

ANNEX I
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

LeukoScan 0.31 mg, powder for solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Kit for the preparation of ^{99m}Tc -labelled LeukoScan.

Each 3 ml vial contains 0.31 mg sulesomab (IMMU-MN3 murine Fab'-SH antigranulocyte monoclonal antibody fragments) for the preparation of ^{99m}Tc labelled LeukoScan. The kit does not include the radioisotope.

Excipient(s) with known effect:

Sucrose (37.8 mg)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for solution for injection.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

LeukoScan is indicated for diagnostic imaging for determining the location and extent of infection/inflammation in bone in patients with suspected osteomyelitis, including patients with diabetic foot ulcers.

LeukoScan has not been employed to diagnose osteomyelitis in patients with sickle cell anaemia.

4.2 Posology and method of administration

The radiolabelled solution should be administered as an intravenous injection. After injection, any remaining portion of the reconstituted solution should be discarded.

LeukoScan is not recommended for use in children.

Formal studies have not been performed in patients with renal or hepatic impairment. However, due to the low dose of protein administered and the short half-life of ^{99m}Tc , dosage adjustment is probably not necessary in such patients.

Radiopharmaceutical agents should be used only by qualified personnel with appropriate government authorisation for the use and manipulation of radionuclides.

This radiopharmaceutical may be received, used and administered only by authorised persons in designated clinical settings. Its receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licenses of local competent official organisations.

Immediately prior to use, contents of the vial are reconstituted in the unlabeled form to prepare LeukoScan [^{99m}Tc]. The unreconstituted contents of the vial before radiolabelling are not to be directly administered to patients.

For instructions on preparation of the medicinal product before administration, see section 6.6.

For readministration see section 4.4.

4.3 Contraindications

Hypersensitivity to the active substance or to mouse proteins or to any of the excipients listed in section 6.1.

Pregnancy.

4.4 Special warnings and precautions for use

Safety and diagnostic accuracy in persons under 21 years of age have not been established. Administration of LeukoScan to young subjects should only be performed after consideration of the possible risks and benefits to the individual subject.

Recommended imaging protocol

Immunoscintigraphy should be performed one to eight hours after injection.

There was essentially no difference in the detection of the presence or absence of osteomyelitis between the 1-2 hour timepoint and the 5-8 hour timepoint after injection. This suggests that imaging can be accomplished anytime between one and eight hours after injection (at the convenience of the nuclear medicine department and the patient).

Planar imaging in all views necessary to adequately visualise the affected area at 1-8 h post-injection with at least 500 k counts or ten minutes per view should be made. Image acquisition in analogue and/or digital word-mode and at least a 128 x 128 matrix is recommended.

Single photon emission computed tomography (SPECT) imaging can also be conducted and may aid in differentiating osteomyelitis from soft tissue infections. SPECT acquisition parameters recommended are: 60 projections in a 360° step-and-shoot technique, 30 seconds per view in at least a 64 x 64 matrix. Data processing by filtered backprojection and reconstruction in three planes (transaxial, coronal, and sagittal) is recommended.

Interpretation of the images

When a bone scan is positive and imaging with LeukoScan is negative, infection is unlikely. When a bone scan is negative, imaging with LeukoScan may rarely show a positive response and this may indicate early osteomyelitis.

Hypersensitivity

Anaphylactic and other hypersensitivity reactions are possible whenever mouse protein materials are administered to patients. Appropriate cardiopulmonary resuscitation facilities and trained personnel should be available for immediate use in the event of an adverse reaction.

Human Anti-mouse Antibody (HAMA)

In clinical trials involving over 350 patients, no induction of human anti-mouse antibody (HAMA) to antibody fragments has been observed nor has there been any elevation of HAMA levels in patients with pre-existing HAMA.

Patients who have previously received murine monoclonal antibody products are more likely to have HAMA. In subjects with HAMA, there may be a greater chance of hypersensitivity reactions and diminished efficacy in imaging.

