SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Techida 30 mg powder for solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One injection vial contains 51.3 mg lyophylisate with the next composition:
Diethyl-acetanilid-imino diacetic acid 30.0 mg.
The radionuclide is not part of the kit.

Excipients:
The product contains 7.86 mg sodium as excipient.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Kit for radiopharmaceutical preparation.
Powder for solution for injection.
The medicinal product must be reconstituted with sodium pertechnetate (^{99m}Tc) solution for injection.
Sterile, pyrogen-free, white powder (lyophilisate).

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

Indication area:
- Isotope diagnostics of hepatobiliar system.
- Dynamic examination of the function of the hepatocytes.
- Liver transplant evaluation.
- Dynamic examination of flow disorders in the hepatobiliary system (blockage in the biliary duct, etc.).
- Examination of the acute cholecystitis.
- Verification of focal nodular hyperplasia.

4.2 Posology and method of administration

Posology:

The recommended dose is 150-200 MBq of ^{99m}Tc-Techida for intravenous use.
The composition contains less than 1 mmol sodium (23 mg) per vial, i.e. practically sodium-free. A single patient dose contains up to 1.96 mg of sodium.

For paediatric examination use Webster's equation (given below) to determine the activity to be administered and see Chapter 4.3.

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

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

Method of administration:
The number of patients to be examined from the labeled composition is determined by the amount of activity level for each assay.
^{99m}Tc-pertechnetate activity for labelling has to be chosen in range of 0.8–1.6 GBq so that individual patient dose should be 150–200 MBq at the time of the investigation.

Method of examination:

For examination of the function of the hepatocytes start imaging and intravenous administration simultaneously. Determine the perfusion, uptake and excretion phases by using the images. Generated curve by using the data of the images should be evaluated quantitatively.

For examination of the hepatobiliary system, take a series of pictures at 2, 5, 10, 15, 30 and 45 minutes after intravenous administration. Determine time-activity curve by using the following ROIs: heart, right lobe of the liver, gallbladder and duodenum.

For instructions on reconstitution of the medicinal product before administration, see section 6.6 and 12.

4.3 Contraindications

- Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.
- Under 18 years of age (See section 4.2) except if the necessity and importance of obtaining the diagnostic information outweights the risk associated with the radiation exposure.
- Pregnancy and lactation (See section 4.6) except if the necessity and importance of obtaining the diagnostic information outweights the risk associated with the radiation exposure.
- The product must not be used if the patient does not provide an oral or written consent of being examined by using radionuclide.

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.
This medicinal product contains radioactive isotope after radiolabelling. Receipt, storage, use, transfer and disposal of the radioactive medicinal products are subject to the regulations and appropriate licences of the competent authorities. Radioactive medicinal products should be received, used and administered only by authorised person in designated clinical settings. Way of handling of radiopharmaceuticals should meet the criteria both of radiation safety and pharmaceutical quality requirements. Appropriate lead shieldings should be used during the preparation of the ^{99m}Tc-Techida injection and the examination, to protect the patient and the staff from the risk of the radiation, as it is possible.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.
No interactions are known.

4.6 Fertility, pregnancy and lactation

Pregnancy
Use of the product is contraindicated in case of pregnancy and lactation except if the necessity and importance of obtaining the diagnostic information outweights the risk associated with the radiation exposure.
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 be considered.
Treatment of women of child bearing potential is recommended in the first 10 days after menstruation.

Lactation:
There is no data of the ^{99m}Tc-Techida secreted in breast milk. Before administering a radioactive medicinal product to a mother who is breast feeding, consideration should be given as to whether the investigation could be reasonably delayed until the mother has ceased breast feeding.
^{99m}Tc is excreted in breast milk. If the administration is considered necessary breast feeding should be interrupted for 12 hours and the expressed milk discarded. During this period the previously collected breast milk should be used. The patient administered by radioactive injection should avoid the close contact with children for 12 hours due to the radiation protection.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Adverse event and reactions have not been reported ever since the authorization of the product (1985) nor registered in the literature. Considering the number of the examinations carried out since, no adverse reactions are expected (frequency lower 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 amount of activity.
According to the table in Chaptert 11, the most endangered organ is the bladder, the dose absorbed by it is 5.1 mGy for standard 120 MBq administered activity; the total dose is 0.12 mGy, i.e. the effective dose remains below 20 mSv.

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. Administration of higher activities than prescribed is unnecessary and must be avoided in order to avoid the excess absorbed radiation dose of 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-Techida. Multiply these specific absorbed radiation dose data by the effectively administered activity (in MBq) to obtain the required absorbed radiation dose data in µGy.

