The tables below show the dosimetry as calculated according to the publication 53 of the ICRP (*International Commission of Radiological Protection, Radiation Dose to Patients from Radiopharmaceuticals,* Pergamon Press, 1987).

Patients with abnormal renal function

Absorbed dose per unit administered activity (mGy/MBq)					
Organ	**Adults**	**15 years**	**10 years**	**5 years**	**1 year**
Adrenals	0.0041	0.0051	0.0078	0.012	0.021
Bladder wall	0.022	0.027	0.04	0.058	0.11
Bone surfaces	0.0044	0.0053	0.0079	0.012	0.021
Breast	0.003	0.003	0.0043	0.0069	0.013
Gastrointestinal tract					
Stomach wall	0.0038	0.005	0.0079	0.011	0.02
Small intestine	0.0047	0.0056	0.0086	0.013	0.023
Upper large intestine wall	0.0044	0.0056	0.0081	0.013	0.022
Lower large intestine wall	0.0047	0.0062	0.0096	0.014	0.025
Kidneys	0.0079	0.0096	0.0014	0.02	0.034
Liver	0.0038	0.0046	0.0071	0.011	0.019
Lungs	0.0033	0.0042	0.0062	0.0095	0.017
Ovaries	0.0049	0.0063	0.0094	0.014	0.024
Pancreas	0.0043	0.0054	0.0081	0.012	0.022
Red Marrow	0.0052	0.0063	0.009	0.013	0.022
Spleen	0.004	0.0048	0.0072	0.011	0.02
Testes	0.0033	0.0045	0.0069	0.011	0.02
Thyroid	0.0025	0.0043	0.0068	0.011	0.019
Uterus	0.0063	0.0075	0.011	0.017	0.029
Other tissue	0.0033	0.004	0.0061	0.0094	0.017
Effective dose mSV/MBq	0.0053	0.0066	0.0097	0.015	0.026

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

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.

As with any pharmaceutical product, if at any time in the preparation of this product the integrity of this vial is compromised, the product should not be used. Therefore, prior to the radiolabelling procedure carefully inspect the vial for the presence of damage, in particular cracks.

PoltechDTPA is designed for labelling with technetium-99m as eluate of sodium pertechnetate-^{99m}Tc obtained from the ^{99}Mo/^{99m}Tc radionuclide generator. The labelling procedure should be performed in the work station protected against ionizing radiation and using method ensuring sterility of the preparation.

Labelling procedure

1. Place the kit vial containing the lyophilisate in an appropriate radioprotective shield.
2. Using a syringe inject (by piercing the rubber stopper) about 5 ml of eluate of sodium pertechnetate ^{99m}Tc (or eluate with desired activity pre-diluted with sterile saline) into the vial containing lyophilized DTPA.
3. Using the same syringe relieve the excess of pressure in the vial by withdrawing the equivalent volume of gas.
4. Shake the contents of the vial until complete dissolution of the powder (about 2 min.). Keep the vial in the shield all the time.
5. The received solution is a ready-to-use solution for injection.

The ^{99m}Tc-DTPA preparation should be used within 6 hours after completion of labelling procedure.
Regulations for safety of work at exposure to ionizing radiation should be strictly observed during preparation and administration of radiopharmaceutical.

Instruction for quality control of radiopharmaceutical ^{99m}Tc-DTPA
Radiochemical purity measurement by Thin Layer Chromatography – two chromatographic systems according to Ph.Eur. Monograph 0642.

Impurity A
1. ITLC-SG plates, (silica gel coated glass-fiber plates)
2. Developing solution: 9 g/l sodium chloride
3. Applying the sample on a plate: apply about 2 µl of the examined solution (with radioactivity from 50 MBq/ml to 200 MBq/ml) about 1.5 cm from the bottom of a 1.5 cm x 12 cm chromatographic plate
4. Developing: immediately, until the solvent front moves to about 4/5 of the plate
5. Drying: in the air
6. Detection: suitable radiation detector

Under these conditions:
- non-bound, reduced ^{99m}Tc and ^{99m}Tc colloidal forms (**Impurity A**) remain at the origin (Rf=0.0-0.1).
- ^{99m}Tc-DTPA complex and free pertechnetate ion $^{99m}TcO_4^-$ migrate with solvent front (Rf=0.9-1.0).

