

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

TEKTROTYD 16 micrograms kit for radiopharmaceutical preparation

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Vial 1 contains 16 µg of HYNIC-[D-Phe¹, Tyr³-octreotide] TFA salt

Vial 2 contains 10 mg of EDDA (Ethylenediamine-N,N'-diacetic acid)

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

White or almost white lyophilisates

For radiolabelling with sodium pertechnetate (^{99m}Tc) solution

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

^{99m}Tc-EDDA/HYNIC-TOC specifically binds to somatostatin receptors.

After radiolabelling with sodium pertechnetate (^{99m}Tc) solution, the solution of ^{99m}Tc-EDDA/HYNIC-TOC obtained is indicated in adult patients with gastro-entero-pancreatic neuroendocrine tumours (GEP-NET) for localizing primary tumours and their metastases (see section 5.1).

For paediatric population see section 4.2.

4.2 Posology and method of administration

Posology

The recommended posology is 370 - 740 MBq for planar scintigraphy and for SPECT studies.

Adults

The suggested activity range is 370 to 740 MBq in one single intravenous injection. The activity to be administered depends on the sensitivity of the available equipment.

Elderly population (above 65 years)

The recommended activity to be given to adults is 370 to 740 MBq in one single intravenous injection. No dose adjustment is required for elderly.

Renal impairment

Careful consideration of the activity to be administered is required since an increased radiation exposure is possible in these patients, see section 4.4.

Hepatic impairment

Dosage reduction in hepatic impairment is not necessary, see section 5.2.

Paediatric population

There are no data on safety and efficacy of technetium ^{99m}Tc-EDDA/HYNIC-TOC for the use in paediatric patients.

Method of administration

This medicinal product should be radiolabeled before administration to the patient.

For instructions for preparation of the radiopharmaceutical, see section 12. ^{99m}Tc-EDDA/HYNIC-TOC is administered intravenously in a single dose.

For patient preparation, see section 4.4.

For each patient, exposure to ionising radiation must be justifiable on the basis of likely diagnostic benefit and risk from radiation exposure.

For more convenient administration, the solution of ^{99m}Tc-EDDA/HYNIC-TOC may be diluted with sodium chloride injection, see section 6.2.

Image acquisition

Image acquisition should be carried out at 1 - 2 and 4 hours after intravenous administration. Images at 1 - 2 hours post-injection may be useful for comparison and evaluation of abdominal activity imaged at 4 hours.

The examination may be complemented depending on the clinical need by acquisition 15 minutes and 24 hours post-injection of the tracer. An additional 24-hour image acquisition can improve specificity in ambiguous cases, especially in the abdomen.

It is recommended to carry out the examinations using Whole Body technique and SPECT (or SPECT/ CT) of selected body areas.

4.3 Contraindications

Hypersensitivity to HYNIC-[D-Phe¹, Tyr³-octreotide] TFA salt, to EDDA (Ethylenediamine-N,N'-diacetic acid) or to any of the excipients or sodium pertechnetate (^{99m}Tc) solution for injection.

4.4 Special warnings and precautions for use

The radiolabelled preparation is intended for single use only.

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 impairment

Careful consideration of the activity to be administered is required since an increased radiation exposure is possible in these patients.

Hepatic impairment

Dosage reductions in hepatic impairment are not necessary, see 5.2.

Paediatric population

For information on the use in paediatric population, see 4.2.

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.

Optimal imaging of the abdominal cavity is obtained after the application of liquid diet starting two days before the examination as well as administration of laxatives on the day before the examination. The method of patient preparation may depend on the applied examination protocol and the localization of imaged lesions.

Regarding patients on octreotide therapy it is recommended to withdraw this therapy temporarily to avoid a possible blockade of somatostatin receptors. This recommendation is given on empirical grounds, the absolute need for such measure has not been demonstrated. In some patients the withdrawal of therapy might not be tolerated and may cause rebound effects. This is notably the case in insulinoma patients, where the danger of sudden hypoglycaemia must be considered, and in patients suffering from the carcinoid syndrome (for proposals for withdrawal refer to section 4.5).

Image interpretation

Positive scintigraphy with ^{99m}Tc-EDDA/HYNIC-TOC reflects the presence of an increased density of tissue somatostatin receptors rather than a malignant disease.

