

**15 December 2020**

**SUMMARY OF PRODUCT CHARACTERISTICS**

**for**

**NanoScan, kit for radiopharmaceutical preparation**

**1. NAME OF THE MEDICINAL PRODUCT**

 NanoScan

**2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each vial contains 0.5 mg nanocolloidal human albumin.

At least 95 % of human albumin colloidal particles have a diameter ≤ 80 nm.

NanoScan is prepared from human serum albumin derived from human blood donations tested according to the EEC Regulations.

The radionuclide is not part of the kit.

Excipient(s) with known effects:

Sodium: 0.045 mmol

For the full list of excipients, see section 6.1

**3. PHARMACEUTICAL FORM**

Kit for radiopharmaceutical preparation

White powder.

Powder for solution for injection.

To be reconstituted with sodium pertechnetate (99mTc) solution for injection.

**4. CLINICAL PARTICULARS**

**4.1 Therapeutic indications**

This medicinal product is for diagnostic use only. This is indicated for adults and for the paediatric population.

After radiolabelling with sodium (99mTc) pertechnetate solution, the solution of nanocolloidal technetium (99mTc) albumin obtained is indicated for:

*Intravenous administration:*

* Bone marrow scanning (The product is not suitable to study the haematopoietic activity of the bone marrow)
* Inflammation scanning in areas other than the abdomen

*Subcutaneous administration:*

* Lymphoscintigraphy to demonstrate the integrity of the lymphatic system and to differentiate venous from lymphatic obstruction.
* Preoperative imaging and intraoperative detection of sentinel lymph nodes in melanoma, breast carcinoma, penile carcinoma, squamous cell carcinoma of the oral cavity and vulvar carcinoma.

**4.2 Posology and method of administration**

The medicinal product should only be administered by trained healthcare professionals with technical expertise in performing and interpreting sentinel lymph node mapping procedures.

Posology

*Adults and elderly population*

Recommended activities are as follows:

*Intravenous administration:*

* Bone marrow scanning: 185-500 MBq as a single intravenous injection.
* Inflammation scanning: 370-500 MBq as a single intravenous injection.

*Subcutaneous administration:*

* Lymphatic scanning: The recommended activity by single or multiple injections by subcutaneous (interstitial) is from 20 to 110 MBq per injection site.
* Sentinel node detection:
	+ The dose depends on the time interval between injection and the image acquisition or the surgery.
	+ Melanoma: 10 to 120 MBq in several doses by intradermal peritumoural injection.
	+ Breast carcinoma: 5-200 MBq in several doses each from 5-20 MBq to be administered by intradermal or subdermal or periareolar injection (superficial tumours) and by intratumoural or peritumoral injection (deep tumours).
	+ Penile carcinoma: 40-130 MBq in several doses each of 20 MBq to be administered intradermally around the tumour.
	+ Squamous cell carcinoma of the oral cavity: 15-120 MBq to be administered by single or

multiple peritumoural injections

* + Vulvar carcinoma: 60-120 MBq to be administered by peritumoural injection.

*Renal impairment/Hepatic impairment*

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

*Paediatric population*

The activities to be administered to children and adolescents is recommended to be calculated according the recommended range of adult activity adjusted to the body weight. The Paediatric Task Group of the European Association of Nuclear Medicine (EANM 1990) recommends calculating the administered activity according to the body weight as shown in the table below.

