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Guideline on core SmPC and Package Leaflet for (^{68}Ge/^{68}Ga) generator

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Executive summary

This guideline describes the information to be included in the Summary of Products Characteristics (SmPC) and package leaflet for (^{68}Ge/^{68}Ga) generator.

1. Introduction (background)

The purpose of this core SmPC and package leaflet is to provide applicants and regulators with harmonised guidance on the information to be included in the Summary of product characteristics (SmPC) for (^{68}Ge/^{68}Ga) generator [1]. This guideline should be read in conjunction with the core SmPC and package leaflet for Radiopharmaceuticals, the QRD product information templates and the guideline on Summary of Product Characteristics.

This core SmPC has been prepared on the basis of national SmPCs, and taking into account the published scientific literature. Any marketing authorisation application or variation of a marketing authorisation for a radiopharmaceutical product containing a (^{68}Ge/^{68}Ga) generator should be accompanied by the required documents for the application to be valid.

The indications in section 4.1 are provided as clinical settings sufficiently documented at the time of publication of this core SmPC. However, this list of clinical settings does not waive the need to submit the required studies to support the claimed indication or an extension of indication.

2. Scope

This core SmPC and package leaflet covers (^{68}Ge/^{68}Ga) generator.

3. Legal basis

This guideline has to be read in conjunction with Article 11 of Directive 2001/83 as amended, and the introduction and general principles (4) and part I of the Annex I to Directive 2001/83 as amended.

4. Core SmPC and Package Leaflet for (^{68}Ge/^{68}Ga) generator

[1]Concept paper on the harmonisation and update of the clinical aspects in the authorised conditions of use for radiopharmaceuticals and other diagnostic medicinal products (EMEA/CHMP/EWP/12052/2008)

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

<▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.> [For medicinal products subject to additional monitoring ONLY]

1. NAME OF THE MEDICINAL PRODUCT

{(Invented) name strength} radionuclide generator

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

The radionuclide generator contains germanium (^{68}Ge) as mother nuclide which decays to the daughter nuclide gallium (^{68}Ga). The germanium (^{68}Ge) used for the production of the (^{68}Ge/^{68}Ga) generator is carrier-free. The total radioactivity due to germanium (^{68}Ge) and gamma-ray-emitting impurities is not more than 0.001%.
The {(Invented) name strength radionuclide generator} is a system for the elution of gallium (^{68}Ga) chloride solution for radiolabelling in accordance with Ph. Eur. 2464. This solution is eluted from a column on which the mother nuclide germanium (^{68}Ge), parent of gallium (^{68}Ga), is fixed. The system is shielded. Physical characteristics of both mother and daughter nuclides are summarized in table 1.

Table 1: Physical characteristics of germanium (^{68}Ge) and gallium (^{68}Ga)

	^{68}Ge	**^{68}Ga**
Half-live	270.95 days	67.71 minutes
Type of physical decay	Electron capture	Positron emission
X-rays	9.225 (13.1%) 9.252 (25.7%) 10.26 (1.64%) 10.264 (3.2%) 10.366 (0.03%)	8.616 (1.37%) 8.639 (2.69%) 9.57 (0.55%)
Gamma-rays		511 keV (178.28%) 578.55 keV (0.03%) 805.83 keV (0.09%) 1,077.34 keV (3.22%) 1,260.97 keV (0.09%) 1,883.16 keV (0.14%)
beta+		Energy max. Energy 352.60 keV 821.71 keV (1.20%) 836.00 keV 1,899.01 keV (87.94%)

Data derived from nudat (www.nndc.bnl.gov)

5 mL of the eluate contains a potential maximum of [X] MBq of ^{68}Ga and [X] kBq of ^{68}Ge *[Product specific]* (0.001 % breakthrough in the eluate). This corresponds to [X] ng of gallium and [X] ng of germanium *[Product specific]*.

The quantity of gallium (^{68}Ga) chloride solution for radiolabelling Ph. Eur. that may be eluted from the generator is dependent on the quantity of germanium (^{68}Ge) present, the volume of eluent used (typically [...] mL) and the lapsed time since the previous elution. If mother and daughter nuclides are in equilibrium, more than 60 % of the present gallium (^{68}Ga) can be eluted.

