravenously, activities may vary widely according to the clinical information required and the equipment employed. The injection of activities greater than local DRLs (Diagnostic Reference Levels) should be justified for certain indications. Recommended activities are as follows:

Adults (70 kg) and the elderly population

- Thyroid scintigraphy: 20 -80MBq
- Salivary gland scintigraphy: 30 to 150 MBq for static images up to 370 MBq for dynamic images
- Meckel's diverticulum scintigraphy: 300 - 400MBq
- Lacrimal duct scintigraphy: 2 - 4 MBq per drop per eye

Renal impairment

Careful consideration of the activity to be administered is required since an increased radiation exposure is possible in these patients.

Paediatric 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 may be calculated according to the recommendations of European Association Nuclear Medicine (EANM) paediatric dosage card; the activity administered to children and to adolescents may be calculated by multiplying a baseline activity (for calculation purposes) by the weight-dependent correction factor given in the table below (see Table 1):

$$A[MBq]_{Administered} = \text{Baseline Activity} \times \text{Multiple}$$

Thyroid scintigraphy: Activity administered [MBq] = 5.6 MBq x correction factor (Table 1). A minimal activity of 10 MBq is necessary for obtaining images of sufficient quality.

Identification/location of ectopic gastric mucosa: Activity administered [MBq] = 10.5 MBq x correction factor (Table 1). A minimal activity of 20 MBq is necessary in order to obtain images of sufficient quality.

Table 1: Weight-dependent correction factors in the paediatric population (for thyroid scintigraphy and identification/location of ectopic gastric mucosa) according to the EANM-May 2008 guidelines

Weight [kg]	Multiple	**Weight [kg]**	Multiple	**Weight [kg]**	Multiple
3	1	**22**	5.29	**42**	9.14
4	1.14	**24**	5.71	**44**	9.57
6	1.71	**26**	6.14	**46**	10.00
8	2.14	**28**	6.43	**48**	10.29
10	2.71	**30**	6.86	**50**	10.71
12	3.14	**32**	7.29	**52-54**	11.29
14	3.57	**34**	7.72	**56-58**	12.00
16	4.00	**36**	8.00	**60-62**	12.71
18	4.43	**38**	8.43	**64-66**	13.43
20	4.86	**40**	8.86	**68**	14.00

Salivary gland scintigraphy: The Paediatric Task Group of EANM (1990) recommends that the activity to be administered to a child should be calculated from the body weight according to the table below (see Table 2) with a minimum dose of 10 MBq in order to obtain images of sufficient quality.

Table 2: Weight-dependent correction factor in the paediatric population (for salivary gland scintigraphy) according to EANM 1990 recommendations

Weight [kg]	Factor	**Weight [kg]**	Factor	**Weight [kg]**	Factor
3	0.1	**22**	0.50	**42**	0.78

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

Lacrimal duct scintigraphy: Recommended activities apply as well for adults as for children.

Method of administration
For intravenous or ocular use.

For multidose use.

For instructions on extemporaneous preparation of the medicinal product before administration, see section 12.

For patient preparation, see section 4.4.

In thyroid scintigraphy, salivary gland scintigraphy and identification/location of ectopic gastric mucosa, the sodium pertechnetate (^{99m}Tc) solution is administered by intravenous injection.

In lacrimal duct scintigraphy, drops are instilled in each eye (ocular use).

Image acquisition

Thyroid scintigraphy: 20 minutes after intravenous injection.

Salivary gland scintigraphy: immediately after intravenous injection and at regular intervals for 15 minutes.

Identification/location of ectopic gastric mucosa (Meckel's Diverticulum): immediately after intravenous injection and at regular intervals for 30 minutes.

Lacrimal duct scintigraphy: dynamic acquisition within 2 minutes after instillation, followed by static images acquired at regular intervals within 20 minutes.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

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 section 11).

Thyroid blocking is of special importance in the paediatric patient population except for thyroid scintigraphy.

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.

To avoid false positives or to minimise irradiation by reduction of pertechnetate accumulation in the thyroid and salivary glands, a thyroid blocking agent should be given prior to lacrimal duct scintigraphy or Meckel's diverticulum scintigraphy. Conversely a thyroid blocking agent must NOT be used before thyroid, parathyroid or salivary glands scintigraphy.

Before the application of sodium pertechnetate (^{99m}Tc) solution for scintigraphy of Meckel's diverticulum the patient must keep an empty stomach for 3 to 4 hours to reduce intestinal peristalsis.

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

After the procedure

Close contact with infants and pregnant women should be restricted during 12 hours.

Specific warnings

Sodium pertechnetate (^{99m}Tc) solution for injection contains 3.54 mg/ml of sodium.

