

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

ELUMATIC III 2-20 GBq radionuclide generator

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Sodium pertechnetate (^{99m}Tc) injection is produced by means of a (⁹⁹Mo/^{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 (⁹⁹Tc) which, in view of its long half-life of 2.13 x 10⁵ years, can be regarded as quasi stable.

The radionuclide generator containing the parent isotope ⁹⁹Mo, adsorbed to a chromatographic column delivers sodium pertechnetate (^{99m}Tc) injection in sterile solution.

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

^{99m} Tc activity (Maximal theoretical eluable activity at calibration date, 12h CET)	2	4	6	8	10	12	16	20	GBq
⁹⁹ Mo activity (at calibration date, 12h CET)	2.5	5	7	9.5	12	14.5	19	24	GBq

Excipient with known effect:

Each mL of sodium pertechnetate (^{99m}Tc) solution contains 3.6 mg of sodium.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Radionuclide generator.

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 radioiodine 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) 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 elderly population:

- Thyroid scintigraphy: 20–80 MBq.
- Salivary gland scintigraphy: 30 to 150 MBq for static images up to 370 MBq for dynamic images.
- Meckel's diverticulum scintigraphy: 300-400 MBq
- 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 must be adapted and may be calculated according to the recommendations of the European Association of Nuclear Medicine (EANM) paediatric dosage card, by multiplying a baseline activity (for calculation purposes) by the weight-dependent correction factor given in the table below (see Table 1).

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

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 minimal adult posology and adapted to the child body weight according to the table below (see Table 2) with a minimum activity 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: 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, the radiation exposure must be justifiable by the likely benefit. The activity administered should in every case be 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, except for thyroid scintigraphy, is of special importance in the paediatric patient 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.

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 should 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 3.6 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 Interaction with other medicinal products and other forms of interaction

Atropine, isoprenaline and analgesics may cause a delay of 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 48 h 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 sulfobromophthalein, 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 child-bearing potential

Where an administration of radiopharmaceuticals to a woman of child-bearing 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.

Breastfeeding

Before administering radiopharmaceuticals to a mother who is breastfeeding, consideration should be given to the possibility of delaying the administration of radionuclide until the mother has ceased breastfeeding, 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, breastfeeding 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 and use machines

No studies on the effects 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) from the Elumatic III radionuclide generator is used for radioactive labelling 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 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.

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 disorders

Frequency not known*: Anaphylactoid reactions (e.g. dyspnoea, coma, urticaria, erythema, rash, pruritus, oedema at various location e.g. face oedema)

Nervous system disorders

Frequency not known*: Vasovagal reactions (e.g. syncope, tachycardia, bradycardia, dizziness, headache, vision blurred, flushing)

Gastrointestinal disorders

Frequency not known*: Vomiting, nausea, diarrhoea

General disorders and administration site conditions

Frequency not known*: 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 pertechnetate (^{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 examination 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 labelled 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:

HPRA Pharmacovigilance

Earlsfort Terrace

IRL - Dublin 2

Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpra.ie

4.9 Overdose

In the event of 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 defecation, 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 ($^{99\text{m}}\text{Tc}$) 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 ($^{99\text{m}}\text{Tc}$) in glandular structures is inhibited by the pre-administration of blocking agents, excretion follows the same pathways but there is a higher renal clearance.

The above data are not valid when sodium pertechnetate ($^{99\text{m}}\text{Tc}$) is used for labelling 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 ($^{99\text{m}}\text{Tc}$) 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 continuous administration.

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

Reproductive toxicity

Placental transfer of $^{99\text{m}}\text{Tc}$ from intravenously administered sodium pertechnetate ($^{99\text{m}}\text{Tc}$) has been studied in mice.

The pregnant uterus was found to contain as much as 60% of the injected $^{99\text{m}}\text{Tc}$ 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

- Bag of solution for elution:
 - Sodium chloride
 - Sodium nitrate
 - Water for injection
- Elution vials:
 - Nitrogen under reduced pressure

6.2 Incompatibilities

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

6.3 Shelf life

Generator: 20 days from manufacturing date.