Impurity B
1. ITLC-SG plates, (silica gel coated glass-fibre plates)
2. Developing solution: methyl ethyl ketone (MEK)
3. Applying the sample on a plate: apply about 2 µl of the examined solution (with radioactivity from 50 MBq/ml to 200 MBq/ml) about 1.5 cm from the bottom of a 1.5 cm x 12 cm chromatographic plate
4. Developing: immediately, until the solvent front moves about 4/5 of the plate
5. Drying: in the air
6. Detection: suitable radiation detector

Under these conditions:
- free pertechnetate ion $^{99m}TcO_4^-$ (**Impurity B**) migrates with the solvent front (Rf=0.9-1.0).
- ^{99m}Tc-DTPA complex and ^{99m}Tc colloidal forms remain at the origin (Rf=0.0-0.1).

Radiochemical purity of ^{99m}Tc-DTPA complex: not less than 95% of total technetium-99m.
Calculate the % of radioactivity ^{99m}Tc-DTPA complex as:

$$100 - (A+B)$$

Where:
A = percentage of Impurity A radioactivity, determined in the test of Impurity A
B = percentage of Impurity B radioactivity, determined in the test of Impurity B

POLATOM

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

PoltechDTPA, 13.25 mg,

kit for radiopharmaceutical preparation

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 vial contains:
sodium diethylenetriaminepentaacetate monohydrate (DTPA) 13.25 mg
The radionuclide is not part of the kit.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Kit for radiopharmaceutical preparation
Lyophilisate for solution for injection

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.
The radiopharmaceutical ^{99m}Tc-DTPA is intended for renal scintigraphic imaging (dynamic renal scintigraphy for GFR measurement of each kidney and evaluation of urinary flow disorders), GFR measurement from the plasma samples, and for the cerebral angiography and brain scanning.

4.2 Posology and method of administration

Product intended for intravenous administration.
This radiopharmaceutical may be used only by authorized persons.
Safety precautions for careful handling this radiopharmaceutical should be observed.
The radiopharmaceutical ^{99m}Tc-DTPA is administered intravenously after labelling with sterile, oxidant-free eluate from a radionuclide generator ^{99}Mo/^{99m}Tc, in accordance with the labelling instructions – see section 12.
For patient preparation – see section 4.4.
For radiolabelling of one vial the 5 ml of sodium pertechnetate (^{99m}Tc) solution (eluate from a radionuclide generator ^{99}Mo/^{99m}Tc) with activity of 740-1500 MBq should be used.
This amount is sufficient to perform the examination in several adult patients.

Image acquisition
Renal scintigraphy with measurement of glomerular filtration rate: Sequential scanning should begin immediately after injection. Optimal static imaging time is 1 hour post injection.
Brain scanning: Sequential dynamic scanning should begin immediately after injection. Static images are obtained 1 hour and, if necessary, several hours after injection.

Posology
Adults
The activity recommended for a renal scintigraphy in adult patient ranges from 74-370 MBq, for measurement of glomerular filtration rate from plasma it ranges 1.8-3.7 MBq, for angiography and brain scanning ranges 370-555 MBq, however depending on indications other activities may be justifiable.

