

## **CORE SmPC FOR RADIOPHARMACEUTICALS**

*The QRD Product Information template with explanatory notes and the convention to be followed for QRD templates provide general guidance on format and text and should be read in conjunction with the core SmPC and the Guideline on Summary of Product Characteristics.*

**ANNEX I**

**SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE MEDICINAL PRODUCT

{(Invented) name strength pharmaceutical form}

*[Trade name = product specific.]*

*[No proprietary or company names should be mentioned in the Core SPCs. The generic name should be that defined as the INN-name. If no such name exists then the EP monograph name (omitting the dosage form) or USAN name will be acceptable. If none of these exist, the EP nomenclature should be adopted.]*

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

*[For radiolabelled radiopharmaceuticals, the physical half-life of the radionuclide should be stated with a summary of the energies of the principal particle and photon emissions.*

*In case of a non-radiolabelled radiopharmaceutical kit, the corresponding information concerning the intended radionuclide should be listed at the beginning of Section 11. In this case should be stated here:] “The radionuclide is not part of the kit“*

<Excipient(s):>

For a full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

*[The pharmaceutical form should be stated according to the full “Standard Terms” published by the Council of Europe, in the singular. Where the Council of Europe short standard term is used on small immediate packaging materials, the short term should be added in brackets. See ' The List of Standard Terms published by the European Directorate for the Quality of Medicines and HealthCare.*

*Route of administration should be specified under 4.2. Posology and method of administration.*

*A description of the visual appearance of the product pharmaceutical form as marketed should be included here. Information on appearance of reconstituted parenteral solution should appear under section 12.]*

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

*[The text should be as short and precise as possible.]*

*[If indications are diagnostic:] This medicinal product is for diagnostic use only.*

*[For kits for radiopharmaceutical preparation:] After radiolabelling with [e.g. sodium (<sup>99m</sup>Tc) pertechnetate solution], [the solution obtained] is indicated in <adults> <children> <aged {x to y}> <years> <months> [if applicable] for ...*

### 4.2 Posology and method of administration

#### Posology

*[Posology should as a general rule*

- *state a suggested activity range*
- *be based on a patient of average weight (70 kg).*

*The activity range should be stated in MBq in round numbers. A statement that “other activities may be justifiable” may also be considered appropriate.*

*Reference to European procedural guidelines should be made if required.]*

*[If applicable]: Paediatric population*

*[Paediatric dosing regimens, when applicable, should be clearly stated when an indication exists in this subgroup. If there are data available which are not sufficient to support an indication in the paediatric population, these data may be summarised in section 5.1 of the SmPC with a cross reference from section 4.2, Paediatric Population. Reference could be made to relevant data proposed by bodies specialised in radiation protection and/or Nuclear Medicine.]*

The use in paediatric 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 to adolescents may be calculated according to *[include here relevant data proposed by bodies specialised in radiation protection and/or Nuclear Medicine]*.

*Patients with hepatic impairment*

*[If applicable] ...*

*Patients with renal impairment*

*[If applicable] ...*

Method of administration

*[For kits for radiopharmaceutical preparation:]* This medicinal product should be reconstituted before administration to the patient.

*[The route of administration should be one of those listed in the 'The List of Standard Terms' published by the European Directorate for the Quality of Medicines and Health Care.]*

*[If applicable]* For patient preparation, see section 4.4.

*<Precautions to be taken before handling or administering the medicinal product>*

For instructions on <reconstitution> <dilution> <extemporaneous preparation> of the medicinal product before administration, see section 12.

*[For a diagnostic radiopharmaceutical intended for imaging or for a therapeutic radiopharmaceutical allowing imaging biodistribution]*

Image acquisition

*[General recommendations should be given about the recommended (minimal) number of imaging times, the delay between administration and imaging, some particular types of acquisition that are recommended in all or some of the indicated clinical settings, such as tomoscintigraphy SPECT, dynamic acquisition (rapid change of biodistribution over time), fusion with another imaging modality ... ]*

### **4.3 Contraindications**

*<Hypersensitivity to the active substance(s), to any of the excipients <or { name of the residue(s)}> or to any of the components of the labelled radiopharmaceutical.>*

*[If pregnancy or breastfeeding is contraindicated, it should be mentioned here. In section 4.6, a cross-reference should be made and further background information provided.]*

### **4.4 Special warnings and precautions for use**

Pregnancy, see section 4.6

### Individual benefit/risk justification

*[The as low as reasonably achievable (ALARA) statement should be included in every radiopharmaceutical:]* 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 *[or, if applicable:]* therapeutic effect.