Readministration

There are, as yet, limited data on safety following repeated use. Readministration should only be considered in patients whose sera are negative for human anti-mouse antibody (HAMA) elevation in the fragment assay. The overall radiation dose received by the patient over time should also be taken into account.

HAMA titers should be determined before repeated administration of LeukoScan.

Paroxysmal nocturnal hemoglobinuria

LeukoScan is not expected to bind to leukocytes in patients with paroxysmal nocturnal hemoglobinuria.

4.5 Interactions with other medicinal products and other forms of interaction

Formal drug interaction studies have not been performed, but no drug interactions have been described to date, including patients receiving antibiotics.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

When it is necessary to administer radioactive medicinal products to women of childbearing potential, information should always be sought about pregnancy. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. Where uncertainty 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 be considered.

Pregnancy

LeukoScan is contraindicated in pregnancy.

Radionuclide procedures carried out on pregnant women also involve radiation doses to the foetus. LeukoScan is contraindicated in pregnancy. Administration of 750 MBq LeukoScan will give an estimated absorbed dose of 4.1 mGy to an embryo or fetus at an early stage.

Breast-feeding

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, bearing in mind the secretion of activity in breast milk. If the administration is considered necessary, breast feeding should be interrupted and the expressed feeds discarded. It is usual to advise that breast feeding can be restarted when the level in the milk will not result in a radiation dose to the child greater than 1 mSv. Due to the short six-hour, half-life of ^{99m}Tc , a dose of less than 1 mSv in mother's milk can be expected 24 hours after the administration of LeukoScan [^{99m}Tc].

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects

The following minor, self-limiting, rare adverse events were reported in the clinical trials and considered at least possibly related to LeukoScan: eosinophilia (3); and facial rash (1). None of these were considered serious, and all resolved without sequelae.

Post-marketing experience currently comprises greater than 70,000 vials sold, with two reports of self-limiting allergic reactions.

1. Statistically significant reductions in white blood cell (WBC) count were observed in the controlled studies at 24 hours post-injection, from a mean value of 8.9 to a mean value of 8.0 ($\times 10^3/\text{mm}^3$), but remained within the normal range, and returned to their pre-injection values by the time of the next measurement at 10 days. By contrast, in non-infected subjects, transient increases in WBC count were seen 24 hours after LeukoScan administration. The eosinophil count increased from 2.7% pre-injection to 2.9% at 24 hours post-injection, and to 3.9% at 10 days, with the magnitude of both increases being statistically significant. The magnitude of these increases were assessed by the investigators to be of no clinical consequence on an individual patient basis.

It is unknown whether the changes in WBC or eosinophil counts observed, although of no clinical significance, are due to a transient effect on WBC function. If so, no inferences concerning the underlying mechanism(s) responsible may be derived from the clinical laboratory results. However, *in vitro* granulocyte function tests did not show significant changes when the sulesomab was added.

In vitro, a positive binding to lymphocytes up to 2-6% has been shown. The effect on lymphocyte function has not been determined.

2. HAMA:
No induction of human anti-mouse antibody (HAMA) reactive with fragment was observed in any patient administered LeukoScan.
3. For each patient, exposure to ionising radiation must be justifiable on the basis of 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 the adverse effects will occur with low frequency because of the low radiation doses incurred.

4. For most diagnostic investigations using a nuclear medicine procedure, the radiation dose delivered (effective dose/EDE) is less than 20 mSv. Higher doses may be justified in some clinical circumstances.

4.9 Overdose

The maximum amount of LeukoScan [^{99m}Tc] that can be administered safely has not been determined. In clinical trials, single doses of 1.0 mg of LeukoScan radiolabelled with 900 ± 200 MBq of ^{99m}Tc were administered to 11 patients with various types of infection and there were no adverse reactions at this dose.

In the unlikely event of a radiation overdose being administered with LeukoScan [^{99m}Tc], the absorbed dose to the patient may be reduced by increased oral or intravenous intake of fluids to promote excretion of the radiolabel.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Diagnostic radiopharmaceuticals. ATC code: VO4D

At the concentrations and activities used for diagnostic procedures, LeukoScan does not appear to exert any pharmacodynamic effects.

