SUMMARY OF PRODUCT CHARACTERISTICS

for

Ceretec, kit for radiopharmaceutical preparation

1. NAME OF THE MEDICINAL PRODUCT

Ceretec

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains exametazime 500 micrograms

Ceretec is reconstituted with Sodium Pertechnetate (^{99m}Tc) Injection (not included in this kit) to prepare Technetium (^{99m}Tc) Exametazime Injection.

Excipients with known effect
The product before reconstitution contains sodium: 1.77 mg/vial. This needs to be taken into consideration for patients on a controlled sodium diet.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Kit for radiopharmaceutical preparation
A white powder

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

This medicinal product is for diagnostic use only.

After radiolabelling with Sodium Pertechnetate (^{99m}Tc) Injection, the solution of technetium (^{99m}Tc) exametazime is indicated in adults, children and adolescents for:

Neurology

Technetium (^{99m}Tc) Exametazime Injection is indicated for use with single photon emission tomography (SPECT). In brain perfusion SPECT, the diagnostic target is detection of abnormalities of regional cerebral blood flow, including:

- Evaluation of patients with cerebrovascular disease (specifically acute stroke, chronic ischaemia and transient ischaemic attack);
- Presurgical lateralisation and localisation of epileptogenic foci;
- Evaluation of patients with suspected dementia (specifically Alzheimer's

disease and frontotemporal dementia);
- Adjuvant technique in the diagnosis of brain death

Infectious or inflammatory diseases
Technetium (^{99m}Tc) Exametazime Injection is also indicated for *in vitro* technetium-99m leukocyte labelling, the labelled leukocytes subsequently being re-injected and scintigraphy carried out to image the sites of localisation. This procedure may be used in the detection of sites of focal infection (e.g. abdominal abscess), in the investigation of pyrexia of unknown origin and in the evaluation of inflammatory conditions not associated with infection such as inflammatory bowel disease.

4.2 Posology and method of administration

The route of administration is direct intravenous injection for brain scintigraphy studies and intravenous injection of labelled leukocytes post labelling *in vitro*.

Posology
Adults
- For brain scintigraphy
  - 555 - 1110 MBq
- For *in-vivo* localisation of technetium-99m-labelled leukocytes
  - 185 - 370 MBq

Paediatric population
The use in children and adolescents has to be considered carefully, based upon clinical needs and assessing the risk/benefit ratio in this patient group.

The activities to be administered to children and adolescents may be calculated according to the recommendations of the European Association of Nuclear Medicine (EANM) Paediatric Dosage Card (Version 5.7.2016) for a given patient weight using the data tabulated below.

Multiple of Baseline Activity

Weight kg	**Multiple**	**Weight kg**	**Multiple**
3	1	32	7.29
4	1.14	34	7.72
6	1.71	36	8.00
8	2.14	38	8.43

10	2.71	40	8.86
12	3.14	42	9.14
14	3.57	44	9.57
16	4.00	46	10.00
18	4.43	48	10.29
20	4.86	50	10.71
22	5.29	52-54	11.29
24	5.71	56-58	12.00
26	6.14	60-62	12.71
28	6.43	64-66	13.43
30	6.86	68	14.00

$$A[MBq]_{\text{Administered}} = BaselineActivity \times Multiple$$

a) For a calculation of the administered activity, the baseline activity value has to be multiplied by the multiples given above

b) If the resulting activity is smaller than the minimum recommended activity, the minimum activity should be administered.

c) The national diagnostic reference levels should not be exceeded!

Recommended Amounts in MBq

	Baseline Activity (for calculation purposes only) MBq	**Minimum Recommended Activity[1] MBq**
^{99m}Tc HMPAO (Brain)	51.8	100
^{99m}Tc HMPAO (WBC)	35.0	40.0

[1] The minimum recommended activities are calculated for commonly used gamma cam eras or positron emission tomographs. Lower activities could be administered when using systems with higher counting efficiency.

Normally a once-only diagnostic procedure.

Method of administration

This medicinal product should be reconstituted before administration to the patient. For instructions on reconstitution of the medicinal product before administration, see section 12.
For patient preparation, see section 4.4

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Potential for hypersensitivity or anaphylactic reactions
The possibility of hypersensitivity including 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.