Table 2 summarizes the activity on the generator and the activity obtained by elution at the start of the shelf-life and at the end of the shelf-life.

Table 2: activity on the generator and activity obtained by elution

Strength	Activity inside the generator at the start of shelf-life	Activity inside the generator at the end of shelf-life	Eluted activity at the start of shelf-life*	Eluted activity at the end of shelf-life*
[Product specific]				

*NLT = not less than * in equilibrium*

More detailed explanations and examples for elutable activities at various time points are given in section 12.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Radionuclide generator
[Appearance product specific]

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is not intended for direct use in patients.

The eluate from the radionuclide generator () is indicated for *in vitro* labelling of various kits for radiopharmaceutical preparation developed and approved for radiolabelling with such solution to be used for positron emission tomography (PET) imaging.

4.2 Posology and method of administration

This medicinal product is for use in designated nuclear medicine facilities only, and should only be handled by specialists experienced with *in vitro* radiolabelling.

Posology

The quantity of the eluate gallium (^{68}Ga) chloride solution required for radiolabelling and the quantity of ^{68}Ga-labelled medicinal product that is subsequently administered will depend on the medicinal product that is radiolabelled and its intended use. Refer to the Summary of Product Characteristics/package leaflet of the particular medicinal product to be radiolabelled.

Paediatric population

Please refer to the Summary of Product Characteristics/package leaflet of the ^{68}Ga-labelled medicinal product for more information concerning its paediatric use.

Method of administration

The gallium (^{68}Ga) chloride solution is not intended for direct use in patients but is used for in vitro radiolabelling of various kits for radiopharmaceutical preparation. The route of administration of the final medicinal product should be adhered to.

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

4.3 Contraindications

Do not administer gallium (^{68}Ga) chloride solution directly to the patient.

The use of ^{68}Ga-labelled medicinal products is contraindicated in case ofhypersensitivity to the active substance or to any of the excipients listed in section 6.1.

For information on contraindications to particular ^{68}Ga-labelled medicinal products prepared by radiolabelling with gallium (^{68}Ga) chloride solution, refer to the Summary of Product Characteristics/package leaflet of the particular medicinal product to be radiolabelled.

4.4 Special warnings and precautions for use

Gallium (^{68}Ga) chloride solution is not to be administered directly to the patient but is used for in vitro radiolabelling of various kits for radiopharmaceutical preparation.

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 information.

General warnings
For information concerning special warnings and special precautions for use of ^{68}Ga-labelled medicinal products refer to the Summary of Product Characteristics/package leaflet of the medicinal product to be radiolabelled.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies of gallium (^{68}Ga) chloride solution with other medicinal products have been performed, because it is for radiolabelling of medicinal products.

For information concerning interactions associated with the use of ^{68}Ga-labelled medicinal products refer to the Summary of Product Characteristics/package leaflet of the medicinal product to be radiolabelled.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential
When an administration of radioactive medicinal products 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.

Breast-feeding
Before administering a radioactive medicinal product to a mother who is breast-feeding, consideration should be given to whether the investigation could be reasonably delayed until the mother has ceased

breast-feeding. If the administration is considered necessary, breast-feeding should be interrupted and the expressed feeds discarded.

Further information concerning the use of a ^{68}Ga-labelled medicinal product in pregnancy and breast-feeding is specified in the Summary of Product Characteristics/package leaflet of the medicinal product to be radiolabelled.

Fertility
Further information concerning the use of a ^{68}Ga-labelled medicinal product concerning fertility is specified in the Summary of Product Characteristics/package leaflet of the medicinal product to be radiolabelled.

4.7 Effects on ability to drive and use machines

Effects on ability to drive and use machines following administration of ^{68}Ga-labelled medicinal products will be specified in the Summary of Product Characteristics/package leaflet of the medicinal product to be radiolabelled.

4.8 Undesirable effects

Possible adverse reactions following the use of a ^{68}Ga-labelled medicinal product will be dependent on the specific medicinal product being used. Such information will be supplied in the Summary of product Characteristics/package leaflet of the medicinal product to be radiolabelled.

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.*

[*For the printed material, please refer to the guidance of the annotated QRD template.]

