SUMMARY OF PRODUCT CHARACTERISTICS
(PHYTATE - F)

1. NAME OF THE MEDICINAL PRODUCT

Technephyte powder for injection, Technephyte, ^{99m}Tc (PHYTATE - F)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

a.) Composition of Technephyte powder for injection:

Denomination of the components	Quantity per vial	Function
Active ingredient		
Calcium-Magnesium Phytate	5.0-15.0 mg	Organ-specific ligand of ^{99m}Tc radionuclide

b.) Composition of ^{99m}Tc -Technephyte radioactive injection:

Denomination of the components	Quantity per vial	Function
Active ingredient		
^{99m}Tc-Technephyte	0.8-1.6 GBq	Provider of organ-specific diagnostic information

3. PHARMACEUTICAL FORM

Pharmaceutical form of Technephyte kit: powder for injection

Pharmaceutical form of ^{99m}Tc -Technephyte: injection

^{99m}Tc -Technephyte injection can be prepared in situ at the site of the use i.e. at isotope laboratories of clinics or hospitals by mixing Technephyte powder for injection (lyophilizate in the vial) and [^{99m}Tc] pertechnate eluate. Sterile, pyrogen free solution of [^{99m}Tc] pertechnate can be obtained by using ^{99}Mo/^{99m}Tc generator.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

INDICATION FIELD: ISOTOPE DIAGNOSTICS

-Diagnosis of benign and malignant liver tumours and monitoring of the therapy

-Lymphoscintigraphy or Sentinel node detection.

4.2 Posology and method of administration

Posology

37 –185 MBq ^{99m}Tc-Technephyte for intravenous or intradermal administration.

For 70 kg of bodyweight 120 MBq is advised.

Method of administration

^{99m}Tc-Technephyte obtained in one labeling reaction can be divided to 3 – 6 doses. Label content of one vial of Technephyte kit by using 0.8 – 1.6 GBq of [^{99m}Tc] pertechnate activity.

^{99m}Tc-pertechnetate activity for labeling must be chosen so that individual patient dose should be 37 – 185 MBq at the time of the investigation.

For pediatric examination use Webster's equation to determine the activity to be administered and see Chapter 4.3.

Achild = [(N+1) Aadult] / (N+7)
where N - age of the child [year]
Achild, Aadult - activity [MBq]

Method of examination

Gamma camera images of the liver–spleen tract can be taken 20 minutes after administration. In case of patients suffering in liver cirrhosis 30 minutes are required. For lymphoscintigraphy or sentinel node detection, images can take 15 - 45 minutes.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients
- Pregnancy and lactation
- Under 18 years of age except if the necessity and importance of obtaining the diagnostic information outweights the risk associated with the radiation exposure

4.4 Special warnings and precautions for use

Patient exposure must be minimized, i.e. the possible lowest activity should be used for the examination to obtain the diagnostic results.

Radioactive medicinal products should be received, used and administered only by authorized person in designated clinical settings.

Receipt, storage, use, transfer and disposal of the radioactive medicinal products are subject to the regulations and appropriate licenses of the competent authorities.

4.5 Interaction with other medicinal products and other forms of interaction

No drug-drug interactions have been described to date.

4.6 Pregnancy and lactation

Use of the product is contraindicated in case of pregnancy and lactation.

There are no information on the secretion of ^{99m}Tc-phytate in breast milk. Therefore, use of the product is contraindicated in case of breast feeding mother.

4.7 Effects on ability to drive and use machines

The product has not direct influence on ability to drive and use machines.

In occurrence of unexpected adverse reactions driving and/or working with machines should be reconsidered.

4.8 Undesirable effects

Exposure to ionizing 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 nor registered in the literature.

Considering the number of the examinations carried out since, no adverse reactions are expected (frequency lower than 1/10000).

The effective dose remains below 20 mSv even in case of the maximal advised dose.

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 7.

Necessity and method of further treatment should be concluded based on these results.

