SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Poltechnet 8.0-175 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 yield and 24 hours time from previous elution and taking into account that branching ratio of ^{99}Mo is about 87%:

^{99m}Tc activity [GBq] at production date	8.0	14	21	28	35	42	53	64	69	88	125	141	175	GBq
^{99m}Tc activity (Maximal theoretical eluable activity at calibration date, 12h CET)	2.3	4.0	6.0	8.0	10	12	15	18	20	25	35	40	50	GBq
99Mo activity (at calibration date, 12h CET)	2.6	4.5	6.8	9.2	11	14	17	21	22	29	41	46	57	GBq

The technetium (99mTc) amounts available by a single elution depend on the real elution yield of generator itself declared by manufacturer and approved by NCA.
Excipient(s) 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.
Sodium pertechnetate (^{99m}Tc) solution: clear and colourless

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.
The eluate from the 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 according to the recommendations of the European Association of 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 the instructions on extemporary 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 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 Special 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, hepatic impairment
Careful consideration of the benefit risk ratio in these patients is required since an increased radiation exposure is possible.
Concomitant application of Sodium perchlorate is associated with reduced uptake of radioactivity in glandular tissue.
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 thryroid 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 (^{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.
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 MR 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.
Thyroid hormones, iodine, iodide, perchlorate, thiocyanate, aluminium containing antacids, sulfonamides and products containing stannous (II) ions may to increased concentrations of Sodium Pertechnetate (99mTc) in the vascular space, in the case of stannous (II) ions and sulfonamides the concentration of Sodium Pertechnetate (99mTc) 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 99mTc-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 99mTc-Pertechnetate from the stomach and the intestine and should not be taken before performing scintigraphy of Meckel's diverticulum.
Administration of laxatives should be withheld since they irritate the gastrointestinal tract. Contrast-enhanced studies (e.g. barium) and upper GI 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 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 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
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 from the Poltechnet 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 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 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 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.
Adverse reactions may be reported to marketing authorization holder.

4.9 Overdose
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 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 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: V09F X01
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 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 (^{99m}Tc) pertechnetate 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
Sodium chloride
Water for injection

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 12 hours. This medicinal product does not require any special storage conditions.
Elution vials: 1 year.
No special requirements concerning storage conditions of medicinal product.

6.4 Special precautions for storage
Generator: Do not freeze.
Eluate: For storage conditions after elution of the medicinal product, see section 6.3.
Vacuum vials: Do not require any special storage conditions.
Storage of radiopharmaceuticals should be in accordance with national regulation on radioactive materials.

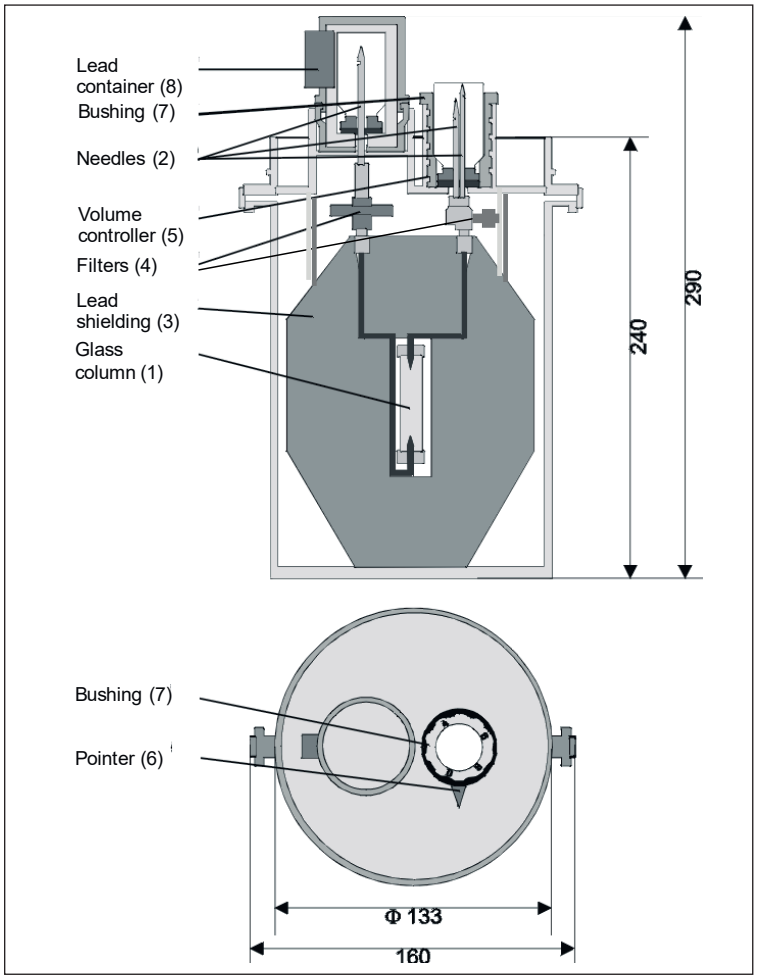
6.5 Nature and contents of container
Poltechnet – generator ^{99}Mo/^{99m}Tc is composed with the following:
- generator sterile, glass column (1) filled with alumina on which molybdenum-99 (fission) is adsorbed. The bottom end of the column is provided with a glass filter to prevent any leakage of alumina from the column. Top and bottom ends of the column are closed with rubber stoppers and caps.
- a set of stainless steel needles (2) which connects generator column with the eluent bottle and eluate vials. During transportation and during breaks between elutions the needles are protected by vials containing bacteriostatic agent (0.02% water solution of lauryl dimethyl benzyl ammonium bromide).
- the column and the needles are placed inside lead shielding (3) of 50 mm wall thickness. This shielding protects personnel from radiation and allows easy operation of the generator.
- filters (4): of the eluate and air filter.
- eluate volume controller (5). Construction of this device enables obtaining of the required eluate volume (by changing the volume of the eluent from 4 to 8 ml). The accuracy of the volume control is within 0,5 ml. This helps to obtain the required radioactive concentration of ^{99m}Tc in the solution. The regulation of the eluate volume is made by turning the bushing (7) of the controller so, that the pointer (6) matches the number of eluate milliliters on the upper surface of the bushing.

