SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

^{99m}Tc-Tektrotyd

16 micrograms
Kit for radiopharmaceutical preparation

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Vial I contains:
HYNIC-[D-Phe^{1},Tyr^{3}-Octreotide]·TFA, 16 micrograms
For a full list of excipients, see section 6.1.
The radionuclide is not part of the kit.

3. PHARMACEUTICAL FORM

Kit for radiopharmaceutical preparation.
Lyophilisate for solution for injection.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

^{99m}Tc-Tektrotyd, kit for radiopharmaceutical preparation is for diagnostic use only. ^{99m}Tc-Tektrotyd is a radiopharmaceutical indicated for diagnostics of pathological lesions in which somatostatin receptors are overexpressed (particularly subtype 2 and, to a lesser extent, subtypes 3 and 5) and which may be imaged by the labelled ligand.
In particular, these are:

- gastro-entero-pancreatic neuroendocrine tumours (GEP-NET);
- pituitary adenomas;
- tumours originating in a sympathetic system; pheochromocytoma, paraganglioma, neuroblastoma, ganglioneurinoma etc.;
- medullary thyroid carcinoma;
- the preparation may be potentially useful in the case of other tumours expressing somatostatin receptors of various intensity. Other tumours which may overexpress somatostatin receptors: breast cancer, melanoma, lymphomas, prostate cancer, NSCLC, sarcoma, renal cell carcinoma, differentiated thyroid carcinoma, astrocytoma according to WHO I-IV (including glioblastoma multiforme G-M), meningiomas, ovarian cancer.

4.2 Posology and method of administration

The medicinal product is for hospital use or in designated nuclear medicine facilities only, by persons experienced in the radiopharmaceuticals application.
^{99m}Tc-Tektrotyd is administered intravenously in a single dose after labelling of the kit using a sterile, oxidant-free sodium pertechnetate (^{99m}Tc) solution for injection (eluate of ^{99}Mo/^{99m}Tc radionuclide generator) in accordance with the instructions for preparation of radiopharmaceutical – see section 12. Technetium-99m in 1 ml of eluate of sodium pertechnetate-^{99m}Tc solution for injection with activity of 740 MBq - 1200 MBq (maximally 2200 MBq) may be used for labelling of one kit. This activity is sufficient for examinations of 1 – 2 adults. Radioactivity of administered dose should be always adjusted with respect to its diagnostic usefulness. The solution of ^{99m}Tc-Tektrotyd may be additionally diluted for more convenient administration. Acquisition should be carried out between 2 – 4 hours after intravenous administration of the preparation. The examination may be complemented by acquisition after 10 minutes, 1 hour and 24 hours after administration of a tracer. It is recommended to carry out the examinations using Whole Body technique and SPECT of selected body areas.

Preparation of the patient for examination

Unless there are indications for other method of the patient preparation, the patient is recommended to stay on light diet one day before examination. On the day of examination, the patient should fast until the end of the first acquisition. If there is a need for examination after 24 hours, it is recommended that a mild laxative be given to the patient starting the evening before. Method of patient preparation may depend on the applied examination protocol and the localization of imaged lesions. However, optimal imaging of abdominal cavity is obtained after the application of liquid diet 2 days before the examination and after administration of laxatives on the day before the examination.

Dosage for adults

The recommended radioactivity dosage for single examination of adult is approximately 370 to 925 MBq.

Dosage for elderly (above 65 years)

Experience from literature data indicates that no dose adjustment is required.

Children

^{99m}Tc-Tektrotyd is not recommended for use in patients under 18 years of age; there are no data for this age group.

Patients with renal impairment

No dosage adjustment is required, see section 4.4

Repeated administration

^{99m}Tc-Tektrotyd is intended for a single intravenous use only. If there is a need for repeated administration, clinical indication and potential adverse events should be considered.

4.3 Contraindications

Hypersensitivity to HYNIC-[D-Phe^{1},Tyr^{3}-Octreotide]·TFA or to any of the excipients or sodium pertechnetate (^{99m}Tc) solution for injection. Pregnancy.
In the case of breastfeeding, see section 4.6. In children and young persons, the dose should be possibly lowered.

4.4 Special warnings and precautions for use

The content of the kit vials is intended for preparation of radiopharmaceutical ^{99m}Tc-Tektrotyd and may be administered to a patient only after completion of labelling procedure – see section 12. The preparation should not be administered before labelling.
Particular attention should be given to patients with renal insufficiency – when renal excretion is prolonged, the patient is exposed to higher dose of radioactivity.
Patients with liver failure should be also provided with particular care.
The radiopharmaceutical should be received, stored and administered to patients only by authorised persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to appropriate regulations and/or appropriate licences of the competent official organisation.
Radiopharmaceuticals intended for administration to patients should be prepared in a manner which satisfies both radiation safety and pharmaceutical quality requirements.
Safety precautions for careful handling this radiopharmaceutical should be observed to ensure protection of the staff and patients against unnecessary exposure to ionising radiation. There are no data on safety and efficacy of the use in children under 18 years of age.

