IZOTOP

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

EC 2 mg kit for radiopharmaceutical preparation

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

2.0 mg EC (Ethylene-dicysteine) in vial A.
Composition of the injection prepared with EC kit: 0.8–1.6 GBq ^{99m}Tc-EC.
The radionuclide is not part of the kit.
For a list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Kit for radiopharmaceutical preparation.
Powder for solution for injection.
Vial-A and vial-B contain white or slightly yellow powder, while content of vial-C is white or yellow paste.
Pharmaceutical form of ^{99m}Tc-EC: injection
^{99m}Tc-EC injection can be prepared in situ at the site of the use ie. at isotope laboratories of clinics or hospitals by mixing EC powder for injection (lyophilisate in the vial) and (^{99m}Tc) pertechnetate eluate. Sterile, pyrogen free solution of (^{99m}Tc) pertechnetate can be obtained by using ^{99m}Tc/^{99}Mo generator. For instructions for preparation, see section 12.
The ^{99m}Tc-EC injection may be colourless or yellow solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.
Indication field: Isotope diagnostics
After radiolabelling with sodium pertechnetate (^{99m}Tc) solution the ^{99m}Tc-EC obtained is indicated for renal tubular functional imaging, dynamic kidney tests by imaging technique, camera renography.

4.2 Posology and method of administration

Posology
Adults
90 –120 MBq of ^{99m}Tc-EC injection for intravenous administration (for an average body weight of 70 kg)
The radiolabelling should be performed in the range of 0.8 – 1.6 GBq of ^{99m}Tc activity to provide sufficient activity at the time of administration. Number of patients to be examined with the labelled content of one vial can be calculated from the activities recommended for the examinations.
Elderly population
Dosing recommendations for older patients are the same as adults.
Renal impairment
Careful consideration of the activity to be administered is required since an increased radiation exposure is possible in these patients.
Hepatic impairment
In general, activity selection for patients with a decreased hepatic function should be cautious, usually starting at the low end of the dosing range.
Pediatric population
The use in children and adolescents has to be considered carefully, based upon clinical needs and assessing the risk/benefit ratio in this patient group.
For paediatric examination use Webster's equation (given below) to determine the activity to be administered

$$A_{child} = \frac{[(N+1)\cdot A_{Adult}]}{N+7}$$

where: N:age of the child [year]
A_{child}, A_{adult}: activity [MBq]

Method of administration:
For intravenous use.
Because of potential tissue damage, extravasal injection of this radioactive product has to be strictly avoided.
For multidose use.
Precautions to be taken before handling or administration of the medicinal product:
This medicinal product should be reconstituted before administration to the patient. For instructions on reconstitution and control of the radiochemical purity of the medicinal product before administration, see section 12.
For patient preparation, see section 4.4.
Image acquisition
The investigation is usually started immediately after administration. The patient should sit or lay, in front of or under the gamma camera adjusted to the back of the patient, to the region of the kidneys. ^{99m}Tc-EC injection should be administered intravenously in the brachial vein, as bolus. Series of pictures should be acquisited as follows:

- 30 frames of 1 second (perfusion phase),
- 120 frames of 20 seconds (uptake and elimination phase).

In case of slow elimination, more than 120 frames of 20 seconds can be acquisited. If needed, elimination can be provoked by administering furosemide injection. The time of furosemide injection should be noted and it should be taken into consideration when kinetic curves are evaluated. The whole time of the renal functional imaging is around 30 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 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.
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 or hepatic impairment
Careful consideration of the benefit risk ratio in these patients is required since an increased radiation exposure is possible (see section 4.2).
Paediatric population
Use of the product is contraindicated for patients under age of 18 years, except if the necessity and importance of obtaining the diagnostic information outweighs the risk associated with the radiation exposure. 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 urged to void as often as possible during the first hours after the examination in order to reduce radiation.
After the procedure
Close contact with infants and pregnant women should be restricted during the initial 12 hours following the injection.
Specific warnings
This medicinal product contains less than 1 mmol sodium (23 mg) per vial, i.e. essentially 'sodium-free'.
For precautions with respect to environmental hazard see section 6.6.