Depending on the time when the injection is administered, the content of sodium given to the patient may in some cases be greater than 1 mmol (23 mg). This should be taken into account in patient on low sodium diet.

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.

In salivary gland scintigraphy a lower specificity of the method should be expected compared to magnetic resonance sialography.

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

4.5 Interactions with other medicinal products and other forms of interaction

Atropine, isoprenaline and analgesics may cause a delay in gastric emptying and thereby cause a redistribution of (^{99m}Tc) pertechnetate in abdominal imaging.

Administration of laxatives should be withheld since they irritate the gastrointestinal tract. Contrast-enhanced studies (e.g. barium) and upper gastro-intestinal examination should be avoided within 48h prior to administration of pertechnetate (^{99m}Tc) for Meckel's diverticulum scintigraphy.

Many pharmacological medicinal products are known to modify the thyroid uptake.

- antithyroid medicinal products (e.g. carbimazole or other imidazole derivatives such as propylthiouracil), salicylates, steroids, sodium nitroprusside, sodium sulfobromophtalein, perchlorate should be withheld for 1 week prior thyroid scintigraphy;
- phenylbutazone and expectorants should be withheld for 2 weeks;
- natural or synthetic thyroid preparations (e.g. sodium thyroxine, sodium liothyronine, thyroid extract) should be withheld for 2-3 weeks
- amiodarone, benzodiazepines, lithium should be withheld for 4 weeks
- intravenous contrast agents should not have been administered within 1-2 months.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

When an administration of radiopharmaceuticals to a woman of childbearing potential, is intended, it is important to determine whether or not she is pregnant. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. If in doubt about her potential pregnancy (if the woman has missed a period, if the period is very irregular, etc.), alternative techniques not using ionising radiation (if there are any) should be offered to the patient.

Pregnancy

Administration of pertechnetate (^{99m}Tc) to a woman who is known to be pregnant should be justified by medical need and a positive individual benefit risk assessment for the mother and the foetus.
Alternative non-irradiating diagnostic modalities should be taken into account.

^{99m}Tc (as free pertechnetate) has been shown to cross the placental barrier.

Breast-feeding

Before administering radiopharmaceuticals to a woman who is breast-feeding, consideration should be given to the possibility of delaying the administration of radionuclide until the mother has ceased breast-feeding and to what is the most appropriate choice of radiopharmaceuticals, bearing in mind the secretion of activity in breast milk. If the administration is considered necessary, breast-feeding should be interrupted for 12 hours post administration and the expressed feeds discarded.

Close contact with infants should be restricted during this period.

4.7 Effects on ability to drive or use machines

Sodium pertechnetate (^{99m}Tc) solution has no influence on the ability to drive and use machines.

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) from the MONTEK radionuclide 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.

Tabulated list of adverse reactions

The frequencies of undesirable effects are defined as follows:

Not known (cannot be estimated from the available data).

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)

* Adverse reactions derived from spontaneous reporting

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose is 5.2 mSv when the maximal recommended activity of 400 MBq is administered these adverse reactions are expected to occur with a low probability.

Description of selected adverse reactions

Anaphylactic reactions (e.g. dyspnoea, coma, urticaria, erythema, rash, pruritus, oedema at various locations [e.g. face oedema])

Anaphylactic reactions have been reported following intravenous injection of sodium perchtechnetate (^{99m}Tc) and include various skin or respiratory symptoms like skin irritations, oedema, or dyspnoea.

Vegetative reactions (nervous system and gastrointestinal disorders)

Single cases of severe vegetative reactions have been reported, however, most of the reported vegetative reactions include gastrointestinal reactions like nausea or vomiting. Other reports include vasovagal reactions like headache or dizziness. Vegetative reactions are rather considered to be related to the examinational setting than to technetium (^{99m}Tc), especially in anxious patients.

General disorders and administration site conditions

Other reports describe local injection site reactions. Such reactions are related to extravasation of the radioactive material during the injection, and the reported reactions rank from local swelling up to cellulitis. Depending on the administered radioactivity and the labeled compound, extended extravasation may necessitate surgical treatment.

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 listed Appendix V.

4.9 Overdose

In the event of the administration of a radiation overdose with sodium pertechnetate (^{99m}Tc), the absorbed dose should be reduced where possible by increasing the elimination of the radionuclide from the body by defaecation, forced diuresis and frequent bladder voiding.

The uptake in the thyroid, salivary glands and the gastric mucosa can be significantly reduced when sodium or potassium 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, various thyroid diagnostic radiopharmaceuticals, ATC code: V09FX01

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

5.2 Pharmacokinetic 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 eliminated, 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. With intact blood brain barrier, sodium pertechnetate (^{99m}Tc) does not penetrate into the brain tissue.