The antibody (IMMU-MN3) recognizes an antigenic structure shared by a surface glycoprotein (NCA-90) of granulocytes and the tumour marker, carcinoembryonic antigen (CEA).

In a single-group, open-label, uncontrolled study of 53 patients with acute or chronic infections of unknown origin or extent, doses of LeukoScan from 0.1 mg to 1.0 mg were studied. There was no dose-response effect for imaging efficacy (sensitivity or specificity) over antibody doses ranging from 0.1 mg to 1.0 mg.

In vitro studies have demonstrated that LeukoScan has no effect on either up-regulation or down-regulation of granulocytes, but LeukoScan does appear to bind more avidly to activated rather than resting granulocytes.

On the basis of two controlled clinical trials of LeukoScan to demonstrate the safety and effectiveness of this product for defining the presence and location of osteomyelitis, in a total of 175 evaluable patients, LeukoScan had a sensitivity of 88.2%, a specificity of 65.6%, an accuracy of 76.6%, a positive predictive value of 70.8%, and a negative predictive value of 85.5%.

In a subgroup of patients in whom LeukoScan was compared directly to the currently available ^{111}In -labelled (occasionally ^{99m}Tc -labelled) autologous white blood cell (WBC) scanning test, LeukoScan showed a statistically significant increase in sensitivity over that achieved by WBC scanning (87.7% vs. 72.6%, $p = 0.003$ by McNemar's Test), with no discernible decrease in specificity as compared to WBC imaging (67.1% vs. 69.4%).

The clinical results indicate that among different presentations of osteomyelitis, LeukoScan can show different results. The product is more sensitive (93.9% vs. 80.6%), but less specific (51.6% vs. 72.9%), in diagnosing osteomyelitis in patients with diabetic foot ulcers than in patients with other sites of long bone osteomyelitis. However, there is an equivalent diagnostic accuracy between these two presentations

(77.5% vs. 75.8%, respectively). This difference is perhaps explained by the anatomically and pathophysiology more complicated clinical setting of osteomyelitis in the diabetic foot, making differentiation of soft tissue and bone infection more difficult than in other presentations of long bone osteomyelitis.

An evaluation of potential clinical impact of LeukoScan demonstrated that LeukoScan could change clinical management in 50.2% or improve clinical outcome in 43.4% of the 175 evaluable patients with suspected osteomyelitis. In 49.7% of the patients, LeukoScan was presumed to provide clinical benefit not achievable by other available diagnostic imaging methods, with the potential that the diagnosis could have been made by LeukoScan alone in 70.3% of the patients. These benefits were also accompanied by a substantial reduction (85.4%) in the number of patients who would require other diagnostic imaging procedures.

Since LeukoScan cross-reacts with CEA, it should be borne in mind that it may interact with CEA producing tumours.

5.2 Pharmacokinetic properties

Pharmacokinetic studies were performed after the intravenous administration of the product. At one hour after infusion, the blood level was 34% of baseline, 17% at four hours and 7% of baseline at 24 hours. The distribution half-life was approximately 1.5 hours; the route of excretion is essentially renal with 41% of the radiolabel excreted in urine over the first 24 hours after administration.

5.3 Preclinical safety data

Only very limited nonclinical studies have been performed with either the labeled or unlabeled agent. These revealed no remarkable findings. It should be noted, however, that these studies did not assess genotoxicity, carcinogenic potential, or toxicity to reproduction.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Stannous chloride, dihydrate	Sodium chloride
Acetic acid, glacial (trace)	Hydrochloric acid (trace)
Sodium potassium tartrate, tetrahydrate	Sodium acetate, trihydrate
Sucrose	Nitrogen

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6 or 12.

6.3 Shelf-life

Kit - 48 months.

Reconstituted and radiolabelled material - 4 hours.

6.4 Special precautions for storage

Kit - Store in a refrigerator (2°C - 8°C). Do not freeze.