4.9 Overdose

Accidental administration of the eluate consisting of 0.1 mol/l hydrochloric acid may cause local venous irritation and, in case of paravenous injection, tissue necrosis. The catheter or affected area should be irrigated with isotonic saline solution.
No toxic effects are to be expected from the free ^{68}Ga after an inadvertent administration of the eluate. The administered free ^{68}Ga decays almost completely to stable ^{68}Zn within a short time (97% are decayed in 6 hours). During this time, ^{68}Ga is mainly concentrated in the blood/plasma (bound to transferrin) and in the urine. The patient should be hydrated to increase the excretion of the ^{68}Ga and forced diuresis as well as frequent bladder voiding is recommended.
Human radiation dose may be estimated using the information given in section 11.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other diagnostic radiopharmaceuticals, ATC code: V09X.

The pharmacodynamic properties of ^{68}Ga-labelled medicinal products prepared by radiolabelling with the generator eluate prior to administration will be dependent on the nature of the medicinal product to be labelled. Refer to the Summary of Product Characteristics/package leaflet of the product to be radiolabelled.

5.2 Pharmacokinetic properties

Gallium (^{68}Ga) chloride solution is not intended for direct use in patients but is used for in vitro radiolabelling of various kits for radiopharmaceutical preparation. Therefore, the pharmacokinetic properties of ^{68}Ga-labelled medicinal products will depend on the nature of the medicinal product to be radiolabelled.

5.3 Preclinical safety data

The toxicological properties of ^{68}Ga labelled medicinal products prepared by radiolabelling with gallium (^{68}Ga) chloride solution, prior to administration, will depend on the nature of the medicinal product to be radiolabelled.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Column matrix:
[Product specific]
Solution for elution:
[Product specific]

6.2 Incompatibilities

Radiolabelling of carrier molecules with gallium (^{68}Ga) chloride is very sensitive to the presence of trace metal impurities.It is important that all glassware, syringe needles etc., used for the preparation of the radiolabelled medicinal product are thoroughly cleaned to ensure freedom from such trace metal impurities. Only syringe needles (for example, non-metallic) with proven resistance to dilute acid should be used to minimise trace metal impurity levels.

It is recommended not to use uncoated chlorobutyl stoppers for the elution vial as they may contain considerable amounts of zinc that is extracted by the acidic eluate.

6.3 Shelf life

Radionuclide generator: [..] months from calibration date. *[Product specific]*
The calibration date and the expiry date are stated on the label.
Gallium (^{68}Ga) chloride eluate: After elution, immediately use the eluate.

6.4 Special precautions for storage

Radionuclide generator: Do not store above [..] °C. *[Product specific]*

Storage of radiopharmaceuticals should be in accordance with national regulations on radioactive materials.

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

[Product specific]

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 licenses 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 generator must not be disassembled for any reason as this may damage the internal components and possibly lead to a leak of radioactive material. Also, disassembly of the casing will expose the lead shielding to the operator.

Administration procedures should be carried out in a way to minimize risk of contamination of the medicinal product and irradiation of the operators. Adequate shielding is mandatory.

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.

The residual activity of the generator must be estimated before disposal.

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

<Date of first authorisation: {DD month YYYY}>
<Date of latest renewal: {DD month YYYY}>

10. DATE OF REVISION OF THE TEXT

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

11. DOSIMETRY

The radiation dose received by the various organs following intravenous administration of a ^{68}Ga-labelled medicinal product is dependent on the specific medicinal product being radiolabelled. Information on radiation dosimetry of each different medicinal product following administration of the radiolabelled preparation will be available in the Summary of Product Characteristics of the particular medicinal product.

The dosimetry tables 3 and 4 below are presented in order to evaluate the contribution of non-conjugated ^{68}Ga to the radiation dose following the administration of ^{68}Ga-labelled medicinal product or resulting from an inadvertent intravenous injection of gallium (^{68}Ga) chloride solution.

The dosimetry estimates were based on a rat distribution study and the calculations were effected using OLINDA - Organ Level INternal Dose Assessment Code. Time points for measurements were 5 minutes, 30 minutes, 60 minutes, 120 minutes and 180 minutes.