Organ uptake

In the blood 70-80% of the intravenously injected sodium pertechnetate (^{99m}Tc) is bound to proteins, primarily in an unspecific way to albumin. The unbound fraction (20-30%) accumulates temporarily in thyroid and salivary glands, stomach and nasal mucous membranes as well as in the plexus chorioideus.

Sodium pertechnetate (^{99m}Tc) in contrast to iodine, nevertheless, is neither used for the thyroid hormone synthesis (organification), nor absorbed in the small intestine. In the thyroid the maximum accumulation, depending on functional status and iodine saturation (in euthyroidism approx. 0.3-3%, in hyperthyroidism and iodine depletion up to 25%) is reached about 20 min after injection and then decreases quickly. This also applies for the stomach mucous membrane parietal cells and the salivary glands acinar cells.

In contrast to the thyroid which releases sodium pertechnetate (^{99m}Tc) in the bloodstream, the salivary glands and the stomach secrete sodium pertechnetate (^{99m}Tc) in the saliva and gastric juice, respectively. The accumulation by the salivary gland lies in the magnitude of 0.5% of the applied activity with the maximum reached after about 20 minutes. One hour after injection, the concentration in the saliva is about 10-30 fold higher than in the plasma. The excretion can be accelerated by lemon juice or by stimulation of the parasympathetic nerve system, the absorption is reduced by perchlorate.

Elimination

Half life in plasma is approximately 3 hours. Sodium pertechnetate (^{99m}Tc) is not metabolised in the organism. One fraction is eliminated very quickly renally, the rest more slowly via faeces, salivary and tear liquid. 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 preadministration of blocking agents, excretion follows the same pathways but there is a higher renal clearance.

The above data are not valid when sodium pertechnetate (^{99m}Tc) is used for labeling of another radiopharmaceutical.

5.3 Preclinical safety data

There is no information on acute, subacute and chronic toxicity from single or repeated dose administration. The quantity of sodium pertechnetate (^{99m}Tc) administered during clinical diagnostic procedures is very small and, apart from allergic reactions, no other adverse reactions have been reported.

This medicinal product is not intended for regular or continous administration.

Mutagenicity studies and long-term carcinogenicity studies have not been carried out.

Reproductive toxicity

Placental transfer of ^{99m}Tc from intravenously administered sodium pertechnetate (^{99m}Tc) has been studied in mice. The pregnant uterus was found to contain as much as 60% of the injected ^{99m}Tc when administered without perchlorate pre-administration. Studies performed on pregnant mice during gestation, gestation and lactation, and lactation alone showed changes in progeny which included weight reduction, hairlessness and sterility.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Aluminium oxide
Molybdenum trioxide
Sodium hydroxide
Hydrogen peroxide 30 %
Sodium hydroxide 1 M (pH adjustment)
Hydrochloric acid 4 M (pH adjustment)
Hydrochloric acid 1 M (pH adjustment)
Sodium chloride 9 mg/ml (0.9%) solution for injection
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except for those mentioned in section 12.

6.3 Shelf life

Generator: 21 days from manufacturing date.

The calibration date and the expiry date are stated on the label.

Sodium pertechnetate (^{99m}Tc) eluate: After elution, use within 8 hours.

Elution vials: 24 months.

Solution for elution: 24 months.

6.4 Special precautions for storage

Store the generator and the eluate, Sodium Pertechnetate (^{99m}Tc) Injection below 25^{o}C in the original package. Do not freeze.

Eluate: For storage conditions after elution of the medicinal product, see section 6.3.

Storage of radiopharmaceuticals should be in accordance with national regulation on radioactive materials.

6.5 Nature and contents of container

Primary packaging

Radionuclide Generator: Type I, colourless, natural glass column and bromobutyl rubber stopper, aluminium cap, stainless steel needle set.
Evacuated vial: 20 ml colourless, Type I natural glass vial and bromobutyl rubber stopper, aluminium cap.
Sodium chloride 9 mg/ml (0.9%) solution for injection. 5 ml, 10 ml: colourless, 20 ml, Type I natural glass vial and bromobutyl rubber stopper, aluminium cap.

Secondary packaging

Radionuclide generator: Lead shield
Evacuated vial: cardboard box
Sodium chloride 9 mg/ml (0.9%) solution for injection of 5 ml, 10 ml: cardboard box

Accessories available
Sodium chloride 9mg/ml (0.9%) solution for injection eluent vials
The sodium chloride 9 mg/ml (0.9%) solution for injection eluent is available in 2 different volumes giving elution volumes of 5 ml and 10 ml to allow the generator eluate to be collected at varying radioactive concentrations.