4.5 Interaction with other medicinal products and other forms of interaction

Interaction studies have not been performed.
Based on clinical experiences, ACE inhibitors may slow-down the kinetics of renal excretion.

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
Radionuclide procedures carried out on pregnant women also involve radiation dose 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 foetus.
Breastfeeding
The ^{99m}Tc is secreted in breast milk.
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 and the expressed feeds discarded. Breastfeeding can be continued when the activity measured in breast milk does not represent a radiation dose exceeding 1 mSv for the child.

4.7 Effects on ability to drive and use machines

The ^{99m}Tc-EC injection has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. Since the effective dose is 0.76 mSv when the recommended maximum activity of 120 MBq is administered, these effects are hardly expected.
Adverse event and reactions have not been reported ever since the authorization of the product (1992) nor registered in the literature. Considering the number of the examinations carried out since, no adverse reactions are expected (frequency less than 1/10000).
Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. However, these effects are hardly expected regarding the applied low amount of activity.
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 one of the contacts (in Hungary: www.ogyei.gov.hu).

4.9 Overdose

No case of overdose has been reported.
The ^{99m}Tc-EC injection should be used and administered only by authorised persons in clinical departments. The potential for pharmacological overdose is negligible. In case of incidental overdose be ready to provide life support. Radiation dose to the body can be reduced by increased and frequent diuresis.
Administration of higher activities than prescribed is unnecessary and must be avoided in order not to cause excess of absorbed radiation dose to the patient and his/her environment. In case of incidental overdose, the effectively administered activity of ^{99m}Tc must be determined (in MBq) and the actual absorbed radiation dose must be calculated by using the data of the dosimetric table of Chapter 11. Necessity and method of further treatment should be concluded based on these results. The table of Chapter 11 contains absorbed radiation dose data in μGy in case of intravenous administration of 1 MBq of ^{99m}Tc-EC. Multiply these specific absorbed radiation dose data by the effectively administered activity (in MBq) to obtain the required absorbed radiation dose data in μGy.
According to the recommendations, quantity of EC in ^{99m}Tc-EC injection administered to one patient is not less than 0.11 mg and not more than 0.30 mg. If the whole content of the vial containing the labelled substance is administered to one patient by mistake, 2 mg of ^{99m}Tc-EC is introduced in the body.
If the labelling differently than recommendation, saturation effect may occur, having negative impact on the pharmacokinetics, i.e. on the diagnostic value.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Diagnostic radiopharmaceutical, ATC code: V09CA

^{99m}Tc-EC has been developed for diagnostic testing of the tubular kidney function. Besides imaging, characteristic parameters of the renogram (T_{max}, $T_{1/2}$) can be determined, from the image series. Determination of the effective quantity of plasma perfusing through the kidneys is also possible. After intravenous administration ^{99m}Tc-EC is rapidly absorbed from the blood and it reaches the kidneys, where it is excreted in the tubular way. Normal pathway of excretion is: kidneys-ureters-urinary bladder even in case of impaired renal functions. Thus, the liver and the spleen do not appear on the images.

Pharmacological properties of ^{99m}Tc-EC are similar to those of PAH and iodohippurane. However, while the plasma binding value of iodohippurane is 33%, the same is 29% for ^{99m}Tc-EC. It is worth to mention that the plasma binding of Tc-99m-MAG3, which is also applied in camera renography and secreted in the tubular way, exceeds 80%. Molecular structure of EC is similar to hippurate, the oxo-oxygen and two oxygen atoms of the adjacent carboxyl group yield a triangle in both compound. These three oxygen atoms are identified by the enzyme of the renal tubules and facilitate selective excretion. These structural characteristics are the reason of excellent imaging properties of ^{99m}Tc-EC.

It is a general principle of nuclear imaging that the radioactive tracer must not have influence on the system to be tested, i.e. the physiological processes of the human body. For the present case the requirement is that the tracer should not have or have only a negligible effect on the tubular filtration of the kidneys. The medical product meets this requirement since not less than 0.11 mg and not more than 0.30 mg EC is administered in ^{99m}Tc-EC injection to a patient. Pharmaceutical effect such small quantities cannot be observed.