Fraction of adult activity:

|  |  |  |
| --- | --- | --- |
|  3 kg = 0.10 |  22 kg = 0.50 |  42 kg = 0.78 |
|  4 kg = 0.14 |  24 kg = 0.53 |  44 kg = 0.80 |
|  6 kg = 0.19 |  26 kg = 0.56 |  46 kg = 0.82 |
|  8 kg = 0.23 |  28 kg = 0.58 |  48 kg = 0.85 |
|  10 kg = 0.27 |  30 kg = 0.62 |  50 kg = 0.88 |
|  12 kg = 0.32 |  32 kg = 0.65 |  52-54 kg = 0.90 |
|  14 kg = 0.36 |  34 kg = 0.68 |  56-58 kg = 0.92 |
|  16 kg = 0.40 |  36 kg = 0.71 |  60-62 kg = 0.96 |
|  18 kg = 0.44 |  38 kg = 0.73 |  64-66 kg = 0.98 |
|  20 kg = 0.46 |  40 kg = 0.76 |  68 kg = 0.99 |

For use in children, it is possible to dilute the product before administration, see section 12.

Method of administration:

For multidose use.

*Intravenous administration:*

* Bone marrow scanning: single intravenous injection.
* Inflammation scanning: single intravenous injection.

*Subcutaneous administration:*

* Lymphoscintigraphy: The product is given by single or multiple subcutaneous injections, depending on the anatomical areas to be investigated and upon the time interval between injection and imaging. The injected volume should not exceed 0.2-0.3 mL. A volume more than 0.5 mL per injection site must not be applied. The subcutaneous injection should be given after checking by aspiration that a blood vessel has not been inadvertently punctured.
* Detection of sentinel lymph nodes:
	+ Melanoma: the activity is administered in four doses surrounding the tumor/scar, by injecting volumes of 0.1-0.2 mL.
	+ Breast carcinoma: a single injection in small volume (0.2 mL) is recommended. Multiple injections may be used in particular circumstances/conditions. When using superficial injections, large volumes of injectate may interfere with normal lymphatic flow; therefore, volumes of 0.05 - 0.5 mL are recommended. With peritumoral injections, larger volumes (e.g. 0.5 - 1.0 mL) may be used.
* Penile carcinoma: the dose should be administered thirty minutes after local spray anaesthesia by intradermal injection into three or four depots of 0.1 mL around the tumour of 0.3–0.4 mL. For large tumours not restricted to the glans, the product can be administered in the prepuce.
* Squamous cell carcinoma of the oral cavity: the activity is administered in two to four doses surrounding the tumor/scar in a total volume of 0.1-1.0 mL.
* Vulvar carcinoma: the activity is administered in four peritumoural doses in a total volume of 0.2 mL.

*Precautions to be taken before handling or administration of the medicinal product*

This medicinal product should be reconstituted before administration to the patient. For instructions on extemporaneous preparation of the medicinal product before administration, see section 12.

For patient preparation, see section 4.4.

This product is not intended for regular or continuous administration.

*Image acquisition*

* Bone marrow scanning: Images may be acquired 45-60 minutes after administration.
* Inflammation scanning: Dynamic imaging is performed immediately. Static imaging comprises an early phase, 15 minutes post-injection and a washout phase, 30-60 minutes post-injection.
* Lymphatic scanning:

When imaging the lower limbs, dynamic images are taken immediately following injection and static imaging 30-60 minutes later.

In parasternal lymph scanning, repeated injections and additional images may be required.

* Sentinel node detection
	+ Melanoma: Lymphoscintigraphic images are acquired starting after injection and regularly thereafter until the sentinel lymph node is visualized.
	+ Breast carcinoma: Scintigraphic images of breast and axillary region can be acquired by early detections (15-30 minutes) and late detections (3-18 hours) after injection.

Penile carcinoma: dynamic imaging can be performed immediately after injection and followed by static imaging at 30 minutes, 90 minutes, and 2 hours post-injection by using dual-head gamma camera.

* + Squamous cell carcinoma of the oral cavity: dynamic acquisition for 20 to 30 minutes starting immediately after injection. Two or three simultaneous static images from one or both sides in the anterior and lateral projections are recommended. Static images can be repeated at 2 hours, 4–6 hours, or just before surgery. SPECT imaging may improve the identification of sentinel lymph nodes, especially close to the injection site. Repeat injection and imaging may be considered; however, proceeding to neck dissection is preferred in order to avoid a false-negative sentinel lymph node.
	+ Vulvar carcinoma: image acquisition is to be obtained starting after the injection and every 30 min thereafter until the sentinel node(s) is visualized. The injection and images can be carried out the day before surgery or on the day of surgery. Planar images acquisition for 3 – 5 minutes in anterior and lateral views, and subsequent SPECT/CT images, are recommended.