Re-injected Ceretec labelled leukocytes only:
When preparing technetium-99m-labelled leukocytes, it is essential that cells are washed free of sedimentation agents before they are re-injected into the patient as materials used in cell separation may cause hypersensitivity reactions.

Individual benefit/risk justification
For each patient, exposure to ionising radiation must be justifiable on the basis of likely benefit. The activity administered should in every case be as low as reasonably achievable to obtain the required diagnostic information.

Renal impairment and hepatic impairment
Careful consideration of the benefit risk ratio in these patients is required since an increased radiation exposure is possible.

Paediatric population
For information on the use in paediatric population, see section 4.2. Careful consideration of the indication 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.

Specific warnings
Depending on the time when you administer the injection, the content of sodium given to the patient may in some cases be greater than 1 mmol. This should be taken into account in patients on low sodium diet.

Precautions with respect to environmental hazard, see section 6.6.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed and no drug interactions have been reported to date.

4.6 Fertility, pregnancy and lactation

Women with childbearing potential
When an administration of radiopharmaceuticals to a woman of childbearing potential is intended, it is important to determine whether or not she is pregnant. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. If in doubt about her potential pregnancy (if the woman has missed a period, if the period is very irregular, etc.), alternative techniques not using ionising radiation (if there are any) should be offered to the patient.

Pregnancy
No data are available on the use of this product in human pregnancy. Animal reproduction studies have not been performed.
Radionuclide procedures carried out on pregnant women also involve radiation doses 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 the foetus.

Breastfeeding
Before administering a radioactive medicinal product to a mother who is breastfeeding, consideration should be given to the possibility of delaying the administration of radionuclide until the mother has ceased breastfeeding and to what is the most appropriate choice of radiopharmaceuticals, bearing in mind the secretion of activity in breast milk. If the administration is considered necessary, breastfeeding should be interrupted for 12 hours and the expressed feeds discarded.

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 frequencies of undesirable effects are defined as follows:

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) and not known (cannot be estimated from the available data)

Congenital and familial/genetic disorders Not known	Hereditary defects[1].
Neoplasms benign and malignant (including cysts and polyps) Not known	Cancer induction[1].
Immune system disorders Not known **Re-injected Ceretec labelled leukocytes only** Not known	Hypersensitivity including rash, erythema, urticaria, angiooedema, pruritus. Hypersensitivity including rash, erythema, urticaria, angiooedema, pruritus, anaphylactoid reaction or anaphylactoid shock
Nervous system disorders Not known	Headache, dizziness, paraesthesia
Vascular disorder Not known	Flushing
Gastrointestinal disorders Not known	Nausea, vomiting
General disorders and administration site conditions Not known	Asthenic conditions (e.g., malaise, fatigue)

[1] Linked with ionising radiation.

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose resulting from the administratin of a (maximal recommended) activity of 1110 MBq for an adult weighing 70 kg is about 10.3 mSv these adverse events are expected to occur with a low probability

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system:

Norway
Statens legemiddelverk
Nettside: www.legemiddelverket.no/meldeskjema

4.9 Overdose

In the event of the administration of a radiation overdose frequent micturition and defaecation should be encouraged in order to minimise the absorbed dose to patient.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Technetium (^{99m}Tc) compounds.
ATC-code: V 09 AA 01, and V 09 HA 02

At the chemical concentrations and activities used for diagnostic procedures technetium-99m exametazime and technetium-99m-labelled leukocytes do not appear to exert any pharmacodynamic effects.

5.2 Pharmacokinetic properties

(1) Direct intravenous injection

The technetium-99m complex of the active ingredient is uncharged, lipophilic and of sufficiently low molecular weight to cross the blood-brain barrier.
It is rapidly cleared from the blood after intravenous injection.
Uptake in the brain reaches a maximum of 3.5-7.0 % of the injected dose within one minute of injection.
Up to 15 % of the cerebral activity washes out of the brain 2 minutes post injection after which there is little loss of activity for the following 24 hours except by physic cal decay of technetium-99m.
The activity not associated with the brain is widely distributed throughout the body particularly in muscle and soft tissue.
About 20 % of the injected dose is removed by the liver immediately after injection and excreted through the hepatobiliary system.
About 40 % of the injected dose is excreted through the kidneys and urine over the 48 hours after injection resulting in a reduction in general muscle and soft tissue background.