Reconstituted and radiolabelled material - Do not store above 25°C. Do not refrigerate or freeze.

6.5 Nature and contents of container

One vial prepared so as to contain 0.31 mg lyophilised LeukoScan monoclonal antibody fragment.

The Type I glass vial is closed with a grey butyl rubber stopper with a green flip-off seal.

Pack size: one vial per carton container.

6.6 Special precautions for disposal and other handling

Read complete directions thoroughly before starting the preparation procedure.

LeukoScan is a sterile, lyophilised formulation, containing 0.31 mg of sulesomab per vial and includes 0.22 mg stannous chloride dihydrate, 3.2 mg potassium sodium tartrate tetrahydrate, 7.4 mg sodium acetate trihydrate, 5.5 mg sodium chloride, glacial acetic acid (trace), hydrochloric acid (trace), 37.8 mg sucrose, nitrogen (vacuum). The imaging agent, technetium-99m LeukoScan [technetium-99m sulesomab] is formed by reconstitution of the contents of the LeukoScan vial with 0.5 mL sodium chloride for injection followed by the addition of 1100 MBq of sodium pertechnetate [^{99m}Tc] in 1 mL of Sodium Chloride for Injection. The resulting solution has a pH of 4.5-5.5 and is intended for intravenous use only.

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, complying with the requirements of Good Manufacturing Practices (GMP) for pharmaceuticals.

Reconstituted radiopharmaceuticals should be handled using waterproof gloves, adequate shielding of radioactivity, and aseptic technique. Following reconstitution, unused radiopharmaceutical and vial should be handled as radioactive waste and disposed of in accordance with local requirements.

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

Method of preparation

1. Obtain 900 ± 200 MBq of freshly eluted ^{99m}Tc sodium pertechnetate eluate from any commercial source which has been eluted within the past 24 hours. Using saline injection, bring the final volume of eluate solution to 1.0 ml.
2. Clean the rubber closure of each vial such as with an alcohol wipe. For reconstitution of lyophilised powder, with a sterile disposable syringe add 0.50 ml of saline injection into the shielded LeukoScan 3-ml vial.
3. Swirl and shake the vial contents gently for 30 seconds to insure dissolution. Radiolabelling must take place immediately after reconstitution of product.
4. Add the prepared eluate into the shielded vial, shake and allow the labelling reaction to proceed for ten minutes. Total volume in vial equals 1.5 ml.

5. Based on the activity measured in the activity calibrator, withdraw a sufficient amount of the product to provide the desired activity (750-1100 MBq of ^{99m}Tc , see Dosage and Administration). LeukoScan [^{99m}Tc] can be used after ten minutes and should be used within four hours after preparation. LeukoScan [^{99m}Tc] can be stored at room temperature after formulation. Do not refrigerate after formulation.
6. Prior to administration, the solution should be inspected visually for particulate matter and discoloration, and quality control should be performed (see section 12). If either are present, the product should be discarded.

7. MARKETING AUTHORISATION HOLDER

Immunomedics GmbH
Paul-Ehrlich-Str. 22
D-63322 Rödermark
Germany

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/97/032/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 14 February 1997

Date of latest renewal: 30 September 2002

10. DATE OF REVISION OF THE TEXT

Date of approval of latest variation or transfer: MM/YYYY

11. DOSIMETRY

For this medicinal product, the effective dose equivalent resulting from an administered activity of 750 MBq is typically 7.7 mSv for a 70 kg individual.

Technetium [^{99m}Tc] disintegrates with the emission of gamma radiation with an energy of 140 keV and a half life of 6 hours to technetium [^{99}Tc] which can be regarded as quasi stable.

The estimated absorbed radiation doses to an average adult patient (70 kg) from an intravenous administration of LeukoScan labeled with 750 MBq of technetium-99m are provided in Table 1. These dose estimates assume a urinary bladder voiding interval of two hours. These values were calculated according to Medical Internal Radiation Dosimetry.