Together with the radionuclide generator, the following elution kits are supplied in cartoon packages:
- 16 vials with 10 ml eluent (9 mg/ml (0.9%) NaCl solution) and 16 evacuated vials (vials for eluate).

A glass vial is the immediate packaging of eluate from generator. 10 ml vial is closed with rubber stopper and aluminium cap type flip-off and placed in the lead container (8).
Exemplary pack sizes:

^{99m}Tc activity [GBq] at production date	8.0	14	21	28	35	42	53	64	69	88	125	141	175	GBq
^{99m}Tc activity (Maximal theoretical eluable activity at calibration date, 12h CET)	2.3	4.0	6.0	8.0	10	12	15	18	20	25	35	40	50	GBq
99Mo activity (at calibration date, 12h CET)	2.6	4.5	6.8	9.2	11	14	17	21	22	29	41	46	57	GBq

Other pack sizes in the range of 8.0-175 GBq at manufacturing date are also available on the customer's request.



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 in the preparation of this product the integrity of this vial is compromised, it should not be used.
Administration procedures should be carried out in a way to minimize 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
Narodowe Centrum Badań Jądrowych
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8. MARKETING AUTHORISATION NUMBER
22500

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
12.06.2015/15.12.2021

10. DATE OF REVISION OF THE TEXT
15.12.2021

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 unit activity administered (mGy/MBq)				
	Adult	**15 Year**	**10 Year**	**5 Year**	**1 Year**
Adrenal glands	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 of activity (mGy/MBq) when blocking agents are administered				
	Adults	**15 years**	**10 years**	**5 years**	**1 year**
Adrenal glands	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
Breasts	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 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 (99mTc) 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 (^{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 depends on many factors. Overall, radiation measurement 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 (99mTc) solution, with a pH between 5.5 and 7.5 and a radiochemical purity greater than 98%.
When sodium pertechnetate (^{99m}Tc) solution is used for kit labelling, please refer to the package leaflet of the concerned kit.
Activity of generators Poltechnet are compatible with the placed order. Nominal activity of generator is determined for 12^{00} CET on calibration day.
For the purposes of safe operation of the generator, it is necessary to follow the instructions of the generator manual.
During handling and administration of the drug, it is necessary to strictly follow the work safety rules in conditions of exposition to ionising radiation.

Mode of action:

CAUTION: Because of the radiation risk to the personnel it is recommended, that elution of the generator and all the other operations with sodium pertechnetate $Na^{99m}TcO_4$ solution are performed behind additional radiation shielding (e.g. 50 mm Pb ledge) and in sterile conditions. Also syringes used for preparation of the radiopharmaceuticals should be protected with lead.

The mode of working with the generator should be in compliance with the following instructions:
- cut off the seals on the transport packaging;
- remove the packaging lid;
- remove the upper plate;
- take out cardboard boxes with kits for elution;
- take out the generator and place it in a working place.