(2) Injection of labelled leukocytes

Technetium-99m-labelled leukocytes distribute between the marginal pools of the liver (within 5 minutes) and spleen (within about 40 minutes), and the circulating pool, (the latter represents approximately 50 % of the leukocyte pool).
Approximately 37 % of the cell associated technetium-99m is recoverable from the circulating pool 40 minutes after injection. Technetium-99m activity is slowly eluted from the cells and is excreted partly by the kidneys and partly via the liver into the gall bladder.
This results in increasing amounts of activity being seen in the intestines.

5.3 Preclinical safety data

There is no additional preclinical safety data of relevance for the prescriber in recognising the safety profile of the product used for the authorised indications.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Stannous chloride dihydrate

6.2 Incompatibilities

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

6.3 Shelf life

Kit before reconstitution: 52 weeks from the day of manufacture.

Reconstituted product: must be injected within 30 minutes of labelling.
Store below 25ºC. Do not refrigerate or freeze.

6.4 Special precautions for storage

For storage conditions of the reconstituted product, see section 6.3.
Storage should be in accordance with national regulations for radioactive materials.

6.5 Nature and contents of container

10 ml Type I Ph.Eur., clear, colourless, borosilicate glass vial sealed with a chlorobutyl rubber closure and oversealed with an aluminium overseal with a blue flip off cap.

Pack sizes: kit contains 2 or 5 vials.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

General warning
Radiopharmaceuticals should 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 licences of the competent official organisation.

Radiopharmaceuticals should be prepared in a manner which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken.

Contents of the vial are intended only for use in the preparation of technetium **(**99mTc) exametazime injection 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 reconstitution is not radioactive. However, after sodium pertechnetate (^{99m}Tc), 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.

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 local requirements.

7. MARKETING AUTHORISATION HOLDER

GE Healthcare AS
P.O.Box 4220 Nydalen
NO-0401 Oslo
Norway

8. MARKETING AUTHORISATION NUMBER

8343

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

12.10.1999/12.10.2009

10. DATE OF REVISION OF THE TEXT

13.12.2022

11. DOSIMETRY

Technetium (^{99m}Tc) is produced by means of a (^{99}Mo/^{99m}Tc) 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 (^{99}Tc) which, in view of its long half-life of 2.13×10^5 years can be regarded as quasi stable.

Brain scintigraphy
The table below shows the dosimetry according to ICRP publication 128 (International Commission of Radiological Protection, Radiation Dose to Patients from Radiopharmaceuticals: A Compendium of Current Information Related to Frequently Used Substances, Ann ICRP 2015).

Organ	Absorbed dose per unit activity administered (mGy/MBq)					
	Adult	15 years	10 years	5 years	1 year	Newborn
Adrenals	0.0053	0.0067	0.0099	0.014	0.024	0.066
Bone surfaces	0.0051	0.0064	0.0094	0.014	0.024	0.073
Brain	0.0068	0.011	0.016	0.021	0.037	0.084
Breast	0.0020	0.0024	0.0037	0.0056	0.0095	0.034
Gallbladder wall	0.018	0.021	0.028	0.048	0.14	0.32
Gastrointestinal tract						
Stomach wall	0.0064	0.0085	0.012	0.019	0.036	0.14
Small intestine wall	0.012	0.015	0.024	0.036	0.065	0.21
Colon wall	0.017	0.022	0.035	0.055	0.10	0.29
(Upper large intestine wall)	0.018	0.024	0.038	0.060	0.11	0.31
(Lower large intestine wall)	0.015	0.019	0.031	0.048	0.090	0.27
Heart wall	0.0037	0.0047	0.0067	0.0097	0.016	0.050
Kidneys	0.034	0.041	0.057	0.081	0.14	0.36
Liver	0.0086	0.011	0.016	0.023	0.040	0.092
Lungs	0.011	0.016	0.022	0.034	0.063	0.17
Muscles	0.0028	0.0035	0.0050	0.0073	0.013	0.045
Oesophagus	0.0026	0.0033	0.0047	0.0069	0.011	0.041
Ovaries	0.0066	0.0083	0.012	0.017	0.027	0.081
Pancreas	0.0051	0.0065	0.0097	0.014	0.023	0.069

