# Public Assessment Report

# Scientific discussion

# Galliapharm
# (Germanium ($^{68}$Ge) chloride, Gallium ($^{68}$Ga) chloride)

# DK/H/2294/001/DC

# Date: 28-10-2014

**This report includes a summary, on pages 10-12.**

**This module reflects the scientific discussion for the approval of Galliapharm. The procedure was finalised at June 18, 2014. For information on changes after this date please refer to the module 'Update'.**

# I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have granted a marketing authorisation for Galliapharm radionuclide generator, 0.74-1.85 GBq, from Eckert & Ziegler Radiopharma GmbH.

The medicinal product is not intended for direct use in patients.
The eluate (gallium (68Ga) chloride solution) is used for in vitro radiolabelling of specific carrier molecules which have been specifically developed and authorised for radiolabelling with this radionuclide to be used for diagnostic imaging with positron emission tomography (PET).
A comprehensive description of the indications and posology is given in the SmPC.

The marketing authorisation has been granted pursuant to Article 8.3 (mixed application) of Directive 2001/83/EC."

As this is considered a new active substance Galliapharm will be subject to additional monitoring.

# II. QUALITY ASPECTS

## II.1 Introduction

The finished product is a radionuclide generator. The generator consists of a pre-assembled column with adsorbed $^{68}$Ge onto titanium dioxide. $^{68}$Ge decays constantly under production of $^{68}$Ga. The generator is supplied with Germanium ($^{68}$Ge/$^{68}$Ga) activity amounts at activity reference time of 0.74 GBq, 1.11 GBq, 1.48 GBq or 1.85 GBq. $^{68}$Ga is eluted from the generator by using 0.1 N hydrochloride acid (typical volume for elution: 5 ml).

*Container/closure system:* The pre-assembled column is a glass column filled with titanium dioxide and sealed with polymer stoppers and tubing (primary packaging). The secondary packaging consists of a lead shielding enclosing the column inside a stainless steel case.

*Accessories for elution*: PP-bag with 250 ml 0.1 N HCl and parts for connecting the generator to the elution solution on the inlet side and to a synthesis module on the outlet side are provided (with tubings, fittings etc.).

Compliance with Good Manufacturing Practice
The RMS has been assured that acceptable standards of GMP (see Directive 2003/94/EC) are in place for this product type at all sites responsible for the manufacturing of the active substance as well as for the manufacturing and assembly of this product prior to granting its national authorisation.

## II.2 Drug Substance

International Non-proprietary Name (INN): not available
Chemical name: $^{68}$Germanium chloride / $^{68}$Gallium chloride

Molecular Formula: [$^{68}$Ge]$GeCl_4$ / [$^{68}$Ga]$GaCl_3$
Molecular Weight: 209.74 g/Mol / 174.29 g/Mol
Structure: not applicable as the active substance is an inorganic substance

The active substance used in the $^{68}$Ge/$^{68}$Ga-generator is Germanium ($^{68}$Ge) chloride and Gallium ($^{68}$Ga) chloride in equilibrium. The radionuclides are no carrier-added.
$^{68}$Ge decays with a half-life of 270.95 d by electron capture into the short lived isotope $^{68}$Ga. The daughter nuclide 68Ga decays with a half-life of 67.71 min by positron emission to stable 68Zn.

The manufacture of 68Ge is performed by Cyclotron Co. Ltd, Obninsk, Russia by irradiation of Ga/Ni alloy as solid target with accelerated protons in a cyclotron. The manufacture of 68Ge solution is adequately described. The 68Ge solution is characterized considering the nuclear reactions using Ga/Ni alloy on copper. The active substance 68Ge in HCl solution is controlled by a specification with requirements to clarity, radionuclidic purity, radioactive concentration, chemical impurities, HCl concentration and residue of hexane. The analytical methods and the validation hereof by calibration/certification are presented. Batch analysis of 5 batches is provided. The presented specification for Ge-68 is acceptable to control the drug substance. The proposed shelf-life, 3 months without storage conditions is considered acceptable on the basis of the physical half-life.

### II.3 Medicinal Product

The composition of the product has been adequately described. The development of the product has generally been well-described. The choice of excipients is justified and their function explained.

The updated manufacturing process and controls have been in sufficient details. Process validation data are provided for four generators and the data demonstrates a robust and reproducible process, including process validation of the sterile-filtration step.