**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. In particular, the use of nanocolloidal technetium (99mTc) albumin is contra-indicated in persons with a history of hypersensitivity to products containing human albumin.

In patients with complete lymph obstruction lymph node scintigraphy is not advisable because of the danger of radiation necroses at the site of injection.

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

**4.4 Special warnings and precautions for use**

Potential for hypersensitivity or anaphylactic reactions

The possibility of hypersensitivity including serious, life-threatening, fatal anaphylactic/ anaphylactoid reactions should always be considered.

If hypersensitivity or anaphylactic reactions occur, the administration of the medicinal product must be discontinued immediately and intravenous treatment initiated, if necessary. To enable immediate action in emergencies, the necessary medicinal products and equipment such as endotracheal tube and ventilator must be immediately available.

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/Hepatic impairment

Careful consideration of the benefit risk ratio in these patients is required since an increased radiation exposure is possible in these patients (see section 4.2).

Paediatric population

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

Careful consideration of the benefits and risks is required since the effective dose per MBq is higher than in adults (see section 11).

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.

After the procedure

Close contact with infants and pregnant women should be restricted during the initial 24 hours following the injection.

Specific warnings

It is strongly recommended that every time that NanoScan is administered to a patient, the name and batch number of the product are recorded, in order to maintain a link between the patient and the batch of the product.

Standard measures to prevent infections resulting from the use of medicinal products prepared from human blood or plasma include selection of donors, screening of individual donations and plasma pools for specific markers of infection, and the inclusion of effective manufacturing steps for the inactivation/removal of viruses. Despite this, when medicinal products prepared from human blood or plasma are administered, the possibility of transmitting infective agents cannot be totally excluded.

This also applies to unknown or emerging viruses and other pathogens.

There are no reports of virus transmissions with albumin manufactured to European Pharmacopoeia specifications by established processes.

Lymphoscintigraphy is not advised in patients with total lymphatic obstruction because of the potential radiation hazard at injection sites. The subcutaneous injection must be made without pressure into loose connective tissue.

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**

No interactions studies have been performed in adults or children.

Iodinated contrast media used in lymphoangiography may interfere with lymphatic scanning using nanocolloidal technetium (99mTc) albumin.

**4.6 Pregnancy and lactation**

Women of childbearing potential

When an administration of radiopharmaceuticals to a women 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.

During pregnancy, lymphoscintigraphy involving the pelvis is strictly contraindicated due to the accumulation in pelvic lymph nodes (see section 4.3).

Breast-feeding

Before administering radiopharmaceuticals to a mother who is breast-feeding 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 13 hours and the expressed feeds discarded.

Close contact with infants should be restricted during the initial 24 hours following injection.

Fertility

No studies on fertility have been performed.

**4.7 Effects on ability to drive and use machines**

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

**4.8 Undesirable effects**

The following table presents how the frequencies are reflected in this section:

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 from the available data)

*Immune system disorders*

Frequently not known: Protein allergic (hypersensitive) reaction, and hypersensitivity reactions (including very rare life-threatening anaphylaxis).

Very rare: local reactions, rash, itching, vertigo, hypotension

*Other disorders*

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose is 3.12mSv when the maximal recommended activity of 500 MBq is administered these adverse reactions are expected to occur with a low probability.

For safety with respect to transmissible agents, see section 4.4.

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:

Lægemiddelstyrelsen

Axel Heides Gade 1

DK-2300 København S

Websted: www.meldenbivirkning.dk

**4.9 Overdose**

In the event of administration of a radiation overdose with nanocolloidal technetium (99mTc) albumin no practical measure can be recommended to satisfactorily diminish tissue exposure as the label is poorly eliminated in urine and faeces.