An adequate hydration of a patient and frequent voiding are necessary to minimize radiation dose to the bladder.
The exposure to radiation can be increased in patients with renal insufficiency. This should be considered in the calculation of the dose to be administered.

Repeated administration of the preparation

If there is a need for repeated examination, clinical indications and potential adverse events should be considered.

4.5 Interaction with other medicinal products and other forms of interactions

In patients subjected to diagnostic examinations with the use of ^{99m}Tc-Tektrotyd, the treatment with somatostatin analogues should be stopped (both "cold" as well as labelled with radioactive isotopes)

- short acting analogues – at least 3 days before the planned examination,
- long acting analogues:
  - lanreotide – at least 3 weeks
  - octreotide – at least 5 weeks before the planned examination.

No interaction studies have been performed. There are limited data concerning possible interactions.

4.6 Fertility, pregnancy and lactation

Pregnancy

The preparation must not be administrated to pregnant women.
When it is necessary to administer radiopharmaceuticals to women of childbearing potential information should always be sought about pregnancy. Pregnancy should be excluded in any women who has had menstrual cycle disturbances. Any women who has missed a period should be assumed to be pregnant until proven otherwise. Examinations using radiopharmaceuticals in women of childbearing potential should be carried out during the first (about 10) days following the onset of menses. Where uncertainty exists it is important to minimize the radiation exposure during examinations. Alternative techniques which do not involve ionising radiation should be considered.

Breast-feeding

Breast-feeding should be interrupted for at least 72 hours following administration of the first dose of radiopharmaceutical product due to potential risk for the child. It can be restarted when radiation dose potentially received by the child during breast-feeding and contact with mother is within the range of approved standards.

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.

4.8 Undesirable effects

Transient headache or epigastric pain may occur very rarely directly after administration of ^{99m}Tc-Tektrotyd. The exposure to radiation should be substantiated by benefits resulting from the performed test. The administered radioactivity should be adjusted in order to achieve the desired diagnostic effect and possibly lower the radiation dose to the patient. The exposure to ionising radiation is potentially related to induction of neoplasm and potential risk for hereditary defects. In case of radiodiagnostic examinations the risk is negligible because of low doses of radiation.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.
Adverse reactions may be reported to Marketing Authorisation Holder.

4.9 Overdose

No case of overdose has been reported.
The risk of overdose in case of diagnostic doses may be ignored. Treatment of overdose should be directed towards the support of vital functions. The dose absorbed by the patient may be reduced by increasing the elimination of the radionuclide from the body by administration of liquids and frequent urine voiding.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: radiopharmaceuticals for cancer diagnostics
ATC code: V09IA07

5.2 Pharmacokinetic properties

After intravenous administration, ^{99m}Tc-Tektrotyd is rapidly eliminated from the blood and already after 10 minutes, accumulation of a marker is seen in the main organs, i.e. liver, spleen and kidneys as well as in tumours expressing somatostatin receptors. These changes are better visible after 2 and 4 hours, while radioactivity accumulated in muscles and in circulating blood decreases. Cancer lesions are still visible after 24 hours. Slight excretion by alimentary tract is observed at this time. Maximal values of the tumour/background ratio are observed at 4 hours after injection. Values of the tumour/liver and tumour/lungs ratios are at the level of 1.4 and 12, respectively.

The preparation is excreted mainly by the renal route with a small contribution of hepatic excretion. ^{99m}Tc-Tektrotyd is rapidly eliminated from the blood. The activity accumulated in the blood cells is below 5% regardless of time after injection. Binding to blood proteins is lower at earlier time points (e.g. 2% - 11% within 5 minutes after injection) in comparison to further time points (33% - 51% after 20 hours). Cumulative urine excretion within 24h falls in the range 24% - 64% of the administered dose.

5.3 Preclinical safety data

The examination of harmlessness of ^{99m}Tc-Tektrotyd carried out in mice, showed that solution of ^{99m}Tc-Tektrotyd radiopharmaceutical is harmless in the maximal injection dose: 0.2 mg of Tektrotyd/kg body weight and 974 MBq/kg body weight. The average increase of mice body weight after two days was about 11%. No clinical studies on the influence of the preparation on fertility and carcinogenicity have been performed.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Vial I:
Tricine (N-[Tris(hydroxymethyl)methyl]glycine
Tin (II) chloride dihydrate
Mannitol
Nitrogen
Vial II:
EDDA (ethylenediamine-N,N'-diacetic acid)
Disodium hydrogen phosphate dodecahydrate
Sodium hydroxide
Nitrogen

6.2 Incompatibilities

No studies on incompatibilities of this preparation have been performed.
^{99m}Tc-Tektrotyd must not be mixed with other medicinal products. It is recommended to administer the preparation by a separate intravenous cannula.