WARNING: *For elution of the generator, use only vials with eluent manufactured by the same manufacturer.*

WARNING: *Do not rinse needles and stoppers with ethyl alcohol, ethyl ether or any detergent solution as this may interfere with the elution process.*

WARNING: *Do not leave the generator unused. The amount of ^{99}Tc will increase in the generator and eluate if the generator is not eluated every day. If the eluate is used after a period of not use of the generator, both ^{99m}Tc and ^{99}Tc will react with the ligande of a kit, but ^{99}Tc will not contribute to the imaging. This will have a negative influence on the quality of the imaging.*

Elution of the generator should be performed as follows:
- unscrew the generator lid;
- place the generator in such a way, that both vials with bacteriostatic agent in the generator sockets are in line parallel to the operator and the settings of the eluate volume controller (6) are well visible;
- remove two vials with bacteriostatic agent from the needles;
- set the controller bushing in the position which matches to the required eluate volume

CAUTION: *Do not screw the bushing out of the socket completely. If the bushing is screwed out of the socket completely, it should be placed again. In such case start with setting the indicator of the bottom of bushing (under digit 4) in front of the indicator of volume regulator.*

- take of plastic disc from the cap from the vial with eluent and evacuated vial
- place the evacuated vial in the eluate shielding container;
- put the vial with eluent on double needle in the controllers socket of the generator. Make the piercing in such way that the vial touches the bottom of the socket;
- place the evacuated vial into the lead container (8) and put the vial on the single needle. Press the vial gently and make piercing in such way that the needle gets to the bottom of the vial;
- elution process has been started now. Time of elution depends on eluate volume and varies approximately from 2 to 3 and 4 minutes to get the eluate volume of 4, 6 and 8 ml, respectively;
- when the elution process is completed remove a lead container with vial with eluate (8) and control the eluted activity of ^{99m}Tc;
- remove the empty eluent vial from double needle.

Attention: *to remove the eluent vial more easy, turn the bushing of the controller down as deep as possible (about 1,5 cm).*

- cover the needles of the generator with the vials containing bacteriostatic agent;
- screw the lid of the generator.

Calculation of the ^{99m}Tc activity
Nominal activity of the radionuclide generator ^{99}Mo/^{99m}Tc (MTcG-4) is expressed as an activity of ^{99m}Tc at 12^{00} at noon on the day of calibration (zero day, *Table 1*).

Activity of the ^{99m}Tc eluted from the generator between 8^{00} and 12^{00} is practically constant and at the level of 96% to 100% of nominal activity on the day of elution.

The highest activities are obtained if the interval between elutions is not shorter than 23-24 hours.

Table 1. Theoretical activity of ^{99m}Tc which can be obtained from the generator on each day of Elution

Day	Generator Activity 99mTc [GBq]																		
	4.00	**5.00**	**6.00**	**7.50**	**8.00**	**10.00**	**12.00**	**13.00**	**15.00**	**17.00**	**18.50**	**20.00**	**23.00**	**25.00**	**30.00**	**35.00**	**40.00**	**50.00**	**82.00**
-5	14.1	17.6	21.2	26.4	28.2	35.3	42.3	45.8	52.9	59.9	65.2	70.5	81.1	88.2	105.8	123.4	141.1	176.3	
-4	11.0	13.7	16.4	20.6	21.9	27.4	32.9	35.6	41.1	46.6	50.7	54.8	63.0	68.5	82.2	95.9	109.6	137.0	
-3	8.5	10.7	12.8	16.0	17.0	21.3	25.6	27.7	32.0	36.2	39.4	42.6	49.0	53.3	63.9	74.6	85.2	106.5	175.0
-2	6.6	8.3	9.9	12.4	13.2	16.6	19.9	21.5	24.8	28.1	30.6	33.1	38.1	41.4	49.7	57.9	66.2	82.8	136.0
-1	5.1	6.4	7.7	9.6	10.3	12.9	15.4	16.7	19.3	21.9	23.8	25.7	29.6	32.2	38.6	45.0	51.5	64.3	105.6
0	**4.00**	**5.00**	**6.00**	**7.50**	**8.00**	**10.00**	**12.00**	**13.00**	**15.00**	**17.00**	**18.50**	**20.00**	**23.00**	**25.00**	**30.00**	**35.00**	**40.00**	**50.00**	**82.00**
1	3.11	3.89	4.66	5.83	6.22	7.77	9.33	10.10	11.66	13.21	14.38	15.54	17.88	19.43	23.32	27.20	31.09	38.86	63.73
2	2.42	3.02	3.62	4.53	4.83	6.04	7.25	7.85	9.06	10.27	11.17	12.08	13.89	15.10	18.12	21.14	24.16	30.20	49.53
3	1.88	2.35	2.82	3.52	3.76	4.69	5.63	6.10	7.04	7.98	8.69	9.39	10.80	11.74	14.08	16.43	18.78	23.47	38.50
4	1.46	1.82	2.19	2.74	2.92	3.65	4.38	4.74	5.47	6.20	6.75	7.30	8.39	9.12	10.95	12.77	14.59	18.24	29.92
5	1.13	1.42	1.70	2.13	2.27	2.84	3.40	3.69	4.25	4.82	5.25	5.67	6.52	7.09	8.51	9.93	11.34	14.18	23.25
6	0.88	1.10	1.32	1.65	1.76	2.20	2.64	2.87	3.31	3.75	4.08	4.41	5.07	5.51	6.61	7.71	8.82	11.02	18.07
7	0.69	0.86	1.03	1.28	1.37	1.71	2.06	2.23	2.57	2.91	3.17	3.43	3.94	4.28	5.14	6.00	6.85	8.56	14.05
8	0.53	0.67	0.80	1.00	1.07	1.33	1.60	1.73	2.00	2.26	2.46	2.66	3.06	3.33	3.99	4.66	5.33	6.66	10.92
9	0.41	0.52	0.62	0.78	0.83	1.03	1.24	1.35	1.55	1.76	1.91	2.07	2.38	2.59	3.10	3.62	4.14	5.17	8.48
10	0.32	0.40	0.48	0.60	0.64	0.80	0.96	1.05	1.21	1.37	1.49	1.61	1.85	2.01	2.41	2.81	3.22	4.02	6.59
11	0.25	0.31	0.38	0.47	0.50	0.63	0.75	0.81	0.94	1.06	1.16	1.25	1.44	1.56	1.88	2.19	2.50	3.13	5.12
12	0.19	0.24	0.29	0.36	0.39	0.49	0.58	0.63	0.73	0.83	0.90	0.97	1.12	1.21	1.46	1.70	1.94	2.43	3.98
13	0.15	0.19	0.23	0.28	0.30	0.38	0.45	0.49	0.57	0.64	0.70	0.76	0.87	0.94	1.13	1.32	1.51	1.89	3.10
14	0.12	0.15	0.18	0.22	0.23	0.29	0.35	0.38	0.44	0.50	0.54	0.59	0.67	0.73	0.88	1.03	1.17	1.47	2.41
15	0.09	0.12	0.14	0.17	0.18	0.22	0.27	0.30	0.34	0.39	0.42	0.46	0.52	0.57	0.68	0.80	0.91	1.14	1.87