Packs of 5 vials containing 5 ml and 5 vials containing10 ml of sodium chloride 9 mg/ml (0.9 %) solution for injection.

The following options are available according to custom order:
Packs of 10 vials containing 5 ml sodium chloride 9 mg/ml (0.9%) solution for injection or 10 vials containing 10 ml sodium chloride 9 mg/ml (0.9%) solution for injection. Vials are packed in 5 vial cartons.

Evacuated elution vials
Packs of 10 vials. Vials are packed in 5 vial cartons.

6.6 Special precautions for disposal and other handling

General warnings

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 competent official organisation.

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

If at any time the integrity of the generator or the vial with the eluted solution is compromised, it should not be used.

Administration procedures should be carried out in a way to minimise risk of contamination of the medicinal product and irradiation of the operators. Adequate shielding is mandatory.

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.

The residual activity of the generator must be estimated before disposal.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORIZATION HOLDER

Monrol Europe SRL
Pantelimon, Str. Gradinarilor, nr.1
ILFOV
Romania

8. MARKETING AUTHORIZATION NUMBER

[To be completed nationally]

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF AUTHORIZATION

Date of first authorisation:
Date of latest renewal:

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

11. DOSIMETRY

The data listed below are from ICRP 80 and are calculated according to the following assumptions:

(I) Without pre-treatment with a blocking agent:

Organ	**Absorbed dose per administered unit of activity (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
Gastrointestinal 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
-Colon	0.042	0.054	0.088	0.14	0.27
-Ascending colon wall	0.057	0.073	0.12	0.20	0.38
-Descending colon 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 bone 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 tissue	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 a blocking agent:

Organ	**Absorbed dose per administered unit activity (mGy/MBq) when blocking agents are administered**				
	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
Gastrointestinal 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
-Colon	0.0036	0.0048	0.0071	0.010	0.018
-Ascending colon wall	0.0032	0.0043	0.0064	0.010	0.017

-Descending colon 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 bone 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 tissue	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 resulting from the intravenous administration of 400 MBq of sodium pertechnetate (^{99m}Tc) to an adult weighing 70 kg is about 5.2 mSv.

After pretreatment of patients with a blocking agent and administration of 400 MBq of sodium pertechnetate (^{99m}Tc) to an adult weighing 70 kg the effective dose is 1.7 mSv.

The radiation dose absorbed by the lens of the eye following administration of sodium pertechnetate (^{99m}Tc) 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 pertechnetate (^{99m}Tc) 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.

The surface dose rates and the accumulated dose depends on many factors. Overall, radiation measurements on the environment and during work are critical and should be practised.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Elution of the generator must be performed in premises complying with the national regulations concerning the safety of use of radioactive products.

The solution eluted is a clear and colourless sodium pertechnetate (^{99m}Tc) solution, with a pH between 4.0 and 8.0 and a radiochemical purity equal to or greater than 95% of the total radioactivity due to ^{99m}Tc.

When sodium pertechnetate (^{99m}Tc) solution is used for kit labelling, please refer to the package leaflet of the concerned kit.

Quality control
Radioactivity and the molybdenum (^{99}Mo) break-through must be checked before administration.

The test for molybdenum (^{99}Mo) break-through can be performed either according to Ph. Eur. or to any other validated methods able to determine a molybdenum (^{99}Mo) content below 0.1 per cent of total radioactivity at the date and hour of administration.

The first eluate obtained from this generator can be normally used, unless otherwise specified. Eluates even eluted later than 24 hours from the last elution can be used for kit labelling, unless it is excluded by the specifications of the relevant kit SmPC.

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

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.

Instructions for elution of the MONTEK 10-40 GBq Radionuclide generator

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) solution, is achieved by placing a sterile evacuated vial onto the elution port.

First elution

1. Remove the generator and accompanying accessories from their packaging. Place the generator on a flat, level surface, in a suitably authorised and shielded location. **Do not remove** needle protector vial until you are ready to carry out the first elution.

2. Select a sodium chloride 9 mg/ml (0.9%) solution for injection vial containing the required volume of sodium chloride 9 mg/ml (0.9%) solution for injection.

3. Remove the flip-top from the sodium chloride 9 mg/ml (0.9%) solution for injection vial and swab the sodium chloride 9 mg/ml (0.9%) solution for injection vial closure using a supplied swab containing 70% isopropyl alcohol and allow drying.

4. Remove the needle protector vial.

5. Place the sodium chloride 9 mg/ml (0.9%) solution for injection vial onto this needle, ensuring that it is fully pushed to the bottom of the inlet well.

