SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Fludeoxyglucose (^{18}F)-Curium 185 MBq/mL solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 mL contains 185 MBq of fludeoxyglucose (^{18}F) at the date and time of calibration.
The activity per vial ranges from 90 MBq to 1850 MBq at the date and time of calibration.
Fluorine (^{18}F) decays to stable oxygen (^{18}O) with a half-life of 110 minutes by emitting a positronic radiation of maximum energy of 634 keV, followed by photonic annihilation radiations of 511 keV.

Excipients with known effects:
Each mL of fludeoxyglucose (^{18}F) contains 9 mg of sodium chloride and less than 4 mg of ethanol.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection
Clear, colourless or slightly yellow solution.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

This medicinal product is for diagnostic use only.
Fludeoxyglucose (^{18}F) is indicated for use with positron emission tomography (PET) in adults and paediatric population.

Oncology
In patients undergoing oncologic diagnostic procedures describing function or diseases where enhanced glucose influx of specific organs or tissues is the diagnostic target. The following indications are sufficiently documented (see also section 4.4):

Diagnosis:
- Characterisation of solitary pulmonary nodules
- Detection of cancer of unknown origin, revealed for example by cervical adenopathy, liver or bones metastases.
- Characterisation of a pancreatic mass

Staging:
- Head and neck cancers including assistance in guiding biopsy
- Primary lung cancer
- Locally advanced breast cancer
- Oesophageal cancer
- Carcinoma of the pancreas
- Colorectal cancer particularly in restaging recurrences
- Malignant lymphoma
- Malignant melanoma, Breslow > 1.5 mm or lymph node metastasis at first diagnosis

Monitoring of therapeutic response:
- Malignant lymphoma
- Head and neck cancers

Detection in case of reasonable suspicion of recurrences:

- Glioma with high grade malignancy (III or IV)
- Head and neck cancers
- Thyroid cancer (non-medullary): patients with increased thyroglobulin serum levels and negative radioactive iodine whole body scintigraphy
- Primary lung cancer
- Breast cancer
- Carcinoma of the pancreas
- Colorectal cancer
- Ovarian cancer
- Malignant lymphoma
- Malignant melanoma

Cardiology

In the cardiologic indication, the diagnostic target is viable myocardial tissue that takes-up glucose but is hypo-perfused, as it must be assessed beforehand using appropriate blood-flow imaging techniques.

- Evaluation of myocardial viability in patients with severe impaired left ventricular function who are candidates for revascularisation when conventional imaging modalities are not contributive.

Neurology

In the neurologic indication the interictal glucose hypometabolism is the diagnostic target.

- Localisation of epileptogenic foci in the presurgical evaluation of partial temporal epilepsy.

Infectious or inflammatory diseases

In infectious or inflammatory diseases, the diagnostic target is tissue or structures with an abnormal content of activated white blood cells.
In infectious or inflammatory diseases, the following indications are sufficiently documented:

Localisation of abnormal foci guiding the aetiologic diagnosis in case of fever of unknown origin.

Diagnosis of infection in case of:

- Suspected chronic infection of bone and/or adjacent structures: osteomyelitis, spondilitis, diskitis or osteitis including when metallic implants are present
- Diabetic patient with a foot suspicious of Charcot's neuroarthropathy, osteomyelitis and/or soft tissue infection
- Painful hip prosthesis
- Vascular prosthesis
- Fever in an AIDS patient
- Detection of septic metastatic foci in case of bacteraemia or endocarditis (see also section 4.4).

Detection of the extension of inflammation in case of:

- Sarcoidosis
- Inflammatory bowel disease
- Vasculitis involving the great vessels

Therapy follow-up:

Unresectable alveolar echinococcosis, in search for active localisations of the parasite during medical treatment and after treatment discontinuation.

4.2. Posology and method of administration

Posology

Adults and elderly population

The recommended activity for an adult weighing 70 kg is 100 to 400 MBq (this activity has to be adapted according to the body weight of the patient, the type of camera used and acquisition mode), administered by direct intravenous injection.

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

Extensive dose-range and adjustment studies with this medicinal product in normal and special populations have not been performed.
The pharmacokinetics of fludeoxyglucose (^{18}F) in renally impaired patients has not been characterised.

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; the activity administered to children and to adolescents may be calculated by multiplying a baseline activity (for calculation purposes) by the weight-dependent multiples given in the table below.

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

The baseline activity for 2D imaging is 25.9 MBq and for 3D imaging 14.0 MBq (recommended in children).