5.2 Pharmacokinetic properties

^{99m}Tc-EC leaves the bloodstream very rapidly, normally; highest activity of the kidneys (T_{max}) can be observed 3 – 3.5 minutes after administration. In case of normal kidney functions, the biological half-life ($T_{1/2}$) is less than 11 minutes. During the dynamic test, which requires 20 – 25 minutes, 75–85 % of ^{99m}Tc-EC is excreted in the urine. In case of impaired renal function, both kinetic parameters (T_{max}, $T_{1/2}$) are increased. It is important that ^{99m}Tc-EC does not remain in the blood and it is not excreted in other ways. As a consequence the liver does not appear on the images even if kidney function is impaired. Of the substances used for kidney-imaging ^{99m}Tc-EC provides the best resolution of images; the parenchyma and the calyx are clearly shown by the pictures.

5.3 Preclinical safety data

Acute toxicity studies on mice showed no clinical symptoms, if less than 11.4 mg/kg of bodyweight is administered. LD_{50} value, obtained in a 14-day long test is 38.4 mg / kg of bodyweight.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Vial-A: Disodium phosphate dihydrate, Mannitol, Ascorbic acid, Disodium edetate
Vial-B: Stannous chloride dihydrate, Tartaric acid, Ascorbic acid
Vial-C: Potassium dihydrogen phosphate, Ascorbic acid.

6.2 Incompatibilities

When preparing ^{99m}Tc-EC injection by using EC 2 mg kit, only physiological saline and sodium pertechnetate (^{99m}Tc) can be used (see ection 12). EC 2 mg kit is incompatible with other materials.

6.3 Shelf life

Kit: 12 months
The radiolabelled injection: after reconstitution and radiolabelling it must be used within 8 hours.
The EC 2 mg kit contains vials for 4 individual labelling, i.e. 4 pieces of vial-A, 4 pieces of vial-B and 4 pieces of vial-C. The 4 labelling can also be carried out at different times, within the expiry date (12 months) indicated on the vial and box labels.

6.4 Special precautions for storage

Kit: Store in refrigerator (at 2-8°C). Keep the bottle in the outer carton in order to protect from light.
The radiolabelled injection: Do not store ^{99m}Tc-EC injection above 25°C, protected from light. Storage of the radiolabelled injection should be in accordance with national regulation on radioactive materials.

6.5 Nature and contents of container

Sterile, type I, 6 ml (colourless, 6R type) injection vial sealed with winered (halobutyl) rubber stopper and flip-off aluminium cap combined with red (Vial A), yellow (Vial B), green (Vial C) polypropylene disc.
Multidose vial.
The EC 2 mg kit contains vials for 4 individual labelling, i.e. 4 pieces of vial-A, 4 pieces of vial-B and 4 pieces of vial-C. The colour of the stripe of the vial labels are different:
for vial-A: red
for vial-B: yellow and
for vial-C: green.
These vials are packed into one paper box, covered by celluloid foil.

6.6 Special precautions for disposal and handling

General warnings
Radiopharmaceuticals should be received, used and administered only by authorized persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licenses of the local competent official organization.
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 ^{99m}Tc-EC injections and are not to be administered directly to the patient without first undergoing the preparative procedure.
For instructions on reconstitution of the medicinal product before administration, see section 12.
If at any time in the preparation of this product the integrity of the 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 content of the kit before extemporary preparation is not radioactive. However, after sodium pertechnetate (^{99m}Tc) solution for injection 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 etc. 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.
Classification: Group II / 3
In accordance with CLIV 1997 on Health Care, (I), which may be used under the conditions provided by providers of outpatient care or inpatient services provided by the outpatient clinic under section 3 (a) of the Act requirements.

7. MARKETING AUTHORISATION HOLDER

Institute of Isotopes Co. Ltd.
Address: 1121 Budapest, Konkoly Thege Miklós str. 29-33.
✉ 1535 Budapest, P.O.B. 851.
Tel.: +36 1 392 2577; 395 9081, Fax: +36 1 395 9247; 392 2575
E-mail: radiopharmacy@izotop.hu

8. MARKETING AUTHORISATION NUMBER(S)

OGYI-T-9141/01

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

First authorization: 03. July 1992.
Renewals: 13. December 2003 and 15. October 2009.

10. DATE OF REVISION OF THE TEXT

28. September 2020.
This SPC was translated by the manufacturer based on the original Hungarian document, authorized by the Hungarian National Institute of Pharmacy on 28.September 2020.