6.3 Shelf life

Shelf life of the kit: 1 year.
Labelled product must be stored at temperature below 25°C and used within 6 hours after preparation.

6.4 Special precaution for storage

Store the kit in a refrigerator at 2°C - 8°C.
During transportation (not longer than 7 days) up to 35°C.
Expiry date is indicated on the package.
After labelling, store the medicinal product for no more than 6 hours at temperature below 25°C using appropriate radiation shielding. Storage of radiopharmaceuticals should be in accordance with national regulations on radioactive materials.

6.5 Nature and content of the container

The kit package contains two glass vials (Vial I and Vial II) of 10 ml volume, closed with a rubber stopper and an aluminium crimp cap. The vials are supplied in cardboard boxes. Vials I and II contain components for preparation of a radiopharmaceutical ^{99m}Tc-Tektrotyd.

6.6 Special precautions for disposal and other handling

See section 12.

7. MARKETING AUTHORISATION HOLDER

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ul. Andrzeja Sołtana 7, 05-400 Otwock, Poland
Phone: +48 22 7180700
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8. MARKETING AUTHORISATION NUMBER(S)

11664

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

29.04.2004/03.12.2008/18.12.2013

10. DATE OF REVISION OF THE TEXT

18.12.2013

11. DOSIMETRY

Technetium-99m disintegrates with the emission of gamma radiation with an energy of 140 keV. The effective dose equivalent (EDE) after administration of ^{99m}Tc-Tektrotyd of 740 MBq radioactivity is about 4.2 mSv (for a 70 kg individual). Half-life of technetium-99m is short and is 6 hours, hence, 60 hours after administration of the preparation, less than 0.1% of the administered dose is retained in the patient's body.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Any unused product, containers and other material which contacted the radioactive substance must be disposed of as radioactive waste in accordance with local requirements.
The kit for preparation of radiopharmaceutical ^{99m}Tc-Tektrotyd is for labelling with technetium-99m in the form of sodium pertechnetate-^{99m}Tc solution for injection, in order to prepare ^{99m}Tc-Tektrotyd, solution for injection.

Labelling procedure:

The administration of radiopharmaceuticals creates risk for other persons from external radiation or contamination from spill of urine or vomiting. Radiation protection precautions in accordance with national regulations must therefore be taken.
Use aseptic technique throughout the preparation and mixing of the components. The user should wear rubber gloves, the shielding must be used at all times when handling vials or syringes containing the radioactive agent.
The radioactivity of the preparation ^{99m}Tc-Tektrotyd should be measured just before administration.

1. For labelling the sodium pertechnetate-^{99m}Tc solution for injection should be used obtained up to two hours prior to start of labelling. The radionuclide generator ^{99}Mo/^{99m}Tc should be previously eluted within the past 24 hours.
2. Place Vial I in a suitable shielding container.
3. Using a syringe, inject 1 ml of water for injection to the Vial II. Stir gently the content of the vial until the components are completely dissolved. Using the syringe, take 0.5 ml of such prepared solution, and inject to the Vial I. Stir thoroughly the content of Vial I and, using a shielded syringe, inject to the same vial (Vial I) the required radioactivity of sodium pertechnetate-^{99m}Tc solution for injection, maximally 2200 MBq, in the volume of maximum 1 ml. Before removing the needle from the vial, relieve the excess of pressure in the vial by withdrawing the equivalent volume of gas. Shake the shielded Vial I gently for about 10 seconds in order to ensure complete dissolution of its content.
4. Place the vial immediately in a water bath or a heating block with a temperature 80°C for 20 minutes maintaining the vial in the upright position. The water bath or heating block should be properly shielded. When the heating is completed, transfer the Vial I to the shielding container and let it cool down at room temperature for not less than 30 minutes in order to cool the preparation. Do not use cold water for cooling the vial as it may impede labelling.
5. Assay the total radioactivity, complete the user radiation label and attach it to the lead shielded vial.
6. Parenteral medicinal products should be inspected visually before administration. In presence of particulate matter or discoloration, the solution should not be administered. Before administration, stir the content of the vial and examine from a safe distance using protective glasses with lead glass.
7. Store the labelled vial upright, at temperature below 25°C. Use within 6 hours after preparation.