Furthermore, positive uptake is not specific for gastro-entero-pancreatic tumours. Positive scintigraphic results require evaluation of the possibility that another disease, characterised by high local somatostatin receptor concentrations, may be present. An increase in somatostatin receptor density can also occur in the following pathological conditions: tumours arising from tissue embryologically derived from the neural crest, (paragangliomas, medullary thyroid carcinomas, neuroblastomas, pheochromocytomas), tumours of the pituitary gland, endocrine neoplasms of the lungs (small-cell carcinoma), meningiomas, mammary carcinomas, lympho-proliferative disease (Hodgkin’s disease, non-Hodgkin lymphomas), and the possibility of uptake in areas of lymphocyte concentrations (subacute inflammations) must be considered.

If the patient is not prepared properly to the examination, bowel uptake might influence the quality of images. Significant nonspecific accumulation occurring within digestive tract could be misinterpreted and misreported as pathologic or could impair the proper images evaluation.

Limitations of use

Tumours which do not bear receptors will not be visualised.

In some patients suffering from GEP-NET the receptor density may be insufficient to allow visualisation with ^{99m}Tc-EDDA/HYNIC-TOC. This has to be considered for patients with insulinoma.

The efficacy of ^{99m}Tc-EDDA/HYNIC-TOC for monitoring the effect of treatment (follow-up) and patient selection for peptide receptor radionuclide therapy has not been established (see section 5.1).

For the limitations of use for staging or re-staging of GEP-NET see section 5.1.

After the procedure

Close contact with infants and pregnant women should be avoided during the first 24 hours after administration of the radiopharmaceutical.

Specific warnings

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially ‘sodium-free’.

Precautions with respect to environmental hazard see section 6.6.

4.5 Interaction with other medicinal products and other forms of interaction

In patients subjected to diagnostic examinations with the use of ^{99m}Tc-EDDA/HYNIC-TOC, it is recommended on an empirical basis to withdraw the treatment with somatostatin analogues temporarily (both “cold” as well as labelled with radioactive isotopes) to avoid a potential blockage of somatostatin receptors:

- 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.

The withdrawal of therapy with somatostatin analogues as a preparatory step to scintigraphy might provoke severe adverse effects, generally of the nature of a return of the symptoms seen before this therapy was started.

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

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

When an administration of a radiopharmaceutical 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.

Breast-feeding

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 24 hours and the expressed feeds discarded.

4.7 Effects on ability to drive and use machines

Effects on the ability to drive or use machines have not to be expected after use of this product.

4.8 Undesirable effects

During the evaluation of adverse reactions, the following frequency data are taken as a basis:

very common (≥1/10)

common (≥1/100 to <1/10)

uncommon (≥1/1,000 to <1/100)

rare (≥1/10,000 to <1/1,000)

very rare (<1/10,000)

not known (cannot be estimated form the available data)

Very rarely transient headache or epigastric pain may occur directly after administration of ^{99m}Tc-EDDA/HYNIC-TOC.

Exposure to ionisation radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose is about 3.8 mSv when the maximal recommended activity of 740 MBq is administered these adverse events are expected to occur with a low probability.

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 Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

No case of overdose has been reported.

Overdose is unlikely when the radiopharmaceutical is administered by diagnostic monodose injection.

In the event of administration of a radiation overdose with ^{99m}Tc-EDDA/HYNIC-TOC the adsorbed dose to the patient should be reduced by increasing the elimination of the radionuclide from the body by administration of liquids and frequent bladder voiding.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:

Diagnostic radiopharmaceuticals, tumour detection, technetium (^{99m}Tc) compounds;

ATC code: V09IA07

Mechanism of action

Technetium (^{99m}Tc) labelled EDDA/HYNIC-TOC binds with high affinity to somatostatin receptor subtypes 2 and 5, also to subtype 3 but with lesser affinity.

Pharmacodynamic effects

At the chemical concentrations used for diagnostic examinations ^{99m}Tc-EDDA/HYNIC-TOC does not appear to have any pharmacodynamic activity.

Clinical efficacy

Direct head-to-head comparison of technical performance (image quality and tumour/tissue uptake) and diagnostic performance (sensitivity and specificity) of technetium ^{99m}Tc-EDDA/HYNIC-TOC versus indium (¹¹¹In) pentetreotide in the same patients and clinical contexts have not been provided in studies recruiting exclusively or mostly GEP-NET.

