ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Quadramet 1.3 GBq/mL solution for injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of solution contains 1.3 GBq Samarium (^{153}Sm) lexidronam pentasodium at the reference date (corresponding to 20 to 80 µg/ml of samarium per vial)

Samarium specific activity is approximately 16 – 65 MBq/µg of samarium.

Each vial contains 2-4 GBq at the reference date.

Samarium-153 emits both medium-energy beta particles and an imageable gamma photon, and has a period of 46.3 hours (1.93 days). The primary radiation emissions of samarium-153 are shown in Table 1.

TABLE 1 : SAMARIUM-153 PRINCIPAL RADIATION EMISSION DATA

Radiation	Energy (keV)*	Abundance
Beta	640	30%
Beta	710	50%
Beta	810	20%
Gamma	103	29%

* Maximum energies are listed for the beta emissions, the average beta particle energy is 233 keV.

Excipient with known effect: sodium 8.1 mg/mL.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

Clear, colourless to light amber solution with pH ranging between 7.0 and 8.5.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Quadramet is indicated for the relief of bone pain in patients with multiple painful osteoblastic skeletal metastases which take up technetium (^{99m}Tc)-labelled biphosphonates on bone scan.

The presence of osteoblastic metastases which take up technetium (^{99m}Tc)-labelled biphosphonates should be confirmed prior to therapy.

4.2 Posology and method of administration

Quadramet should only be administered by physicians experienced in the use of radiopharmaceuticals and after full oncological evaluation of the patient by qualified physicians.

Posology
The recommended dose of Quadramet is 37 MBq per kg body weight.

Paediatric population
Quadramet is not recommended for use in children below the age of 18 years due to a lack of data on safety and efficacy.

Method of administration

Quadramet is to be administered by slow intravenous route through an established intravenous line over a period of one minute. Quadramet should not be diluted before use.

Patients who respond to Quadramet generally experience the onset of pain relief within 1 week after treatment. Relief of pain may persist for 4 weeks up to 4 months. Patients who experience a reduction in pain may be encouraged to decrease their use of opioid analgesics.

Repeat administration of Quadramet should be based on an individual patient's response to prior treatment and on clinical symptoms. A minimum interval of 8 weeks should be respected, subject to recovery of adequate bone marrow function.

The data on the safety of repeated dosing are limited and based on compassionate use of the product.

For instructions on preparation of the medicinal product before administration, see section 12.

4.3 Contraindications

- Hypersensitivity to the active substance (ethylenediaminetetramethylenephosphonate (EDTMP) or similar phosphonates) or to any of the excipients excipients listed in section 6.1.
- in pregnant women (See section 4.6).
- in patients having received chemotherapy or hemi-body external radiation therapy in a preceding period of 6 weeks.

Quadramet is used only as a palliative agent and should not be used concurrently with myelotoxic chemotherapy as this may enhance myelotoxicity.

It should not be used concurrently with other biphosphonates if an interference is shown on the technetium (^{99m}Tc)-labelled biphosphonate bone scans.

4.4 Special warnings and precautions for use

In absence of clinical data, the injected activity should be adapted to the renal function.

Use of Quadramet in patients with evidence of compromised bone marrow reserve from previous therapy or disease involvement is not recommended unless the potential benefit of the treatment outweighs its risks.

Because of potential bone marrow suppression after administration, blood counts should be monitored weekly for at least 8 weeks, beginning 2 weeks after administration of Quadramet, or until recovery of adequate bone marrow function.

The patient should be encouraged to ingest (or receive by intravenous administration) a minimum of 500 ml of fluids prior to injection and should be encouraged to void as often as possible after injection to minimise radiation exposure to the bladder.

The clearance of Quadramet being rapid, the precautions relating to the excreted urinary radioactivity need not be taken after 6-12 hours following administration.

Special precautions, such as bladder catheterisation, should be taken during six hours following administration to incontinent patients to minimise the risk of radioactive contamination of clothing, bed linen, and the patient's environment. For the other patients the urine should be collected for at least six (6) hours**.**

Bladder catheterisation should be undertaken in patients with urinary obstruction.

Radiopharmaceuticals 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 the appropriate licences of the 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 Practice for pharmaceuticals.