Table 1

Summary of Normal Organ Dosimetry to an Average Adult Patient (70 kg) from an Intravenous Dose of LeukoScan Labelled with 750 MBq of Technetium-99m [Dose Estimate from 13 Subjects 26 Administrations]	
LeukoScan [^{99m} Tc]	
Organ	Average Dose μ Gy/MBq
Kidneys	44.9
Urinary Bladder Wall	21.5
Spleen	15.7
Heart Wall	11.8
Lungs	10.0
Liver	9.0
Bone Surfaces	8.0
Adrenals	7.2
Red Marrow	7.1
Pancreas	6.8
Thyroid	6.7
Gall Bladder Wall	6.2
Uterus	5.9
Ovaries	4.9
Small Intestine	4.8
Stomach	4.8
Upper Large Intestinal Wall	4.7
Lower Large Intestinal Wall	4.7
Thymus	4.5
Total Body	4.2
Muscle	3.5
Testes	3.0
Breasts	2.8
Brain	2.4
Skin	2.1
Effective Dose Equivalent*	10.3
Effective Dose*	8.0
* Effective Dose Equivalent and Effective Dose are in units of μ Sv/MBq.	

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Quality control

LeukoScan is reconstituted with 0.5 ml isotonic sodium chloride injection. Following reconstitution, 1 ml sodium pertechnetate [^{99m}Tc] is added.

The recommended adult dose is 0.25 mg of Fab' fragment labelled with 900 ± 200 MBq of technetium ^{99m}Tc pertechnetate (approximately 1.2 ml).

After radiolabelling the antibody and diluting a 10 μ l sample with 1.5 ml saline, immediately determine the radiochemical purity by Instant Thin Layer Chromatography on silica gel impregnated glass fiber

strips, 1 × 9 cm using acetone as the solvent. When the solvent front is within 1 cm of the top of the strip, remove it, cut it in half and place each into a glass tube. Count each tube in a gamma scintillation counter, dose calibrator or radiochromatogram analyzer. Calculate the percent free technetium as follows:

$$\% \text{ Free Technetium} = \frac{\text{Activity in top half of strip}}{\text{Total Activity}} \times 100$$

The radiolabelled product should not contain more than 10% free technetium.

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

ANNEX II

- A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**
- C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**
- D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

**A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND
MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE**

Name and address of the manufacturer(s) of the biological active substance(s)

Immunomedics, Inc.
300 American Road
Morris Plains, New Jersey 07950, USA

Name and address of the manufacturer responsible for batch release

Immunomedics GmbH
Paul-Ehrlich-Str. 22
D-63322 Rödermark
Germany

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription

**C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING
AUTHORISATION**

- **Periodic Safety Update Reports**

The requirements for submission of periodic safety update reports for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

**D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE
USE OF THE MEDICINAL PRODUCT**

- **Risk Management Plan (RMP)**

Not applicable.

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

CONTAINER PACKAGE LABEL

1. NAME OF THE MEDICINAL PRODUCT

LeukoScan 0.31 mg, powder for solution for injection
sulesomab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One vial contains 0.31 mg sulesomab

3. LIST OF EXCIPIENTS

Each vial contains stannous chloride, sodium chloride, sodium potassium tartrate, sodium acetate, sucrose, nitrogen.

4. PHARMACEUTICAL FORM AND CONTENTS

0.31 mg sulesomab
Powder for solution for injection

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For intravenous use.

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

For diagnostic use only.

After mixing with Tc, the final product must be disposed of as radioactive waste in accordance with local law.

8. EXPIRY DATE

EXP MM/YYYY

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C-8°C). Do not freeze.

Reconstituted and radiolabelled material – Do not store above 25°C. Do not refrigerate or freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

After use, the container should be disposed of as radioactive waste.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Immunomedics GmbH
Paul-Ehrlich-Str. 22
63322 Rödermark
Germany
Telephone: +49-6074-2153-600
Fax: +49-6074-2153-619
Email: europe@immunomedics.de

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/97/032/001

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

<Justification for not including Braille accepted.>

17. UNIQUE IDENTIFIER – 2D BARCODE

<Not applicable.>

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

<Not applicable.>

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

LeukoScan 0.31 mg, powder for solution for injection
0.31 mg lyophilised sulesomab, stannous chloride and stabilizers.
For intravenous use.