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 (^{99m}Tc) which, in view of its long half-life of 2.13 x 10^5 years, can be regarded as quasi stable.

The data listed below are from ICRP publication 106 in 2008.
Normal renal function
^{99m}Tc 6.01 h

Organ	Absorbed dose per unit activity administered (mGy/MBq) (Normal renal function)				
	Adult	15 years	10 years	5 years	1 year
Adrenals	0.00053	0.00068	0.0011	0.0017	0.003
Bladder	0.095	0.12	0.17	0.22	0.026
Bone surfaces	0.0014	0.0017	0.0025	0.0034	0.0048
Brain	0.00022	0.00028	0.00045	0.00073	0.0013
Breasts	0.0002	0.00026	0.00041	0.0007	0.0013
Gall bladder	0.0007	0.001	0.0024	0.0024	0.0031
Gastrointestinal tract:					
Stomach	0.00052	0.00065	0.0013	0.0019	0.0029
Small intestine	0.0022	0.0028	0.0045	0.006	0.0072
Colon	0.0032	0.004	0.0062	0.0078	0.0088
Upper large intestine	0.0017	0.0022	0.0037	0.0053	0.0063
Lower large intestine	0.0052	0.0065	0.0096	0.011	0.012
Heart	0.00033	0.00043	0.00066	0.001	0.0019
Kidneys	0.0034	0.0041	0.0059	0.0085	0.014
Liver	0.00045	0.00059	0.001	0.0017	0.0026
Lungs	0.00028	0.00038	0.00058	0.00091	0.0017
Muscles	0.0014	0.0016	0.0024	0.0032	0.0041
Oesophagus	0.00027	0.00035	0.00054	0.00086	0.0015
Ovaries	0.0049	0.0062	0.009	0.011	0.012
Pancreas	0.00055	0.00068	0.0012	0.0019	0.0031
Red marrow	0.00096	0.0012	0.0018	0.0021	0.0024
Skin	0.0005	0.00061	0.001	0.0014	0.002
Spleen	0.0005	0.00065	0.0011	0.0017	0.0028
Testes	0.0034	0.0048	0.0084	0.011	0.013
Thymus	0.00027	0.00035	0.00054	0.00086	0.0015
Thyroid	0.00027	0.00034	0.00055	0.00089	0.0016
Uterus	0.011	0.013	0.02	0.024	0.026
Remaining organs	0.0014	0.0017	0.0023	0.0027	0.0034
Effectiv dose (mSv/MBq)	0.0063	0.008	0.012	0.015	0.018

Bladder wall contributes 76% of the effective dose.
The effective dose resulting from the administration of a maximal recommended activity of 120 MBq for an adult weighing 70 kg is about 0.76 mSv. The typical radiation dose to the target organ (kidney) is 0.41 mGy and the typical radiation dose to the critical organ (bladder and uterus) is 11.40 mGy and 1.32 mGy.

Abnormal renal function
^{99m}Tc 6.01 h

Organ	Absorbed dose per unit activity administered (mGy/MBq) (Abnormal renal function)				
	Adult	15 years	10 years	5 years	1 year
Adrenals	0.0026	0.0033	0.005	0.0074	0.013
Bladder	0.044	0.056	0.081	0.1	0.13
Bone surfaces	0.0036	0.0043	0.0064	0.0092	0.016
Brain	0.0015	0.0018	0.003	0.0048	0.0085
Breasts	0.0013	0.0016	0.0023	0.0037	0.007
Gallbladder	0.0027	0.0036	0.0059	0.0083	0.01
Gastrointestinal tract:					
Stomach	0.0022	0.0029	0.0047	0.0065	0.011
Small intestine	0.0031	0.0039	0.006	0.0088	0.014
Colon	0.0034	0.0044	0.0067	0.0096	0.014
Upper large intestine	0.0028	0.0037	0.0056	0.0086	0.013
Lower large intestine	0.0048	0.0053	0.0082	0.011	0.016
Heart	0.0021	0.0026	0.0039	0.0058	0.01
Kidneys	0.011	0.013	0.018	0.026	0.045
Liver	0.0028	0.0035	0.0053	0.0075	0.013