**5. PHARMACOLOGICAL PROPERTIES**

**5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Technetium (99mTc), particles and colloids

ATC code: V 09 DB 01

Pharmacodynamic effects

At the chemical concentrations and activities used for diagnostic examinations, nanocolloidal technetium (99mTc) albumin does not appear to have any pharmacodynamic activity.

**5.2 Pharmacokinetic properties**

Distribution

Reticuloendothelial cells in liver, spleen as well as in bone marrow are responsible for blood clearance after intravenous injection. A small fraction of 99mTc radioactivity passes through kidneys and is eliminated in urine.

The maximum concentration in the liver and spleen is reached after about 30 minutes, but in the bone marrow after only 6 minutes.

The proteolytic breakdown of the colloid begins immediately after its uptake by the RES, the products of degradation being excreted through the kidneys into the bladder.

After subcutaneous injection into connective tissue, 30-40% of the administered nanocolloidal technetium (99mTc) albumin particles are filtered into lymphatic capillaries. The technetium (99mTc) albumin nanosized colloidal particles are then transported along the lymphatic vessels to regional lymph nodes and main lymphatic vessels and are finally trapped into the reticular cells of functionary lymph nodes.

Elimination

A fraction of the injected dose is phagocytized by histiocytes at the injection site. Another fraction appears in the blood and accumulates mainly in the RES of the liver, spleen and bone marrow; faint traces are eliminated via the kidneys.

**5.3 Preclinical safety data**

Toxicological studies with mice and rats have demonstrated that with a single intravenous injection of 800 mg and 950 mg, respectively, no deaths and no gross pathological changes at necropsy were observed. No local reactions were observed in either mice or rats following subcutaneous injection of 1g nanocolloidal albumin particles/kg body weight with 0.9 % saline injection. These doses correspond to the contents of 50 vials per kg body weight, which is the 3,500-fold compared to the maximum human dose.

This medicinal product is not intended for regular or continuous administration. Mutagenicity studies and long-term carcinogenicity studies have not been carried out. Studies of toxicity to reproduction are not available.

**6. PHARMACEUTICAL PARTICULARS**

**6.1 List of excipients**

Stannous (II) Chloride dihydrate

Glucose monohydrate

Sodium dihydrogen phosphate dihydrate, di-Sodium hydrogen phosphate dihydrate

Nitrogen

Hydrochloric acid

Sodium hydroxide

**6.2 Incompatibilities**

This medicinal product must not be mixed with other medicinal products except those mentioned in section 12.

**6.3 Shelf-life**

18 months.

After radiolabelling: 8 hours.

Do not store above 25 °C after radiolabelling.

**6.4 Special precautions for storage**

Do not store above 25 °C.

Keep the vials in the outer carton 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**

8 ml colourless, Type I, brosilicate glass multi-dose vials, closed with chlorobutyl rubber stopper and plastic-aluminium caps (polypropylene-aluminium caps) with turned up edge.

Pack sizes

1 pack contains 6 vials.

Sample package: 2 vials.

Bundle pack of 2 packs of 6 vials.

Bundle pack of 4 packs of 6 vials.

Not all pack sizes may be marketed.

**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/or appropriate licensees of the competent official organization.

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 preparation of nanocolloidal technetium (99mTc) albumin 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 this 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 extemporary preparation is not radioactive. However, after reconstitution with *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 spill of urine, vomiting etc. Radiation protection precautions in accordance with national regulations must therefore be taken.

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

**7. MARKETING AUTHORISATION HOLDER**

Radiopharmacy Laboratory Ltd.