2. METHOD OF ADMINISTRATION

For intravenous use.

Read the package leaflet before use.

3. EXPIRY DATE

EXP MM/YYYY

4. BATCH NUMBER

Batch

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Contains 0.31 mg lyophilised sulesomab, stannous chloride and stabilizers.

6. OTHER

Rehydrate with sterile, non-pyrogenic ^{99m}Tc Na pertechnetate.

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

LeukoScan 0.31 mg, powder for solution for injection (sulesomab)

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What LeukoScan is and what it is used for
2. What you need to know before you are given LeukoScan
3. How LeukoScan is administered
4. Possible side effects
5. How to store LeukoScan
6. Contents of the pack and other information

1. What LeukoScan is and what it is used for

LeukoScan contains the active substance sulesomab and is a diagnostic radiopharmaceutical.

LeukoScan is used in adults.

An antibody is a natural substance made by the body which binds to foreign substances to help remove them from your body. You produce many different kinds of antibodies.

LeukoScan (sulesomab) is a special kind of antibody which binds to the surface of certain kinds of blood cells called leukocytes. It is produced in mice and purified so that it can be used in humans. When it is combined to the radioactive technetium isotope and injected into your vein, it finds an abnormal accumulation of white blood cells and attaches to them. One to eight hours later after the injection you will be placed on a special table and pictures will be taken with standard nuclear cameras. This helps your doctor make a diagnosis and evaluate the extent of your illness. The doctor does this by using a special imaging camera that reveals areas of radioactivity to see where the infections are located. This medicine is for diagnostic use only.

LeukoScan is used to determine the presence of infections in long bones. Shortly after mixing the LeukoScan with the radioactive technetium isotope, the doctor will inject it into your vein. One to eight hours later you will be placed on a special table and pictures will be taken with standard nuclear cameras to see where the infections are located.

LeukoScan is an antibody fragment which is linked to a radioactive substance called technetium. LeukoScan is used in patients with suspected infection of the bone called osteomyelitis. The antibody is able to bind to the surface of white blood cells which infiltrate the area of infection. When the radioactive antibody binds to the white blood cells, your doctor can determine where the infection is located by using a special imaging camera that reveals areas of radioactivity. The doctor can also determine how much disease there is. This will help the doctor determine whether there is infection in the bone and what kind of treatment to use.

2. What you need to know before you are given LeukoScan

You should not be given LeukoScan 0.31 mg, powder for solution for injection

- if you are allergic to sulesomab or any protein which comes from a mouse or any of the other ingredients of this medicine (listed in section 6), tell your doctor. You must then not be given LeukoScan.
- if you are pregnant.

Warning and precautions

- It is possible to have a serious allergic reaction to LeukoScan. Therefore, your doctor should keep you under close observation for a short time after he has given you this medicine.
- If you have ever received LeukoScan or another product made from a mouse antibody, your doctor should take a sample of blood for testing to be sure that you have not developed an allergy to it.
- If the prepared solution of LeukoScan appears discoloured or contains particles, it should not be used.
- LeukoScan is not expected to work in patients with paroxysmal nocturnal hemoglobinuria

Children and adolescents

This medicine is not recommended for use in patients below 21 years of age because the safety and diagnostic accuracy of the product have not been established.

Other medicines and LeukoScan

Tell your doctor if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

No interactions with other medicines have been described to date.

LeukoScan with food and drink

No studies effects of food/drink have been performed.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before you are given this medicine.

You must inform the doctor before the administration of LeukoScan if there is a possibility you might be pregnant, if you have missed your period or if you are breast-feeding. When in doubt, it is important to consult your nuclear medicine doctor who will supervise the procedure.

Pregnancy

- You should not be given LeukoScan if you are pregnant.