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

Sodium pertechnetate ($^{99\text{m}}\text{Tc}$) eluate: after elution, store in a refrigerator ($2^{\circ}\text{C} - 8^{\circ}\text{C}$) and use within 10 hours.

Elution vials: 24 months.

6.4 Special precautions for storage

Generator: Do not store above 25°C . Store preferably inside the specific lead shielding for storage and elution "PROTEC-ELU" (available on request), or behind a lead shielding of appropriate thickness.

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.

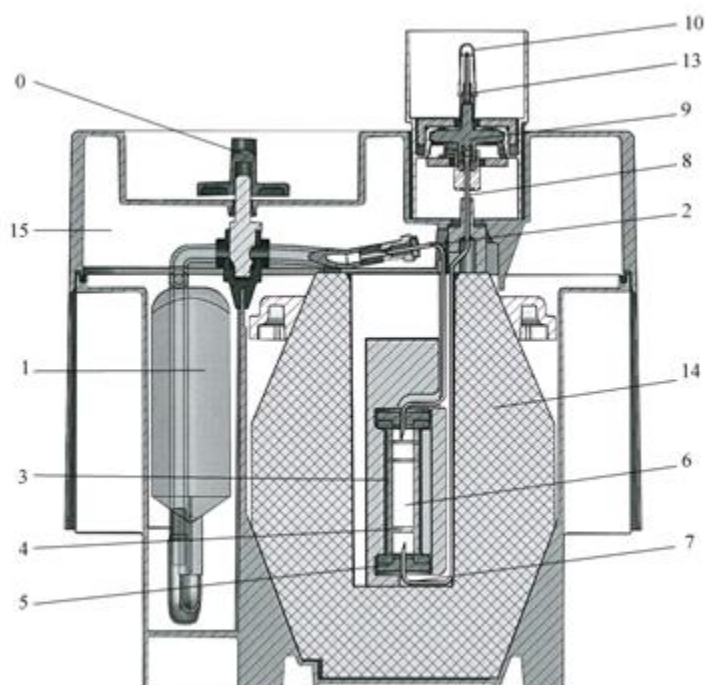
6.5 Nature and contents of container

The generator ELUMATIC III includes:

- A supple plastic bag (1) containing the eluent (0.9% sodium chloride and 0.005 % sodium nitrate aqueous solution). The bag is connected by a stainless needle (2) to the top of the chromatographic column.
- A glass chromatographic column (3) with a filter at the bottom (4) to prevent any leakage of alumina. The column is obturated at both ends by caps maintained by metallic capsules (5). This column contains the alumina (6) which adsorbs the molybdate ions and is inert towards the pertechnetate ions.
- A needle with one end connected to the bottom of the column (7). The other end (8) is connected to a sterilising filtration assembly (9). The sterility of the elution needle (13) of the assembly is secured by a protective cap (10).

The column and the needles are protected by a cylindro-conical lead shielding (14) with a minimal thickness of 52 mm. The whole system is placed in a parallelepipedic cover (23 x 21 x 14 cm) made of moulded nylon (15).

Near the elution station is a cavity with a safety valve (0) turned off during the transport (O).



The generator is delivered in a tight metal drum and includes:

- Ten sterilised needle caps, for single use only
- A packet of ten 15 mL elution vials (TC-ELU 5), sterile, pyrogen-free and under partial vacuum allowing elution of 5 mL.

An elution container is supplied with the first order.

Elution vials are 15 mL, colourless, European Pharmacopeia type I, drawn glass vial, closed with chlorobutyl rubber stoppers and aluminium capsules.

Pack size: the generator contains 2, 4, 6, 8, 10, 12, 16 or 20 GBq of sodium pertechnetate (^{99m}Tc) at calibration date.

