SUMMARY OF PRODUCT CHARACTERISTICS for Nanopt, kit for radiopharmaceutical preparation

1. NAME OF THE MEDICINAL PRODUCT
Nanopt

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Human serum albumin colloidal particles 500 micrograms/vial
At least 95 % of human albumin colloidal particles have a diameter ≤ 80 nm. Nanopt is prepared from human serum albumin derived from human blood donations tested according to the EEC Regulations and found non-reactive for:
- Hepatitis B surface antigen (HBsAg)
- Antibodies to human immunodeficiency virus (anti-HIV 1/2)
- Antibodies to hepatitis C virus (anti-HCV)
Nanopt is reconstituted with Sodium Pertechnetate ([99mTc] Tc) Injection (not included in this kit) to prepare technetium-99m albumin nanocolloidal in-fusion.

Technetium-99m decays with the emission of gamma radiation with an energy of 140 keV and a half-life of 6 hours to technetium-99 which can be regarded as quasi stable.

3. PHARMACEUTICAL FORM
Kit for radiopharmaceutical preparation
Powder for solution for injection

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
This medicinal product is for diagnostic use only.

- After radiolabelling with Sodium Pertechnetate ([99mTc] Tc) solution, the solution so obtained is indicated in adults, children aged 1-18 years and neonates for:
  - Intravenous administration:
    - Bone marrow scanning. (The product is not suitable to use in the abdomen, including the bony marrow).
    - Infusion scanning in areas other than the abdomen.
  - Subcutaneous administration:
    - Lymphoscintigraphy to demonstrate integrity of the lymphatic system and also to visualize the sentinel node in malignant diseases such as melanoma, breast, prostate, penis, head and neck, female pelvis (cervix and vulva) cancer and to differentiate between venous and lymphatic obstruction.

4.2 Posology and method of administration
Posology
Adults
Recommended activities in adults are as follows:

Conventional lymphoscintigraphy
The recommended activity by single or multiple subcutaneous (intertitial) injection ranges from 18.5-110 MBq per site injection. For identifying sentinel node, see below.
- The injection site is given subcutaneously, after checking by aspiration, that a blood vessel has not been inadvertently punctured.

Sentinel node detection
- Melanoma: Intraderrmal injection 20-120 MBq, administered in four doses in the vicinity of the primary lesion or biopsy scar.
- Breast Cancer: 20-370 MBq in several doses each of 5-20 GBq to be injected intradermally, subcutaneously, or subperiosteally (superficial tumors) and intratumorally or peritumorally (deep tumors).
- Prostate Cancer: 65-400 MBq median of 250 MBq in one to four doses is recommended to be injected intra prostate under ultrasound guidance.
- Pelvic Cancer: 40 - 131 MBq in several doses each of 20 MBq to be injected intratumorally or peritumorally (deep tumors).
- Head and Neck Cancer: 30 - 100 MBq in one-more doses to be injected intratumorally or peritumorally (deep tumors).

4.3 Contraindications
Hypersensitivity to the active substance(s), to any of the excipients listed in section 6.1 or to any of the components of the labelled radiopharmaceutical preparation. In particular, the use of F2 humans albumin colloidal particles is contraindicated in persons with a history of hypersensitivity to products containing human albumin.

During pregnancy, lymphoscintigraphy and sentinel node detection involving the pelvis is strictly contraindicated due to the accumulation in lymph nodes.

4.4 Special warnings and precautions for use
Pregnancy, see section 4.6.

4.5 Indication for radiopharmaceutical preparation
Individual benefit/risk justification
It is always the case that the benefit of radiopharmaceutical preparation 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.
Lymphoscintigraphy is not advised in patients with total lymphatic obstructions (e.g. radiation damage to the lymphatic system). However, a limited number of patients may still be contraindicated, due to the possible accumulation in pelvic lymph nodes, see section 4.3.

4.6 Pregnancy and lactation
Woman of childbearing potential
When an administration of radiopharmaceuticals to a woman of child-bearing 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 irregular etc.), alternative techniques not using ionising radiation (if there are any) should be offered to the patient.

4.7 Effects on ability to drive and use machines
Nanopt has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects
The frequencies of undesirable effects are defined as follows:
Very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1000 to <1/100), rare (≥1/10,000 to <1/1000), very rare (≤1/10,000) and not known (cannot be estimated from the available data).

Congenital, familial and genetic disorders
Frequency not known (cannot be estimated from the available data).

Neoplasms benign, malignant and unspecified (including cysts and polyps)
Frequency not known (cannot be estimated from the available data).

Immune system disorders
Frequency not known (cannot be estimated from the available data).

Hypersensitivity reactions
Including very rare (radiation inducing).

Cancer induction.

Exposure to ionising radiation is linked with cancer induction and a potential neoplastic risk. As the effect is dose related, a dose of 2.3 mBq when the maximum recommended activity of 500 MBq is administered these adverse events are expected to occur with a low probability.

For safety with respect to transmissible agents see section 4.4.

4.9 Overdose
The risk of overdose lies in an unintentional high exposure to ionising radiation.

5.1 In the event of an overdose of radioactivity being administered when using technetium 99m albumin colloid, no practical measure can be recommended to satisfactorily diminish tissue exposure as the label is poorly eliminated in urine and faeces.
The technetium-99m albumin colloidal particles are then transported throughout the body. After radiolabelling the medicinal product does not require any special precautions. The radiation dose estimation for a number of organs is based on MIRD principles. The ready to use injection suspension should not contain more than 5 % free [99mTc]-pertechnetate and must be used within 6 hours after the vial is reconstituted.

6.3 Shelf life

Kit before reconstitution: 24 months from the date of manufacture. Reconstituted product: should be used within 6 hours after labelling. After radiolabelling the medicinal product does not require any special storage conditions.