Organ	Absorbed dose per unit activity administered (mGy/MBq) (Abnormal renal function)				
	Adult	15 years	10 years	5 years	1 year
Lungs	0.0018	0.0023	0.0034	0.0052	0.0095
Muscles	0.0021	0.0026	0.004	0.0058	0.01
Oesophagus	0.0018	0.0022	0.0033	0.0052	0.0093
Ovaries	0.0043	0.0054	0.0079	0.011	0.016
Pancreas	0.0026	0.0033	0.0049	0.0074	0.013
Red marrow	0.0021	0.0026	0.004	0.0056	0.0093
Skin	0.0013	0.0016	0.0025	0.0039	0.007
Spleen	0.0023	0.003	0.0046	0.0068	0.012
Testes	0.0029	0.0029	0.0064	0.0092	0.014
Thymus	0.0018	0.0022	0.0033	0.0052	0.0093
Thyroid	0.0018	0.0022	0.0036	0.0057	0.01
Uterus	0.0069	0.0083	0.013	0.017	0.022
Remaining organs	0.0022	0.0028	0.0042	0.0064	0.011
Effective dose (mSv/MBq)	0.0046	0.0059	0.0088	0.012	0.018

The effective dose resulting from the administration of a maximal recommended activity of 120 MBq for an adult weighing 70 kg is about 0.55 mSv. The typical radiation dose to the target organ (kidney) is 1.32 mGy and the typical radiation dose to the critical organ (bladder and uterus) is 5.3 mGy and 0.83 mGy.

Acute unilateral renal blockage
^{99m}Tc 6.01 h

Organ	Absorbed dose per unit activity administered (mGy/MBq) (Acute unilateral renal blockage)				
	Adult	15 years	10 years	5 years	1 year
Adrenals	0.011	0.015	0.023	0.033	0.057
Bladder	0.049	0.062	0.091	0.12	0.14
Bone surfaces	0.0031	0.0041	0.006	0.0089	0.017
Brain	0.00011	0.00014	0.00024	0.0004	0.00079
Breasts	0.0004	0.00053	0.0011	0.0017	0.0031
Gallbladder	0.0064	0.0075	0.011	0.016	0.023
Gastrointestinal tract:					
Stomach	0.004	0.0046	0.0073	0.0097	0.013
Small intestine	0.0043	0.0055	0.0088	0.012	0.019
Colon	0.0038	0.0048	0.0074	0.01	0.014
Upper large intestine	0.004	0.0051	0.0078	0.011	0.016
Lower large intestine	0.0035	0.0044	0.0068	0.0094	0.012
Heart	0.0014	0.0017	0.0028	0.0042	0.0063
Kidneys	0.2	0.24	0.34	0.48	0.84
Liver	0.0046	0.0056	0.0084	0.012	0.017
Lungs	0.0011	0.0017	0.0026	0.004	0.0074
Muscles	0.0022	0.0027	0.0038	0.0055	0.0088
Oesophagus	0.00039	0.00056	0.00088	0.0016	0.0023
Ovaries	0.0036	0.0047	0.0072	0.01	0.014
Pancreas	0.0077	0.0093	0.014	0.019	0.029
Red marrow	0.003	0.0036	0.0051	0.0064	0.0084
Skin	0.00082	0.001	0.0016	0.0023	0.0042
Spleen	0.01	0.013	0.019	0.027	0.041
Testes	0.0018	0.0025	0.0045	0.0061	0.0084
Thymus	0.00039	0.00056	0.00088	0.0016	0.0023
Thyroid	0.00018	0.00024	0.00047	0.00096	0.0017
Uterus	0.0065	0.0079	0.012	0.016	0.02
Remaining organs	0.0022	0.0027	0.0037	0.0046	0.0068
Effective dose (mSv/MBq)	0.0099	0.012	0.018	0.024	0.037