Red marrow	0.0034	0.0041	0.0059	0.0080	0.014	0.042
Skin	0.0016	0.0019	0.0029	0.0045	0.0083	0.032
Spleen	0.0043	0.0054	0.0082	0.012	0.020	0.059
Testes	0.0024	0.0030	0.0044	0.0061	0.011	0.039
Thymus	0.0026	0.0033	0.0047	0.0069	0.011	0.041
Thyroid	0.026	0.042	0.063	0.14	0.26	0.37
Urinary bladder wall	0.023	0.028	0.033	0.033	0.056	0.15
Uterus	0.0066	0.0081	0.012	0.015	0.025	0.075
Remaining organs	0.0032	0.0040	0.0060	0.0092	0.017	0.053
Effective dose (mSv/MBq)	0.0093	0.011	0.017	0.027	0.049	0.12

The effective dose resulting from the administration of a (maximal recommended) activity of 1110 MBq for an adult weighing 70 kg is about 10.3 mSv. For an administered activity of 740 MBq the typical radiation dose to the target organ (brain) is 5.0 mGy and the typical radiation dose/doses to the critical organ (kidneys) is 25.2 mGy.

***In-vivo* localisation of technetium-99m-labelled leukocytes**

The table below shows the dosimetry according to ICRP publication 128 (International Commission of Radiological Protection, Radiation Dose to Patients from Radiopharmaceuticals: A Compendium of Current Information Related to Frequently Used Substances: Ann ICRP 2015.)

Organ	**Absorbed dose per unit activity administered (mGy/MBq)**				
	Adult	15 years	10 years	5 years	1 year
Adrenals	0.012	0.012	0.018	0.026	0.043
Bone surfaces	0.016	0.021	0.034	0.061	0.15
Brain	0.0023	0.0029	0.0044	0.0070	0.013

Breast	0.0024	0.0029	0.0049	0.0076	0.013
Gallbladder wall	0.0084	0.010	0.016	0.025	0.036
Gastrointestinal tract					
Stomach wall	0.0081	0.0096	0.014	0.020	0.032
Small intestine wall	0.0046	0.0057	0.0087	0.013	0.021
Colon wall	0.0043	0.0054	0.0084	0.012	0.021
(Upper large intestine wall)	0.0047	0.0059	0.0093	0.014	0.023
(Lower large intestine wall)	0.0037	0.0048	0.0073	0.010	0.018
Heart wall	0.0094	0.012	0.017	0.025	0.044
Kidneys	0.012	0.014	0.022	0.032	0.054
Liver	0.020	0.026	0.038	0.054	0.097
Lungs	0.0078	0.0099	0.015	0.023	0.041
Muscles	0.0033	0.0041	0.0060	0.0089	0.016
Oesophagus	0.0035	0.0042	0.0058	0.0086	0.015
Ovaries	0.0039	0.0050	0.0072	0.011	0.018
Pancreas	0.013	0.016	0.023	0.034	0.053
Red marrow	0.023	0.025	0.040	0.071	0.14
Skin	0.0018	0.0021	0.0034	0.0055	0.010
Spleen	0.15	0.21	0.31	0.48	0.85
Testes	0.0016	0.0021	0.0032	0.0051	0.0092
Thymus	0.0035	0.0042	0.0058	0.0086	0.015
Thyroid	0.0029	0.0037	0.0058	0.0093	0.017
Urinary bladder wall	0.0026	0.0035	0.0052	0.0078	0.014
Uterus	0.0034	0.0043	0.0065	0.0097	0.016

Remaining organs	0.0034	0.0042	0.0063	0.0095	0.016
Effective dose (mSv/MBq)	**0.011**	**0.014**	**0.022**	**0.034**	**0.062**

The effective dose resulting from the administration of a (maximal recommended) activity of 370 MBq for an adult weighing 70 kg is about 4.1 mSv.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

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

Method of preparation of technetium-99m exametazime for intravenous injection or *in-vitro* leukocyte labelling:

Use aseptic technique throughout.