*[If applicable:]* In patients with reduced kidney function, careful consideration of the indication is required since an increased radiation exposure is possible in these patients.

*[Peculiarities concerning radiopharmaceuticals with biliary excretion or pulmonary excretion may also be stated here.]*

### Paediatric population

Paediatric population, see section 4.2. or 5.1., as appropriate.

*[If applicable:]* careful consideration of the indication is required since the effective dose per MBq is higher than in adults (see section 11 “Dosimetry”)

### Patient preparation

*[If applicable:]* 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 study in order to reduce radiation.

*[or, in case of administration of higher activities:]* Patients should be encouraged to increase oral fluids and urged to void as often as possible to reduce bladder radiation, especially after high activities e.g. for the treatment of [...]. Patients with bladder voiding problems should be catheterized after high activity [...] administration.

### 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 by the user in a manner which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken.

*[For kits for radiopharmaceutical preparation:]* Contents of the vial are intended only for use in the preparation of [...] and are not to be administered directly to the patient without first undergoing the preparative procedure.

### Specific warnings

*[If applicable:]* This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially ‘sodium-free’.

*[If applicable:]* According to the time of conditioning injection for the patient, the content of sodium may in some cases be greater than 1 mmol. This should be taken into account in patient on low sodium diet.

*[In case hypersensitivity or anaphylactic reactions with general or life-threatening manifestation have been observed:]* 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.

*Precautions with respect to environmental hazard are in Section 6.6.*

## **4.5 Interaction with other medicinal products and other forms of interaction**

*[Interactions should be presented as brief as possible perhaps with a table of interactions. Only generic names of interacting substances should be used. Only true drug interactions should be included i.e. those which may produce inaccuracies in diagnostic accuracy or interfere with therapeutic efficacy.]*

*[The following statement may be used where appropriate:]* No drug-drug interactions have been described to date.

<No interaction studies have been performed.>

*[If applicable:] <Paediatric population>*  
<Interaction studies have only been performed in adults.>

#### **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.

*[If applicable:] Contraception in males and females*

##### Pregnancy

*[For radiopharmaceuticals in which pregnancy is not a contraindication:]* Radionuclide procedures carried out on pregnant women also involve radiation dose to the foetus. Only imperative investigations should therefore be carried out during pregnancy, when the likely benefit far exceeds the risk incurred by the mother and foetus.

##### Breastfeeding

*[The fact whether or not radioactivity will be excreted into breast milk should be mentioned here if applicable.]*

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 [...] hours and the expressed feeds discarded.

*[If applicable:]* Close contact with infants should be restricted during this period.

*[If applicable:] Fertility*

#### **4.7 Effects on ability to drive and use machines**

<{Invented name} has <no or negligible influence> <minor influence> <moderate influence> <major influence> on the ability to drive and use machines.>  
<Not relevant.>

#### **4.8 Undesirable effects**

The following table presents how the frequencies are reflected in this section:

Very common ( $\geq 1/10$ )
Common ( $\geq 1/100$ to $< 1/10$ )
Uncommon ( $\geq 1/1,000$ to $< 1/100$ )
Rare ( $\geq 1/10,000$ to $< 1/1,000$ )
Very rare ( $< 1/10,000$ )
Not known (cannot be estimated from the available data)

*[Use MedDRA system organ classes (SOCs). The frequency of individual undesirable effects should be stated where possible. The order of presentation should be (1) classical side effects like e.g. anaphylaxis (which should be listed with all observed symptoms in the SOC Immune System Disorders/ subheading anaphylactic reactions) (2) side effects due to radiation exposure.]*

*[The following statement should be included in this section of each radiopharmaceutical:]* Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary

defects. *[For diagnostic agents:]* As the effective dose is [...] mSv when the maximal recommended activity of [...] MBq is administered these adverse events are expected to occur with a low probability. *[For therapeutic agents:]* The radiation dose resulting from therapeutic exposure may result in higher incidence of cancer and mutations *[specify if known]*. In all cases it is necessary to ensure that the risks of the radiation are less than from the disease itself. *[If applicable:]* The effective dose is [...] mSv when the maximal recommended activity of [...] MBq is administered.

