1. NAME OF THE MEDICINAL PRODUCT

SENTI-SCINT 1.0 mg powder for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:
Human Serum Albumin millimicroaggregate 1.0 mg per vial
Excipients:
Contains 15.0 mg Glucose

For full list of excipients see 6.1

3. PHARMACEUTICAL FORM

Powder for injection. Kit for radiopharmaceutical preparation.
The kit contains lyophilised, sterile, pyrogen free inactive preparation, sealed in nitrogen atmosphere. After reconstitution with the prescribed quantity of Technetium–99m sterile solution, the solution is clear, particle free and complies with the criteria of sterile injections.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.
The product is a cold radiopharmaceutical. After reconstitution with sodium ^{99m}Tc-pertechnetate solution the agent may be used for Sentinel node lymphoscintigraphy in melanoma malignum and in breast cancer.

4.2 Posology and method of administration

Administration

For the labelling of one vial of lyophilised powder, use 1-5 ml of sterile 99mTc sodium pertechnetate solution with a maximum radioactivity of 5.5 GBq.
Depending on the activity of the ^{99m}Tc solution used for labelling, the injection can be distributed into three-five portions.

The recommended activity per examination for adults with a mean body weight of 70 kg is 60-100 MBq.

Pediatric doses:
The activity for children may be calculated from the recommended range of adult activity and adjusted according to body weight.
The Paediatric Task Group of EANM recommends calculating the administered activity from the body weight according to the following table.

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

Method of Administration

Three-five subcutaneous injections are administered near to the lesion. Volume of 0.2 - 0.5 ml and 20 - 20 MBq per injection site is used.
Imaging is carried out 20 minutes after injection and repeated 1-5 hours later until the appearance of the first lymph node.

4.3 Contraindications

Hypersensitivity to the active substance or to the excipients. The use of human albumin colloidal particles is contraindicated in persons with a history of hypersensitivity to products containing human albumin. Adequate medication and reanimation equipment must therefore always be kept available during the investigation.

4.4 Special warnings and precautions for use

The activity administered must be such that the resulting radiation dose is as low as reasonably achievable, bearing in mind the need to obtain the intended diagnostic result.
The subcutaneous injection must be made without pressure into loose connective tissue.
Prior to injection, an aspiration test should ascertain that no blood vessel was inadvertently punctured.
The patient to be investigated should not eat anything for 4 hours before the investigation, and should eat only light food after the injection in order to facilitate the elimination of the radiopharmaceutical from the body.
When a protein-containing radiopharmaceutical such as 99mTc-Senti-Scint is administered to a patient, hypersensitivity reactions may develop
Adequate medication and reanimation equipment must therefore always be kept available during the investigation.
It cannot be administered to pregnant or lactating mothers or patients less than 18 years of age except when the value of the desired clinical information exceeds the risk of the radiation burden incurred by the patient.
With women of child- bearing potential, the investigation should be performed during the first 10 days after the onset of menses.
The labelled preparation can be used within 6 hours.
The labelled preparation can be diluted, if needed, by the addition of sterile, isotonic saline.
The reconstituted product should be stored at any temperature below 25 ^{o}C and protected against oxidants.
The reconstituted product should be stored in agreement with national regulations for radioactive materials.
Radiopharmaceutical should be used only by physicians who are qualified by training and experience in the safe use and handling of radionuclides and whose experience and training have been approved by the appropriate government agency authorized to licence the use of radionuclides.
The preparation without reconstitution with sodium 99mTc-pertechnetate must not be administered to patients.

4.5 Interaction with other medicinal products and other forms of interaction

Not known.

4.6 Pregnancy and lactation

Women of childbearing potential
When it is necessary to inject radiopharmaceuticals to women of childbearing potential, information should always be thought about pregnancy. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. Where uncertainly exists it is important that radiation exposure should be the minimum consistent with achieving the desired clinical information. Alternative techniques, which do not involve ionising radiation should always considered.
Pregnancy
Radionuclide procedures carried out on pregnant women also involve radiation dose to the foetus. Only imperative investigations should-therefore be carried out during pregnancy, when the likely benefit far exceeds the risk incurred by the mother and fetus.
Lactation
Before administering a radioactive medicinal product to a mother who is breast feeding consideration should be given as to whether the investigation could be reasonably delayed until the mother has ceased breast feeding and as to whether the most appropriate choice of radiopharmaceutical has been made. Breast feeds should be banked prior to injection and the subsequent ones discarded after injection. Breast feeding can be restarted 12 hours post injection.
Lactation can be started if the child does not receive more than 1 mSv radiation dose due to the breast feeding.

4.7 Effects on ability to drive and use machines

Effects on ability to drive and use machines have not been described.

4.8 Undesirable effects

Rare: hypersensitivity
When a protein-containing radiopharmaceutical such as 99mTc-Senti-Scint is administered to a patient, hypersensitivity reactions may develop. Adequate medication and reanimation equipment must therefore always be kept available during the investigation.
For each patient, exposure to ionising radiation must be justifiable on the basis of the likely benefit.
The activity administered must be such that the resulting radiation dose is as low as reasonably achievable, bearing in mind the need to obtain the intended diagnostic result.
Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects.
For diagnostic nuclear medicine investigations the current evidence suggests that these adverse effects will occur with low frequency because of the low radiation doses incurred.
For most diagnostic investigations using a nuclear medicine procedure the radiation dose delivered (EDE) is less than 20 mSv.