Weight [kg]	Multiple	**Weight [kg]**	Multiple	**Weight [kg]**	Multiple
3	1	**22**	5.29	**42**	9.14
4	1.14	**24**	5.71	**44**	9.57
6	1.71	**26**	6.14	**46**	10.00
8	2.14	**28**	6.43	**48**	10.29
10	2.71	**30**	6.86	**50**	10.71
12	3.14	**32**	7.29	**52-54**	11.29
14	3.57	**34**	7.72	**56-58**	12.00
16	4.00	**36**	8.00	**60-62**	12.71
18	4.43	**38**	8.43	**64-66**	13.43
20	4.86	**40**	8.86	**68**	14.00

Method of administration
For intravenous use.
For multidose use.
The activity of fludeoxyglucose (^{18}F) has to be measured with activimeter immediately prior to injection.
The injection of fludeoxyglucose (^{18}F) must be intravenous in order to avoid irradiation as a result of local extravasation, as well as imaging artefacts.

For intructions on dilution of the medical product before administration, see section 12.
For patient preparation, see section 4.4.

Image acquisition
The emission scans are usually started 45 to 60 minutes after the injection of fludeoxyglucose (^{18}F). Provided a sufficient activity remains for adequate counting statistics, fludeoxyglucose (^{18}F)-PET can also be performed up to two or three hours after administration, thus reducing background activity.

If required, repeated fludeoxyglucose (^{18}F) PET examinations can be reiterated within a short period of time.

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

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 products and equipment such as endotracheal tube and ventilator must be immediately available.

Individual benefit/risk justification

For each patient, the radiation exposure must be justifiable by the likely benefit. The activity administered should in every case be as low as reasonably achievable to obtain the required diagnostic information.

Renal and hepatic impairment

Due to the major renal excretion of fludeoxyglucose (^{18}F), in patients with reduced kidney function, careful consideration of the benefit risk ratio in these patients is required since an increased radiation exposure is. Activity should be adjusted if necessary.

Paediatric population
For information on the use in paediatric population, see sections 4.2 or 5.1.
Careful consideration of the indication is required since the effective dose per MBq is higher than in adults (see section 11.).

Patient preparation

Fludeoxyglucose (^{18}F)-Curium should be given to sufficiently hydrated patients fasting for a minimum of 4 hours, in order to obtain a maximum target activity, since glucose uptake in the cells is limited ("saturation kinetics"). The amount of liquid should not be limited (beverages containing glucose must be avoided).
In order to obtain images of best quality and to reduce the radiation exposure of the bladder, patients should be encouraged to drink sufficient amounts and to empty their bladder prior to and after the PET examination.

- *Oncology and neurology and infectious diseases*
In order to avoid hyperfixation of the tracer in muscle, it is advisable for patients to avoid all strenuous physical activity prior to the examination and to remain at rest between the injection and examination and during acquisition of images (patients should be comfortably lying down without reading or speaking).
The cerebral glucose metabolism depends on the brain activity. Thus, neurological examinations should be performed after a relaxation period in a darkened room and with low background noise.

A blood glucose test should be performed prior to administration since hyperglycaemia may result in a reduced sensitivity of Fludeoxyglucose (^{18}F)-Curium, especially when glycaemia is greater than 8 mmol/L. Similarly, PET with fludeoxyglucose (^{18}F) should be avoided in subjects presenting uncontrolled diabetes.

- *Cardiology*
Since glucose uptake in the myocardium is insulin-dependent, for a myocardial examination a glucose loading of 50 g approximately 1 hour prior to the administration of Fludeoxyglucose (^{18}F)-Curium is recommended. Alternatively, especially for patients with diabetes mellitus, the blood sugar level can be adjusted by a combined infusion of insulin and glucose (Insulin-Glucose-Clamp) if needed.

Interpretation of the PET with fludeoxyglucose (^{18}F) images
In the exploration of inflammatory bowel diseases, diagnostic performance of fludeoxyglucose (^{18}F) has not been directly compared with that of scintigraphy using labelled white blood cells which may be indicated prior to fludeoxyglucose (^{18}F) PET or after fludeoxyglucose (^{18}F) PET when inconclusive.

Infectious and/or inflammatory diseases as well as regenerative processes after surgery can result in a significant uptake of fludeoxyglucose (^{18}F) and therefore lead to false positive results, when search for infectious or inflammatory lesions is not the aim of the fludeoxyglucose (^{18}F) PET.