The effective dose resulting from the administration of a maximal recommended activity of 120 MBq for an adult weighing 70 kg is about 1.19 mSv. The typical radiation dose to the target organ (kidney) is 24 mGy and the typical radiation dose to the critical organ (bladder and uterus) is 5.9 mGy and 0.78 mGy.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Withdrawals should be performed under aseptic conditions. The vials must not be opened before disinfecting the stopper, the solution should be withdrawn via the stopper using a single dose syringe fittedwith suitable protective shielding and a disposable sterile needle.
If the integrity of this vial is compromised, the product should not be used.
Method of preparation
Remove the protective foil and lift up the upper part of the paper box to access the vials. Never administer EC 2 mg kit or its components to patients, only the ^{99m}Tc-EC injection is allowed for human use.
^{99m}Tc-EC injection contains radioactive isotope. For handling, shipping and storage of this product the rules and regulations referring to the radioactive materials should be observed.
The labelling procedure to obtain ^{99m}Tc-EC injection by using EC 2 mg kit is described below.
Labelling procedure: One piece of Vial A is placed in a small lead container of 3 mm wall thickness. 2 ml of sterile sodium pertechnetate (^{99m}Tc) (0.8-1.6 GBq) is injected into the vial through the rubber stopper with a sterile single-use syringe under aseptic circumstances. Shake well.
Content of Vial B is dissolved in 2 ml of 0.9% sterile sodium-chloride solution. 0.5 ml of this solution is injected to Vial A, which is then allowed to stand for 15 minutes while it is shaken once or twice.
Content of Vial C is dissolved in 1 ml of 0.9% sterile sodium-chloride solution and the whole solution is added to Vial A and shaked. Now the solution in vial-A, which has a pH value in the range of 5 - 8, is ready for administration to patients
^{99m}Tc-EC injection should be used within 8 hours after labelling. The quantity of the radiochemical impurities does not exceed 5% at 15 min. after labelling and 10 % at expiry date.
Control of the drug product
Radiochemical purity of ^{99m}Tc-EC injection is tested by using thin layer chromatography.
Stationary phase: Kieselgel 60 (F254, catalogue code: Merck 5554) 1.5 x 20 strips
Mobile phase: 96 % ethanol,
Development is carried out at room temperature (20–25 ºC).
Development of chromatograms
Three strips are prepared and 5 – 5 µl-s of test solution are dropped at 1.5 cm from the bottom of the strips. Chromatograms are developed up to a front distance of 15 cm.
Evaluation: Dry the strips at room temperature and determine the radioactivity by using a scanner.
Radiochemical purity is calculated by using the data of three replicates.
Information on R_f values:

Reduced ^{99m}Tc + hydrolysed ^{99m}Tc	0.0 – 0.1
Labelled complex	0.4 – 0.5
Free $^{99m}TcO_4^-$	0.9 – 1

Radiochemical purity is calculated by using the peak areas. Total activity of the strip is considered 100% and activity percentage due to ^{99m}Tc-EC peak is the radiochemical purity, which is not less than 95 % at 15 min. after labelling and 90% at expiry date.
Any unused product or waste material should be disposed of in accordance with national regulation on radioactive materials.

Package leaflet: Information for the patient

EC 2 mg kit for radiopharmaceutical preparation
Ethylene-dicysteine

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your nuclear medicine doctor.
- If you get any side effects, talk to your nuvlear medicine doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What ^{99m}Tc-EC is and what it is used for

This medicine is radiopharmaceutical product (containing radioactive isotope) for diagnostic use only.
^{99m}Tc-EC injection prepared from EC kit is a diagnostic radiopharmaceuticals contains (^{99m}Tc)-technecium isotope radioactive sterile injection for intravenous administration. Use of EC is permitted only in departments of nuclear medicines.
The ^{99m}Tc-EC injection is colourless or yellow solution for intravenous use. This radiopharmaceutical is taken up by the kidneys from the blood and is excreted by the urinary tract, providing a modality for dynamic renal examinations.
As the medicine contains gamma-emitter radioactive isotope, it can be detected from outside the body using gamma cameras. The pictures taken by this camera show the distribution of the radioactive isotope in your body and organs. The pictures can give your doctor valuable information about the structure and working of the organ helping this way to choose the best treatment.
This radiopharmaceutical is for detection of the impaired renal functions.
The use of ^{99m}Tc-EC injection does involve exposure to small amounts of radioactivity. Your nuclear medicine doctor has considered that the clinical benefit that you will obtain from the procedure with the radiopharmaceutical outweighs the risk due to radiation.