Quantity of ^{99m}Tc-Techida administered to one patient is not less than 2.8 mg and not more than 7.5 mg if administration is complying with the recommendations. If the whole content of the vial containing the labelled substance is administered to one patient by mistake 30 mg of ^{99m}Tc-Techida is introduced in the body.

Acute toxicity studies on mice showed no clinical symptoms if less than 9 mg/kg of bodyweight is administered. If the whole content of the vial containing the labelled substance is administered to one patient by mistake, it represents 0.43 mg/kg of bodyweight level (calculated on 70 kg average bodyweight). This is equivalent to 4.8 % of the no observed effect level. Thus, no toxic effects are expected in case of overdose.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Diagnostic radiopharmaceutical, ATC code: V09DA02

After administered intravenously ^{99m}Tc-Techida binds to plasma proteins and is transported to the liver where hepatocytes uptake it by active transport in a anionic process which is similar to that of bilirubin. Uptake of ^{99m}Tc-Techida by the hepatocytes highly depends on the liver function. High levels of serum bilirubin inhibit the excretion of ^{99m}Tc-Techida via the liver which brings about that the significant percentage of the activity is excreted via the kidneys. In this case, the bladder appears intensively on the images of the gamma camera test.

The following three factors predominantly govern the excretion of ^{99m}Tc-Techida by the liver: the plasma albumin concentration, the intensity of the blood flow through the liver, and the hepatocyte function.

^{99m}Tc-Techida is excreted either in a non-metabolised form or bound to bile acids. The normal way of elimination is: liver – gallbladder – duodenum – intestines.

5.2 Pharmacokinetic properties

^{99m}Tc-Techida rapidly eliminates from the blood; one hour after administration less than 1 % of the substance is present. It appears in the liver one minutes after administration and reaches its highest activity after 10–15 minutes. Hepatic excretion normally has a half-life of 20–25 minutes. The half life highly depends on the plasma albumin concentration, intensity of blood circulation and hepatocyte function. 15 minutes after administration the bile duct appears on the images and after 30 minutes the gallbladder becomes visible. Highest activity in the gallbladder is reached after 30 – 40 minutes. 40 – 45 minutes after administration duodenum is well visible on the images.

5.3 Preclinical safety data

An intravenous acute toxicity study of mice showed no clinical symptoms up to 9 mg/kg of bodyweight. Quantity of ^{99m}Tc-Techida, if administration is complying with the recommendations, is not less than 5 mg and not more than 10 mg. With a mean body weight of 70 kg, the minimum and maximum amounts are equivalent to 0.8 and 1.6 % of the no observed effect level, respectively. Thus, there is no special hazard for humans and the use of the product is safe.

Further advantage of the product is that the activity of [^{99m}Tc]pertechnetate in the range of 0.8–1.6 GBq does not affect the radiochemical purity of the preparation. Quantity of radiochemical impurities is always less than 10 %, therefore the kit is safe from the point of view of labelling.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Stannous chloride dihydrate, ascorbic acid, sodium chloride.

6.2 Incompatibilities

This medicine can only be mixed with the medicines listed in section 12.

Stannous chloride component of Techida kit is a reducing agent. It reduces free pertechnetate from +7 oxidation state to +4 oxidation state, in which technetium readily forms complex with Techida. It is important to keep away the content of the vials from moisture and oxidising agents, for example chemical oxidation agents or oxygen of the air. Alkaline media facilitate the oxidation of Sn(II) before the labelling reaction this is why the product is incompatible with bases. As a result of these incompatibilities it is recommended to remove the closure of the closed injection vials just before the labelling reaction. Perform the labelling by observing the instructions detailed in Chapter 12.

For preparation of ^{99m}Tc-Techida only ^{99m}Tc-pertechnetate- and physiological NaCl solution can be used (See chapter 12). The Techida kit is incompatible with other materilas.

6.3 Shelf life

Kit: 24 months from production date.
The expiry date is also available on the outer carton and on the vial label.
After radiolabelling: After dissolution and radiolabelling, the labelled formulation should be used within 6 hours.

6.4 Special precautions for storage

Kit: Store in refrigerator (2-8°C) in its original box.
Radiolabelled medicinal product: is to be stored in refrigerator (2 - 8°C).
The reconstituted injection maintains its stability at 2 - 8°C for 6 hours. From a microbiological aspect, the preparation should be used immediately after preparation of the solution. If not used immediately, the user is responsible for the duration and conditions of pre-use storage of the reconstituted solution.
Storage of radiopharmaceuticals should be in accordance with national regulations on radioactive material.