In the intended population of GEP-NET, three published studies assessed diagnostic performance of ^{99m}Tc-EDDA/HYNIC-TOC based on composite reference standards (histopathology or surgery or clinical imaging follow-up). In the study of Gomez et al. 2010, recruiting 32 patients with histologically proven or clinically suspected GEP-NET (22 carcinoid, 2 insulinomas, 2 gastrinomas and 6 non-specific), sensitivity and specificity

were 94 % (16/17) and 100 % (15/15), respectively, for detection of primary tumour and 79 % (11/14) and 100 % (18/18), respectively, for detection of metastases. Sepulveda et al. 2012 with 56 patients with suspected neuroendocrine tumours, mostly GEP-NET, undergoing scintigraphy with ^{99m}Tc-EDDA/HYNIC-TOC for detection of primary tumour or metastases obtained a sensitivity and specificity of 88.4 % (78 - 97 %) and 92.3 % (64 - 100 %), respectively. In the study of Gabriel et al. 2005, scintigraphy with ^{99m}Tc-EDDA/HYNIC-TOC performed in 88 proven GEP-NET resulted in a sensitivity of 77.5 % (31/40) and specificity of 50 % (1/2) for initial staging, and of 83.3 % (25/30) and 100 % (16/16), respectively, for restaging.

5.2 Pharmacokinetic properties

Distribution

After intravenous administration, ^{99m}Tc-EDDA/HYNIC-TOC is rapidly eliminated from the blood. Already after 10 minutes, accumulation of the ^{99m}Tc-EDDA/HYNIC-TOC is seen in the main organs, i.e. liver, spleen and kidneys as well as in tumours expressing somatostatin receptors.

Uptake

Maximal values of the tumour/background ratio are observed at 4 hours after injection. Cancer lesions are still visible after 24 hours. Slight excretion by the alimentary tract is observed in late images.

Elimination

The activity is excreted mainly by the renal route with a small contribution of hepatic excretion. ^{99m}Tc-EDDA/HYNIC-TOC is rapidly eliminated from the blood. The activity accumulated in the blood cells is below 5 % regardless of time after injection.

5.3 Preclinical safety data

In studies performed in mice and rats no effects of acute toxicity at dose level of 40 µg/kg bodyweight have been found.

Toxicity with repeated administration of ^{99m}Tc-EDDA/HYNIC-TOC was not tested. This agent is not intended for regular or continuous administration. Mutagenicity studies performed in a bacterial reverse mutation assay showed no ^{99m}Tc-EDDA/HYNIC-TOC induced gene mutations.

Long-term carcinogenicity studies have not been carried out.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Vial 1:

Tricine (N-[tris(hydroxymethyl)methyl]glycine)

Stannous chloride dihydrate

Mannitol

Nitrogen (as protective gas)

Vial 2:

Disodium hydrogen phosphatedodecahydrate

Sodium hydroxide

Nitrogen (as protective gas)

6.2 Incompatibilities

After radiolabelling a dilution with up to 5 mL physiological saline is possible.

^{99m}Tc-EDDA/HYNIC-TOC must not be mixed with other medicinal products.

6.3 Shelf life

1 year

After radiolabelling 4 hours when stored below 25 °C.

6.4 Special precautions for storage

Store in a refrigerator at 2 °C - 8 °C.

Store in the original package in order to protect from light.

For storage conditions after radiolabelling of the medicinal product, see section 6.3.

Storage of radiopharmaceuticals should be in accordance with national regulation on radioactive materials.

6.5 Nature and contents of container

Glass vials (Type I Ph. Eur.) of 10 mL nominal capacity, sealed with a rubber stopper and an aluminium cap with flip off seal.

Vials 1 and 2 contain components for the radiopharmaceutical preparation of ^{99m}Tc-EDDA/HYNIC-TOC.

Each vial contains a white or nearly white lyophilisate for preparation of a solution for injection.

Vial 1: active substance: HYNIC-[D-Phe¹, Tyr³-octreotide] TFA salt, excipients: stannous chloride dihydrate, tricine (N-[Tris(hydroxymethyl)methyl]glycine), mannitol, nitrogen

Vial 2: active substance: EDDA (ethylenediamine-N,N'-diacetic acid), excipients: disodium hydrogen phosphate dodecahydrate, sodium hydroxide, nitrogen

Pack size: 2 vials

6.6 Special precautions for disposal

Tektrotyd is supplied as kit consisting of two vials which cannot be used separately.

The radionuclide is not part of the kit.

General warning

Contents of the kit vials are intended only for use in the preparation of ^{99m}Tc-EDDA/HYNIC-TOC and are not to be administered directly to a patient without first undergoing the preparative procedure.

After radiolabelling of Tekrotyd the common protective measures for radioactive medicinal product must be applied.