It is possible to obtain eluate in time interval shorter than 23 hours from previous elution. In such case the activity of ^{99m}Tc will be respectively lower. In the *Table 2* there are values of correction factors which help to calculate ^{99m}Tc activity depending on the time intervals between elutions.

Table 2. The values of factors allowing to calculate the activity of technetium-99m, depending on the time following the previous elution.

Time following the previous elution [h]	0	2	4	6	8	10	12	14	16	18	20	23
Decay factor of ^{99}Mo	1.0	0.979	0.960	0.940	0.919	0.900	0.881	0.863	0.845	0.828	0.811	0.785
Growth factor of ^{99m}Tc	0.0	0.21	0.39	0.51	0.62	0.71	0.79	0.85	0.89	0.93	0.96	1.0

Examples of calculations:
● Generator with nominal activity of 15 GBq was eluted on day "+2" at 9^{00}, and then on the same day the second elution was performed at 13^{00}, that is after 4 hours from the last elution.
Activity of the first elution is: 9.06 GBq (see *Table 1*).
Activity of the second elution is: 9.06 x 0.960 x 0.39 = 3.39 GBq (correction factors from *Table 2)*.
● Generator with nominal activity of 23 GBq was eluted on day "+4" at 8^{00}, and then on the same day the second elution was performed at 14^{00}, that is after 6 hours from the last elution.
Activity of the first elution is: 8.39 GBq (see *Table 1*).
Activity of the second elution is: 8.39 x 0.940 x 0.51 = 4.02 GBq (correction factors from *Table 2)*.

Quality control
Clarity of the solution, pH, 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. 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 SmPC
Characteristics of the eluate from the generator:

Radioactivity/Elution yield	90 - 110%
Radiochemical purity of the eluate	≥ 98%
Assay of ^{99}Mo in the eluate	≤ 0.1% (A/A)
Assay of Al^{3+} in the eluate	< 5.0 µg/ml
pH of the eluate	5.5 – 7.5

Control at the user's level
Activity measurement: perform by optional method which gives the accuracy of 10% related to the end time of elution.
Radiochemical purity: perform by ascending paper chromatography using Whatman 1MM chromatographic paper and acetone as a developing solution.
R_f value for the spot of sodium pertechnetate-^{99m}Tc is 0.9 - 1.0
Assay of aluminum in the eluate: performed by colorimetric method on the strip of chromatographic paper which was impregnated with 0.05% solution of chromazurol S.

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