(1) Place the vial in a shielding container and swab the closure with the sanitising swab provided.
(2) Using a 10 ml syringe, inject into the shielded vial 5 ml of sterile eluate from a technetium-99m generator (see notes a - f). Before withdrawing the syringe from the vial withdraw 5 ml of gas from the space above the solution to normalise the pressure in the vial. Shake the shielded vial for 10 seconds to ensure complete dissolution of the powder.
(3) Assay the total activity and calculate the volume to be injected or used for *in vitro* technetium-99m-leukocyte labelling.
(4) Complete the label provided and attach to the vial.
(5) Use within a maximum of 30 minutes after reconstitution. Discard any unused material.

Note:

a) For the highest radiochemical purity reconstitute with freshly eluted technetium-99m generator eluate.
b) Use only eluate which was eluted less than 2 hours previously from a generator which was eluted within 24 hours.
c) 0.37-1.11 GBq (10-30 mCi) technetium-99m may be added to the vial.
d) Before reconstitution the generator eluate may be adjusted to the correct radioactive concentration (0.37-1.11 GBq in 5 ml) by dilution with sodium chloride for injection.
e) Pertechnetate complying with the specifications prescribed by the USP and BP/Ph.Eur. Monographs on Sodium Pertechnetate (^{99m}Tc) Injection should be used.
f) The pH of the prepared injection/labelling agent is in the range 9.0-9.8.

Procedure for separation of leukocytes and subsequent *in-vitro* labelling with technetium-99m exametazime:

Use aseptic technique throughout.

1) Draw 9 ml of acid-citrate-dextrose (ACD) (see note a) into each of two 60 ml plastic non-heparinized syringes.
2) Withdraw 51 ml of patient's blood into each syringe, using a 19G Butterfly needle infusion set. Close the syringes with sterile hubs.
3) Dispense 2 ml sedimentation agent (see note b) into each of 5 Universal containers or tubes.
4) Without attaching a needle to the syringes dispense 20 ml of blood into each of the 5 Universal tubes containing sedimentation agent. Dispense the remaining 20 ml of blood into a tube without sedimentation agent.

TIP: To avoid bubbles and frothing run the blood gently down the sides of the tubes.

5) Mix the blood and sedimentation agent with one gentle inversion. Remove the cap of the Universal tube and burst the bubble formed at the top using a sterile needle. Replace the cap and allow the tubes to stand for 30-60 minutes for erythrocyte sedimentation to take place.

TIP: The period of time for erythrocyte sedimentation depends on the patient's condition. As a guideline it should be stopped when the blood has sedimented to give approximately half the volume as sedimented red cells.

6) Meanwhile centrifuge the tube containing 20 ml of blood and no sedimentation agent at 2000 g for 10 minutes. This will yield supernatant cell-free plasma (CFP) containing ACD which is retained, at room temperature, for use as a cell labelling and re-injection medium.
7) When sufficient red cell sedimentation has taken place (see (5)) carefully transfer 15 ml aliquots of the cloudy straw-coloured supernatant into clean Universal tubes. Take care to avoid withdrawing any sedimented erythrocytes. The supernatant is leukocyte-rich, platelet-rich plasma (LRPRP).

TIP: Do not use needles on sampling syringes to avoid unnecessary cell damage.

8) Centrifuge the LRPRP at 150 g for 5 minutes to give supernatant, platelet-rich plasma (PRP) and a pellet of "mixed" leukocytes.
9) Remove as much of the PRP as possible into clean Universal tubes and further centrifuge at 2000 g for 10 minutes to give more supernatant, CFP containing sedimentation agent. This will be used to wash the cells after labelling.
10) Meanwhile loosen the pellets of "mixed" leukocytes by *very* gently tapping and swirling the Universal tubes. Using a syringe, without an attached needle, pool all the cells into one tube then, using the same syringe, add 1ml of cell-free plasma containing ACD (from 6) and *gently* swirl to resuspend.
11) Reconstitute a vial of Ceretec with 5 ml of technetium-99m generator eluate containing approximately 500 MBq (13.5 mCi) of $^{99m}TcO_4^-$ (using the procedure described above).