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 spills 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 AUTHORISATION HOLDER

CIS bio international
B.P. 32 – 91192
Gif-sur-Yvette Cedex
France

8 MARKETING AUTHORISATION NUMBER

PA 0677/010/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 03 April 1998

Date of last renewal: 03 April 2008

10 DATE OF REVISION OF THE TEXT

December 2016

11 DOSIMETRY

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

(i) Without pre-treatment with blocking agent:

Organ	Absorbed dose per unit activity administered (mGy/MBq)				
	Adults	15 years	10 years	5 years	1 year
Adrenals	0.0037	0.0047	0.0072	0.011	0.019
Bladder	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
Gall bladder	0.0074	0.0099	0.016	0.023	0.035
Gastro-intestinal tract					
Stomach	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
Upper large intestine	0.057	0.073	0.12	0.20	0.38
Lower large intestine	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
Remaining organs	0.0035	0.0043	0.0064	0.0096	0.017
Effective dose (mSv/MBq)	0.013	0.017	0.026	0.042	0.079

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.

(ii) With pre-treatment with blocking agent:

Organ	Absorbed dose per unit activity administered (mGy/MBq) when blocking agents are given				
	Adults	15 years	10 years	5 years	1 year
Adrenals	0.0029	0.0037	0.0056	0.0086	0.016
Bladder	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
Gall bladder	0.0030	0.0042	0.0070	0.010	0.013
Gastro-intestinal tract					
Stomach	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
Upper large intestine	0.0032	0.0043	0.0064	0.010	0.017
Lower large intestine	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
Remaining organs	0.0025	0.0031	0.0048	0.0073	0.013
Effective dose (mSv/MBq)	0.0042	0.0054	0.0077	0.011	0.019

After pre-treatment 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 about 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 (^{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.

The surface dose rates and the accumulated dose depend 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 5 and 7 and a radiochemical purity equal to or greater than 95%.

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

Elution

Usual precautions regarding sterility and radiation safety should be respected.
Disinfect the stopper of elution vials before each elution.

Warning:

Do not use ethanol or ethyl ether to disinfect the needle or the stopper of the elution vial, as this may interfere with the elution process.

Between two elutions, protect the elution needle (13) from possible bacterial contamination by placing one of the ten sterilised needle caps (12) over this needle.

Observe the following sequences to obtain satisfactory results.

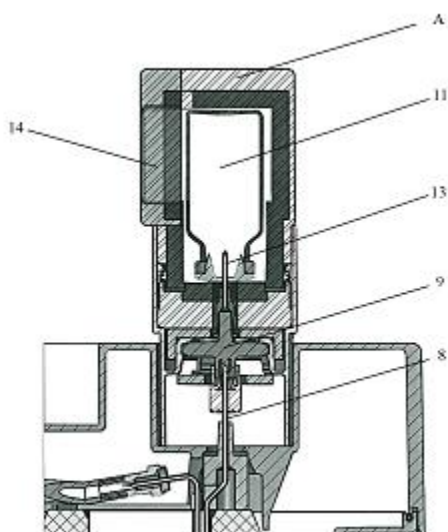
First elution:

When starting using the generator, OPEN the safety valve (n° 0 : ⊕), BEFORE putting the elution vial in place. NEVER turn off the valve between two elutions. Turn it off only when the generator is not being used any more.

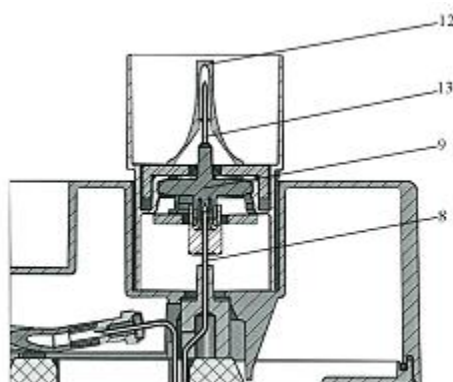
To elute the generator, replace the protective cap of the elution needle (10) by the elution container (A) with an elution vial (11) corresponding to the elution volume required.