The product specifications have been adequately set in line with the Ph. Eur. monograph Gallium ($^{68}$Ga) chloride solution for injection which came into force from July 1$^{st}$ 2013. Validations of the analytical methods have been presented, and cross-evaluations of in-house methods against the Ph. Eur. methods are performed. Batch analysis has been performed on 7 batches. The three additional batch analysis results show that the finished products meet the specifications proposed.

The suitability of the primary packaging parts has been confirmed by extractables and leachables studies. Satisfactory specifications on primary packaging parts have been set.

The conditions used in the stability studies are not according to the ICH stability guideline, which is acceptable for this special kind of product. On the basis of the current stability data the following shelf-life/storage condition is acceptable: 12 months with the storage restriction ‘do not store above 25°C, Store in appropriate shielding in accordance with national provisions regarding radiation safety is acceptable. The eluate should be used immediately. The proposed shelf-life (18 months) for the ultrapure 0.1 N HCl solution in PP-bag is considered acceptable with the commitment to initiate a new stability study cf. ICH conditions.

The following shelf-life/storage conditions are acceptable on the basis of the current data presented:

- Generator: 12 months, do not store above 25 °C
- Eluate: Immediately use
- Sterile ultrapure 0.1N HCl solution in PP-bag: 18 months (committed to be confirmed by a new stability study cf. ICH conditions)

### II.4 Discussion on chemical, pharmaceutical and biological aspects

The active substance and finished product have been adequately described.
From a quality point of view, the benefit/risk ratio of the product is considered positive.

## III. NON-CLINICAL ASPECTS

### III.1 Introduction

No biopharmaceutical studies, no studies on the clinical pharmacology and no studies on efficacy is carried out, since Galliapharm is a radiopharmaceutical precursor and is not intended to be administered directly to the patient.

## III.2 Pharmacology

No pharmacology studies have been performed by the MAH in support of the current marketing authorisation for GalliaPharm. The lack of any specific studies on the pharmacology is acceptable. The MAH has provided summarised overview of the available literature on elemental gallium, gallium chloride and Gallium complexes lige Ga-EDTA and Ga-DOTA-TOC.

$^{68}$Ga decays in 89% by positron emission with a short half-life of 67.71 min, making it a potential radioisotope for PET-imaging. It decays to stable $^{68}$zinc. The total amount of accidentally administered $^{68}Ga^{3+}$, e.g. 5 mL eluate containing 1850 MBq $^{68}$Ga (1.2 ng gallium), would amount to 1.2 ng zinc by approximately 6 hours (5 half lives of 67.71 minutes). In the EMA guideline on limits residues on metal catalysts or reagents (EMEA/CHMP/SWP/4446/2000) permitted daily exposure (PDE) levels are specified, in which zinc is characterized as a class 3 metal (with minimal safety concern), and a PDE of 1300 µg/day.

The patient administered $^{68}$Ga through a radio-labelled medicinal product, will be exposed to radiation in a limited time frame, and the radioactive molecule $^{68}$Ga will decay to zinc in amounts far below what is allowed to be administered on a daily basis as a metal residue. The slight and transient heart rate decrease observed in cardiac cells after exposure to GaCl resulting in concentrations of $Ga^{3+}$ of 0.5, 2 and 8 ng/L (Leperre et al 1994), is not considered to be of any safety concern for patients receiving a $^{68}$Ga -labelled medicinal product. The $^{68}$Ga will be bound to a carrier molecule and the doses exceed any potential exposure with $^{68}$Ga from GalliaPharm.

The lack of any pharmacodynamic drug interaction studies with GaCl is acceptable, as the pharmacodynamic properties of the drug product to be labelled will be more relevant. As no carrier molecule has been defined in the current application, no relevant drug interaction studies can be suggested.

## III.3 Pharmacokinetics

As expected, following an intravenous injection, the maximum plasma concentration (based on observed radioactivity) was observed 5 minutes after injection (first sampling time point). Further samples (plasma and tissue) were obtained at 30, 60, 120, and 180 minutes after intravenous injection of diluted $^{68}$Ge/$^{68}$Ga-generator eluate. Diluted $^{68}$Ge/$^{68}$Ga-generator eluate with a total radioactivity of 47±4 MBq was administered to each animal.