*[If applicable:]* Paediatric population

#### 4.9 Overdose

*[Brief, appropriate and useful statements should be included. Although overdose is unlikely when a radiopharmaceutical is administered by authorised personnel, the opportunities available to reduce excessive radiation exposure should be outlined. E.g: ]*

In the event of administration of a radiation overdose with [...] the absorbed dose to the patient should be reduced where possible by increasing the elimination of the radionuclide from the body by frequent micturition *[if applicable:]* and defecation *[or:]* by forced diuresis and frequent bladder voiding. It might be helpful to estimate the effective dose that was applied.

*[If applicable:]* Paediatric population

### 5. PHARMACOLOGICAL PROPERTIES

#### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: {group}, ATC code: {code} <not yet assigned>

<Mechanism of action>

<Pharmacodynamic effects>

*[If applicable:]* At the chemical concentrations used for diagnostic examinations, [...] does not appear to have any pharmacodynamic activity.

#### Indication A

...

#### Indication B

...

*[Statements should be appropriate to the concentrations of radiopharmaceutical and excipients administered by the advised route.]*

<Clinical efficacy and safety>

<Paediatric population>

<The European Medicines Agency has waived the obligation to submit the results of studies with {(Invented) Name} in all subsets of the paediatric population in {condition as per Paediatric Investigation Plan (PIP) decision, in the granted indication} (see section 4.2 for information on paediatric use).>

<The European Medicines Agency has deferred the obligation to submit the results of studies with {(Invented) Name} in one or more subsets of the paediatric population in {condition, as per Paediatric Investigation Plan (PIP) decision in the granted indication} (see section 4.2 for information on paediatric use).>

<This medicinal product has been authorised under a so-called ‘conditional approval’ scheme.

This means that further evidence on this medicinal product is awaited.

The European Medicines Agency will review new information on the product every year and this SmPC will be updated as necessary.>

<This medicinal product has been authorised under ‘exceptional circumstances’.  
This means that due to <the rarity of the disease> <for scientific reasons> <for ethical reasons> it has not been possible to obtain complete information on this medicinal product.  
The European Medicines Agency will review any new information which may become available every year and this SmPC will be updated as necessary.>

## **5.2 Pharmacokinetic properties**

### Distribution

...

### Organ uptake

...

### Elimination

...

*[State major metabolic pathway for clearance]*

### Half-Life

...

*[State biological half-life and effective half-life (including biological and physical half-lives)]*

*[The provided data should relate entirely to the human species.]*

*[If applicable:]* Paediatric population

## **5.3 Preclinical safety data**

*[The LD<sub>50</sub> should be replaced by a safety factor or NOED.]*

Toxicological studies with [mice/rats] have demonstrated that with a single [IV injection] of [...] and [...] mg/kg no deaths were observed. Toxicity with repeated administration of [...] mg/kg/day over [...] days in ... [rats] ... was not observed. This agent is not intended for regular or continuous administration.

*[If applicable:]* Mutagenicity studies und long-term carcinogenicity studies have not been carried out.

<Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.>

<Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.>

<Adverse reactions not observed in clinical studies, but seen in animals at exposure levels similar to clinical exposure levels and with possible relevance to clinical use were as follows:>

<Environmental Risk Assessment (ERA)>

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

*[Product specific]*

### **6.2 Incompatibilities**

*[Product specific]*

<Not applicable.>

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

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



### 6.3 Shelf life

*[Shelf life after radiolabelling and first opening should be provided here.]*

<...> <6 months> <...> <1 year> <18 months> <2 years> <30 months> <3 years> <...>

### 6.4 Special precautions for storage

*[Storage conditions are product specific and are defined during the marketing authorisation procedure.]*

For storage conditions of the <reconstituted> <diluted> medicinal product, see section 6.3. Storage of radiopharmaceuticals should be in accordance with national regulation on radioactive materials.

### 6.5 Nature and contents of container <and special equipment for use, administration or implantation>

*[Product specific, it should be specified here and in the labelling if multidose or for single use only. This information of multidose/single use is also to be included in the labelling.]*

<Not all pack sizes may be marketed.>

### 6.6 Special precautions for disposal <and other handling>

*[Only for kits for radiopharmaceutical preparation:]* The content of the kit before extemporaneous preparation is not radioactive. However, after *[e.g. sodium pertechnetate (<sup>99m</sup>Tc) Injection, Ph. Eur.]* is added, adequate shielding of the final preparation must be maintained.

