



SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

EC kit for radiopharmaceutical preparation

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

2.0 mg EC (Ethylene-dicysteine) in vial A.

For a list of excipients, see section 6.1.

Composition of the injection prepared with EC kit: 0.8–1.6 GBq ^{99m}Tc -EC.

3. PHARMACEUTICAL FORM

Pharmaceutical form of EC kit: powder for injection (lyophilisate)
Pharmaceutical form of ^{99m}Tc -EC: injection

^{99m}Tc -EC injection can be prepared *in situ* at the site of the use i.e. 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 / ^{99}Mo generator.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.
 ^{99m}Tc -EC is used for renal tubular functional imaging, dynamic kidney tests by imaging technique, camera renography.

4.2 Posology and method of administration

The recommended doses for adults (of 70 kg average body weight) are in the range of 90–120 MBq of ^{99m}Tc -EC.

^{99m}Tc -EC injection, obtained in one labelling procedure, can be divided for 3–6 patients.

^{99m}Tc -pertechnetate activity for labelling is chosen so that individual patient dose should be 90–120 MBq in the time of the investigation.

For paediatric examination use Webster's equation (given below) to determine the activity to be administered

$$A_{\text{child}} = [(N+1)A_{\text{adult}}] / (N+7)$$

where: N: age of the child [year]

A_{child} : activity [MBq]

Method of 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 acquired 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 acquired. 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.

4.4 Special warnings and precautions for use

The demand for an isotope diagnostic test should be well indicated, based on the previous diagnosis of the patient and the possible lowest activity should be used.

Radioactive medicinal products should be received, used and administered only by authorised person in designated clinical settings. Receipt, storage, use, transfer and disposal of the radioactive medicinal products are subject to the regulations and appropriate licences of the competent authorities.

Appropriate lead shieldings should be used during the preparation and the examination, to protect the patient and the staff from the risk of the radiation, as it is possible.

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. In this case, lowered activity should be used (see section 4.2).

Use of the product is contraindicated in case of pregnancy and lactation except if the necessity and importance of obtaining the diagnostic information outweighs the risk associated with the radiation exposure (see section 4.6).

The patient should not contact small children during 12 hours post injection.

4.5 Interaction with other medicinal products and other forms of interaction

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

4.6 Pregnancy and lactation

Pregnancy:
There is no clinical experience of the use of ^{99m}Tc -EC injection in pregnant women. When it is necessary to administer radioactive medicinal products to women of childbearing potential, information should always be sought about pregnancy. Any woman who has missed a period should be assumed pregnant until proven otherwise. Alternative techniques which do not involve ionising radiation should also be considered.

Treatment of women of child bearing potential is recommended in the first 10 days after menstruation.

Lactation:
Although there is no evidence of excretion of ^{99m}Tc -EC into the breast milk, it should be considered that the isotope diagnostic examination could be postponed until the end of the lactation period. If the examination cannot be postponed, lactation should be ceased for 12 hours and the breast milk produced during this period, should not be used. If possible, breast milk obtained before the administration of the radioactive injection should be collected and used in that 12 hrs period.

From radiation protection reasons, the patient should not contact small children during 12 hours post injection.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.
In occurrence of unexpected adverse reactions driving and/or working with machines should be reconsidered.

4.8 Undesirable effects

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.

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. LD₅₀ value, obtained in a 14-day long test is 38.4 mg / kg of bodyweight.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

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

6.2 Incompatibilities

Vial-A: disodium hydrogenphosphate dihydrate, mannitol, ascorbic acid sodium edetate
Vial-B: stannous chloride dihydrate, tartaric acid, ascorbic acid
Vial-C: potassium dihydrogenphosphate, ascorbic acid.

6.3 Shelf life

Shelf life of EC kit is 12 months from the day of production.
The ^{99m}Tc -EC injection should be used within 8 hours after labelling.

6.4 Special precautions for storage

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

6.5 Nature and contents of container

The 6 ml injection vials, containing the freeze-dried product, are closed with rubber stopper and tear-off kombicap (aluminium and plastic).
The EC 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

The rest of labelled solution and the stripes used chromatography must be handled as radioactive waste, in accordance with the regulations on radiation.
Any unused product or waste material should be disposed of in accordance with local requirements.
Never administer EC kit or its components to patients, only the ^{99m}Tc -EC injection is allowed for human use. The labelling procedure to obtain ^{99m}Tc -EC by using EC kit is described in section 12.

4.9 Overdose

No case of overdose has been reported.

In case of overdose, the elimination of the radioisotope can be facilitated 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 1.1. Necessity and method of further treatment should be concluded based on these results. The table of Chapter 1.1 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 ^{99m}Tc -EC administered to one patient is not less than 0.33 mg and not more than 0.67 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, which may correspond to 0.029 mg/kg in case of 70 kg body weight.

Acute toxicity studies on mice shows there are not any clinical symptom, if less than 11.4 mg/kg of bodyweight is administered. LD₅₀ value, which was obtained in a 14-day long test, is 38.4 mg / kg of bodyweight. Therefore appearance of clinical symptoms is not expected even if the whole content of the vial containing the labelled substance (2 mg of ^{99m}Tc -EC) is administered to one patient by mistake.

At the same time, if the labelled ^{99m}Tc -EC is divided to less than 3 patients, 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-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 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 0.33 mg and not more than 0.67 mg of ^{99m}Tc -EC is administered to a patient. Pharmaceutical effect such small quantities cannot be observed.