4.9 Overdose

In the event of an overdose of radioactivity being administered when using 99mTc-Senti-Scint, no practical measure can be recommended to satisfactory diminish tissue exposure as the label is poorly eliminated in urine and faeces. In the experiments with the Senti-Scint preparation in rats no signs indicative of toxicity were observed.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutical group: diagnostic radiopharmacon, does not containing the labelling isotope, ATC code : V09DB03

At the chemical concentrations and activities used for diagnostic procedures 99mTc-Senti-Scint does not appear to exert any pharmacodynamic effects.

5.2 Pharmacokinetic properties

The Senti-Scint colloidal product produced from human serum albumin consists of particles between 100-600 nm in size.
After subcutaneous injection into connective tissue the 99mTc-albumin colloidal particles are filtered into lymphatic capillaries. The 99mTc-albumin 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.
^{99m}Tc radioactivity passes through kidneys and is eliminated in urine.

5.3 Preclinical safety data

Pathological investigations during preclinical studies did not reveal pathological lesions in the organs of the laboratory animals. Mutagenicity, teratogenicity or carcinogenicity of the product has not been reported in the relevant literature.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Stannous(II) Chloride Dihydrate, Sodium Phosphate Monobasic, Sodium Phosphate Dibasic, Glucose, Nitrogen gas

6.2 Incompatibilities

Not known.

6.3 Shelf life

– The labelled product should be used within 6 hours after reconstitution with sodium 99mTc-pertechnetate injection. Sodium pertechnetate [99mTc] injection should comply with European Pharmacopoeia specification.
– The expiry date of the kit is 18 months. The expire date is indicated on the packaging material.

6.4 Special precaution and storage

The freeze-dried product is to be stored below 25°C, protected from light and oxidants.
The reconstituted product should be stored and handled in accordance with national regulations for radioactive materials.
Radiopharmaceutical should be used only by physicians who are qualified by training and experience in the safe use and handling of radionuclides and whose experience and training have been approved by the appropriate government agency authorized to licence the use of radionuclides.

6.5 Nature and contents of container

Sterile, colourless, 8 ml glass vials, European Pharmacopoeia Type I, closed with sterile rubber stopper and plastic-aluminium flip-off caps with turned up edge.

6.6 Special precautions for disposal and additional information of the product

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

7. MARKETING AUTHORISATION HOLDER

Name: MEDI-RADIOPHARMA LTD.
Address: 2030, Érd, Szamos st. 10-12., Hungary
Tel: 36-23-521-261
Fax: 36-23-521-260
e-mail: mediradiopharma-ltd@t-online.hu, www.mediradiopharma.com

8. MARKETING AUTHORISATION NUMBER(S)

Hungary:	OGYI-T-8665
Czech Republic:	88/100/01-C
Slovak Republic:	88/0045/04-S
Turkey:	RF-04-0006

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Hungary:	14. September 1999/22. February, 2010
Czech Republic:	07. March 2001./13. September, 2006.
Slovakian Republic:	27. February 2004
Turkey:	06. July 2004

10. DATE OF REVISION OF THE TEXT

22. February, 2010

11. DOSIMETRY

Adults and Children

Absorbed doses						
Organs	Adult µGy/MBq	Child				Newborn µGy/MBq
		15yrs µGy/MBq	10yrs µGy/MBq	5yrs µGy/MBq	1yr µGy/MBq	
Liver	16.0	20.3	30.2	42.2	75.6	161
Bladder wall	9.96	13.2	18.6	27.5	50.0	111
Gall bladder wall	8.08	10.1	15.2	22.7	31.4	73.0
Pancreas	6.37	7.98	11.9	18.0	30.8	63.6
Adrenals	6.31	7.71	11.4	16.3	28.2	59.0
Uterus	5.82	7.16	10.9	16.4	28.5	58.9
Ovaries	5.75	6.51	11.5	18.1	20.7	46.6
Red marrow	5.72	6.63	10.3	16.8	34.0	95.7
Bone surface	5.68	6.86	10.9	16.3	36.1	95.7
Intestinal wall, upper colon	5.57	7.22	10.8	17.3	28.2	60.1
Intestine	5.51	6.88	10.5	16.1	27.7	58.7
Kidneys	5.41	6.64	10.1	15.0	25.5	54.7
Myocardium	5.32	6.69	9.90	14.6	25.5	54.5
Intestinal wall, lower colon	5.20	6.56	10.3	14.9	26.9	53.4
Stomach	4.93	6.60	10.6	15.2	26.6	56.8
Lung	4.68	5.99	8.70	13.1	23.2	49.8
Whole body	4.48	5.49	8.42	13.0	23.3	52.4
Thymus	4.20	5.33	7.79	12.0	21.5	46.6
Spleen	4.11	5.44	8.27	12.1	20.9	45.3
Thyroid	4.05	5.14	8.14	13.0	23.1	49.5
Muscle	3.96	4.91	7.40	11.2	20.7	46.6
Testes	3.49	5.58	7.83	11.0	19.4	43.8
Brain	3.34	4.17	6.77	10.9	19.2	43.0
Breast	3.05	3.87	5.63	8.89	16.8	38.0
Skin	2.69	3.23	5.14	8.20	15.2	35.9