Table 3: Absorbed dose per unit activity administered –inadvertent administration in women

	Absorbed dose per administered unit of activity (mGy/MBq)					
Organ	**Adult (57 kg)**	**15 years (50 kg)**	**10 years (30 kg)**	**5 years (17 kg)**	**1 year (10 kg)**	**Newborn (5 kg)**
Adrenals	0.0114	0.0112	0.0164	0.0238	0.0403	0.0782
Brain	0.0180	0.0159	0.0176	0.0206	0.0292	0.0667
Breasts	0.0059	0.0058	0.0110	0.0163	0.0269	0.0545
Gallbladder Wall	0.0096	0.0092	0.0127	0.0201	0.0390	0.0750
Lower large intestine Wall	0.0032	0.0032	0.0050	0.0077	0.0133	0.0292
Small Intestine	0.0039	0.0039	0.0062	0.0099	0.0178	0.0376
Stomach Wall	0.0057	0.0056	0.0088	0.0133	0.0250	0.0502
Upper large intestine Wall	0.0040	0.0039	0.0067	0.0104	0.0199	0.0425
Heart Wall	0.1740	0.1940	0.3010	0.4830	0.8730	1.7200
Kidneys	0.0385	0.0421	0.0600	0.0888	0.1600	0.4150
Liver	0.0972	0.0974	0.1480	0.2200	0.4270	0.9890
Lungs	0.1860	0.2240	0.3190	0.4930	0.9840	2.7100
Muscle	0.0073	0.0076	0.0131	0.0319	0.0622	0.0954
Ovaries	0.0188	0.0203	0.0566	0.0988	0.2250	0.4590
Pancreas	0.0187	0.0218	0.0406	0.0547	0.1120	0.3400
Red Marrow	0.0225	0.0256	0.0415	0.0777	0.1770	0.5710
Osteogenic Cells	0.1160	0.1140	0.1840	0.3100	0.7350	2.3500
Skin	0.0029	0.0029	0.0044	0.0067	0.0122	0.0271
Spleen	0.0055	0.0056	0.0086	0.0130	0.0238	0.0492
Thymus	0.0100	0.0102	0.0133	0.0190	0.0297	0.0570
Thyroid	0.2210	0.2980	0.4600	1.0200	1.9300	2.6300
Urinary Bladder Wall	0.0023	0.0022	0.0038	0.0063	0.0110	0.0222
Uterus	0.0792	0.0802	1.3400	2.0300	3.6900	1.4700
Total Body	0.0177	0.0178	0.0289	0.0468	0.0920	0.2340
Effective Dose (mSv/MBq)	0.0483	0.0574	0.1230	0.2090	0.4100	0.7170

Table 4: Absorbed dose per unit activity administered – inadvertent administration in men

	Absorbed dose per administered unit of activity (mGy/MBq)					
Organ	**Adult (70 kg)**	**15 years (50 kg)**	**10 years (30 kg)**	**5 years (17 kg)**	**1 year (10 kg)**	**Newborn (5 kg)**
Adrenals	0.0093	0.0112	0.0165	0.0235	0.0377	0.0749
Brain	0.0134	0.0137	0.0148	0.0170	0.0241	0.0563
Breasts	0.0062	0.0074	0.0142	0.0213	0.0350	0.0725
Gallbladder Wall	0.0081	0.0096	0.0137	0.0213	0.0409	0.0803
Lower large intestine Wall	0.0015	0.0020	0.0031	0.0051	0.0091	0.0204
Small Intestine	0.0022	0.0029	0.0048	0.0080	0.0146	0.0309
Stomach Wall	0.0048	0.0066	0.0099	0.0153	0.0287	0.0560
Upper large intestine Wall	0.0027	0.0033	0.0058	0.0094	0.0182	0.0385
Heart Wall	0.3030	0.3930	0.6110	0.9830	1.7800	3.4900