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: commerce@izotop.hu

8. MARKETING AUTHORISATION NUMBER(S)

OGYI-T-09141/01

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

First authorization: 03. July 1992.
Renewals: 13. December 2003 and 14. October 2009.

10. DATE OF REVISION OF THE TEXT

14. October 2009.

This SPC was translated by the manufacturer based on the original Hungarian document, authorized by the Hungarian National Institute of Pharmacy on 14.10.2009.

11. DOSIMETRY



PACKAGE LEAFLET: INFORMATION FOR THE USER

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Radiation properties:

Physical half life	6 hrs
Energy and yield of emitted photons	140 keV, 100 %
Energy and yield of beta particles	- , -

During the decay of ^{99m}Tc radioisotope, ^{99}Tc is formed from $^{99}\text{Mo}/^{99m}\text{Tc}$ generator, by beta decay of ^{99}Mo radionuclide. As side product of the decay, ^{99}Tc is also formed.

Organ	Absorbed dose [$\mu\text{Gy}/\text{MBq}$]
Kidneys	17.0
Liver	5.0
Urinary bladder	43.0
Ovaries, testes	7.0
Whole body	1.0

1. WHAT EC KIT IS AND WHAT IT IS USED FOR

This medicine is for diagnostic use only. ^{99m}Tc -EC, prepared from EC kit at the site of utilisation, is a radioactive sterile injection for intravenous use and can be applied for the dynamic studies of kidney (function of kidney) by imaging technique. Use of EC kit 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. This labelling procedure to obtain ^{99m}Tc -EC by using EC 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 $[^{99m}\text{Tc}]$ perchlorate (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 shook. 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. Within this period the quantity of the radiochemical impurities does not exceed 10%. Control of the drug product.

Radiochemical purity of ^{99m}Tc -EC 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 °C). 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 1.5 cm. Evaluation. Dry the strips and impregnate them with 5% polystyrene solution. Determine the radioactivity by using a scanner. Radiochemical purity is calculated by using the data of three replicates.

Information on R_f values:
Reduced $^{99m}\text{Tc} +$ hydrolysed ^{99m}Tc 0.0 – 0.1
Labelled complex 0.4 – 0.5
Free $^{99m}\text{TcO}_4^-$ 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 90% at expiry date.

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

EC kit for radiopharmaceutical preparation

Ethylen-L,L-dicystein

Read all of this leaflet carefully before this medicine is used for your examination.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

In this leaflet:

1. What EC kit is and what it is used for
2. Before you use EC kit
3. How to use EC kit
4. Possible side effects
5. How to store EC kit
6. Further information

2. BEFORE YOU USE EC KIT

Important information about some of the ingredients of EC kit

When you are given ^{99m}Tc -EC you receive a small amount of radiation. The absorbed dose in this case is usually smaller than those of certain X-ray examinations (e.g. CT). Your doctor will always consider the possible risks and advantages.

If you have any further questions on the use of this medicine, ask your doctor.

3. HOW TO USE EC KIT

^{99m}Tc -EC prepared with EC is administered intravenously.

Amount of the administered activity, method and timing of imaging is decided by your doctor according to the type of examination and your state of health.

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. Therefore, ^{99m}Tc -EC can only be used in hospitals or institutes. EC can be handled, used and administered only by people specialized for handling of radioactive materials and waste. These people give you instructions about the precautions and warnings. Comply with their instructions.

Since ^{99m}Tc -EC is given by a doctor under controlled conditions, the probability of overdose is low. In the unlikely event of overdose your 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 special care.

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. If you have any further questions on the use of this medicine, ask your doctor.

4. POSSIBLE SIDE EFFECTS

Like every medicinal product, EC kit might cause adverse reactions, but such effects do not appear in every case. If any adverse reaction becomes serious, inform your doctor.

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. The amount of radioactivity in the body from ^{99m}Tc -EC 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.

5. HOW TO STORE EC KIT

It is the responsibility of the hospital staff to ensure that the product is stored correctly and not used after expiry date stated on the label. Keep out of the reach and sight of children and people who are not authorized to handle, use or transport this product!

Radioactive ^{99m}Tc -EC is to be stored below 25°C, considering the regulations for radiation safety. The storage conditions as well as the expiry date are indicated on the vial and box labels.

6. FURTHER INFORMATION

What EC kit contains ?

The active substance is 2.0 mg ethylene-L,L-dicystein (EC) in vial-A. Other ingredients are:
- vial-A: disodium hydrogenphosphate dihydrate, mannitol, ascorbic acid, sodium edetate .
- vial-B: stannous chloride dihydrate, tartaric acid, ascorbic acid .
- vial-C: potassium dihydrogenphosphate, ascorbic acid .

How EC kit and ^{99m}Tc -EC injection look like and what is the contents of the pack?

^{99m}Tc -EC injection is colourless or yellow solution which is prepared in the hospital isotopes laboratory by using EC kit and ^{99m}Tc -perchlorate. EC kit consists of vial-A, vial-B and vial-C. The injection vials containing the sterile, pyroge-free, freeze-dried product are closed with rubber stopper and tear-off kombicap (aluminium and plastic). One paper box of EC kit contains 4 vial-A, 4 vial-B and 4 vial-C. The content of vial-A is homogenous, white powder, while that of vial-B and vial-C can be pale yellow or yellow.

Marketing Authorisation Holder and Manufacturer

Institute of Isotopes Co. Ltd.
Addressee: 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: ragyoo@izotop.hu

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