*[This section should include, where appropriate, precautions for relatives, carers and hospital staff:]*

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.

*[In case of administration of higher activities:]* This preparation is likely to result in a relatively high radiation dose to most patients. The administration of [...] may result in significant environmental hazard. This may be of concern to the immediate family of those individuals undergoing treatment or the general public depending on the level of activity administered. Suitable precautions in accordance with national regulations should be taken concerning the activity eliminated by the patients in order to avoid any contaminations.

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

<No special requirements.>

## 7. MARKETING AUTHORISATION HOLDER

{Name and address}

<{tel}>

<{fax}>

<{e-mail}>

## 8. MARKETING AUTHORISATION NUMBER(S)

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<{DD/MM/YYYY}> <{DD month YYYY}>

## 10. DATE OF REVISION OF THE TEXT

{MM/YYYY}

**<11. DOSIMETRY>**

*[For radiopharmaceutical kits the physical half-life of the radionuclide with a summary of the energies of the principal particle and photon emissions should be stated in the first paragraph of this section. E.g. for technetium (<sup>99m</sup>Tc) labelled radiopharmaceuticals:]*

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

*[In the second paragraph of this section the biokinetic model used for the ICRP calculations of radiation exposure should be stated shortly: ]*

The data listed below are from ICRP [*insert volume number*] and are calculated according to the following assumptions: [...]

*[Tabulated data should be included on dosimetry as established from biodistribution studies in man preferably cited from ICRP [volume number]. If for a new radiopharmaceutical a citation from the ICRP is not possible new data should be provided with the respective model.]*

Organ	Dose absorbed per activity administered [mGy/MBq]				
	Adults	15 year old	10 year old	5 year old	1 year old
[...]	[...]	[...]	[...]	[...]	[...]
[...]	[...]	[...]	[...]	[...]	[...]
<b>Effective dose</b> [mSv/MBq]	[...]	[...]	[...]	[...]	[...]

*[The following statement should be included after the table:]*

*[For diagnostic agents:]* The effective dose resulting from the administration of a (maximal recommended) activity of [...] MBq [...] for an adult weighing 70 kg is about [...] mSv. For an administered activity of [...] MBq the typical radiation dose to the target organ [*specify which*] is [...] mGy and the typical radiation dose/doses to the critical organ/organs [*specify which*] is/are Z1 Z2 etc. mGy, respectively.

*[For therapeutic agents:]* Radiation dose to specific organs, which may not be the target organ of therapy, can be influenced significantly by pathophysiological changes induced by the disease process. This should be taken into consideration when using the following information. For an administered activity of [...] MBq the typical radiation dose to the target organ [*specify which*] is [...] mGy and the typical radiation dose/doses to the critical organ/organs [*specify which*] is/are Z1 Z2 etc. mGy, respectively.

**12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS**

*Section 12 is designated to describe the dilution of a ready-to-use (multidose) radiopharmaceutical or the reconstitution of a kit radiopharmaceutical with the eluate of a generator containing the radionuclide. The required quality control should be included if required.*

As with any pharmaceutical product, if at any time in the preparation of this product the integrity of this vial is compromised it should not be used.

*[For ready-to-use radiopharmaceuticals:]*

*[Instructions on the dilution of the ready-to-use radiopharmaceutical before administration could be given here (e. g. with 9 mg/ml sodium chloride solution). Information on the appearance of the diluted parenteral solution should appear here.]*

*[For kits for radiopharmaceutical preparation]*

**Method of preparation**

*[Instructions on reconstitution/extemporary preparation of the medicinal product before administration should be included here.*

*Information on the appearance of the reconstituted parenteral solution should appear here.]*

*[Section 12 is also designated to describe the extemporaneous preparation of radiopharmaceuticals which requires several steps.]*

**Quality control**

*[This section should describe convenient method(s) for quality control of the radiopharmaceutical which could be carried out in any nuclear medicine centre or radiopharmacy, for example, the way to check the rate of radionuclide labelling in case of doubt or when it is performed periodically or systematically.]*

*[Additional requirements for diluents, etc. should appear here.]*

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