12) *Immediately* following reconstitution add 4 ml of the resulting technetium-99m exametazime solution to the "mixed" leukocytes in CFP (from 10).
13) *Gently* swirl to mix and incubate for 10 minutes at room temperature.
14) If required, immediately spot the chromatography strips for assessment of radiochemical purity of the technetium-99m exametazime, as instructed overleaf.
15) On completion of incubation *carefully* add 10ml of CFP containing sedimentation agent (from 9) to the cells, in order to stop labelling. Gently invert the cells to mix.
16) Centrifuge at 150 g for 5 minutes.
17) Remove and retain all of the supernatant.

TIP: It is critical that all the supernatant which contains unbound technetium-99m exametazime is removed at this stage. This can be best achieved using a syringe with a wide-bore (19G) needle.

18) Gently resuspend the technetium-99m labelled mixed leukocyte preparation in 5-10 ml of CFP containing ACD from (6). Gently swirl to mix.
19) Measure the radioactivity in the cells and in the supernatant from (17). Calculate the labelling efficiency (LE) which is defined as the activity in the cells as a percentage of the sum of the activity in the cells and the activity in the supernatant.

TIP: Labelling efficiency depends on the patient's leukocyte count and will vary according to the volume of the initial blood sample. Using the volumes in (2), a LE of about 55 % might be expected.

20) Without attaching a needle, carefully draw up the labelled cells into a plastic, non-heparinised syringe and close it with a sterile hub. Measure the radioactivity.
21) Labelled cells are now ready for re-injection. This should be performed without delay.

Note:

a) Acid-citrate-dextrose (ACD) should be made up as follows:
NIH Formula A. For 1 litre add 22 g trisodium citrate, 8 g citric acid, 22.4 g dextrose and make up to 1 litre with Water for injections. The product should be manufactured under aseptic condition. Commercial preparations of the product are also available. The product should be stored under the conditions recommended by the manufacturer and should be used only up to the expiry date given by the manufacturer.
b) Sedimentation agents should be manufactured under aseptic conditions. Commercial sedimentation agents are available. Handling and use of sedimentation agents should be in accordance with the recommendation and instructions of the manufacturer.

Quality control

Three potential radiochemical impurities may be present in the prepared exametazime injection. These are a secondary ^{99m}Tc exametazime complex, free pertechnetate and reduced-hydrolysed-technetium-99m. A combination of two

chromatographic systems is necessary for the determination of the radiochemical purity of the injection.

Test samples are applied by needle approximately 2.5 cm from the bottom of two Glass Microfiber Chromatography Paper impregnated with Silicic Acid (GMCP-SA) strips (2 cm (±2 mm) x 20 cm). The strips are then immediately placed in prepared ascending chromatography development tanks, one containing butan-2-one and the other 0.9 % aq. sodium chloride (1cm depth fresh solvent). After a 14 cm elution the strips are removed, solvent fronts marked, the strips dried and the distribution of activity determined using suitable equipment.

Interpretation of chromatograms
System 1 (GMCP-SA:butan-2-one (methyl ethyl ketone))
Secondary ^{99m}Tc exametazime complex and reduced-hydrolysed-technetium remain at the origin.
Lipophilic ^{99m}Tc exametazime complex and pertechnetate migrate at Rf 0.8-1.0.

System 2 (GMCP-SA: 0.9% sodium chloride)
Lipophilic ^{99m}Tc exametazime complex, secondary ^{99m}Tc exametazime complex and reduced-hydrolysed-Tc remain at the origin.
Pertechnetate migrates at Rf 0.8-1.0.

(1) Calculate the percentage of activity due to both secondary ^{99m}Tc exametazime complex and reduced-hydrolysed-technetium-99m from System 1 (A %). Calculate the percentage of activity due to pertechnetate from System 2 (B %).

(2) The radiochemical purity (as percentage lipophilic ^{99m}Tc exametazime complex) is given by:

100 - (A %+B %) where:

A % represents the level of secondary ^{99m}Tc exametazime complex plus reduced-hydrolysed technetium-99m.
B % represents the level of pertechnetate.

A radiochemical purity of at least 80% may be expected provided the test samples have been taken and analysed within 30 minutes of reconstitution.