Gyár st. 2

2040 Budaörs

Hungary

**8. MARKETING AUTHORISATION NUMBER(S)**

02248

**9. DATE OF FIRST AUTHORISATION**

6 September 2011

**10. DATE OF REVISION OF THE TEXT**

15 December 2020

**11. DOSIMETRY**

Technetium (99mTc) 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 6.02 hours to technetium (99Tc) which, in view of its long half-life of 2.13 x 105 years can be regarded as quasi stable.

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

**Adult and Children Category**

**Estimated Absorbed Radiation Dose after administration of**

**Technetium 99mTc NanoScan injection**

|  |
| --- |
| **Absorbed doses** |
| Organs | AdultmGy/MBq | Child | **Newborn****mGy/MBq** |
| **15yrs****mGy/MBq** | **10yrs****mGy/MBq** | **5yrs****mGy/MBq** | **1yr****mGy/MBq** |
| Adrenals | 0.00631 | 0.00771 | 0.0114 | 0.0163 | 0.0282 | 0.059 |
| Bladder wall | 0.00996 | 0.0132 | 0.0186 | 0.0275 | 0.050 | 0.111 |
| Bone surfaces | 0.00568 | 0.00686 | 0.0109 | 0.0163 | 0.0361 | 0.0957 |
| Brain | 0.00334 | 0.00417 | 0.00677 | 0.0109 | 0.0192 | 0.043 |
| Breast | 0.00305 | 0.00387 | 0.00563 | 0.00889 | 0.0168 | 0.038 |
| Gall bladder wall | 0.00808 | 0.0101 | 0.0152 | 0.0227 | 0.0314 | 0.073 |
| Gastrointestinal tract. |  |  |  |  |  |  |
| Stomach | 0.00493 | 0.0066 | 0.0106 | 0.0152 | 0.0266 | 0.0568 |
| Intestin | 0.00551 | 0.00688 | 0.0105 | 0.0161 | 0.0277 | 0.0587 |
| Intestinal wall upper colon | 0.00557 | 0.00722 | 0.0108 | 0.0173 | 0.0282 | 0.0601 |
| Intestinal wall, lower colon | 0.0052 | 0.00656 | 0.0103 | 0.0149 | 0.0269 | 0.0534 |
| Myocardium | 0.00532 | 0.00669 | 0.0099 | 0.0146 | 0.0255 | 0.0545 |
| Kidneys | 0.00541 | 0.00664 | 0.0101 | 0.015 | 0.0255 | 0.0547 |
| Liver | 0.016 | 0.0203 | 0.0302 | 0.0422 | 0.0756 | 0.161 |
| Lung | 0.00468 | 0.00599 | 0.0087 | 0.0131 | 0.0232 | 0.0498 |
| Muscles | 0.00396 | 0.00491 | 0.00740 | 0.0112 | 0.0207 | 0.0466 |
| Ovaries | 0.00575 | 0.00651 | 0.0115 | 0.0181 | 0.0207 | 0.0466 |
| Pancreas | 0.00637 | 0.00798 | 0.0119 | 0.018 | 0.0308 | 0.0636 |
| Red bone marrow | 0.00572 | 0.00663 | 0.0103 | 0.0168 | 0.034 | 0.0957 |
| Skin | 0.00269 | 0.00323 | 0.00514 | 0.00820 | 0.0152 | 0.0359 |
| Spleen | 0.00411 | 0.00544 | 0.00827 | 0.0121 | 0.0209 | 0.0453 |
| Testes | 0.00349 | 0.00558 | 0.00783 | 0.011 | 0.0194 | 0.0438 |
| Thymus | 0.0042 | 0.00533 | 0.00779 | 0.012 | 0.0215 | 0.0466 |
| Thyroid | 0.00405 | 0.00514 | 0.00814 | 0.013 | 0.0231 | 0.0495 |
| Uterus | 0.00582 | 0.00716 | 0.0109 | 0.0164 | 0.0285 | 0.0589 |
| **Effective Dose per unit activity administered (mSv/MBq)** | **0.00624** | **0.00764** | **0.0147** | **0.0205** | **0.0341** | **0.0732** |