4.5 Interaction with other medicinal products and other forms of interaction

Because of the potential for additive effects on bone marrow, the treatment should not be given concurrently with chemotherapy or external beam radiation therapy. Quadramet may be given subsequent to either of these treatments after allowing for adequate marrow recovery.

4.6 Fertility, pregnancy and lactation

Pregnancy
Quadramet is contra-indicated (see 4.3) in pregnancy. The possibility of pregnancy must strictly be ruled out. Women of childbearing potential have to use effective contraception during the treatment and the whole period of follow-up.

Breast-feeding
There are no available clinical data relating to the excretion of Quadramet in human milk. If therefore Quadramet administration is deemed necessary, formula feeding should be substituted for breast-feeding 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

Decreases in white blood cell and platelet counts and anaemia were observed in patients receiving Quadramet.
In clinical trials white blood cell and platelet counts decreased to a nadir of approximately 40 % to 50 % of baseline 3 to 5 weeks after a dose, and generally returned to pre-treatment levels by 8 weeks post treatment.

The few patients who experienced Grade 3 or 4 hematopoietic toxicity usually either had a history of recent external beam radiation therapy or chemotherapy or had rapidly progressive disease with probable bone marrow involvement.

Postmarketing reports of thrombocytopenia have included isolated reports of intracranial haemorrhage, and cases in which the outcome was fatal.

A small number of patients have reported a transient increase in bone pain shortly after injection (flare reaction). This is usually mild and self-limiting and occurs within 72 hours of injection. Such reactions are usually responsive to analgesics.

Adverse drug reactions such as nausea, vomiting, diarrhoea and sweating were reported.

Hypersensitivity reactions including rare cases of anaphylactic reaction have been reported after Quadramet administration.

A few patients experienced cord/root compressions, disseminated intravascular coagulation and cerebrovascular accidents. The occurrence of these events may be linked to the patients' disease evolution. When there are spinal metastases at the cervico-dorsal level, an increased risk of spinal cord compression cannot be excluded.

The radiation dose resulting from therapeutic exposure may result in higher incidence of cancer and mutations. In all cases, it is necessary to ensure that the risks of the radiation are less than from the disease itself.

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 listed in Appendix V.

4.9 Overdose

The product should only be administered by qualified personnel in authorised settings. The possibility of pharmacological overdose is therefore remote.

The risks to be expected are associated with the inadvertent administration of excess radioactivity. Radiation dose to the body can be limited by promoting a diuresis and frequent voiding of urine.

5. PHARMACOLOGIC PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Various pain palliation radiopharmaceuticals.
ATC Code: V10BX02

Mechanism of action
Quadramet has an affinity for skeletal tissue and concentrates in areas of bone turnover in intimate association with hydroxyapatite.

Pharmacodynamic effects
Studies in rats have demonstrated that Quadramet is cleared rapidly from the blood and localises to growing areas of bone matrix, specifically the layer of osteoid undergoing mineralisation.

Clinical efficacy and safety
In clinical studies employing planar imaging techniques, Quadramet accumulates with a lesion-to-normal bone ratio of approximately 5 and a lesion-to-soft tissue ratio of approximately 6. Thus, areas of metastatic involvement can accumulate significantly greater amounts of Quadramet than surrounding normal bone.

5.2 Pharmacokinetic properties

Absorption
Total skeletal uptake of Quadramet in studies of 453 patients with a variety of primary malignancies was 65.5 ± 15.5 % of the administered activity. A positive correlation was found between skeletal uptake and the number of metastatic sites. In contrast, skeletal uptake was inversely proportional to plasma radioactivity at 30 minutes.

Elimination
In patients, Quadramet is rapidly cleared from the blood. Thirty minutes after injection of the agent to 22 patients, only 9.6 ± 2.8 % of the administered activity remained in plasma. At 4 and 24 hours, plasma radioactivity had decreased from 1.3 ± 0.7 % to 0.05 ± 0.03 %.

Urinary excretion occurred predominantly during the first 4 hours (30.3 ± 13.5 %). At 12 hours, 35.3 ± 13.6 % of the administered activity had been excreted into the urine. Less urinary excretion occurred in patients who had extensive bony metastases, regardless of the amount of radiopharmaceutical administered.