In both males and females, the estimated terminal half life of $^{68}$Ga was 188 to 254 hours (male and females respectively), which is significantly longer than the physical half life of 67.71 minutes. This was attributed to a relative high plasma concentration measured at 180 minutes, which was that last sampling time point. A more accurate estimate may have been made, had the study design included more samples at later time points, e.g. including 6 hour post treatment, which corresponds to approximately 5 half lives of $^{68}$Ga. However, as the current study design has most likely resulted in overestimating the human exposure, there is no need for any further investigations.

The MAH's biodistribution study show that following intravenous injection of the $^{68}$Ge/$^{68}$Ga-generator eluate, $^{68}$Ga-radioactivity was cleared relatively slowly from blood circulation and excreted in the urine. $^{68}$Ga-radioactivity in the female genital organs (uterus and ovaries) was quite high, this was attributed to small sample size, however Uchino (1990) have previously observed higher concentrations of some elements, including iron in female rat organs. As $^{68}Ga^{3+}$ is transported into tissues in a similar way to $Fe^{3+}$, this may also explain some of the sex difference observed in the MAH's study.

The tissue distribution data from male and female rats was utilised to extrapolate human residence time and radiation dosimetry estimates. The MAH has provided the updated human radiation dosimetry data to reflect male and female respectively.

$^{68}$Ge radiation was also evaluated and showed low residual radioactivity in all organs, being highest in urine, liver, thyroids and spleen, respectively. The biodistribution study showed minimal the retention of $^{68}$Ge in bone. The biodistribution of intraperitoneally administered $GeCl_4$ in rats has been

reported by Sabbioni and co-workers (Sabbioni 2010). At 24 h post-exposure Ge was poorly retained in rat tissues (kidney, liver, intestine, femur, spleen and the heart were the organs with the highest Ge concentration). In the blood, Ge was rapidly cleared, being almost equally distributed between plasma and red blood cells. The excretion was mainly via the urine. The results obtained in the MAH's study are in accordance with the Sabbioni's results, except the low observed $^{68}$Ge-radioactivity in the bone.

The lack of any metabolism studies is acceptable, as the metabolism of the final radiolabelled medicinal product will depend on the medicinal product to be labelled. Furthermore the $^{68}$Ga will decay to $^{68}$Zn, with a half life of 67.71 minutes.

The excretion of the radiolabelled medicinal product will depend on the excretion of the medicinal product to be labelled. Unbound $^{68}$Ga will be excreted mainly through the urine.

The MAH has not supplied any literature on any pharmacokinetic drug interaction or any other pharmacokinetic studies, as they have not been able to identify any relevant studies.

## III.4 Toxicology

No specific non-clinical toxicity studies on the $^{68}$Ge/$^{68}$Ga eluate have been performed. Literature references have been quoted, and references to the single dose biodistribution study. The lack of any new studies is accepted

In order to justify the lack of nonclinical studies on $^{68}$Zn, the MAH has made references to the EMA guideline on limits residues on metal catalysts or reagents (EMEA/CHMP/SWP/4446/2000). Although the source of Zn exposure of the patients in the case of the current application is not as a residue, the 1.2 ng Zn following decay of $^{68}$Ga after the full dose of 1.2 ng $^{68}$Ga is well below the limit of 1300 µg/day Zn per day, allowed as a residue in medicinal products administered parenterally on a daily base to patients. As the amount of Zn that results after $^{68}$Ga decay is much smaller than what is allowed as a residue, the lack of any new studies and any toxicological evaluation of zinc exposure is accepted

No dedicated single dose toxicity studies have been performed in support of the current application. The MAH has provided a literature reference (Dudley and Levine, 1949), in which the toxicity of gallium lactate was investigated in rats and rabbits at doses up to 75 and 70 mg/kg gallium lactate, respectively. The lowest concentrations of gallium lactate administered were 15-20 mg/kg in rabbits and rats respectively, and LD50 values of 46 mg/kg (rat) and 43 mg/kg (rabbit) were specified. These doses are far in excess of the accidental exposure to the total 1.2 ng gallium per 5 mL eluate. Accidental injection of the 5 mL eluate would therefore result in a maximum single intravenous dose of 20 pg $^{68}$Ga/kg in a 60 kg person. Therefore, the quoted article has described toxicity following exposure to levels of gallium far exceeding the potential exposure from GalliaPharm, and there is no need for any new single dose toxicity studies.