The table of Chapter 10 contains absorbed radiation dose data in μGy in case of intravenous administration of 1 MBq of ^{99m}Tc-Technephyte.
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 Technephyte introduced to one patient is not less than 2.5 mg and not more than 5.0 mg if administration is complying with the recommendations. If the whole content of the vial containing the labeled substance is administered to one patient by mistake 15.0 mg of Technephyte is introduced in the body.
Acute toxicity studies on rats showed that there are not any clinical symptom, if less than 4 mg/kg of bodyweight is administered.
If the whole content of the vial containing the labeled substance is administered to one patient by mistake, it represents 0.21 mg/kg of bodyweight level (calculated on 70 kg average bodyweight). This is equivalent to 5.25 % 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: Radiopharmaceuticals
After administered intravenously ^{99m}Tc-phytate forms a microdisperse system (colloid) with calcium ions of the blood. The cells of the liver and the spleen, the Kupffer-cells and the reticuloendothelial system extract that system from the blood (phagocytosis). 90-95% of the activity appears in the liver. Further 5-10% is deposited in the spleen and the bone marrow. The colloid leaves the liver in the way of slow degradation and hydrolysation of the micro-particles.
In case of impaired liver function the bone marrow radioactivity is increased and some activity appears in the lungs. However, diffuse liver diseases result in an increased spleen activity.

5.2 Pharmacokinetic properties

^{99m}Tc-phytate introduced intravenously leaves the bloodstream in two parallel processes described by two exponential curves:

Fast process	T1/2 = 2.4-7 min
Slow process	T1/2 = 69-105 min

The fast process is the result of the operation of the reticuloendothelial system.
The liver uptake is quick, it can be observed even some minutes after administration. After thirty minutes 90% of the radioactivity is accumulated in the liver. However, excretion from the liver is extremely slow.

5.3 Preclinical safety data

Acute toxicity study of rats showed no clinical symptoms up to 4 mg/kg of body weight. Quantity of the administered ^{99m}Tc-Technephyte, if complying with the recommendations, is not less than 2.5 mg and not more than 5.0 mg. Calculated on an average 70 kg of bodyweight the smallest and the greatest quantities are equivalent to 0.9 and 1.8 % of the no observed effect level, respectively. Thus, the use of the product considered 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

Component	Quantity per Vial	Function
Excipients		
Stannous chloride	1.0 mg	Reducing agent of

dehydrate		[^{99m}Tc]pertechnetate
Sodium-chloride	10.0 mg	Filler

6.2 Incompatibilities

One component of Technephyte kit is stannous chloride, which is a reducing agent. It reduces free pertechnetate, which (+7 oxidation state) to +4 oxidation state, in which technetium readily forms complex with Technephyte. It is important to keep away the content of the vials from moisture and oxidising agents, e.g. 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 of Chapter 8.

6.3 Shelf life

Shelf life of Technephyte kit lyophilised, non-radioactive components in injection vials closed with rubber stopper and aluminium cap) is 12 month from the date of the manufacture.
One paper box contains 6 of injection vials, which can be labelled at different times within the expiry time.
^{99m}Tc-labelled Technephyte must be used within 5 hours.

6.4 Special precautions for storage

Do not store Technephyte kit above 25°C.
Do not store ^{99m}Tc-Technephyte injection above 25°C. Comply with the regulations for radiation safety.

6.5 Nature and contents of container

The injection vials of Technephyte kit contain the sterile, pyrogen-free and freeze-dried components. The labelled 10 ml injection vials are closed with rubber stopper and tear-off aluminium cap.
The labelled vials are supplied in a white, 150 x 100 x 60 mm carton box. Position of the vials inside the box is fixed by a carton insert, which prevents the moving of the vials. One box contains six(6) vials, one Instruction Manual and a Quality Certificate.

6.6 Special precautions for disposal and other handling

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

7. DOSIMETRY

Individual patient dose is 74 – 185 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	92	
Spleen (at spleen scintigraphy)	57	
Bone marrow	7.3	
Testes	0.3	
Ovaries	1.5	
Radiation physical properties		
Physical half-life	6 hours	
Energy and intensity of the emitted gamma photons	140 keV	100 %
Energy and intensity of the emitted beta particles	–	–

8. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Remove the protective foil and lift up the upper part of the paper box to access the vials.

Fiton kit can only be administered to patient after labeling with ^{99m}Tc. Never administer Technephyte kit without performing the labelling.

^{99m}Tc -Technephyte injection contains radioactive isotope. For handling, shipping and storage of this product besides pharmaceutical regulations the rules and regulations referring to the radioactive materials should be observed.

Labelling procedure.

Place the vial containing the freeze-dried powder in a small lead container with a wall thickness of 3 mm. Under aseptic circumstances inject 0.8 – 1.6 GBq of sterile sodium pertechnetate 3-6 ml, into the vial through the rubber stopper with a sterile syringe. Gently swirl the content. Allow the preparation 2-3 minutes incubation at room temperature. This solution can be used for intravenous or intradermal administration.

Utilize the labelled solution in 5 hours. Over this period the percentage of radiochemical impurities should not be more than 10%.