Biotransformation
Analysis of urine samples found the radioactivity to be present as the intact complex

5.3 Preclinical safety data

The radiolysis products of Sm-EDTMP showed a renal toxicity in rats and dogs with a no effect level of 2.5 mg/kg.

Repeated dose administration of samarium (^{153}Sm)-EDTMP to dogs indicated a slightly longer time for depressed bone marrow and peripheral haematological parameters to recover when compared to recovery following only single dose administration.

Radioactive Sm-EDTMP has not been tested for mutagenicity/carcinogenicity but due to the radiation dose resulting from therapeutic exposure it should be regarded as presenting a genotoxic/carcinogenic risk.

Non-radioactive Sm-EDTMP showed no mutagenic potential in a battery of *in vivo* and *in vitro* tests. The same results were observed for Sm-EDTMP enriched with radiolysis degradants.

In a carcinogenic potential study of EDTMP, osteosarcomas occurred in rats at high doses. In the absence of genotoxic properties, these effects can be assigned to the EDTMP chelatant properties leading to osseous metabolism disturbances.

No studies have been performed to assess the effect of Quadramet on reproduction.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Total EDTMP (as EDTMP.H2O)
Calcium-EDTMP sodium salt (as Ca)
Total sodium (as Na)
Water for Injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with the other medicinal products.

6.3 Shelf-life

1 day from the activity reference time stated on the label.

Use within 6 hours of thawing. After thawing, do not freeze again.

6.4 Special precautions for storage

Quadramet is delivered frozen in dry ice.
Store in a freezer at -10°C to -20°C in the original package.

Storage procedures should be in accordance with local regulations for radioactive substances.

6.5 Nature and contents of container

15 ml colourless European Pharmacopoeia Type I drawn glass vial closed with Teflon-coated chlorobutyl/natural rubber stopper and aluminium flip-off overseal.

Each vial contains 1.5 ml (2 GBq at calibration) to 3.1 ml (4 GBq at calibration) of solution for injection.

6.6 Special precautions for disposal and other handling

The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spills of urine, vomiting etc. Radiation protection precautions in accordance with national regulations must therefore be taken.

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

(See section 12, for detailed instructions of product preparation)

7. MARKETING AUTHORISATION HOLDER

CIS bio international
Boîte Postale 32
F-91192 GIF-SUR-YVETTE Cedex
FRANCE

8. MARKETING AUTHORISATION NUMBER

EU/1/97/057/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

Date of first authorisation: 05 February 1998
Date of latest renewal: 12 December 2007

10. DATE OF REVISION OF THE TEXT

11. DOSIMETRY

The estimated absorbed radiation doses to an average adult patient from an intravenous injection of Quadramet are shown in Table 2. The dosimetry estimates were based on clinical biodistribution studies using methods developed for radiation dose calculations by the Medical Internal Radiation Dose (MIRD) Committee of the Society of Nuclear Medicine.

Because Quadramet is excreted in the urine, radiation exposure was based on a urinary voiding interval of 4.8 hours. Radiation dose estimates for bone and marrow assume that radioactivity is deposited on bone surfaces, in accordance with autoradiograms of bone samples taken from patients who received Quadramet.

Radiation dose to specific organs, which may not be the target organ of therapy, may be influenced significantly by pathophysiological changes induced by the disease process. This should be taken into consideration when using the following information:

TABLE 2 : RADIATION ABSORBED DOSES

Organ	**Absorbed dose per injected activity (mGy/MBq)**
Adrenals	0.009
Brain	0.011
Chest	0.003
Gallbladder	0.004
Ascending colon wall	0.005
Descending colon wall	0.010
Small intestine	0.006
Myocardial wall	0.005
Kidneys	0.018
Liver	0.005
Lungs	0.008
Muscle	0.007
Ovaries	0.008
Pancreas	0.005
Red marrow	1.54
Bone surfaces	6.76
Skin	0.004
Spleen	0.004
Stomach	0.004
Testes	0.005
Thymus	0.004
Thyroid	0.007
Urinary bladder wall	0.973
Uterus	0.011
Effective dose (mSv/MBq)	0.307

For this product the effective dose resulting from an injected activity of 2 590 MBq is 796 mSv.