6.5 Nature and contents of container

Type I glass injection vial (volume 6 ml) closed with rubber stopper and tear-off combicap (aluminum and plastic).
A box contains 6 vials for labelling. The white carton is sealed with celluloid shrink foil.

Content of the package:
Six vials, Summary of Product Characteristic (SPC) and Patient Information Leaflet (PIL) and six label with radioactive symbol.

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 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.

Contents of the vial are intended only for use in the ^{99m}Tc-Techida injection 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 minimise risk of contamination of the medicinal product and irradiation of the operators. Adequate shielding is mandatory.
The content of the kit before reconstitution is not radioactive. However, after sodium pertechnetate (^{99m}Tc) Ph. Eur. 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 or any other body fluid. 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.

7. MARKETING AUTHORISATION HOLDER

Institute of Isotopes Co. Ltd.
Addresse: 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: izotop@izotop.hu; radiopharmacy@izotop.hu

8. MARKETING AUTHORISATION NUMBER(S)

OGYI-T-9210/01

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 19 March 1985.
Date of latest renewal: 17 December 2009.

10. DATE OF REVISION OF THE TEXT

25 May 2017.

11. DOSIMETRY

Individual patient dose is 150–200 MBq. Estimated absorbed dose values of 1 MBq of the injection for an average body weight of 70 kg are given in the table below.

Organ	Absorbed dose [µGy/MBq]
Liver	20.5
Choledoctus	246.0
Kidneys	12.0
Ovaries	16.7
Whole body	4.3

The ^{99m}Tc isotope is generated in a ^{99}Mo generator during β decay.

Radiation physical properties of the labelled medicinal product:

Physical half-life	6 hours	
Energy and intensity of the emitted gamma photons	140 keV	100 %
Energy and intensity of the emitted beta particles	_	_

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Preparation of ^{99m}Tc-Techida:
Remove the protective foil and lift up the upper part of the paper box to access the vials.
Techida vial can only be administered to patient after labelling with sodium pertechnetate (^{99m}Tc) solution fo injection (Ph. Eur.). Only the labelled ^{99m}Tc-Techida injection can be administered.

Labelling procedure:
All procedures have to be carried out under aseptic conditions.
Place the vial containing the freeze-dried powder in a small lead container with a wall thickness of 3 mm and inject 0.8–1.6 GBq of sterile sodium pertechnetate (minimal volume: 2 ml, max. volume:5 ml) into the vial through the rubber stopper with a sterile syringe.
Shake well and allow to stand at room temperature for 15 minutes. The ^{99m}Tc-Techida injection can be used for intravenous administration. pH of the medicinal product is in the range of pH = 5–7.

Quality control

Radiochemical purity of the injection Ph. Eur. 2.2.27

Determination of radiochemical purity of the injection (according to Ph. Eur. 2.2.27)

Preparation of injection: place one vial of Techida into a lead container. Inject the ^{99m}Tc eluate of having activity of 800 to 1600 MBq in no more than 5 ml volume into the vial without removing its cap (through rubber stopper). Shake thoroughly allow 15 minutes for the reaction to take place. Label one vial and develop three replicate chromatograms in a test.

Development of chromatograms: Examine by thin-layer chromatography using F254 fluorescent silicic acid as the coating substance on a glass plate (Merck 105808). Heat the plate at 110°C for 10 minutes cool down before use. Apply to the plate 5 µl of the injection to be examined without drying. Develop immediately over a path of 15 cm using a 9 g/l solution of sodium chloride (saline). After that allow the plate to dry. Determine the distribution of radioactivity by gamma scanner.

Specification:
Expected Rf values are:
Colloidal technetium 0.0-0.2 (start)
Labelled complex 0.5-0.7 (middle)
Pertechnetate ion 0.8-1.0 (front)

The radiochemical purity (the relative amount of labelled complex) is not less than 90%.

PACKAGE LEAFLET: INFORMATION FOR THE PATIENT

Techida 30 mg powder for solution for injection
diethyl-acetanilid-imino diacetic acid

Read all of this leaflet carefully before you take 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 doctor or health care professional.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Techida 30 mg powder for solution for injection is and what it is used for?

This medicine is for diagnostic use only.

^{99m}Tc-Techida injection prepared from Techida kit is a colourless, sterile solution that contains radioactive isotope. Use of Techida is permitted only in departments of nuclear medicines.
^{99m}Tc-Techida injection is administered intravenously. After intravenous administration, ^{99m}Tc- Techida is transported to the liver via the blood circulation. As the medicine contains gamma-radiator 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 liver, gallbladder and duodenum helping this way to choose the best treatment.