In cases where fludeoxyglucose (^{18}F) accumulation can be caused by either cancer, infection or inflammation, additional diagnostic techniques for the determination of the causative pathologic alteration may be required to supplement the information obtained by PET with fludeoxyglucose (^{18}F). In some settings e.g. staging of myeloma, both malignant and infectious foci are searched for and may be distinguished with a good accuracy on topographic criteria e.g. uptake at extramedullary sites and/or bone and joint lesions would be atypical for multiple myeloma lesions and identified cases associated with infection. There are currently no other criteria to distinguish infection and inflammation by means of fludeoxyglucose (^{18}F) imaging.

Because of the high physiologic uptake of fludeoxyglucose (^{18}F) within brain, heart and kidneys, PET/CT with fludeoxyglucose (^{18}F) has not been evaluated for the detection of septic metastatic foci in these organs when the patient has been referred due to bacteraemia or endocarditis.
False positive or false negative PET with fludeoxyglucose (^{18}F) results cannot be excluded after radiotherapy within the first 2-4 months. If the clinical indication is demanding an earlier diagnosis by PET with fludeoxyglucose (^{18}F), the reason for earlier PET with fludeoxyglucose (^{18}F) examination must be reasonably documented.

A delay of at least 4-6 weeks after the last administration of chemotherapy is optimal, in particular to avoid false negative results. If the clinical indication is demanding an earlier diagnosis by PET with fludeoxyglucose (^{18}F), the reason for earlier PET with fludeoxyglucose (^{18}F) examination must be reasonably documented. In case of chemotherapy regimen with cycles shorter than 4 weeks, the PET with fludeoxyglucose (^{18}F) examination should be done just before re-starting a new cycle.
In low-grade lymphoma, lower oesophagus cancer and suspicion of recurrent ovarian cancer, only positive predictive values have to be considered because of a limited sensitivity of PET with fludeoxyglucose (^{18}F).
Fludeoxyglucose (^{18}F) is not effective in detecting brain metastases.
The accuracy of fludeoxyglucose (^{18}F) PET imaging is better using PET/CT than PET cameras alone.

When a hybrid PET-CT scanner is used with or without administration CT contrast media, some artefacts may occur on the attenuation-corrected PET images.

After the procedure
Close contact with infants and pregnant women should be restricted during the initial 12 hours following the injection.

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 (23 mg).

This should be taken into account in patient on low sodium diet.
This medicinal product contains ethanol (alcohol), less than 100 mg per administration.

Precautions with respect to environmental hazard see section 6.6.

4.5. Interaction with other medicinal products and other forms of interaction

All medicinal products that modify blood glucose levels can affect the sensitivity of the examination (e.g. corticosteroids, valproate, carbamazepine, phenytoin, phenobarbital and catecholamines).
Under administration of colony-stimulating factors (CSFs), there is an increased uptake of fludeoxyglucose (^{18}F) in the bone marrow and the spleen for several days. This must be taken into account for the interpretation of PET imaging. Separating CSF therapy from PET imaging by an interval of at least 5 days may diminish this interference.

The administration of glucose and insulin influences the influx of fludeoxyglucose (^{18}F) into the cells. In the case of high blood glucose levels as well as low plasma insulin levels, the influx of fludeoxyglucose (^{18}F) into organs and tumours is reduced.
No formal studies on the interaction between fludeoxyglucose (^{18}F) and any contrast for computed tomography have been performed.

4.6. Fertility, pregnancy and lactation

Women of 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
Radionuclide procedures carried out on pregnant women also involve radiation dose to the foetus.
Only essential investigations should therefore be carried out during pregnancy, when the likely benefit far exceeds the risk incurred by the mother and foetus.

Breastfeeding
Before administering radiopharmaceuticals 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.
Close contact with infants should be restricted during the initial 12 hours following injection.

Fertility
No studies on fertility have been performed.

4.7. Effects on ability to drive and use machines

Not relevant.

4.8. Undesirable effects

Tabulated list of adverse reactions
The following table includes the adverse reactions sorted by system organ classes according to MedDRA.
The frequencies are defined as follows: very common ≥ 1/10; common from ≥ 1/100 to <1/10; uncommon from ≥ 1/1,000 to <1/100, rare from ≥ 1/10,000 to <1/1,000; very rare <1/10,000; frequency not known (cannot be estimated from the available data).