For an administered activity of 2 590 MBq, the typical radiation dose to the target organ, skeletal metastases, is 86.5 Gy and the typical radiation doses to the critical organs are: normal bone surfaces 17.5 Gy, red marrow 4.0 Gy, urinary bladder wall 2.5 Gy, kidneys 0.047 Gy and ovaries 0.021 Gy.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Allow the product to thaw at room temperature before administration.

The solution for injection should be visually inspected before use. It should be clear without particles. The operator should be careful to protect the eyes while inspecting the solution for clarity.

The activity should be measured by a dose calibrator immediately before administration. Verification of the dose to be administered and patient identification are necessary prior to administration of Quadramet.
For radiation safety reasons, the patient should be treated in a facility with the appropriate agreement for the therapeutic use of radioactive non-sealed sources. He/she will be released when exposure rates comply with the limits prescribed by the regulations in force.

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

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. 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) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

CIS bio international
Boîte Postale 32
F-91192 Gif-sur-Yvette cedex
France

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (See Annex I: Summary of Product Characteristics, section 4.2)

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

Pharmacovigilance system
The MAH must ensure that the system of pharmacovigilance presented in Module 1.8.1. of the Marketing Authorisation, is in place and functioning before and whilst the medicinal product is on the market.

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

Not applicable

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

METALLIC BOX / LEADPOT

1. NAME OF THE MEDICINAL PRODUCT

Quadramet 1.3 GBq/mL solution for injection
Samarium (^{153}Sm) lexidronam pentasodium

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Samarium (^{153}Sm) lexidronam pentasodium : 1.3 GBq/ml at reference date.
(Corresponding to 20 to 80 µg/ml of samarium)

3. LIST OF EXCIPIENTS

Total EDTMP (as EDTMP.H2O)
Calcium-EDTMP sodium salt (as Ca)
Total sodium (as Na)
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection in a single-dose vial.

_____ ml

_____ GBq/vial, _____ (12 h CET)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use

For intravenous 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

8. EXPIRY DATE

EXP: DD/MM/YYYY (12 h CET)

9. SPECIAL STORAGE CONDITIONS

Store in a freezer at -10°C to -20°C in the original package

Use within 6 hours of thawing

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

CIS bio international,
Boîte Postale 32,
91192 GIF-SUR-YVETTE Cedex,
FRANCE

12. MARKETING AUTHORISATION NUMBER

EU/1/97/057/001

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>

MINIMUM PARTICULARS TO APPEAR ON SMALL INTERMEDIATE PACKAGING UNITS

GLASS VIAL

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

Quadramet 1.3 GBq/mL solution for injection
Samarium (^{153}Sm) lexidronam pentasodium
For intravenous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP: DD/MM/YYYY (12 h CET)

4. BATCH NUMBER

Batch: _____

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

_____ ml

_____ GBq/vial,_____ (12 h CET)

6. OTHER

Manufacturer: CIS bio international.

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Quadramet 1.3 GBq/mL solution for injection
Samarium (^{153}Sm) lexidronam pentasodium.

Read all of this leaflet carefully before you start taking 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 your pharmacist.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Quadramet is and what it is used for

Quadramet is a medicinal product for therapeutic use only.

This radiopharmaceutical is used for the treatment of bone pain due to your disease.

Quadramet has a high affinity for skeletal tissue. Once injected it concentrates in bone lesions. Because Quadramet contains small amounts of a radioactive element, samarium-153, radiations are delivered locally to the bone lesions, allowing to develop the palliative action on bone pain.

2. What you need to know before you take Quadramet

Do not take Quadramet:
- If you are allergic to ethylene diamine tetramethylene phosphonic acid (EDTMP) or similar phosphonate compounds or any of the other ingredients of this medicine (listed in section 6),
- If you are pregnant,
- If you have received chemotherapy or hemibody field external radiation therapy in a preceding period of 6 weeks.

Warnings and precautions
Talk to your doctor before taking Quadramet.

Your doctor will take blood samples weekly for at least 8 weeks to check your platelets, white and red blood cell counts which may slightly decrease due to the therapy.

During 6 hours following the injection of Quadramet, your physician will encourage you to drink and void as often as possible. He will decide at which time you will be authorised to leave the nuclear medicine department.

In the case of urine incontinence or urinary obstruction you will get a urine catheter for about 6 hours. For the other patients the urine should be collected for at least 6 hours.