6.4 Special precautions for storage

The medicinal product does not require any special storage conditions. Storage should be in accordance with national regulations for radiopharmaceuticals. For storage conditions of the reconstituted product, see section 6.3.

6.5 Nature and contents of container

10 ml glass vial (Type 1 Ph.Eur.) sealed by bromobutyl rubber stopper and metal flip off cap, placed in a polystyrene tray and a packet insert, inserted in a cardboard box.

Pack sizes: Each Kit contains 5 vials.

6.6. Special precautions for disposal and other handling

Radiopharmaceuticals should be used, administered only by 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 by the user in a manner which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken. Contents of the vial are in the form of technetium-99m-human albumin colloidal particles 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.

The content of the kit before reconstitution is not radioactive. However, after Sodium Pertechnetate ([99mTc] 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 spills of urine, vomitings, etc. Provision of protection precautions in accordance with national regulations must therefore be taken.

Normal safety precautions for handling radioactive materials should be observed. After use, all materials associated with the preparation and administration of radiopharmaceuticals, including any unused product and its container, should be decontaminated or treated as radioactive waste and disposed of in accordance with the conditions specified by the local competent authority. Contaminated material must be disposed of as radioactive waste via an authorised route.

7. MARKETING AUTHORISATION HOLDER

ROTOP Pharmaka GmbH
Bautzner Landstraβe 400
01328 Dresden
Tyrkland

8. MARKETING AUTHORISATION NUMBER(S)

56210

9. DATE OF FIRST AUTHORISATION

26 June 2017

10. DATE OF REVISION OF THE TEXT

4 October 2017

11. DOSIMETRY

Technetium-99m is produced by means of a (99Mo/99mTc) generator and decays with the emission of gamma radiation with a mean energy of 140 keV and a half-life of 6 hours to technetium (99mTc) which, in view of its long half-life of 2.13 x 10^8 years, can be regarded as quasi stable. The radiation dose estimation for a number of organs is based on MIRD reference term and MIRD S values, and has been calculated from biological data on organ uptake and blood clearance.

The radiation dose absorbed by a patient weighing 70 kg, after intravenous injection of 99mTc-human albumin colloidal particles, are reported hereafter.

Intravenous injection

The radiation dose absorbed by a patient weighing 70 kg, after intravenous injection of 99mTc-human albumin colloidal particles, are reported hereafter.

- **Liver**
- **Urine bladder (wall)**
- **Spleen**
- **Bone marrow (red)**
- **Ovaries**
- **Testes**
- **Whole body**

For an administered activity of 500 MBq the typical radiation dose to the critical organ (liver) is 39 mGy and the typical radiation dose to the critical organ (red bone marrow) is 7.0 mGy.

For an administered activity of 110 MBq the typical radiation dose to the organ target (lymph nodes) is 65 mGy and to the critical organ (injection site) 1320 mGy.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

The content of the kit before preparation is not radioactive. However, after Sodium Pertechnetate ([99mTc] solution Ph. Eur. is added, adequate shielding of the final preparation must be maintained.

The labeled HSA remains at the start, [99mTc]pertechnetate can be found near the solvent front. If the integrity of this vial is compromised, the product should not be used.

This agent is not intended for regular or continuous administration.

Method of preparation

Nanotop does not contain preservatives.

Aseptic preparation and the attention of the radiation protection are necessary.

The formation of the [99mTc]-nano sized albumin colloid depends on a sufficient content of tin in the reduced state. Oxidation can affect the quality of the preparation. Air inlet has to be avoided strictly.

The specific activity of the applied [99mTc]-nano sized albumin colloid should be as high as possible, since only approx. 1 - 2 % of the activity is enriched in lymph nodes after subcutaneous administration. Therefore, it is recommended to use fresh eluate of a generator eluted shortly before the radiolabelling. Labelling should be accomplished with the highest possible activity shortly after administration.

For use in children, it is possible to dilute the product up to 1:50 with 0.9 % sodium chloride injection.

Radiochemical marking / preparation of an injection suspension

1. Place the vial in a lead shield. Sanitize the closure with a suitable alcohol swab and allow to air dry.
2. Add 1.85 to 5.050 MBq in 1 - 5 ml of sodium pertechnetate ([99mTc] solution into the vial using a sterile syringe.
3. Then withdraw the same volume of nitrogen from the vial using the same syringe for pressure compensation. Do not use a breather needle.
4. Swirl gently to ensure complete resuspension (including upside down motions) and allow to react for 10 minutes at room temperature.
5. If required, dilute the radiochemical up to 1:50 with saline solution (0.9%).
6. Swirl the injection suspension immediately before withdrawing a dose from the vial. Swirl the syringe several times before injection.

Characteristics of the ready to use suspension

- **Volume**
- **Colour**
- **pH Value**
- **Radionuclided colloid**
- **pH value**

The radiochemical purity of the ready to use injection suspension can be controlled by thin layer chromatography.

The test solution has to be taken after 10 minutes and after 6 hours (for stability testing) from the method for particle size determination.

Method A: TLC plate

- **TLC plate**
- **Solvent**
- **Run distance**
- **Start**
- **Detector**

Method B: TLC plate

- **TLC plate**
- **Solvent**
- **Run distance**
- **Sample**
- **Detector**

After development remove the strips from the chromatographic chamber, dry in air and laminate with adhesive foil at both sides.

The spreading of activity is measured and displayed in a chromatogram. The percentages of the single peaks are calculated.

[99mTc]-Nano sized albumin colloids remain at the start, free [99mTc]-pertechnetate can be found near the solvent front.

The ready to use injection suspension should not contain more than 3 mg free [99mTc]-pertechnetate and must be used within 6 hours.