System Organ Class (SOCs)	Adverse reactions*	Frequency
Immune system disorders	Hypersensitivity , anaphylactic and anaphylactoid reactions such as anaphylactic shock, cardiac arrest, dyspnoea, bronchospasm, angioedema, hypotension, rash, rash erythematous, rash pruritic, rash maculo-papular, urticaria, pruritus, erythema, dermatitis, skin reaction, localised oedema, face oedema, cough, mouth swelling, lip swelling, ocular hyperaemia, eye irritation, eye disorder, nausea and vomiting	Not known

* Adverse reactions derived from spontaneous reporting

Hypersensitivity is not preventable by usual means.
Symptoms may appear with a latency ranged from immediately to 10 days with a median latency of 3 hours. In the majority of cases, the latency was of 24 hours or less.

Hypersensitivity reactions are ranging from mild (such as rash, pruritus) requiring symptomatic/supportive treatments to serious/severe (anaphylaxis) which may require emergency support (hospitalization).

Prior to administration, patients should be asked about their allergy history, medical histories, and current medications. Re-exposure to the drug is at risk of a recurrent reaction.

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose is 7.6 mSv when the maximal recommended activity of 400 MBq is administered these adverse reactions 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:
ADR Reporting
Website: www.medicinesauthority.gov.mt/adrportal

4.9. Overdose

In the event of administration of a radiation overdose with fludeoxyglucose (^{18}F) the absorbed dose to the patient should be reduced where possible by increasing the elimination of the radionuclide from the body by forced diuresis and frequent bladder voiding. It might be helpful to estimate the effective dose that was applied.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: diagnostic radiopharmaceutical, other diagnostic radiopharmaceuticals for tumour detection,ATC code: V09IX 04

Pharmacodynamic effects

At the chemical concentrations used for diagnostic examinations, fludeoxyglucose (^{18}F) does not appear to have any pharmacodynamic activity.

5.2. Pharmacokinetic properties

Distribution

Fludeoxyglucose (^{18}F) is a glucose analogue, which is accumulated in all cells using glucose as primary energy source. Fludeoxyglucose (^{18}F) is accumulated in tumours with a high glucose turnover.
Following intravenous injection, the pharmacokinetic profile of fludeoxyglucose (^{18}F) in the vascular compartment is biexponential. It has a distribution time of 1 minute and an elimination time of approximately 12 minutes.
In healthy subjects, fludeoxyglucose (^{18}F) is widely distributed throughout the body, particularly in the brain and heart, and to a lesser degree in the lungs and liver.

Organ uptake

The cellular uptake of fludeoxyglucose (^{18}F) is performed by tissue-specific carrier systems, which are partly insulin-dependent and, thus, can be influenced by eating, nutritional condition and the existence of a diabetes mellitus. In patients with a diabetes mellitus a reduced uptake of fludeoxyglucose (^{18}F) into the cells occurs due to a changed tissue distribution and glucose metabolism.

Fludeoxyglucose (^{18}F) is transported via the cell membrane in similar fashion to glucose, but only undergoes the first step of glycolysis resulting in formation of fludeoxyglucose (^{18}F)-6-phosphate, which remains trapped within the tumour cells and is not further metabolised. Since the following dephosphorylation by intracellular phosphatases is slow, fludeoxyglucose (^{18}F)-6-phosphate is retained in the tissue over several hours (trapping-mechanism).

Fludeoxyglucose (^{18}F) passes the blood-brain barrier. Approximately 7 % of the injected dose are accumulated in the brain within 80-100 minutes after injection. Epileptogenic foci exhibit a reduced glucose metabolism in the seizure free phases.
Approximately 3 % of the injected activity are taken-up by the myocardium within 40 minutes. The distribution of fludeoxyglucose (^{18}F) in normal heart is mainly homogenous, however, regional differences of up to 15 % are described for the interventricular septum. During and after a reversible myocardial ischemia, an increased glucose uptake occurs into the myocardial cell.
0.3 % and 0.9 - 2.4 % of the injected activity are accumulated in pancreas and lung.

Fludeoxyglucose (^{18}F) is also bound to a lesser extent to ocular muscle, pharynx and intestine. Binding to muscle may be seen following recent exertion and in the event of muscular effort during the examination.

Elimination
Elimination of fludeoxyglucose (^{18}F) is chiefly renal, with 20 % of activity being excreted in urine in the 2 hours following injection.
Binding to renal parenchyma is weak, but because of renal elimination of fludeoxyglucose (^{18}F), the entire urinary system, particularly the bladder, exhibits marked activity.