If your renal function is decreased, the amount of product will be adapted.

Children and adolescents
Quadramet is not recommended for use in children below 18 years of age.

Other medicines and Quadramet
Tell your doctor if you are taking or have recently taken or might take any other medicines.

Pregnancy and breast-feeding:
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 taking this medicine.

Quadramet must not be administered to pregnant women.
If Quadramet administration to a breastfeeding woman is deemed necessary, breastfeeding should be stopped.

3. How to take Quadramet

Your doctor will want to carry out a special scan before administering Quadramet to ascertain whether you are likely to benefit from Quadramet.

Dosage
One single dose of 37 megabecquerel (Becquerel is the unit in which radioactivity is measured) of Quadramet per kilogram of body weight is to be injected.

If you have the impression that the effect of Quadramet is too strong or too weak, talk to your doctor or pharmacist.

Method and route of administration
Quadramet is to be administered by slow injection into a vein.

Frequency of administration
This medicinal product is not intended to be injected on a regular or continuous basis. The administration can however be repeated after 8 weeks following injection, subject to the evolution of your disease.

Duration of treatment
You will be authorised to leave the nuclear medicine department after a dosimetric follow-up (generally within 6 hours following Quadramet injection).

If you take more Quadramet than you should
Quadramet being supplied as a single-dose vial, an accidental overdose is unlikely to occur.
Radiation dose to the body can be limited by increasing fluid intake and frequent voiding of urine.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

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

The undesirable effects due to Quadramet administration are linked with a decrease of red and white blood cells, and platelets. Cases of bleeding have been reported, some of which have been serious.

This is the reason why your blood counts will be monitored strictly for a few weeks following Quadramet injection.

You may exceptionally feel a slight increase in bone pain a few days after Quadramet injection. You should not be alarmed at this; in such case, your pain medicine will be slightly increased. This effect is moderate and brief and will disappear after some hours.

Adverse drug reactions such as nausea, vomiting, diarrhoea and sweating were reported.

Hypersensitivity reactions including rare cases of anaphylactic reaction have been reported after Quadramet administration.

In rare cases, the following undesirable effects have been observed: neuralgia, coagulation disorders, cerebrovascular accidents. These effects were deemed to be related to the progression of the disease.

If you experience back pain or sensory abnormalities, please inform your physician as soon as possible.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. 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 Quadramet

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

Do not use Quadramet after the expiry date which is stated on the label.
Quadramet expires 1 day from the activity reference time stated on the label.

Store at –10°C to –20°C in a freezer in its original packaging.

Quadramet should be used within 6 hours of thawing. After thawing, do not freeze again.

The product label includes the appropriate storage conditions and the expiry date for the batch of product. Hospital personnel will ensure that the product is stored correctly and not administered to you after the stated expiry date.

Storage procedures should be in accordance with national regulations for radioactive materials.

6. Contents of the pack and other information

What Quadramet contains
The active substance is samarium (^{153}Sm) lexidronam pentasodium.
Each ml of solution contains 1.3 GBq Samarium (^{153}Sm) lexidronam pentasodium at the reference date (corresponding to 20-80 µg/ml of samarium per vial).

The other ingredients are total EDTMP (as EDTMP.H2O), calcium-EDTMP sodium salt (as Ca), total sodium (as Na), water for injections.

What Quadramet looks like and contents of the pack
Quadramet is a solution for injection.

This medicinal product is a clear, colourless to light amber solution which is packed in a 15 ml colourless European Pharmacopoeia Type I drawn glass vial closed with Teflon-coated chlorobutyl/natural rubber stopper and aluminium flip-off overseal.

Each vial contains 1.5 ml (2 GBq at reference) to 3.1 ml (4 GBq at reference) of solution for injection.

Marketing authorisation holder and manufacturer

CIS bio international
Boîte Postale 32
F-91192 Gif-sur-Yvette cedex
France

The leaflet was last revised in {MM/YYYY}

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

The following information is intended for medical or healthcare professionals only:
The complete SmPC of Quadramet is provided as a separate document in the product package, with the objective to provide healthcare professionals with other additional scientific and practical information about the administration and use of this radiopharmaceutical.

Please refer to the SmPC (SmPC should be included in the box)