6. 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 provided and allow drying. Then, place elution vial inside the elution vial shield.

7. Place the prepared shield containing elution vial on the needle. 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 locked with the plunger and the vial is fully located on the elution needle

8. You may realize air bubbles on the sodium chloride 9 mg/ml (0.9%) solution for injection vial and also you may realize the solution level in this vial is decreasing. Allow at least 3 minutes for the elution to proceed to completion. **Do not remove either the sodium chloride 9 mg/ml (0.9%) solution for injection vial or elution vial before the elution is complete.**

9. 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.

10. Leave the empty sodium chloride 9 mg/ml (0.9%) solution for injection vial in place until the next elution to preserve sterility.

Subsequent elution

Using a new sanitised sodium chloride 9 mg/ml (0.9%) solution for injection vial of the required volume and an elution vial repeat steps 1–10.

Elution activity and yield of technetium-99m

MONTEK 10-40 GBq radionuclide generator is calibrated in terms of the amount of molybdenum loaded on the column. The available ^{99m}Tc 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 3 - 5 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 3 (which allows for decay of ^{99}Mo). Then multiply the product by the appropriate factor from Table 5 (which allows for the growth of ^{99m}Tc and for decay characteristics of ^{99}Mo) or if you elute once you may use Table 6 directly if you elute the generator once a day. You may use Table 4 (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.

Table 3 ^{99}Mo decay Table (^{99}Mo half-life 66 hours)

T (hours)	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 4 ^{99m}Tc decay Table (^{99m}Tc half-life 6.01hours)

Min. / Hour	**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 5 Factors allowing for growth of ^{99m}Tc at various times following the previous elution

(^{99m}Tc half-life 6.01 hours)

Hours	Factor	Hours	Factor	Hours	Factor	Hours	Factor	Hours	Factor	Hours	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 6: TABLE of (^{99m}Tc) ACTIVITIES OBTAINED FROM MONTEK 10-40 GBq RADIONUCLIDE GENERATORS

DAYS		MONTEK 10		MONTEK 15		MONTEK 20		MONTEK 25		MONTEK 30		MONTEK 35		MONTEK 40	
		mCi	MBq	mCi	MBq	mCi	MBq	mCi	MBq	mCi	MBq	mCi	MBq	mCi	MBq
-6	Friday	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
-5	Saturday	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
-4	Sunday	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
-3	Monday	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	Tuesday	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	Wednesday	292	10,804	441	16,317	590	21,830	740	27,380	889	32,893	1,038	38,406	1,188	43,956
0	**Thursday**	**225**	**8,325**	**340**	**12,580**	**455**	**16,835**	**570**	**21,090**	**685**	**25,345**	**800**	**29,600**	**915**	**33,855**
+1	Friday	173	6,401	261	9,657	350	12,950	438	16,206	527	19,499	616	22,792	704	26,048
+2	Saturday	133	4,921	201	7,437	269	9,953	337	12,469	406	15,022	474	17,538	542	20,054
+3	Sunday	102	3,774	155	5,735	207	7,659	260	9,620	312	11,544	365	13,505	417	15,429
+4	Monday	79	2,923	119	4,403	159	5,883	200	7,400	240	8,880	281	10,397	321	11,877
+5	Tuesday	60	2,220	92	3,404	123	4,551	154	5,698	185	6,845	216	7,992	247	9,139
+6	Wednesday	46	1,702	70	2,590	94	3,478	118	4,366	142	5,254	166	6,142	190	7,030
+7	Thursday	36	1,332	54	1,998	73	2,701	91	3,367	109	4,033	128	4,736	146	5,402
+8	Friday	27	999	42	1,554	56	2,072	70	2,590	84	3,108	98	3,626	113	4,181
+9	Saturday	21	777	32	1,184	43	1,591	54	1,998	65	2,405	76	2,812	87	3,219
+10	Sunday	16	592	24	888	33	1,221	41	1,517	50	1,850	58	2,146	67	2,479
+11	Monday	12	444	19	703	25	925	32	1,184	38	1,406	45	1,665	51	1,887
+12	Tuesday	9	333	14	518	19	703	24	888	29	1,073	34	1,258	39	1,443
+13	Wednesday	7	259	11	407	15	555	19	703	22	814	26	962	30	1,110
+14	Thursday	5	185	8	296	11	407	14	518	17	629	20	740	23	851
+15	Friday	4	148	6	222	9	333	11	407	13	481	15	555	18	666

*Elution Activity is the activity obtained from a generator eluted at 8 A.M (GMT +3) 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.