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/or 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.

For instructions on radiolabelling 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, the product 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 extemporary preparation is not radioactive. However, after sodium pertechnetate (^{99m}Tc) injection, Ph. Eur. 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.

7 MARKETING AUTHORISATION HOLDER

ROTOP Pharmaka GmbH
Bautzner Landstrasse 400
01328 Dresden
Germany

8 MARKETING AUTHORISATION NUMBER(S)

PL 45925/0001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

18/12/2020

10 DATE OF REVISION OF THE TEXT

18/12/2020

11 DOSIMETRY

Technetium(^{99m}Tc) is obtained from a ⁹⁹Mo/^{99m}Tc radionuclide generator and decays by gamma emission (energy 141 keV) with a physical half-life of 6.02 hours to technetium-99, which in view of its long half-life of 2.13 x 10⁵ years may be regarded as quasi stable.

Patient-specific 3-dimensional (3D) image-based dosimetry of ^{99m}Tc-EDDA/HYNIC-TOC in NETs was assessed with the OLINDA/EXAM software with time-integrated activity coefficients estimated from a hybrid planar/SPECT technique in the study of Grimes et al. 2011. The average organ absorbed doses and effective dose of ^{99m}Tc-EDDA/HYNIC-TOC are given in the table below.

Dose absorbed per unit activity administered (mGy/MBq)	
Organ	Adult
Adrenals	0.0060
Brain	0.0022
Breasts	0.0021
Gallbladder Wall	0.0062
LLI Wall	0.0038
Small Intestine	0.0041
Stomach Wall	0.0049
ULI Wall	0.0042
Heart Wall	0.0050
Kidneys	0.0208
Liver	0.0118
Lungs	0.0036
Muscle	0.0030
Ovaries	0.0042
Pancreas	0.0071
Red Marrow	0.0030
Osteogenic Cells	0.0079
Skin	0.0019
Spleen	0.0296
Testes	0.0024
Thymus	0.0029
Thyroid	0.0040
Urinary Bladder Wall	0.0142
Uterus	0.0045
Total Body	0.0035
Effective Dose (mSv/MBq)	0.0051

The effective dose resulting from the administration of a maximal recommended activity of 740 MBq for an adult weighing 70 kg is about 3.8 mSv. For an administered activity of 740 MBq the typical radiation dose to the critical organ, i.e. the kidneys, is 15.4 mGy.

Reference:

Grimes J, Celler A, Birkenfeld B, et al. Patient-Specific Radiation Dosimetry of ^{99m}Tc-HYNIC-Tyr³-octreotide in Neuroendocrine Tumours. J Nucl Med 2011; 52: 1474-1481.

12 INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Withdrawals should be performed under aseptic conditions.

Usual safety precautions for the handling of radioactive materials should be followed.

The vials must not be opened before disinfecting the stopper, the solution should be withdrawn via the stopper using a single dose syringe fitted with suitable protective shielding and a disposable sterile needle or using an authorised automated application system.

If the integrity of this vial is compromised, the product should not be used.

Method of preparation

The kit consists of 2 vials:

Vial 1 with the active ingredient HYNIC-[D-Phe¹, Tyr³-octreotide] TFA salt

Vial 2 with the active ingredient EDDA (ethylenediamine-N,N'-diacetic acid)

Preparation of technetium ^{99m}Tc-EDDA/HYNIC-TOC injection from the Tekrotyd kit is to be done according to the following aseptic procedure:

1. Sanitize the closure of the two vials with a suitable alcohol swap and allow to air dry.
2. Add 1 mL of water for injection to the vial 2 using a sterile syringe. Shake gently for 15 seconds to ensure complete dissolution (including upside-down motions).
3. Transfer 0.5 mL coligand/buffer solution from vial 2 to vial 1, using a sterile syringe, and with the same syringe withdraw an equal volume of gas in order to equalize the pressure. Shake gently for about 30 seconds to ensure complete dissolution (including upside-down motions).
4. Place the vial 1 in a suitable shielding container.
5. Add 1 mL of sodium pertechnetate (^{99m}Tc) solution (up to 1,600 MBq) to vial 1 using a shielded sterile syringe and equalize the pressure. Heat the vial in a boiling water bath or heating block at 100 °C for 10 min.
6. Leave the vial to cool down to room temperature (30 minutes). Do not speed up, e.g. by cool water.
7. If required, dilute the radiopharmaceutical up to 5 mL with 0.9 % sodium chloride solution for injection.
8. Store the labelled vial at temperature below 25 °C. Use within 4 hours after preparation.
9. Radiochemical purity should be checked prior to patient administration according to one of the methods detailed below. **Note:** Do not use the radiopharmaceutical if the radiochemical purity is less than 90 %.
10. Dispose any unused material and its container via an authorised route.