Kidneys	0.0198	0.0241	0.0345	0.0510	0.0911	0.2310
Liver	0.0766	0.1030	0.1570	0.2330	0.4500	1.0400
Lungs	0.1340	0.2000	0.2850	0.4390	0.8720	2.3800
Muscle	0.0051	0.0074	0.0129	0.0326	0.0636	0.0961
Pancreas	0.0187	0.0257	0.0480	0.0646	0.1310	0.4030
Red Marrow	0.0138	0.0154	0.0243	0.0441	0.0980	0.3110
Osteogenic Cells	0.0431	0.0558	0.0901	0.1510	0.3560	1.1300
Skin	0.0020	0.0024	0.0036	0.0057	0.0103	0.0232
Spleen	0.0041	0.0056	0.0084	0.0130	0.0227	0.0469
Testes	0.0011	0.0018	0.0075	0.0094	0.0138	0.0239
Thymus	0.0139	0.0158	0.0194	0.0276	0.0417	0.0794
Thyroid	0.1980	0.3250	0.5020	1.1200	2.1100	2.8800
Urinary Bladder Wall	0.0011	0.0013	0.0022	0.0039	0.0070	0.0152
Total Body	0.0115	0.0147	0.0237	0.0383	0.0748	0.1900
Effective Dose (mSv/MBq)	0.0338	0.0506	0.0756	0.1340	0.2600	0.5550

The effective dose resulting from an accidental intravenously injected activity of 250 MBq is 12.1 mSv for a 57-kg female adult and 8.45 mSv for a 70-kg male adult.

Data on the radiation dose to patients of gallium (^{68}Ga) citrate listed in the table 5 below are from ICPR 53 and may be used to estimate distribution after inadvertent application of unbound ^{68}gallium from the generator eluate, even though the data were obtained using a different salt.

Table 5: Absorbed dose per unit activity inadvertent administration of gallium (^{68}Ga) citrate

	Absorbed dose per administered unit of activity (mGy/MBq)				
Organ	**Adult**	**15 years**	**10 years**	**5 years**	**1 year**
Adrenals	0.034	0.044	0.064	0.088	0.140
Bone surface	0.037	0.048	0.080	0.140	0.310
Breast	0.014	0.014	0.023	0.037	0.074
Lower large intestine Wall	0.018	0.022	0.036	0.059	0.110
Small Intestine	0.064	0.080	0.140	0.230	0.450
Stomach Wall	0.014	0.017	0.027	0.044	0.084
Upper large intestine Wall	0.053	0.064	0.110	0.180	0.360
Kidneys	0.026	0.032	0.046	0.068	0.120
Liver	0.027	0.035	0.053	0.079	0.150
Lungs	0.013	0.016	0.025	0.041	0.080
Pancreas	0.014	0.018	0.029	0.047	0.089
Red Marrow	0.046	0.064	0.110	0.210	0.450
Spleen	0.036	0.051	0.080	0.130	0.240
Testes	0.013	0.015	0.024	0.039	0.077
Thyroid	0.012	0.015	0.025	0.042	0.081
Urinary Bladder Wall	0.014	0.016	0.026	0.044	0.081
Other tissue	0.013	0.015	0.025	0.041	0.080
Effective Dose (mSv/MBq)	0.027	0.034	0.056	0.095	0.190

External radiation exposure

[Product specific].

The average surface or contact radiation for the (^{68}Ge/^{68}Ga) radionuclide generator is less than [..] µSv/h per MBq of ^{68}Ge. For example, a [..] GBq generator will reach a maximum surface dose rate of ..] µSv/h. It is generally recommended that the generator is stored within auxiliary shielding to minimize dose to operating personnel.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Elution of the generator must be performed in premises complying with the national regulations concerning the safety of use of radioactive products.

Elution should be performed under aseptic conditions.

Preparation
[Product specific]

Quality control
Clarity of the solution, pH and the radioactivity must be checked before radiolabelling.

^{68}Ge breakthrough *[Product specific]*
A small amount of ^{68}Ge is washed from the column with each elution. ^{68}Ge breakthrough is expressed as a percentage of total ^{68}Ga eluted from the column, corrected for decay. The ^{68}Ge breakthrough is not more than 0.001 % of the eluted ^{68}Ga activity. The breakthrough for this generator typically begins as low as [….] % at the point of release and may rise slightly with the number of elutions. To keep the breakthrough low, the generator should be eluted at least once per working day. When used according to these instructions, the breakthrough should stay below 0.001 % for 12 months. For testing the ^{68}Ge breakthrough the activity level of the ^{68}Ga and the ^{68}Ge in the eluate should be compared. For further details please refer to Ph. Eur. monograph 2464.