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 for children is adjusted according to body weight or surface area:
Pediatric activity (MBq) = Adult dosage (MBq) x Child weight (kg)/70
Pediatric activity (MBq) = Adult dosage (MBq) x Child body surface (m^2)/1.73
The activities to be administered to children and adolescents may be calculated 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 multiples given in the table below

3 kg = 0.10	22 kg = 0.50	42 kg = 0.78
4 kg = 0.14	24 kg = 0.53	44 kg = 0.80
6 kg = 0.19	26 kg = 0.56	46 kg = 0.82
8 kg = 0.23	28 kg = 0.58	48 kg = 0.85
10 kg = 0.27	30 kg = 0.62	50 kg = 0.88
12 kg = 0.32	32 kg = 0.65	52-54 kg = 0.90
14 kg = 0.36	34 kg = 0.68	56-58 kg = 0.92
16 kg = 0.40	36 kg = 0.71	60-62 kg = 0.96
18 kg = 0.44	38 kg = 0.73	64-66 kg = 0.98
20 kg = 0.46	40 kg = 0.76	68 kg = 0.99

In very young children (up to one 1 year) a minimum dose of 20 MBq is necessary in order to obtain images of sufficient quality, when the medicinal product is used for kidney studies.

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

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

If hypersensitivity or anaphylactic reactions occurs, 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.
Pregnancy, see section 4.6.

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.
In patients with renal impairment careful consideration of the indication is required since an increased exposure is possible in these patients. This must be taken into account when calculating the activity to be administered – see section 11.

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.

Patient preparation
The patient should be well hydrated before the start of the examination and should void before scanning and as often as possible during the first hours after the study in order to reduce radiation to the bladder wall.
After the procedure close contact with infants and pregnant women should be restricted during 24 h.
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.
The content of the vial is intended for preparation of radiopharmaceutical ^{99m}Tc-DTPA and may be administered to the patient only after completion of labelling procedure.

Specific warnings
This medicinal product contains less than 1 mmol sodium (23 mg) per vial, i.e. essentially „sodium free".

4.5 Interactions with other medicinal products and other forms of interactions

Many drugs may affect the function of tested organ and modify the uptake ^{99m}Tc-DTPA, i.e.,

Diagnostic use of captopril: Dynamic renal scanning performed under controlled conditions and again one hour after oral administration of captopril (25-50 mg) may reveal haemodynamic changes in a kidney affected by renal artery stenosis. The blood pressure should be carefully monitored as patients with vascular disease are at risk of significant hypotension and renal impairment.

Diagnostic use of furosemide: The administration of intravenous furosemide during dynamic renal scanning increases elimination of ^{99m}Tc-DTPA which may help to distinguish whether true obstruction exists in a dilated renal tract.

Cerebral angiography: Psychotropic drugs increase blood flow in the territory of the external carotid artery. This may lead to the rapid uptake of tracer in the nasopharyngeal area during the arterial and capillary phases (hot nose phenomenon).

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.
Examinations using radiopharmaceuticals in women of childbearing potential should be carried out during the first 10 days following the onset of menses.
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.
Examinations using radiopharmaceuticals in women of childbearing potential should be carried out during the first (about 10) days following the onset of menses.

Pregnancy

Radionuclide procedures carried out on pregnant women also involve radiation doses to the foetus. Only essential investigations should therefore be carried out during pregnancy, when the likely benefit far exceeds the risk incurred by the mother and the foetus.

Administration of 555 MBq ^{99m}Tc-DTPA to a patient results in an absorbed dose to the uterus of 4.4 mGy. Doses above 0.5 mGy would be regarded as a potential risk for the foetus.

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 4 hours and the expressed feeds discarded.

4.7 Effects on ability to drive and use machines

The radiopharmaceutical has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The frequency of adverse reactions reported after administration of the product is presented in the table below.

Undesirable effects	**Frequency**
Nervous system disorders: dizziness	Very rare (<1/10,000)
Vascular disorders: hypotension, flushing	Very rare (<1/10,000)
Respiratory, thoracic and mediastinal disorders: dyspnoea	Very rare (<1/10,000)
Skin and subcutaneous tissue disorders urticaria, pruritus	Very rare (<1/10,000)
Neoplasms benign and malignant (incl. cysts and polyps): cancer induction*	Frequency not known (cannot be estimated from the available data)
Congenital and familial/genetic disorders: hereditary defects*	Frequency not known (cannot be estimated from the available data)

*linked with ionising radiation

For each patient, exposure to ionising radiation must be justified on the basis of likely benefit. The activity administered must be such that the resulting radiation dose is as low as reasonably achievable bearing in mind the need to obtain the intended diagnostic result.