Dose calculations were made with the standard MIRD method (MIRD Pamphlet No.1, Society of Nuclear Medicine, 1976). The Effective Dose Equivalence (EDE) was determined as specified in ICRP 80 (Ann. ICRP 18 (1-4), 1988). This value varied as follows: 6.24x10-3 mSv/MBq for adults and 7.64x10-3 mSv/MBq, 1.47x10-2mSv/MBq, 2.05x10-2 mSv/MBq, 3.41x10-2mSv/MBq and 7.32x10-2mSv/MBq respectively, for children aged 15, 10, 5 and 1 years and for newborns.

**Pregnancy Category**

**Estimated Absorbed Radiation Dose after administration of**

**Technetium 99mTc-NanoScan injection**

|  |  |  |
| --- | --- | --- |
| Organs | Pregnant womenmGy/MBq | Duration of Pregnancy |
| **3 months****mGy/MBq** | **6 months****mGy/MBq** | **9 months****mGy/MBq** |
| Adrenals | 0.00205 | 0.00205 | 0.00203 | 0.00203 |
| Bladder wall | 0.000081 | 0.000081 | 0.000088 | 0.000082 |
| Bone surfaces | 0.00304 | 0.00304 | 0.00304 | 0.00304 |
| Brain | 0.000103 | 0.000103 | 0.000103 | 0.000103 |
| Breast | 0.358 | 0.358 | 0.358 | 0.358 |
| Gall bladder wall | 0.00147 | 0.00147 | 0.00161 | 0.00161 |
| Gastrointestinal tract. |  |  |  |  |
| Stomach | 0.00268 | 0.00268 | 0.00331 | 0.00331 |
| Intestin | 0.00032 | 0.00032 | 0.00057 | 0.00193 |
| Intestinal wall upper colon | 0.00049 | 0.00049 | 0.00159 | 0.00178 |
| Intestinal wall, lower colon | 0.000117 | 0.000117 | 0.000360 | 0.000270 |
| Myocardium | 0.020 | 0.020 | 0.0211 | 0.0211 |
| Kidneys | 0.00082 | 0.00082 | 0.00081 | 0.00081 |
| Liver | 0.00293 | 0.00293 | 0.00344 | 0.00344 |
| Lung | 0.00811 | 0.00811 | 0.00839 | 0.00839 |
| Muscles | 0.00174 | 0.00174 | 0.00175 | 0.00180 |
| Ovaries | 0.000117 | 0.000117 | 0.000139 | 0.000142 |
| Pancreas | 0.00257 | 0.00257 | 0.00253 | 0.00253 |
| Red bone marrow | 0.00189 | 0.00189 | 0.00189 | 0.00189 |
| Skin | 0.00278 | 0.00278 | 0.00288 | 0.00293 |
| Spleen | 0.00172 | 0.00172 | 0.00171 | 0.00171 |
| Thymus | 0.0103 | 0.0103 | 0.00916 | 0.00916 |
| Thyroid | 0.00124 | 0.00124 | 0.00125 | 0.00125 |
| Uterus | 0.000127 | 0.000126 | 0.000641 | 0.000830 |
| Foetus | - | 0.000158 | 0.000580 | 0.000710 |
| Placenta | - | - | 0.00126 | 0.00156 |
| **Effective Dose per unit activity administered (mSv/MBq)** | **0.0574** | **0.0574** | **0.0576** | **0.0576** |

Dose calculations were made with the standard MIRD method (MIRD Pamphlet No.1, Society of Nuclear Medicine, 1976). The Effective Dose Equivalence (EDE) was determined as specified in ICRP 80 (Ann. ICRP 18 (1-4), 1988). This value varied as follows: 5.74x10-2 mSv/MBq for women and 5.74x10-2 mSv/MBq, 5.76x10-2 mSv/MBq and 5.76x10-2mSv/MBq respectively, for pregnant women in 3, 6 or 9-months.