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 53 (Ann. ICRP 18 (1-4), 1988). This value varied as follows: $6.24x10^{-3}$ mSv/MBq for adults and $7.64x10^{-3}$ mSv/MBq, $1.47x10^{-2}$mSv/MBq, $2.05x10^{-2}$ mSv/MBq, $3.41x10^{-2}$mSv/MBq and $7.32x10^{-2}$mSv/MBq respectively, for children aged 15, 10, 5 and 1 years and for newborns.

Pregnancy Category

Absorbed doses				
Organs	Pregnant women µGy/MBq	Duration of Pregnancy		
		3 months µGy/MBq	6 months µGy/MBq	9 months µGy/MBq
Breast	358	358	358	358
Myocardium	20.0	20.0	21.1	21.1
Thymus	10.3	10.3	9.16	9.16
Lung	8.11	8.11	8.39	8.39
Whole body	4.22	4.22	4.09	4.14
Bone surface	3.04	3.04	3.04	3.04
Skin	2.78	2.78	2.88	2.93
Liver	2.93	2.93	3.44	3.44
Stomach	2.68	2.68	3.31	3.31
Pancreas	2.57	2.57	2.53	2.53
Adrenals	2.05	2.05	2.03	2.03
Red marrow	1.89	1.89	1.89	1.89
Muscle	1.74	1.74	1.75	1.80
Spleen	1.72	1.72	1.71	1.71
Gall bladder wall	1.47	1.47	1.61	1.61
Thyroid	1.24	1.24	1.25	1.25
Kidneys	0.82	0.82	0.81	0.81
Intestinal wall, upper colon	0.49	0.49	1.59	1.78
Intestine	0.32	0.32	0.57	1.93
Uterus	0.127	0.126	0.641	0.830
Foetus		0.158	0.580	0.710
Placenta			1.26	1.56
Intestinal wall, lower colon	0.117	0.117	0.360	0.270
Ovaries	0.117	0.117	0.139	0.142
Brain	0.103	0.103	0.103	0.103
Bladder wall	0.081	0.081	0.088	0.082

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 53 (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 $5.76x10^{-2}$mSv/MBq respectively, for pregnant women in 3, 6 or 9-months.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Method of Preparation

Usual precaution regarding sterility and radioprotection should be respected.
Place the vial containing the lyophilised substance in a lead shield having 3 mm wall thickness.
Inject sterile 99mTc-sodium pertechnetate solution Ph. Eur. (max. 5.5 GBq) aseptically into the vial in a volume of 1-5 ml. Before removing the syringe, withdraw an equal volume (1-5 cm^3) of the nitrogen gas to normalise the pressure in the vial. (Do not use a breather needle.)
Dissolve the lyophilised material by gently swirling, incubate at room temperature (20-25 °C) for 20 min., and then shake gently before injection.
Fill out the enclosed label and place onto the vial.

Quality Control

Method: ascending thin layer chromatography

Materials, reagents:

1. 2.0x20 cm silica gel coated plate (Kieselgel 60 DC-Alufolien)
2. Eluent: Acetone
3. Chromatographic tank
4. Syringe, needle, scissors, tweezers, radiation detector

Test:

1. Fill eluent to the chromatographic tank (2cm deep)
2. Apply the (5-10 µl) of sample solution and 99mTc sodium pertechnetate solution as reference at a distance of 3 cm from the lower edge and from the sides of the plate. Place the plate vertically into the chromatographic tank. The spots should be above the eluent level. Close the tank lid.
3. After development dry the plate nad cut into 1 cm stripes. Use tweezers during the operation.
4. Measure the activity by NK-350 automatic or other suitable radiation detector.
5. After development in acetone the labelled product remains at the start point (R_f=0.0), and the unbound $^{99m}TcO^{4-}$ is at the solvent front (R_f=0.9-1.0).
6. After measuring the activity , calculate the percentage of total activity bound to the carrier molecule, and the percentage of unbound $^{99m}TcO^{4-}$ and other radiochemical impurity.

Calculation of labelling efficacy:

$$^{99m}\text{Tc-SENTI-SCINT (\%)} = \frac{\text{Activity value (cpm) at } R_f=0.0}{\text{Total activity of thin layer plate (cpm)}} \times 100$$

Calculation of radiochemical impurities:

$$\text{Radiochemical impurities (\%)} = \frac{\text{Activity value (cpm) at } R_f=1.0}{\text{Total activity of thin layer plate (cpm)}} \times 100$$

Labelling efficacy should be not less than 90%, and the radiochemical impurities should be not more than 10 %.