2. What you need to know before ^{99m}Tc-EC is used

^{99m}Tc-EC must not be used
if you are allergic to Ethylene-dicysteine or any of the other ingredients of this medicine (listed in section 6).
Warnings and precautions
Inform the nuclear medicine specialist if any of the following apply to you:
- if you are pregnant or believe you may be pregnant
- if you are breast-feeding

When using ^{99m}Tc-EC injection, you are given a small amount of radioactive radiation. Although this effect is less than in some X-rays, your doctor will always take into account potential risks and benefits. If you have any doubt, it is important to consult your nuclear medicine doctor before receiving the product.
Make sure you carry out the doctor's instructions both before and after the examination in order to avoid radioactive exposure of other people and the radioactive contamination of the environment. The radioactive isotope is excreted in the urine, faeces, sweat and other secretions temporarily contaminating the environment this way according to the short half-life of (^{99m}Tc)-technecium.

Before administration of ^{99m}Tc-EC injection
Before administration drink plenty of water and to be well hydrated before the start of the examination in order to urinate as often as possible during the first hours after the study.

Children and adolescents
Talk to your nuclear medicine doctor, if you are under 18 years old.

Other medicines and ^{99m}Tc-EC
Please tell your nuclear medicine doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription, since they may interfere with the interpretation of the images.

Using ^{99m}Tc-EC with food and drink
You can take ^{99m}Tc-EC with any food or drink.

Pregnancy and breast-feeding
You must inform the nuclear medicine doctor before the administration of ^{99m}Tc-EC if this is a possibility you might be pregnant, if you have missed your period or if you are breast-feeding. When in doubt, it is important to consult your nuclear medicine doctor who will supervise the procedure.
Pregnancy
Your nuclear medicine doctor will only administer this medicine during pregnancy if a benefit is expected which would outweigh the risks.
Examination of radioactive radiation on pregnant women is a risk to the fetus as well. During pregnancy, therefore, only indispensable examinations can be carried out when the expected benefit outweighs the risk to the mother and the child.
Breastfeeding
Since radioactivity can be absorbed into breast milk the consideration should be given to the possibility of delaying the administration of radionuclide until the mother has ceased breastfeeding.
If you are breastfeeding and the doctor decides to perform the examination, the breastfeeding should be discontinued for as long as it is recommended by the doctor. During that time, pour out breast milk until radioactivity is clearing from your body. At the time the infant should be nourished artificially. Nuclear medicine doctor tells you when you can resume breast-feeding.

Driving and using machines
It is considered unlikely that ^{99m}Tc-EC injection will affect your ability to drive or to use machines.

3. How ^{99m}Tc-EC is used

There are strict laws on the use, handling and disposal of radiopharmaceutical products. ^{99m}Tc-EC will only be used in special controlled areas. This product will only be handled and given to you by people who are trained and qualified to use it safely. These persons will take special care for the safe use of this product and will keep you informed of their actions.
^{99m}Tc-EC injection is prepared by mixing the content EC 2 mg kit and radioactive (^{99m}Tc)-pertechnate at the site of the use (hospitals, clinics). The ^{99m}Tc-EC injection is administered intravenously.
The nuclear medicine doctor supervising the procedure will decide on the quantity of ^{99m}Tc-EC injection to be used in your case. It will be the smallest quantity necessary to get the desired information.

Use in children and adolescents
In children and adolescents, if the doctor decides to perform the examination the quantity to be administered will be adapted to the child's weight.

Duration of the procedure
Your nuclear medicine doctor will inform you about the usual duration of the procedure.

After administration of ^{99m}Tc-EC injection
Drink large amounts of fluid and urinate frequently in order to eliminate the product from your body. This prevents the radioactive substance from accumulating in the bladder.
The nuclear medicine doctor will inform you if you need to take any special precautions after receiving ^{99m}Tc-EC. Contact your nuclear medicine doctor if you have any questions.