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. For diagnostic nuclear medicine investigations the current evidence suggests that these adverse reactions are expected to occur with a low probability.

For most diagnostic investigations using a nuclear medicine procedure the radiation dose delivered (effective dose/ EDE) is less than 20 mSv. Higher doses may be justified in some clinical circumstances.

According to the literature data (J.Nucl.Med., 1996, 37, 185-192, 1064-1067), after the intravenous administration of the radiopharmaceutical ^{99m}Tc-DTPA the following adverse reactions have been reported sporadically: fever, nausea, vomiting, flushing, erythema, pruritus, urticaria, headache, hypertension, aseptic meningitis.

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 Authorisation Holder.

4.9 Overdose

In the event of the administration of a radiation overdose with ^{99m}Tc-DTPA injection, the absorbed dose to the patient should be reduced where possible by increasing the elimination of the radionuclide from the body by forced diuresis and frequent bladder voiding.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: diagnostic radiopharmaceutical, technetium (^{99m}Tc) compounds, ATC code:V09CA01

At the chemical concentrations used for diagnostic procedures ^{99m}Tc-DTPA and excipients do not appear to exert any pharmacodynamic activity.

5.2 Pharmacokinetic properties

PoltechDTPA is intended for technetium-^{99m}Tc labelling.

Distribution

Less than 5% of the injected dose is bound to the plasma proteins. There is also a negligible binding of ^{99m}Tc-DTPA to red blood cells. After administration ^{99m}Tc -DTPA does not cross the normal blood-brain barrier but diffuses weakly in breast milk.

Elimination

Plasma clearance is multiexponential with a dominant fast component.
The complex remains stable in vivo, more than 98% of urine radioactivity is in the form of a chelate.

Approximately 90% of the injected dose is eliminated in the urine within the first 24 hours mainly by glomerular filtration. No retention of the compound has been demonstrated in the kidneys.
Plasma clearance may be delayed in patients with renal disease.

Following intravenous injection ^{99m}Tc-DTPA disappears from blood rapidly.

5.3 Preclinical safety data

This product is not intended for regular or continuous administration. Repeated intravenous administration of $CaNa_3DTPA$ to rabbits and dogs for 14 days of doses that were 100 and 1000 times (respectively) the normal dose for humans, produced no evidence of toxicity. The minimum dose of CaDTPA causing abortion and fetal death in mice was approximately 3600 times the dose of $CaNa_3DTPA$ that is proposed for diagnosis in women.
Mutagenicity studies and long-term carcinogenicity studies have not been carried out.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Stannous chloride dihydrate
Sodium chloride
Nitrogen

6.2 Incompatibilities

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

6.3 Shelf life

Kit - 1 year.
After radiolabelling with sodium pertechnetate (^{99m}Tc) solution: 6 hours.
Store below 25°C in a suitable radiation lead shield.

6.4 Special precautions for storage

Store in a refrigerator (2°C- 8°C).
During transportation (not longer than 7 days) up to 35°C.
For storage conditions after radiolabelling 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

10 ml multi-dose glass vials sealed with a rubber stopper and aluminium cap in cardboard box.
3 vials
6 vials
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

General warning

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 licenses 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.
Contents of the vial are intended only for use in the preparation of medicinal product and are not to be administered directly to the patient without first undergoing the preparative procedure.
The content of the kit before extemporary preparation is not radioactive. However, after sodium pertechnetate (^{99m}Tc) is added, adequate shielding of the final preparation must be maintained.
The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spill of urine, vomiting or any other biological fluids. Radiation protection precautions in accordance with national regulations must therefore be taken.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.
For instructions on extemporary preparation of the medicinal product before administration, see section 12.