The radiation doses absorbed by a patient weighing 70 kg, after subcutaneous injection of 99mTc-human albumin colloidal particles, are reported hereafter. The data listed below is based on MIRD reference man and MIRD S values, and has been calculated from biological data of organ uptake and blood clearance.

|  |  |
| --- | --- |
| Organ | Absorbed doseµGy/MBq |
| Injection site | 12000 |
| Lymph nodes | 590 |
| Liver | 16 |
| Urinary bladder (wall) | 9.7 |
| Spleen | 4.1 |
| Bone marrow (red) | 5.7 |
| Ovaries | 5.9 |
| Testes | 3.5 |
| Whole body | 4.6 |

The effective dose resulting from the subcutaneous administration of a maximal recommended activity of 110 MBq for an adult weighing 70 kg is about 0.44 mSV.

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

In the case of subcutaneous administration for sentinel node detection it is assumed that the dose to the injection site, which varies greatly with location, injected volume, number of injections and retention, can be ignored due to the relatively low radio sensitivity of skin and the small contribution this makes to the overall effective dose.

In the case of sentinel node detection of breast carcinoma the data listed below (ICRP 106) assumes no leakage occurs and the absorbed dose to the remaining breast is equal to the dose to the lungs.

|  |  |
| --- | --- |
| **Organ** | **Absorbed dose per unit activity administered (mGy/MBq)** |
| **6 h to removal** |  | **18 h to removal** |
| **Adult** | **15 years** |  | **Adult** | **15 years** |
| Adrenals | 0.00079 | 0.00093 |  | 0.0014 | 0.0016 |
| Bladder | 0.000021 | 0.000039 | 0.000036 | 0.000068 |
| Bone surfaces | 0.0012 | 0.0015 | 0.0021 | 0.0026 |
| Brain | 0.000049 | 0.000058 | 0.000087 | 0.0001 |
| Breast (remaining) | 0.0036 | 0.0039 | 0.0064 | 0.0069 |
| Gall bladder | 0.00053 | 0.00072 | 0.00093 | 0.0013 |
| GI-tract |  |  |  |  |
| Stomach | 0.0013 | 0.00092 | 0.0023 | 0.0016 |
| Small Intestine | 0.00015 | 0.00011 | 0.00027 | 0.0002 |
| Colon | 0.00019 | 0.000083 | 0.00033 | 0.00014 |
| (Upper large intestine | 0.00028 | 0.00012 | 0.00049 | 0.0002 |
| (Lower largeintestine | 0.00007 | 0.000038 | 0.00012 | 0.000066 |
| Heart | 0.0041 | 0.0052 | 0.0071 | 0.0091 |
| Kidneys | 0.00031 | 0.00042 | 0.00054 | 0.00073 |
| Liver | 0.0011 | 0.0014 | 0.0019 | 0.0024 |
| Lungs | 0.0036 | 0.0039 | 0.0064 | 0.0069 |
| Muscles | 0.00066 | 0.00083 | 0.0012 | 0.0015 |
| Oesophagus | 0.0036 | 0.005 | 0.0062 | 0.0087 |
| Ovaries | 0.000041 | 0.000048 | 0.000071 | 0.000083 |
| Pancreas | 0.00097 | 0.0011 | 0.0017 | 0.002 |
| Bone marrow (red) | 0.0086 | 0.00092 | 0.0015 | 0.0016 |
| Skin | 0.0012 | 0.0014 | 0.0021 | 0.0024 |
| Spleen | 0.00068 | 0.00083 | 0.0012 | 0.0015 |
| Thymus | 0.0036 | 0.005 | 0.0062 | 0.0087 |
| Thyroid | 0.00047 | 0.00062 | 0.00082 | 0.0011 |
| Uterus | 0.000041 | 0.000064 | 0.000071 | 0.00011 |
| Remaining organs | 0.00066 | 0.00083 | 0.0012 | 0.0015 |
| **Effective dose (mSv/MBq)** | **0.0012** | **0.0014** |  | **0.002** | **0.0024** |

The effective dose resulting from the subcutaneous administration of a maximal recommended activity of 200 MBq with the removal of the injection site 18 hours post-injection for an adult weighing 70 kg is about 0.4 mSv.