The lack of any dedicated repeat-dose toxicity studies is acceptable, although no literature has been published on repeated treatment with $^{68}$Ga. With regards to gallium nitrate $LD_{50}$ values of 80 and 67.5 mg/kg has been reported for mice and rats respectively. In a study by Dudly and Levine, $LD_{50}$ following a single intravenous injection in rats was establisted to 46 mg/kg. The MAH attribute this to an increased excretion rate, as a 17 year old female showed increased excretion rate with reduced $^{67}$Ga retention and plasma levels, following repeated administrations of high doses (300 mg/m$^2$) of $^{67}$Ga.
With regards to the current application, as $^{68}GaCl_3$ is intended for the *in-vitro* radio-labelling of specific carriers for diagnostic PET-imaging, and any one patient would most likely only receive one treatment with $^{68}GaCl_3$. Therefore, the lack of any repeat-dose toxicity studies is acceptable.

The lack of any studies on genotoxicity is acceptable as according to Annex 1 Part III of Dir 2001/83/EC, in the specific case of a radiopharmaceutical precursor intended solely for radiolabelling purposes, mutagenicity studies on the radio-nuclide are not considered to be useful.

As $^{68}$Ga is intended for radio-labelling a pharmaceutical substance, prior to the patient undergoing a PET scan, GalliaPharm is not expected to be used repeatedly. Therefore no carcinogenicity studies are needed.

The lack of any dedicated reproductive studies performed by the MAH in support of the current application is acceptable. The MAH has found two reproductive toxicity studies have been performed with gallium sulphate and $^{68}$Ga-labelled human serum albumin ($^{68}$Ga-HSA) in hamsters and rabbits respectively. Ferm and Carpenter (1970) conclude that Ga-nitrate at a dose of 40 mg/kg is not a serious teratogen in their experiment. Lorenz et al (1970) actually recommend $^{68}$Ga-HSA for placentography in their summary.

$^{68}$Ga from GalliaPharm will be used as a radio-label of another medicinal product. As such, in the SmPC (4.6) for GalliaPharm, the MAH has specified that "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." Regardin breastfeeding and fertility, the GalliaPharm SmPC refer to the SmPC of the medicinal product to be radiolabelled. This is acceptable based on the provided literature, and in line with the core SmPC for radiopharmaceuticals.

The lack of any dedicated local tolerance studies performed by the MAH in support of the current application is acceptable. The MAH has cited literature, and has concluded that no local reactions are to be expected. However, $GaCl_3$ has been cited to cause marked localised reactions (attributed to formation of gallium hydroxide and protein precipitation) at the injection site, and no doses were stated. As $^{68}$Ga will be bound to the carrier molecule, this is unlikely to occur under treatment with a $^{68}$Ga-labelled medicinal product.
In case of accidental administration of the $^{68}$Ga eluate, the highly acidic nature (pH 1) of the eluate may cause local reactions of tissue damage and necrosis. As this can be determined based on the pH of the eluate, no need for any further animal studies to establish this risk is needed. It has been described in the SmPC, that the catheter or affected area should be irrigated/flushed with saline.

The lack of any studies with regards to antigenicity, immunotoxicity, dependence, metabolites or studies on impurities is acceptable, as the nature of the product does not warrant any such studies.

## III.5 Ecotoxicity/environmental risk assessment (ERA)

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. Any unused medicinal product or waste material must be disposed of in accordance with local requirements.
Additionally, according to the Guideline on the environmental risk assessment of medicinal products for human use (EMEA/CHMP/SWP/4447/00) an environmental risk assessment is not required, because inorganic salts representing electrolytes are considered not to pose a risk to the environment. Moreover, as the product is a radiopharmaceutical, the Product Information contains adequate relevant warnings and precautions regarding handling and disposal. Therefore, an ERA specifically addressing the effect of the 68Ge/68Ga-generator on the environment is not deemed necessary.
A justifying why an ERA has not been performed is accepted. As The MAH has sufficiently described why no ERA is needed, an experimentally determined LogKow is not necessary.

## III.6 Discussion on the non-clinical aspects

From a non-clinically point of view the benefit/risk ratio of the product is considered positive.