Caution

1. The volume of sodium pertechnetate-^{99m}Tc solution for injection which is added to the Vial I of the kit for preparation of radiopharmaceutical ^{99m}Tc-Tektrotyd must not exceed 1 ml.
2. The radioactivity of technetium-99m added to the Vial I must not exceed 2200 MBq. The radioactivity dose is calculated to the time of injection to the patient, to obtain the total vial radioactivity within a range of 740 – 1200 MBq at the moment of administration.
3. If the radioactive concentration of labelled preparation is too high, it may be diluted after labelling to a maximum of 3 ml with 0.9% sodium chloride solution for injection. The volume of solutions used in the labelling procedure should not be increased.
4. The medicinal product shows to have radiochemical purity above 90% measured by ITLC method prior to administration.
5. The content of the vials of the kit for preparation of radiopharmaceutical ^{99m}Tc-Tektrotyd is not radioactive. After addition of sodium pertechnetate-^{99m}Tc solution for injection, proper radiation shielding must be used.
6. The labelling of ^{99m}Tc-Tektrotyd depends on maintenance of tin(II) chloride dihydrate in a reduced state. The presence of oxidizer in the sodium pertechnetate-^{99m}Tc solution might negatively affect the quality of the radiolabelled preparation.
7. The content of the kit for preparation of the radiopharmaceutical ^{99m}Tc-Tektrotyd is sterile. The vials do not contain bacteriostatic agents.

The preparation of the radiopharmaceutical ^{99m}Tc-Tektrotyd must be carried out in aseptic conditions, following the provided instruction for use.

Quality control

Determination of radiochemical purity may be performed using the described chromatographic procedure.

Equipment and reagents

1. two ITLC SG strips (2 cm x 10 cm)
2. two developing chambers with a cover
3. methylethylketone (MEK)
4. the mixture of acetonitrile and water in a volume ratio of 1:1 (preparation of the mixture – see below)
5. 1 ml syringe with a needle for subcutaneous injections
6. suitable counting equipment

The mixture of acetonitrile and water (in a volume ratio of 1:1) (ACNW)

Mix carefully the same volumes of acetonitrile and water. The mixture should be prepared every day.

The method of determination

1. Fill in the developing chambers with the prepared solutions of MEK and ACNW to the height of 0.5 cm. Cover the chambers and allow to equilibrate with the solvents vapours.
2. Mark two ITLC SG strips with a pencil at 1 cm from their bottom margin (the place of putting a drop of analysed preparation) and a section of 0.5 cm from their upper margin (the place where front of the developing solution will move).
3. Spot the drop (about 5 – 10 µl) of the solution of ^{99m}Tc-Tektrotyd for injection using a needle for subcutaneous injections, in the middle of the line marked at 1 cm of the bottom margin of each strip, do not allow the spots to dry. CAUTION: Do not touch the surface of the strip with a needle.
4. Place the chromatographic chambers behind the lead shielding.
5. Place one ITLC SG strip in a chamber with a MEK solution and another ITLC SG strip in ACNW solution. Place the strips upright to ensure that the place of spotting ^{99m}Tc-Tektrotyd is above the solution line, the upper end of the strip leaned against the side of the chamber.

CAUTION: the strip surface may not contact the walls of the chamber.
The chambers should be covered.

6. Wait until the front of the solution moves to the line determining the distance of 0.5 cm from the upper margin of the strip.
7. Remove the strips from the chambers and allow to dry behind the lead shielding.
8. Cut the strips as described below:
   ITLC SG MEK: in the middle between the front of the solution and the line determining the place of putting the drop of the preparation (R_f = 0.5 to 1.0)
   ITLC SG ACNW: in a distance of 3.5 cm from the bottom margin of the strip (R_f = 0 to 0.3).
9. Measure the radioactivity of each part of the strip and calculate the results as follows:

Percent of pertechnetate-^{99m}Tc = A

$$A = 100 \times \frac{\text{Radioactivity of the upper section of the strip ITLC SG MEK } (R_f \text{ 0.5 to 1.0})}{\text{Total radioactivity of both parts of ITLC SG MEK strip}}$$

Percent of technetium [^{99m}Tc] in colloidal form = B

$$B = 100 \times \frac{\text{Radioactivity of the lower section of the strip ITLC SG ACNW } (R_f \text{ 0 to 0.3})}{\text{Total radioactivity of both parts of ITLC SG ACNW strip}}$$

10. Percent of the content of complex ^{99m}Tc-Tektrotyd : 100 – (A + B). In the properly prepared preparation, ready for administration to the patient, the content of the complex should be at least 90%.

POLATOM