Control of drug product

Principle: Radiochemical purity of ^{99m}Tc-Technephyte is tested by using paper chromatography.

Method: Stationary phase: Whatman ET31 (catalogue code: 3031915) 1.5x20 cm paper strips

Mobile phase: Acetone, 10 % CaCl2 solution. Temperature: Room temperature: 20-25°C.

Fresh prepared ^{99m}Tc-Technephyte injection is tested by two chromatographic processes:

-Determination of free $^{99m}TcO_4^-$ by paper chromatography

Use 3 pieces of 1.5 x 20 cm ET-31 paper strips. Apply to the strips 5 – 5 µl (approximately 1 MBq/ µl) of the solution to be tested at 1.5 cm from the end of the paper. Develop the strips over a 15 cm path in acetone. 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 Rf values^{99m}Tc -Technephyte complex: 0–0.3, Free $^{99m}Tc\ O_4^-$: 0.8–1

-Examination of the disperse system formed with Ca++ ions by paper chromatography

Use 3 pieces of 1.5 x 20 cm ET-31 paper strips. Apply to the strips 5 – 5 µl of the solution to be tested at 1.5 cm from the end of the paper. Develop the strips over a 15 cm path in 10% CaCl2. 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 Rf values:

^{99m}Tc -phytate and Ca disperse system 0.3–0.4

Free $^{99m}TcO_4^-$ 0.7–1.0

Radiochemical purity is calculated by using the peak areas. Total activity of the strip is considered 100% and activity percentage due to ^{99m}Tc -Technephyte 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.

PACKAGE LEAFLET: INFORMATION FOR THE USER

Technephyte 15 mg powder for injection

Sodium phytate

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:

WHAT TECHNEPHYTE IS AND WHAT IT IS USED FOR

This medicine is for diagnostic use only.

^{99m}Tc-Technephyte injection prepared from Technephyte kit is a sterile solution that contains radioactive isotope. Use of Technephyte is permitted only in departments of nuclear medicines.

^{99m}Tc-Technephyte injection is administered intravenously. After intravenous administration, ^{99m}Tc-Technephyte 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. For lymphoscintigraphy or sentinel node detection it is administered intradermal.

^{99m}Tc-Technephyte is suitable for morphological examination of the liver, diagnosis of benign and malignant liver tumours and monitoring of the therapy

BEFORE YOU USE TECHNEPHYTE

Do not use Technephyte

- if you are allergic (hypersensitive) to the active substance or any of the other ingredients of Technephyte.
- 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

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.

Using other medicines

Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Using Technephyte with food and drink

You can take Technephyte with any food or drink.

Pregnancy and breast-feeding

It is important to tell your doctor if there is any possibility that you are pregnant or if you breast-feeding.
In these cases your doctor will consider the necessity of the radioisotope diagnostics. The radioisotope can be dangerous to the foetus and the infant, and it is excreted in mother's milk. Therefore, it is possible that your doctor will choose other, non-radioactive method. Trust your doctor, because the decision will be made in accordance with 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 restart of breast -feeding.

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

Important information about some of the ingredients of Technephyte
When you are given ^{99m}Tc-Technephyte you receive a small amount of radiation. The adsorbed 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.

HOW TO USE TECHNEPHYTE
^{99m}Tc- Technephyte injection is prepared by mixing the content Technephyte kit and radioactive ^{99m}Tc-pertechnate at the site of the use (hospitals, clinics). The injection is administered intravenously or intradermal.
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-Technephyte can only be used in hospitals or institutes.
Technephyte 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- Technephyte 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 and eat lots of high-fiber foods
which will accelerate the elimination of the drug from your body. You should take all necessary precautions against the contamination of yourenvironment with radioactivity. Comply with the instructions given by your doctor.
^{99m}Tc- Technephyte 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.

POSSIBLE SIDE EFFECTS
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. Considering the number of the examinations carried out since, no adverse reactions are expected.
The amount of radioactivity in the body from ^{99m}Tc-Technephyte 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.

FURTHER INFORMATION
What Technephyte contains
- The active substance is 15 mg filtered sodium phytate per vial, particle mean size, 50 - 150 nm.
- Other ingredients are: Stannous chloride dihydrate, sodium chloride
- The active substance of the labelled, radioactive Technephyte: ^{99m}Tc-Technephyte

What Technephyte looks like and contents of the pack
The injection vials (10 ml) containing the sterile, pyrogen-free freeze dried product are closed with rubber stopper and tear-off kombicap (aluminium and plastic).
Five vials of Technephyte kit are packed into one paper box.