# IV. CLINICAL ASPECTS

## IV.1 Introduction

No biopharmaceutical studies, no studies on the clinical pharmacology and no studies on efficacy is carried out, since 68GaCL3 is a radiopharmaceutical precursor and is not intended to be administered directly to the patient. An overview of the most important clinical diagnostic indications and the 68Ga-complexes used has been performed.

## IV.2 Risk Management Plan

The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Galliapharm.

- Summary table of safety concerns as approved in RMP

| | |
|---|---|
| Important identified risks | Not applicable |
| Important potential risks | • Accidental direct use in patients<br>• $^{68}$Ge breakthrough |
| Missing information | Not applicable |

- Summary of Safety Concerns and Planned Risk Minimisation Activities as approved in RMP

| **Safety concern** | **Routine risk minimisation measures** |
|---|---|
| **Accidental direct use in patients** | Proposed text in SmPC<br>• Instruction / information / warning in section 2, 4.1, 4.2, 4.4, 5.2:<br>"not intended for direct use in patients"<br>• Contraindication in section 4.3:<br>"Do not administer gallium (68Ga) chloride solution directly to the patient."<br>• Instructions in case of accidental use in section 4.9:<br>"Accidental administration of the eluate consisting of 0.1 N 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 inactive $^{68}$Zn within a short time (97 % is 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."<br>• Information in case of accidental use in section 11:<br>"The dosimetry table below is 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 accidental intravenous injection of gallium ($^{68}$Ga) chloride solution." (Dosimetry table 1 provided in SmPC).<br>"For this product, 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." |

| Safety concern | Routine risk minimisation measures |
|---|---|
| | Radiopharmaceutical;<br>Receipt, use and administration restricted to authorized persons in designated clinical settings |
| **$^{68}$Ge breakthrough** | Proposed text in SmPC<br>• Instruction of extensive instructions in section 12.<br>• Information/warning in section 12:<br>"$^{68}$Ge breakthrough<br>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 0.0001 % 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 approx. 400 elutions or 12 months.<br><br>**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 0.1 N HCl 7 - 24 hours prior to the intended use."<br><br>Radiopharmaceutical;<br>Receipt, use and administration restricted to authorized persons in designated clinical settings |

### IV.3 Discussion on the clinical aspects

From a clinically point of view the benefit/risk ratio of the product is considered positive.

## V. USER CONSULTATION

The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the PIL was English.
The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

## VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

Galliapharm radionuclide generator, 0.74-1.85 GBq has a proven chemical-pharmaceutical quality.

No biopharmaceutical studies, no studies on the clinical pharmacology and no studies on efficacy is carried out, since 68GaCL3 is a radiopharmaceutical precursor and is not intended to be administered directly to the patient. An overview of the most important clinical diagnostic indications and the 68Ga-complexes used has been performed.

Agreement between Member States was reached during a written procedure. There was no discussion in the CMD(h). The Concerned Member States, concluded based on the data submitted, that the befit/risk of Galliapharm was positive. The decentralised procedure was finalised on June 18, 2014.
Galliapharm was authorised in Denmark on September 15, 2014.

**Summary of pharmacovigilance system master file (sPSMF)**
The MAH has provided written confirmation that systems and services are in place to ensure compliance with their pharmacovigilance obligations.

**Periodic Safety Update Report (PSUR)**
DK/H/2294/01/DC, Galliapharm, radionuclide generator, Germanium ($^{68}$Ge) chloride, Gallium($^{68}$Ga)chloride, is authorised via art. 8(3) of Directive 2001/83/EC.
The marketing authorisation holder shall submit the first periodic safety update report for this product within 6 months following authorisation. Subsequently, the marketing authorisation holder shall submit periodic safety update reports for this product in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal.

**Additional monitoring (Black Triangle)**
Medicines that are subject to additional monitoring are:

- medicines authorised after 1 January 2011 that contain a new active substance
- biological medicines for which there is limited post-marketing experience;
- medicines with a conditional approval or approved under exceptional circumstances;
- medicines for which the marketing-authorisation holder is required to carry out a postauthorisation safety study (PASS).

As this is considered as an application for a new active substance Galliapharm will be subject to additional monitoring.