Caution

The labelling of Tekrotyd depends on maintenance of stannous chloride dihydrate in its reduced state. The content of the kit for preparation of the radiopharmaceutical ^{99m}Tc-EDDA/HYNIC-TOC is sterile. The vials do not contain bacteriostatic agents.

Quality control

Determination of radiochemical purity should be performed using one of the alternative chromatographic procedures, A or B, described below.

Procedure A. Thin-layer chromatography

Equipment and eluents

1. Two ITLC SG strips (2 cm x 10 cm): Silica gel impregnated glass fibre strips
2. Two developing chambers with a cover
3. Solvents:
 - Methylethylketone (MEK) for impurity A, [^{99m}Tc]pertechnetate
 - Mixture of acetonitrile and water in a volume ratio of 1:1 (ACNW) for impurity B, [^{99m}Tc]technetium in colloidal form: Mix carefully the same volumes of acetonitrile and water. The mixture should be prepared every day.
4. 1 mL syringe with a needle for subcutaneous injections
5. Suitable counting equipment

Method

1. Fill in the developing chambers with the prepared solutions of MEK and ACNW to the height of not more than 0.5 cm. Cover the chambers and allow to equilibrate with the solvent's 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 µl) of the solution of ^{99m}Tc-EDDA/HYNIC-TOC 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 MEK and another ITLC SG strip in ACNW solution. Place the strips upright to ensure that the place of spotting ^{99m}Tc-EDDA/HYNIC-TOC is above the solution line, the upper end of the strip leaned against the side of the chamber.

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

7. 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.

8. Remove the strips from the chambers and allow to dry behind the lead shielding.

9. 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).

10. Measure the radioactivity of each part of the strip. Relate activity of the pieces to total activity. Calculate the percentages of the impurities.

TLC with MEK: Impurity A: R_f = 0.5 to 1.0

TLC with ACNW: Impurity B: R_f = 0 to 0.3

11. Calculate the percentage of radioactivity of ^{99m}Tc-EDDA/HYNIC-TOC using the following formula: 100 % - (([%]A +[%]B). Limit: minimum 90 per cent of the total activity.

Procedure B. Thin-layer chromatography

Equipment and eluents

1. Two ITLC-SA strips (1 cm x 8 cm): Silica acid impregnated glass fibre strips
2. Two developing chambers with a cover
3. Solvents:
 - Methylethylketone (MEK) for impurity A, [^{99m}Tc]pertechnetate
 - Water/acetonitrile/glacial acetic acid 1:1:2 (WAG) for impurity B, [^{99m}Tc]technetium in colloidal form
4. 1 mL syringe with a needle for subcutaneous injections
5. Suitable counting equipment

Method

1. Fill in the developing chambers with the prepared solutions of MEK and WAG to the height of 0.5 cm. Cover the chambers and allow to equilibrate with the solvent's vapours.
2. Mark two ITLC-SA strips with a pencil at 1 cm from their bottom margin (the place of putting a drop of analysed preparation) and a section of 2 cm from their upper margin (the place where front of the developing solution will move). Mark also cutting positions.
3. Spot the drop (about 1 - 2 µl) of the solution of ^{99m}Tc-EDDA/HYNIC-TOC for injection in the middle of the origin line. **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-SA strip in a chamber with MEK solution and another ITLC-SA strip in WAG solution. Place the strips upright to ensure that the place of spotting ^{99m}Tc-EDDA/HYNIC-TOC is above the solution line.

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

7. Wait until the front of the solution moves to the marked front line.

8. Remove the strips from the chambers and allow to dry behind the lead shielding.

9. Scan the ITLC-SA strips or cut them in case of TLC with MEK at 1 cm below the front line and in case of TLC with WAG at 0.5 cm above the origin. Measure activity of each piece. Relate activity of the pieces to total activity. Calculate the percentages of the impurities.

TLC with MEK: Impurity A: R_f > 0.8

TLC with WAG: Impurity B: R_f < 0.2

10. Calculate the percentage of radioactivityof ^{99m}Tc-EDDA/HYNIC-TOC using the following formula: 100 % - (([%]A +[%]B). Limit: minimum 90 per cent of the total activity.