The elution may be observed through the lead glass window (14) of container (A). Wait for at least 3 minutes for total elution.

Before use, check the clarity of the eluate. If the eluate is not clear, it should be discarded.



After elution, immediately replace the elution vial in the container (A) by one of the sterilised needle caps (12) over the needle.

**Elution volumes**

The generator ELUMATIC III is designed to elute all the available technetium-99m activity in 5 mL. Fractionated elutions are therefore unnecessary. On the other hand, elution may be performed in larger volumes such as 10 or 15 mL.

Possibilities of use

The activity quoted on the label of the ELUMATIC III is expressed in available technetium-99m at the calibration time (12 h CET).

The available activity of technetium-99m depends on:

- the molybdenum-99 activity at the time of elution;
- the time elapsed since the last elution was performed.

The maximal radioactivity of eluable sodium pertechnetate (^{99m}Tc) for each content of generator can be determined by reference to the following table:

Table 3:

Days GBq	-8	-7	-6	-5	-4	-3	-2	-1	0	+1	+2	+3	+4	+5	+6	+7	+8	+9	+10	+11	+12	+13	+14
2	15.02	11.67	9.07	7.05	5.48	4.26	3.31	2.57	2	1.55	1.21	0.94	0.73	0.57	0.44	0.34	0.27	0.21	0.16	0.13	0.10	0.08	0.06
4	30.03	23.34	18.14	14.10	10.96	8.52	6.62	5.15	4	3.11	2.42	1.88	1.46	1.13	0.88	0.69	0.53	0.41	0.32	0.25	0.19	0.15	0.12
6	45.05	35.01	27.21	21.15	16.44	12.78	9.93	7.72	6	4.66	3.62	2.82	2.19	1.70	1.32	1.03	0.80	0.62	0.48	0.38	0.29	0.23	0.18
8	60.07	46.69	36.29	28.20	21.92	17.04	13.24	10.29	8	6.22	4.83	3.76	2.92	2.27	1.76	1.37	1.07	0.83	0.64	0.50	0.39	0.30	0.24
10	75.08	58.36	45.36	35.25	27.40	21.30	16.55	12.87	10	7.77	6.04	4.70	3.65	2.84	2.20	1.71	1.33	1.04	0.80	0.63	0.49	0.38	0.29
12	90.10	70.03	54.43	42.31	32.88	25.56	19.86	15.44	12	9.33	7.25	5.63	4.38	3.40	2.65	2.06	1.60	1.24	0.96	0.75	0.58	0.45	0.35
16	120.13	93.37	72.57	56.41	43.84	34.08	26.49	20.59	16	12.44	9.67	7.51	5.84	4.54	3.53	2.74	2.13	1.66	1.29	1.00	0.78	0.60	0.47
20	150.16	116.71	90.72	70.51	54.80	42.59	33.11	25.73	20	15.54	12.08	9.39	7.30	5.67	4.41	3.43	2.66	2.07	1.61	1.25	0.97	0.76	0.60

Note: The days with a minus sign are the days preceding the date shown on the label (calibration date) and the date with plus sign are the days after this date.

Activities of technetium-99m available with elutions performed every 24 hours can be calculated with table 4:

TABLE 4

Previous days								Calibration date
-8	-7	-6	-5	-4	-3	-2	-1	0
751	584	454	353	274	213	166	129	100
Available activity in percent of ^{99m} Tc at the calibration date (round values)								

Calibration date	Following days													
0	+1	+2	+3	+4	+5	+6	+7	+8	+9	+10	+11	+12	+13	+14
100	78	60	47	36	28	22	17	13	10	8	6	5	4	3
Available activity in percent of ^{99m} Tc at the calibration date (round values)														

It is also possible, to elute the ELUMATIC III before 24 hours have elapsed thus performing "partial time" elutions. Table 5 shows the percentage of activity in technetium-99m which can be collected after times varying from 0 to 23 hours:

TABLE 5

Time elapsed since the last elution was performed (hours)	0	1	2	3	4	5	6	8	10	12	14	16	18	20	22	23
Corrective factor	0.00	0.11	0.21	0.30	0.39	0.45	0.51	0.62	0.71	0.79	0.85	0.89	0.93	0.96	0.99	1.00
Decay of ⁹⁹ Mo	100	98.95	97.92	96.90	95.89	94.88	93.97	91.94	90.03	88.16	86.33	84.53	82.78	81.05	79.37	78.54
% of ^{99m} Tc available (round values)	0	11	21	29	37	43	48	57	64	70	73	75	77	78	79	79

Available activity in percent of ^{99m}Tc activity at the time of previous elution
(if performed about 24 hours after the previous one)

Examples

- a) A 10 GBq generator is eluted 24 hours after the calibration date. The technetium-99m activity collected is (table 4):
 $10 \times = 7.8 \text{ GBq}$
- b) The same generator is eluted 6 hours later. The technetium-99m activity collected is (tables 4 and 5):
 $7.8 \times = 3.7 \text{ GBq}$
- c) The same generator is eluted 18 hours later i.e. 48 hours after the calibration date. The 24 hours needed to reach the ⁹⁹Mo–^{99m}Tc equilibrium have not elapsed and the technetium-99m activity collected will be instead of 6.0 GBq (tables 6 and 7 : corrective factor):
 $6.0 \times = 5.6 \text{ GBq}$

This is summarised in the following table:

TABLE 6

	Monday	Tuesday	Wednesday		Thursday		Friday
Time of elution	8 a.m.	8 a.m.	8 a.m.		8 a.m.		8 a.m.
Radioactivity eluted 10 GBq on Tuesday	13	10	7.8		6.0		4.7
Time of elution	8 a.m.	8 a.m.	8 a.m.	2 p.m.	8 a.m.	12 a.m.	8 a.m.
Same generator eluted at different times (GBq)	13	10	7.8	3.7	5.6	2.1	4.5

N.B.:
In case the user waits for 48 hours or more between two elutions, he will obtain the activity indicated in table 4 multiplied by 1.1 (this factor accounts for the "rate equilibrium" which appears after 48 hours between molybdenum-99 and technetium-99m). This remark applies mainly:

- to the first elution: the previous elution was performed in the production laboratory, several days before;
- when the generator has a high activity.

Interest of partial time elutions

The potential utilisation of a generator can be notably increased by partial time elutions. ELUMATIC III has the advantage of a small elution volume. When choosing an appropriate volume for the elution vial, the desired volumic activity can be obtained even when the period of time between two elutions is of a few hours.

Example:

An elution of 10 GBq has been performed at 10 a.m. in 15 mL. The volumic activity is 0.67 GBq/mL. A new elution performed at 2 p.m., 4 hours after the first one, will give 3.7 GBq. If this activity is collected in 5 mL instead of 15 mL as previously, the volumic activity, 0.74 GBq/mL will be higher than in the morning.

Table 7 shows that a comparatively constant volumic activity can be obtained all along the week:

TABLE 7

	Calibration date	Elutions on following days				
	0	+ 1	+ 2	+ 3	+ 4	+ 5
Eluted activity GBq	10	7.8	6.0	4.7	3.6	2.8
Elution volume mL	15	15	10	8*	5	5
Volumic activity GBq/mL	0.67	0.52	0.60	0.59	0.72	0.56

* To reach a final volume of 8 mL, 3 mL of 0.9% sodium chloride injection are added to the 5 mL eluted in a vial TC-ELU-5.