5.3. Preclinical safety data

Toxicological studies with mice and rats have demonstrated that with a single intravenous injection of 0.0002 mg/kg no deaths were observed. Toxicity with repeated administration was not performed because fludeoxyglucose (^{18}F) is administered in a single dose. This medicinal product is not intended for regular or continuous administration.
Mutagenecity studies and long-term carcinogenicity studies have not been carried out.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Sodium chloride 9 mg/mL
Ethanol
Water for injections

6.2. Incompatibilities

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

6.3. Shelf life

14 hours at the end of the manufacturing time.
Date and time of expiry are indicated on the packaging and on the vial.

After first withdrawal, store below 25°C and use within 12 hours without exceeding the expiry time.

6.4. Special precautions for storage

Store in the original package.
Storage of radiopharmaceuticals should be in accordance with national regulation on radioactive materials.
For storage conditions after first withdrawal see section 6.3.

6.5. Nature and contents of the container

15 mL, colourless glass vial, European Pharmacopoeia Type I, closed with a Teflon chlorobutyl stopper and an aluminium seal.

Packsize: One multidose vial contains 0.5 to 10 mL of solution, corresponding to 90 to 1850 MBq at calibration time.

6.6. Special precautions, for disposal and other handling

General warnings
Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate 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.

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.

7. MARKETING AUTHORISATION HOLDER

CURIUM INTERNATIONAL
Boulevard Bischoffsheim 39 boîte 4
1000 Bruxelles
BELGIUM

8. MARKETING AUTHORISATION NUMBER

Country specific

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 5 December 2002
Date of latest renewal: 15 July 2014

10. DATE OF REVISION OF THE TEXT

12/2023

11. DOSIMETRY

The data listed below are from ICRP 106 publication.

ORGAN	ABSORBED DOSE PER UNIT ACTIVITY ADMINISTERED (mGy/MBq)				
	Adult	15 years	10 years	5 years	1 year
Adrenals	0.012	0.016	0.024	0.039	0.071
Bladder	0.13	0.16	0.25	0.34	0.47
Bone surfaces	0.011	0.016	0.022	0.034	0.064
Brain	0.038	0.039	0.041	0.046	0.063
Breast	0.0088	0.011	0.018	0.029	0.056
Gall bladder	0.013	0.016	0.024	0.037	0.070
Gastrointestinal tract					
Stomach	0.011	0.014	0.022	0.035	0.067
Small Intestine	0.012	0.016	0.025	0.040	0.073
Colon	0.013	0.016	0.025	0.039	0.070
(Upper Large Intestine	0.012	0.015	0.024	0.038	0.070
(Lower Large Intestine	0.014	0.017	0.027	0.041	0.070
Heart	0.067	0.087	0.13	0.21	0.38
Kidneys	0.017	0.021	0.029	0.045	0.078
Liver	0.021	0.028	0.042	0.063	0.12
Lungs	0.020	0.029	0.041	0.062	0.12
Muscles	0.010	0.013	0.020	0.033	0.062
Oesophagus	0.012	0.015	0.022	0.035	0.066
Ovaries	0.014	0.018	0.027	0.043	0.076
Pancreas	0.013	0.016	0.026	0.040	0.076
Red marrow	0.011	0.014	0.021	0.032	0.059
Skin	0.0078	0.0096	0.015	0.026	0.050
Spleen	0.011	0.014	0.021	0.035	0.066
Testes	0.011	0.014	0.024	0.037	0.066
Thymus	0.012	0.015	0.022	0.035	0.066
Thyroid	0.010	0.013	0.021	0.034	0.065
Uterus	0.018	0.022	0.036	0.054	0.090
Remaining organs	0.012	0.015	0.024	0.038	0.064
Effective dose (mSv/MBq)	**0.019**	**0.024**	**0.037**	**0.056**	**0.095**

The effective dose resulting from the administration of a maximal recommended activity of 400 MBq of fludeoxyglucose (^{18}F) for an adult weighing 70 kg is about 7.6 mSv.
For an administered activity of 400 MBq, the typical radiation doses delivered to the critical organs, bladder, heart and brain are respectively: 52 mGy, 27 mGy and 15 mGy, respectively.

12. INTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Method of preparation

The package must be checked before use and the activity measured using an activimeter.
The medicinal product may be diluted with sodium chloride 9 mg/mL solution for injection.
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 authorized automated application system.
If the integrity of this vial is compromised, the product should not be used.

Quality control

The solution should be inspected visually prior to use. Only clear solutions, free of visible particles should be used.

Detailed information on this medicinal product is available on the website of {name of MS/Agency}.