**Follow-up measures**
The following post-approval commitments were made during the procedure:

- Eckert & Ziegler Radiopharma GmbH commits to perform a stability study on the 0.1 mol/l hydrochloric acid in 250 ml PP bags used to elute the GalliaPharm Radionuclide generator. The study is planned to begin within 6 months from the approval of the generator and will last for 18 months with the option for a prolongation to 24 months.
- Eckert & Ziegler Radiopharma GmbH commits to submit additional data supporting the pharmacokinetic table for 68Gallium citrate added to the SmPC.

# Summary Public Assessment Report

# non-generics

# Galliapharm
# (Germanium ($^{68}$Ge) chloride, Gallium ($^{68}$Ga) chloride)

# DK/H/2294/001/DC

# Date: 28-10-2014

# Summary Public Assessment Report

# Galliapharm

# Germanium (68Ge) chloride, Gallium (68Ga) chloride, radionuclide generator, 0.74-1.85 GBq.

This is a summary of the public assessment report (PAR) for Galliapharm. It explains how Galliapharm was assessed and its authorisation recommended as well as its conditions of use. It is not intended to provide practical advice on how to use Galliapharm.

For practical information about using Galliapharm, patients should read the package leaflet or contact their doctor or pharmacist.

**What is Galliapharm and what is it used for?**
This medicine is a radiopharmaceutical product for diagnostic use only.

The obtained gallium (68Ga) chloride solution is used for radiolabelling, a technique in which a substance is tagged (radiolabelled) with a radioactive compound, here 68Ga.
GalliaPharm is used to label certain medicines that have been specially developed for the use with the active substance gallium (68Ga) chloride. These medicines act as carriers to take the radioactive 68Ga 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.

**How does Galliapharm work?**
The effect of Galliapharm 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.

**How is Galliapharm used?**
The pharmaceutical form of Galliapharm is radionuclide generator.
Galliapharm is only to be used by specialists who have experience in radiolabelling. Galliapharm is never given directly to the patient.
GalliaPharm must be used only in combination with another medicine which has been specifically developed for being combined (radiolabelled) with GalliaPharm. Only the final radiolabelled product will be given to the patient.
Radiolabelling of a medicine takes place outside the body in a laboratory setting. The radiolabelled medicine is then given to the patient according to the instructions in that medicine's summary of product characteristics (SmPC).

Please read section 3 of the PL for detailed information on dosing recommendations, the route of administration, and the duration of treatment.

**What benefits of Galliapharm have been shown in studies?**
No biopharmaceutical studies, no studies on the clinical pharmacology and no studies on efficacy is carried out, since Galliapharm is a radiopharmaceutical precursor and is not intended to be administered directly to the patient. An overview of the most important clinical diagnostic indications and the 68Ga-complexes used has been performed.

These studies have shown that medicines radiolabelled with Galliapharm is effective in recognising particular type of cells in the body, including tumour cells (cancer).

**What are the possible side effects from Galliapharm?**
After the medicine radiolabelled with GalliaPharm is administered, it will deliver low amounts of ionising radiation with the least risk of cancer and hereditary abnormalities.

For the full list of all side effects reported with Galliapharm, see section 4 of the package leaflet.

Galliapharm must not be given directly to any patient. Medicines radiolabelled with Galliapharm should not be used in people who may be hypersensitive (allergic) to gallium (68Ga) chloride or any of the other ingredients.

For the full list of restrictions, see the package leaflet.

**Why is Galliapharm approved?**
The member states involved in the procedure concluded that Galliapharms's benefits are greater than its risks and recommended that it can be approved for use.

**What measures are being taken to ensure the safe and effective use of Galliapharm?**
A risk management plan has been developed to ensure that Galliapharm is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Galliapharm, including the appropriate precautions to be followed by healthcare professionals and patients.

This medicine is subject to additional monitoring. This will allow quick identification of new safety information. Known side effects are continuously monitored. Furthermore new safety signals reported by patients/healthcare professionals will be monitored/reviewed continuously as well.

**Other information about Galliapharm**
The marketing authorisation for Galliapharm was granted on September 15th 2014.

The full PAR and the package leaflet for Galliapharm can be found on the website http://mri.medagencies.org/Human/.
For more information about treatment with Galliapharm, read the package leaflet or contact your doctor or pharmacist.

This summary was last updated in 10-2014.