Quality control

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

To obtain an approximate estimate of molybdenum-99, prior to use of the injection, take a volume of eluate equivalent to 37 MBq and determine the gamma-ray spectrum using a sodium iodide detector with a shield of lead, of thickness 6 mm, interposed between the sample and the detector. The response in the region corresponding to the 0.740 MeV photon of molybdenum-99 does not exceed that obtained using 37 kBq of a standardised solution of molybdenum-99 measured under the same conditions, when all measurements are calculated with reference to the date and hour of administration.

Warning:

The maximal radioactivity contained in the generator at the time of reception can be higher than that indicated on the label on the corresponding calibration date. Refer to table 5, showing the maximal radioactivity of elutable sodium pertechnetate (^{99m}Tc) for each content of generator, to determine the maximal radioactivity contained in the generator at the time of reception.

The first eluate obtained from this generator can be normally used, unless otherwise specified. The eluate can be used for kit labelling even eluted after 24 hours from the last elution, except if the use of fresh eluate is specified in the relevant kit SPC.

Weight of (^{99m}Tc + ⁹⁹Tc) in the eluate

The molybdenum-99 is transformed into technetium-99m (87.6% of the molybdenum-99 disintegrations) and technetium-99 (12.4% of the molybdenum-99 disintegrations). Thus, the eluted solution is not "carrier free". The calculation of the total weight (⁹⁹Tc + ^{99m}Tc) expressed in µg present in the eluate can be done with the following simplified formula:

W (µg) = $\frac{{}^{99m}\text{Tc activity in the eluate} \times k}{F}$

k = 5.161.10⁻³ when activity is expressed in GBq.

F is the ratio between the number of technetium-99m (N_{99m}) and the total number of technetium atoms (N_t):

F = $\frac{N_{99m}}{N_t}$

The values of this ratio in terms of time elapsed between two elutions are given in the table 8 hereunder:

TABLE 8

Hours	Days						
	0	1	2	3	4	5	6
0	-	0.277	0.131	0.076	0.0498	0.0344	0.0246
3	0.727	0.248	0.121	0.072	0.0474	0.0329	0.0236
6	0.619	0.223	0.113	0.068	0.0452	0.0315	0.0227
9	0.531	0.202	0.105	0.064	0.0431	0.0302	0.0218
12	0.459	0.184	0.098	0.061	0.0411	0.0290	0.0210
15	0.400	0.168	0.092	0.058	0.0393	0.0278	0.0202
18	0.352	0.154	0.086	0.055	0.0375	0.0266	0.0194
21	0.311	0.141	0.081	0.052	0.0359	0.0256	0.0187

Examples:

- 1) The technetium-99m from an ELUMATIC III has been eluted in 5 mL; the activity measured is 10 GBq; the previous elution was performed 27 hours earlier. The weight of technetium carrier will be:

$$W\ (\mu\text{g}) = \frac{10 \times 5.161 \cdot 10^{-3}}{0.248} = 0.208\ \mu\text{g}$$

corresponding to 0.042 µg/mL.

- 2) The technetium-99m is eluted from an ELUMATIC III 4 days after the preparation, this being the first elution for the user. For an activity of 10 GBq eluted in 5 mL, the weight of technetium carrier is:

$$W\ (\mu\text{g}) = \frac{10 \times 5.161 \cdot 10^{-3}}{0.0498} = 1.036\ \mu\text{g}$$

corresponding to 0.207 µg/mL, which is 5 times as much carrier as in the former example. Although small, this amount of technetium may affect the labelling yield of some compounds.

This remark applies not only to ELUMATIC III but to all technetium-99m generators.

Table 9 shows the variation in the weight of technetium carrier on a 10 GBq generator from Tuesday and eluted every day at an interval of 24 hours, assuming that the previous elution was performed 3 days after that performed on Monday.

TABLE 9

	Monday	Tuesday	Wednesday	Thursday	Friday
Radioactivity eluted GBq	13	10	7.8	6.0	4.7
Weight of technetium carrier in µg for the whole eluate	0.883	0.186	0.145	0.112	0.088

Detailed information on this medicinal product is available on the website of the Health Products Regulatory Authority (www.hpra.ie).