Breast-feeding

- If you are breast feeding, you should stop breast feeding your baby for at least 24 hours after you have been given LeukoScan.

Use of radiopharmaceutical agents

- Radiopharmaceutical agents should be used only by qualified personnel with appropriate government authorisation for the use and manipulation of radionuclides.
- This radiopharmaceutical may be received, used and administered only by authorised persons in designated clinical settings. Its receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licenses of local competent official organisations.
- 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, complying with the requirements of Good Manufacturing Practices (GMP) for pharmaceuticals.
- After use, the container should be disposed of as radioactive waste.

Driving and using machines

No studies on the effects on the ability to drive and use machines have been performed.

LeukoScan contains sucrose

If you have been told that you have an intolerance to some sugars, inform your doctor before you are given this medicine.

3. How LeukoScan is administered

Dosage

You will receive a single dose of 0.25 mg of LeukoScan. It will contain the radioactive technetium isotope in an amount called 740-1110 MBq.

Method and/or route(s) of administration

Your doctor will prepare the LeukoScan and the radioactive isotope technetium in a volume of 1.5 ml. 0.25 mg of LeukoScan will be labelled with 740-1110 MBq of technetium. This material will then be injected into your vein. This dose of radioactivity is safe and will be gone from the body in about 24 hours.

Frequency of administration

LeukoScan is prepared for a single injection. If your doctor decides to give it to you again after several weeks or several months, your blood should be tested first to see if you have developed an allergy to LeukoScan.

Use in children and adolescents

LeukoScan is not intended to be used in children and adolescents.

If you are given more LeukoScan than you should

The maximum amount of LeukoScan that can be administered has not been determined. Patients have been given four times the amount you will receive with no adverse reactions.

In the unlikely event of the administration of a radiation overdose with LeukoScan, the absorbed dose to the patient may be reduced by increased oral or intravenous intake of fluids to promote excretion of the radiolabel.

If you forget to use LeukoScan

Not applicable

If you stop using LeukoScan

Not applicable. LeukoScan is prepared for a single injection.

If you have any further questions on the use of this diagnostic medicine, ask your doctor or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Uncommon side effects

A small increase in the number of certain white blood cells called eosinophils (but without any apparent symptoms)

Rash

Some side effects, although not common, have been reported. These include a small increase in the number of certain white blood cells called eosinophils (but without any apparent symptoms) and rash.

Reporting of side effects

If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store LeukoScan

Keep this medicine out of the sight and reach of children.

Expiry date and storage conditions

Do not use this medicine after the expiry date which is stated on the label and the carton. The expiry date refers to the last day of that month. (Kit - 48 months.)

Store in a refrigerator (2°C-8°C). Do not freeze.

Reconstituted and radiolabelled material - 4 hours. Do not store above 25°C. Do not refrigerate or freeze.

After use, the container should be disposed of as radioactive waste.

6. Contents of the pack and other information

What LeukoScan contains

Kit for the preparation of ^{99m}Tc-labelled LeukoScan.

The kit does not include the radioisotope.

The active substance is sulesomab.

Each 3 ml vial contains 0.31 mg sulesomab (IMMU-MN3 murine Fab'-SH antigranulocyte monoclonal antibody fragments).

The other ingredients are:

Stannous chloride, dihydrate

Acetic acid, glacial (trace)

Sodium potassium tartrate, tetrahydrate

Sodium chloride

Hydrochloric acid (trace)

Sodium acetate, trihydrate

Sucrose

Nitrogen

What LeukoScan looks like and contents of the pack

Powder for solution for injection.

One vial prepared so as to contain 0.31 mg lyophilised LeukoScan monoclonal antibody fragment.
The Type I glass vial is closed with a grey butyl rubber stopper with a green flip-off seal.

Pack size: one vial per carton container.

Marketing Authorisation Holder and Manufacturer

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This leaflet was last revised in 10/2016.

Detailed information on this medicine is available on the European Medicines Agency web site:

<http://www.ema.europa.eu>