2. What you need to know before you Techida 30 mg powder for solution for injection is used for your examination

Do not use Techida 30 mg powder for solution for injection:
- if you are allergic (hypersensitive) to the diethyl-acetanilid-imino diacetic acid or any of the other ingredients of Techida (section 6).
- if you are pregnant or breast feeding, except if your doctor decides otherwise.
- if you are under 18 years of age, except if your doctor decides otherwise.

Warnings and precautions
Talk to your doctor before using Techida 30 mg powder for solution for injection.
The administered ^{99m}Tc-Techida injection will deliver low amount of ionising radiation. The adsorbed dose in this case is usually smaller than those of certain X-ray examinations (CT) and doctor will always consider the possible risks and advantages.
Should you have any further question please ask your doctor before administration. 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.

Children and adolescents
Use of ^{99m}Tc-Techida is not recommended for patients under 18 years of age. Your doctor will consider the necessity and importance of the radioisotope diagnostics.

Other medicines and Techida
Tell your doctor if you are taking, have recently taken or might take any other medicines.

Techida 30 mg powder for solution for injection with food and drink
You can take Techida with any food or drink.

Pregnancy and breast-feeding
You must inform your doctor if you are pregnanat or breastfeed.
In these cases your doctor will consider the necessity of the radioisotope diagnostics. The radioisotope can be dangerous to the foetus and the infant, as it is excreted in mother's milk partially. Therefore, it is possible that your doctor will choose other, non-radioactive method. Trust your doctor, his /her makes medical decision according to the strict regulations.
If you are breast-feeding and you will be examined with this product, you should stop breast-feeding for the period recommended by your doctor. During this time the radioactive isotope will be eliminated from your body. Use formula feed for your child. The breast milk should be expressed and collected and spilled out after dilution. You can restart breast-feeding when the radiation dose for the child is less than 1 mSv. Your doctor will decide about the restarting.

Driving and using machines
^{99m}Tc-Techida injection has no influence on the ability to drive and use machines.

Techida 30 mg powder for solution for injection contains stannous chloride dihydrate, ascorbic acid, sodium chloride.
The composition contains less than 1 mmol sodium (23 mg) per vial, i.e. practically sodium-free. A single patient dose contains up to 1.96 mg of sodium.

3. How to use Techida 30 mg powder for solution for injection?

^{99m}Tc- Techida injection is prepared by mixing the content Techida kit and radioactive ^{99m}Tc-pertechnetate at the site of the use (hospitals, clinics). The injection 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.

If you have been administerd more than you should
There are strict rules and regulations on handling, use and disposal of radioactive materials. Therefore, ^{99m}Tc-Techida injection can only be used in hospitals or institutes.
Techida 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- Techida 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 against the contamination of your environment with radioactivity. Comply with the instructions given by your doctor.
If you have any further questions on the use of this medicine, ask your doctor.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Any side effect becomes serious please contact your doctor.
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, frequency lower than 1/10000.
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 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 to store Techida powder for solution for injection

Keep this medicine out of the reach and sight of children!

Hospital staff will ensure that the product is stored correctly and not used after expiry date stated on the label.

Kit: Store in refrigerator (2 - 8°C) in its original box.
Radiolabelled medicinal product: is to be stored in refrigerator (2 - 8°C) considering the radiation protection rules.
Injection can be used within 6 hours after reconstitution.
Expiry and storage conditions are stated on the label.

6. Contents of the pack and other information

What Techida 30 mg powder for solution for injection contains?
- The active substance is 30 mg diethyl-acetanilid-imino diacetic acid.
- Other ingredients are: stannous chloride dihydrate, ascorbic acid, sodium chloride.
- The active substance of the labelled, radioactive Techida: ^{99m}Tc-Techida.

What Techida 30 mg powder for solution for injection looks like and contents of the pack?

Type I glass injection vial (6 ml) containing the sterile, pyrogen-free lyophilised powder are closed with rubber stopper and tear-off kombicap (aluminium and plastic).
Six vials of Techida powder for solution for injection are packed into one paper box, with six label with radioactive symbol.

Marketing Authorisation Holder and Manufacturer
Institute of Isotopes Co. Ltd.
Addresse: 1121 Budapest, Konkoly Thege Miklós str. 29-33.
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OGYI-T-9210/01

For any information about this medicine, please contact the local representative of the Marketing Authorization Holder:
Hungary
National Institute of
Pharmacy and Nutrition
Box: 450.
H-1372 Budapest
Website: www.ogyei.gov.hu

This leaflet was translated by the manufacturer based on the original Hungarian document, authorized by the Hungarian National Institute of Pharmacy in May 2017.