What should you do if you received overdose of the medicinal product?
There are strict rules and regulations on handling, use and disposal of radioactive materials.
Since ^{99m}Tc-EC is given by a doctor under controlled conditions, the probability of overdose is low. However, in the case of an overdose, you will receive the appropriate treatment. In particular, the nuclear medicine doctor will advise you to drink lots of liquid which will accelerate the elimination of the drug from your body. You should take all necessary precautions against the contamination of your environment with radioactivity. Comply with the instructions given by your doctor. ^{99m}Tc-EC which is temporarily present in your body and the excreted material loose their radioactivity in a natural way.
Should you have any further questions on the use of this medicine, please ask the nuclear medicine doctor who supervises the procedure.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
The use of ^{99m}Tc-EC injection does involve exposure to small amounts of radioactivity. Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. However, these effects are hardly expected regarding the applied amount of activity.
Adverse event and reactions have not been reported ever since the authorization of the product (1992). Considering the number of the examinations carried out since, no adverse reactions are expected, less than 1/10000.
The amount of radioactivity in the body from ^{99m}Tc-EC injection is small. It will be passed out of the body in a few days without any intervention. If you have any further questions on the use of this medicine, ask your doctor.
Reporting of side effects
If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system one of the contacts (In Hungary: www.ogyei.gov.hu). By reporting side effects you can help provide more information on the safety of this medicine.

5. How ^{99m}Tc-EC is stored

You will not have to store this medicine. This medicine is stored under the responsibility of the specialist in appropriate premises. Storage of radiopharmaceuticals will be in accordance with national regulation on radioactive materials.
Hospital staff will ensure that the product is stored correctly and not used after expiry date stated on the label.
The following information is intended for the specialist only.
Keep out of the reach and sight of children.
Keep out of the reach and sight of the people who are not authorized to handle, use or transport this product.
EC 2 mg kit should be stored in refrigerator at 2 – 8 ºC. Keep the bottle in the outer carton in order to protect from light.
The radiolabelled injection (^{99m}Tc-EC injection) is to be stored below 25°C and protected from light.
Storage of the radiolabelled injection should be in accordance with national regulation on radioactive materials.
^{99m}Tc-labelled EC must be used within 8 hours.
This medicine must not be used after the expiry date (EXP) which is stated on the label of vial and box. The expiry date refers to the last day of that month.

6. Contents of the pack and other information

What EC 2 mg kit contains
- The active substance is 2.0 mg ethylene-dicysteine (EC) in vial-A.
- Other ingredients are:
  - vial-A: Disodium phosphate dihydrate, Mannitol, Ascorbic acid, Disodium edetate.
  - vial-B: Stannous chloride dihydrate, Tartaric acid, Ascorbic acid.
  - vial-C: Potassium dihydrogen phosphate, Ascorbic acid.
- The active substance of the labelled, radioactive EC: ^{99m}Tc-EC.

What EC 2 mg kit looks like and contents of the pack

^{99m}Tc-EC injection is colourless or yellowish solution.
EC 2 mg kit for radiopharmaceutical preparation consists of vial-A, vial-B and vial-C. The injection vials containing the sterile, pyroge-free, freeze-dried product. The content of vial-A and vial-B are white or slightly yellow powder, while vial-C is white or yellow paste.
Sterile, type I, 6 ml (colourless, 6R type) injection vial sealed with winered (halobutyl) rubber stopper and flip-off aluminium cap combined with red (Vial A), yellow (Vial B), green (Vial C) polypropylene disc.
Multidose vial.
The EC 2 mg kit contains vials for 4 individual labelling, i.e. 4 pieces of vial-A, 4 pieces of vial-B and 4 pieces of vial-C. Position of the vials inside the box is fixed by a carton insert, which prevents the moving of the vials. The colour of the stripe of the vial labels are different:
for vial-A: red
for vial-B: yellow and
for vial-C: green.
These vials are packed into one paper box, covered by celluloid foil.

Marketing Authorisation Holder and Manufacturer

Institute of Isotopes Co. Ltd.
Addresse: 1121 Budapest, Konkoly-Thege Miklós str. 29-33.
✉ 1535 Budapest, P.O.B. 851.
Tel.: +36 1 391 0859; +36 1 391 0860, Fax: +36 1 395 9070
E-mail: radiopharmacy@izotop.hu

This leaflet was last revised in: 09/2020
This leaflet was translated by the manufacturer based on the original Hungarian document, authorized by the Hungarian National Institute of Pharmacy on 28.09.2020.
OGYI-T-9141/01