Warning: Breakthrough of ^{68}Ge can increase above 0.001 % if the generator is not eluted for more than 2 days. If the generator has not been used for 3 days or more, it should be pre-eluted with 10 mL of sterile ultrapure 0.1 mol/l hydrochloric acid 7 - 24 hours prior to the intended use.

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu<, and on the website of {name of MS Agency (link)}>.

PACKAGE LEAFLET

Package leaflet: Information for the patient

{(Invented) name strength} radionuclide generator

Gallium (^{68}Ga) chloride solution

< ▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.> [For medicinal products subject to additional monitoring ONLY]

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

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your nuclear medicine doctor who will supervise the procedure.
- If you get any side effects talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What {(Invented) name} is and what it is used for.
2. What you need to know before the gallium (^{68}Ga) chloride solution obtained with {(Invented) name} is used.
3. How gallium (^{68}Ga) chloride solution obtained with {(Invented) name} is used.
4. Possible side effects
5. How {(Invented) name} is stored
6. Contents of the pack and other information

1. What {(Invented) name} is and what it is used for

This medicine is a radiopharmaceutical product not intended for direct use in patients.
{(Invented) name} is a germanium (^{68}Ge)/gallium (^{68}Ga) radionuclide generator, a device used to obtain a solution of gallium (^{68}Ga) chloride.

The obtained gallium (^{68}Ga) chloride solution is used for radiolabelling, a technique in which a substance is tagged (radiolabelled) with a radioactive compound, here ^{68}Ga.

{(Invented) name} is used to label certain medicines that have been specially developed and approved for the use with the active substance gallium (^{68}Ga) chloride. These medicines act as carriers to take the radioactive ^{68}Ga to where it is needed. These may be substances that have been designed to recognise a particular type of cell in the body, including tumour cells (cancer). The low amount of radioactivity administered can be detected outside of the body by special cameras to obtain images of the body. Please refer to the package leaflet of the medicine that is to be radiolabelled with gallium (^{68}Ga) chloride.

The nuclear medicine doctor will explain to you what type of examination will be performed with this product.

The use of a ^{68}Ga-labelled medicinal product does involve exposure to small amounts of radioactivity. Your doctor and the nuclear medicine doctor have considered that the clinical benefit that you will obtain from the procedure with the radiopharmaceutical overcomes the risk due to radiation.

2. What you need to know before the gallium (^{68}Ga) chloride solution obtained with {(Invented) name} is used

The gallium (^{68}Ga) chloride solution obtained with {(Invented) name} must not be used

- if you are allergic to gallium (^{68}Ga) chloride or any of the other ingredients of this medicine (listed in section 6).

If you are using a ^{68}Ga-labelled medicinal product, you should read information on contraindications in the package leaflet of the product to be radiolabelled.

Warnings and precautions

For information concerning special warnings and special precautions for use of ^{68}Ga labelled medicinal products please refer to the Package Leaflet of the medicinal product to be radiolabelled.

Children and adolescents

Please speak to your nuclear medicine doctor if you or your child are under 18 years old.

Other medicines and gallium (^{68}Ga) chloride solution

Tell your nuclear medicine doctor if you are taking, have recently taken or might take any other medicines since they may interfere with the interpretation of the images.

It is not known whether gallium (^{68}Ga) chloride solution may interact with other medicines as specified studies have not been carried out.

For information concerning interactions associated with the use of ^{68}Ga-labelled medicinal products refer to the Package Leaflet of the medicinal product to be radiolabelled.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your nuclear medicine doctor for advice before you are given medicines radiolabelled with {(Invented) name}.

You must inform the nuclear medicine doctor before the administration of medicines radiolabelled with {(Invented) name} if there is a possibility you might be pregnant, if you have missed your period or if you are breast-feeding.

When in doubt, it is important to consult your nuclear medicine doctor who will supervise the procedure.

<u>If you are pregnant</u>

The nuclear medicine doctor will only administer this medicine during pregnancy if a benefit is expected which would outweigh the risks.

<u>If you are breast-feeding</u>

You will be asked to stop breast-feeding. Please ask your nuclear medicine doctor when you can resume breast-feeding.

Driving and using machines

There could be effects on your ability to drive and to use machines due to the medicine used in combination with {(Invented) name}. Please read the package leaflet of that medicine carefully.