7. MARKETING AUTHORISATION HOLDER

Narodowe Centrum Badań Jądrowych
ul. Andrzeja Sołtana 7
05-400 Otwock, Poland
Phone: (+48) 22 7180700
Fax: (+48) 22 7180350
e-mail: polatom@polatom.pl

8. MARKETING AUTHORISATION NUMBER

Marketing authorization number: R/3453

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization:16.05.1989
Date of latest renewal: 27.08.2013

10. DATE OF APPROVAL/REVISION OF THE TEXT

30.08.2016

11. DOSIMETRY

Technetium (^{99m}Tc) is produced by means of a (^{99}Mo/^{99m}Tc) radionuclide generator and decays with the emission of gamma radiation with an energy of 140 keV and a half-life of 6.02 hours to technetium (^{99}Tc) which, in view of its long half-life of 2.13 x 10^5 years, can be regarded as quasi stable.
The projected radiation doses to organs and tissues of a patient after intravenous injection of ^{99m}Tc-DTPA are given in the table below. These data are adopted from ICRP publications 53 and 80. The data listed below are from publication 80 of the ICRP (*International Commission of Radiological Protection, Radiation Dose to Patients from Radiopharmaceuticals*, Pergamon Press, 1998)

Patients with normal renal function

Absorbed dose per unit administered activity (mGy/MBq)					
Organ	**Adults**	**15 years**	**10 years**	**5 years**	**1 year**
Adrenals	0.0013	0.0017	0.0026	0.0038	0.007
Bladder	0.062	0.078	0.097	0.095	0.17
Bone surfaces	0.0023	0.0028	0.004	0.0055	0.0099
Brain	0.00084	0.001	0.0017	0.0027	0.0048
Breast	0.00071	0.0009	0.0013	0.0021	0.004
Gall bladder	0.0015	0.002	0.0036	0.0046	0.006
Gastrointestinal tract					
Stomach	0.0013	0.0016	0.0027	0.0037	0.0067
Small intestine	0.0025	0.0031	0.0045	0.0057	0.0098
Colon	0.003	0.0038	0.0054	0.0064	0.011
(ULI	0,0021	0.0027	0.004	0.0054	0.009
(LLI	0.0043	0.0053	0.0073	0.0077	0.013
Heart	0.0011	0.0014	0.0021	0.0032	0.0058
Kidneys	0.0039	0.0047	0.0067	0.0096	0.017
Liver	0.0012	0.0015	0.0024	0.0035	0.0063
Lungs	0.00099	0.0013	0.0019	0.0029	0.0053
Muscles	0.0016	0.002	0.0028	0.0037	0.0067
Oesophagus	0.001	0.0013	0.0019	0.0029	0.0053
Ovaries	0.0042	0.0053	0.0069	0.0078	0.013
Pancreas	0.0014	0.0018	0.0027	0.004	0.0072
Red marrow	0.0014	0.0018	0.0026	0.0033	0.0056
Skin	0.00085	0.001	0.0016	0.0023	0.0043
Spleen	0.0012	0.0016	0.0024	0.0036	0.0066
Testes	0.0029	0.004	0.006	0.0069	0.013
Thymus	0.001	0.0013	0.0019	0.0029	0.0053
Thyroid	0.001	0.0013	0.002	0.0032	0.0058
Uterus	0.0079	0.0095	0.013	0.013	0.022
Remaining organs	0.0017	0.002	0.0028	0.0037	0.0064
Effective dose mSV/MBq	**0.0049**	**0.0062**	**0.0082**	**0.009**	**0.016**
Bladder wall contributes up to 57% of the effective dose.					
The effective dose if bladder is emptied 0.5 or 1 hour after administration					
1 hour	0.0038	0.0048	0.0065	0.0077	0.014
30 minutes	0.0043	0.0053	0.007	0.0079	0.014

The effective dose equivalent resulting from an administered activity of 555 MBq to a patient of 70 kg body weight is 2.7 mSv.