**12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS**

The preparation contains no bacteriostatic preservative.

99mTc-NanoScan is to be used within eight (8) hours from reconstitution. The vial is reconstituted with an activity ranging from 185MBq to 5.5 GBq of oxidant-free sterile Sodium (99mTc) pertechnetate.

Withdrawals should be performed under aseptic conditions. 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.

In children, it is possible to dilute the product up to 1:50 with sodium chloride for injection.

This agent is not intended for regular or continuous administration.

**Method of preparation**

Use aseptic procedure throughout and take precautions to minimize radiation exposure by the use of suitable shielding. Water-proof gloves should be worn during the preparation procedure.

1. Remove the protective disc from the vial and swab the closure with an alcohol swab.
2. Place the vial in a suitable lead vial shield which has a minimum wall thickness of 3 mm (1/8 inch) and which has a fitted lead cap. Obtain 1-5 ml of sterile, non-pyrogenic, addictive-free Sodium pertechnetate (99mTc) Injection Ph.Eur. (activity: 185 MBq to 5.5 GBq) using shielded syringe.
3. Add the Sodium Pertechnetate (99mTc) solution to the vial, while avoiding the build-up of excessive pressure in the vial. Pressure build-up may be avoided by injecting several millilitres of pertechnetate solution into the vial, then withdrawing several millilitres nitrogen gas (present to prevent oxidation of the complex) into the syringe. The procedure is repeated as necessary until the entire amount of pertechnetate is added to the vial and normal pressure is established within the vial.
4. Place the lead cap on the vial shield and mix the contents of the shielded vial by repeated gentle inversion until all the material is suspended. Than allow standing for 20 minutes at room temperature (15-25 °C). Using proper shielding, the vial should be visually inspected to ensure that the suspension is free of foreign matter before proceeding, if it is not, the radiopharmaceutical should not be used.
5. Assay the product in a suitable calibrator, record the radioassay information on the label which has a radiation warning symbol. Also note the time and date of preparation. Apply the label to the vial shield.
6. The radiochemical purity of the finished product should be determined prior the patient administration. The radiochemical purity should not be less than 95 %.
7. Withdrawals for administration must be made aseptically using sterile needle and syringe. Since the vials contain nitrogen, the vials should not be vented. If repeated withdrawals are made, the replacement of the contents of the vial with air should be minimized.
8. The finished preparation should be discarded after 8 hours. It should also be retained during its life in a lead vial shield with the lead cap in place. Do not store the labelled product above +25 °C.
9. After reconstitution the container and any unused contents should be disposed of in accordance with local requirements for radioactive materials.

**Quality Control**

The quality of labelling (radiochemical purity) can be controlled according to the following procedure:

Materials

GMCP-SA

Methyl ethyl keton

Capintec or equivalent instrument for measuring radioactivity in the 0.01 MBq-6 GBq range. The resolution value is 0.001 MBq

1 ml syringe with a 22-26 gauge needle.

Small developing tank with cover

**Procedure**

Pour enough Methyl ethyl keton into the developing tank (beaker) to have a depth of 3-4 mm of solvent.

Saturation time: 30 minutes.

Apply 1 drop (5 µl) of the kit solution to the GMCP-SA 2 cm from the bottom.

Develop immediately.

Develop the plate a distance of minimum 5 cm from the spot.

Determine the distribution of radioactivity using suitable detector

99mTc-Human Serum Albumin colloid remains at the starting point (Rf: 0.0-0.2) and free pertechnetate ions and other soluble impurities migrate with the solvent front (Rf: 0.8-1.0).

Do not use the material if the radiochemical purity is less than 95 %.