3. How gallium (^{68}Ga) chloride solution obtained with {(Invented) name} is used

There are strict laws on the use, handling and disposal of radiopharmaceutical products. {(Invented) name} will only be used in special controlled areas. This product will only be handled and given to you by people who are trained and qualified to use it safely. These persons will take special care for the safe use of this product and will keep you informed of their actions.

The nuclear medicine doctor supervising the procedure will decide on the quantity of medicine radiolabelled with {(Invented) name} to be used in your case. It will be the smallest quantity necessary to achieve the appropriate outcome, depending on the final product and its intended use. Please read the package leaflet of the medicine that is to be radiolabelled for more information.

Administration of gallium (^{68}Ga) chloride solution and conduct of the procedure
You will not get the gallium (^{68}Ga) chloride solution, but another product radiolabelled with {(Invented) name}. Gallium (^{68}Ga) chloride solutionmust be used only in combination with another medicine which has been specifically developed and approved for being combined (radiolabelled) with {(Invented) name}. You will only be given the final radiolabelled product.

Duration of the procedure
Your nuclear medicine doctor will inform you about the usual duration of the procedure after the administration of the medicine radiolabelled with {(Invented) name}.

After administration of the medicine radiolabelled with {(Invented) name} has been performed
The nuclear medicine doctor will inform you if you need to take any special precautions after receiving the medicine radiolabelled with {(Invented) name}. Contact your nuclear medicine doctor if you have any questions.

If you have been given more medicine radiolabelled with {(Invented) name} than you should
An overdose is unlikely, because you will only receive the medicine radiolabelled with {(Invented) name} precisely controlled by the nuclear medicine doctor supervising the procedure. However, in the case of an overdose, you will receive the appropriate treatment.

Should you have any further question on the use of this product, please ask the nuclear medicine doctor who supervises the procedure.

4. Possible side effects

Like all medicines, the medicine radiolabelled with {(Invented) name} can cause side effects, although not everybody gets them.

After the medicine radiolabelled with {(Invented) name} is administered, it will deliver low amounts of ionising radiation with the least risk of cancer and hereditary abnormalities.

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

[*For the printed material, please refer to the guidance of the annotated QRD template.]

5. How {(Invented) name} is stored

You will not have to store this medicine. This medicine is stored under the responsibility of the specialist in appropriate premises. Storage of radiopharmaceuticals will be in accordance with national regulation on radioactive materials.

The following information is intended for the specialist only.
The radionuclide generator must not be used after the expiry date stated on the container after “EXP”.

Do not dismantle the case. Do not store above [::]°C. *[Product specific]*

The gallium (^{68}Ga) chloride solution obtained with {(Invented) name} must be used immediately.

6. Contents of the pack and other information

What {(Invented) name} contains
The active substance is gallium (^{68}Ga) chloride solution.

The other ingredients are: [..] (matrix) *[Product specific]*
[..] (solution for elution) *[Product specific]*

What {(Invented) name} looks like and contents of the pack
You will not need to obtain or handle this medicine.

Marketing Authorisation Holder and Manufacturer
{Name and address}
<{tel}>
<{fax}>
<{e-mail}>

This medicinal product is authorised in the Member States of the EEA under the following names:

Country	**Product name**

This leaflet was last revised in <{MM/YYYY}><{month YYYY}>.
<This medicine has been given 'conditional approval'. This means that there is more evidence to come about this medicine.
The European Medicines Agency will review new information on the medicine every year and this leaflet will be updated as necessary.>

<This medicine has been authorised under 'exceptional circumstances'. This means that <because of the rarity of this disease> <for scientific reasons> <for ethical reasons> it has been impossible to get complete information on this medicine.
The European Medicines Agency will review any new information on the medicine every year and this leaflet will be updated as necessary.>

<Other sources of information>

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu<, and on the website of {name of MS Agency (link)}>. <There are also links to other websites about rare diseases and treatments.>

<This leaflet is available in all EU/EEA languages on the European Medicines Agency website.>

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The following information is intended for medical or healthcare professionals only:

The complete SmPC of {(Invented) name } is provided <as a separate document> <as a tear-off section at the end of the printed leaflet> 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].