

## PRODUCT MONOGRAPH

### **Gallium (Ga 67) Citrate Injection**

Gallium (Ga 67) Citrate

Solution, 74 MBq/mL

Radiodiagnostic agent

Curium Canada Inc.  
2572 boul. Daniel-Johnson, Suite 245-249  
Laval, QC, H7T-2R3  
CANADA

Date of Revision: April 26<sup>th</sup>, 2019

Distributed by:  
Curium Canada Inc.  
Laval, QC, H7T-2R3  
CANADA

**CURIUM™**

**Control No: 225104**

## Table of Contents

<b>PART I: HEALTH PROFESSIONAL INFORMATION.....</b>	<b>3</b>
SUMMARY PRODUCT INFORMATION .....	3
DESCRIPTION.....	3
INDICATIONS AND CLINICAL USE .....	5
CONTRAINDICATIONS .....	5
WARNINGS AND PRECAUTIONS.....	5
ADVERSE REACTIONS.....	7
DRUG INTERACTIONS .....	7
DOSAGE AND ADMINISTRATION .....	7
RADIATION DOSIMETRY .....	8
OVERDOSAGE .....	9
ACTION AND CLINICAL PHARMACOLOGY .....	9
STORAGE AND STABILITY.....	10
SPECIAL HANDLING INSTRUCTIONS .....	10
DOSAGE FORMS, COMPOSITION AND PACKAGING .....	10
<b>PART II: SCIENTIFIC INFORMATION .....</b>	<b>11</b>
PHARMACEUTICAL INFORMATION.....	11
CLINICAL TRIALS .....	12
DETAILED PHARMACOLOGY .....	12
TOXICOLOGY .....	12
REFERENCES .....	13
<b>PART III: CONSUMER INFORMATION.....</b>	<b>14</b>

# Gallium (Ga 67) Citrate Injection

Gallium (Ga 67) Citrate

## PART I: HEALTH PROFESSIONAL INFORMATION

### SUMMARY PRODUCT INFORMATION

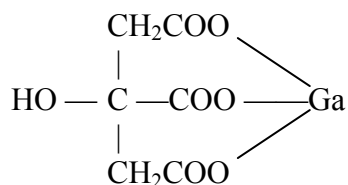
Route of Administration	Dosage Form / Strength	Clinically Relevant Non-medicinal Ingredients
Intravenous injection	Solution, 74 MBq/mL	Benzyl alcohol, sodium chloride and sodium citrate dihydrate.  <i>For a complete listing see <b>DOSAGE FORMS, COMPOSITION AND PACKAGING.</b></i>

### DESCRIPTION

Gallium (Ga 67) Citrate Injection is supplied in a 10 milliliter vial as an isotonic, sterile, non-pyrogenic solution. Each milliliter of the isotonic solution contains 74 megabecquerels (2 millicuries) of gallium (Ga 67) on the calibration date as a complex formed from 8.3 nanograms gallium (Ga 67) chloride, 1.9 milligrams of sodium citrate dihydrate, 7.8 milligrams of sodium chloride and 0.9 percent benzyl alcohol (v/v) as a preservative. The pH is adjusted between 5.5 and 8.0 with hydrochloric acid and/or sodium hydroxide solution.

Gallium (Ga 67), with a half-life of 78.3 hours, is cyclotron produced by the proton irradiation of enriched zinc. At the time of calibration the drug contains no more than 0.02% gallium (Ga 66) and no more than 0.2% of zinc (Zn 65). The concentration of each radionuclidic impurity changes with time. At expiration, the drug contains no more than 0.001% gallium (Ga 66) and no more than 1.0 % zinc (Zn 65). No carrier has been added.

Gallium citrate has the following chemical structure:



## Physical Characteristics

Gallium (Ga 67) with a physical half-life of 78.3 hours<sup>1</sup> decays by electron capture to stable zinc (Zn 67). Photons that are useful for imaging studies are listed in Table 1.

**Table 1. Principal Radiation Emission Data<sup>1</sup>**

<b>Radiation</b>	<b>Mean % Per Disintegration</b>	<b>Energy (keV)</b>
Gamma-2	3.2	91.3
Gamma-3	39.2	93.3
Gamma-4	21.2	184.6
Gamma-5	2.4	209.0
Gamma-6	16.8	300.2
Gamma-7	4.7	393.5

## External Radiation

The specific gamma ray constant for Gallium (Ga 67) is 0.8 R\*cm<sup>2</sup>/mCi\*hour. The first half-value thickness of lead (Pb) is 0.086 cm. A range of values for the relative attenuation of the radiation emitted by this radionuclide that results from interposition of various thickness of lead is shown in Table 2. For example, the use of 1.2 cm of lead will decrease the radiation exposure by a factor of about 100.

**Table 2. Radiation Attenuation by Lead Shielding<sup>2</sup>**

<b>Shield Thickness (Pb), cm</b>	<b>Coefficient of Attenuation</b>
0.086	0.5
0.48	10 <sup>-1</sup>
1.4	10 <sup>-2</sup>
3.4	10 <sup>-3</sup>

To correct for physical decay of this radionuclide, the fractions that remain at selected time intervals after the time of calibration are shown in Table 3.

**Table 3. Physical Decay Chart; Gallium (Ga 67) Half-Life 78.3 Hours**

<b>Hours</b>	<b>Fraction Remaining</b>		<b>Hours</b>	<b>Fraction Remaining</b>
0*	1.000		72 (3d)	0.529
6	0.948		78	0.501
12	0.899		84	0.475
18	0.853		90	0.451
24 (1d)	0.809		96 (4d)	0.427
30	0.767		108	0.384
36	0.727		120 (5d)	0.345
42	0.689		132	0.311
48 (2d)	0.654		144 (6d)	0.279
54	0.620		156	0.251
60	0.588		168 (7d)	0.226
66	0.557			

\*Calibration Time

### **INDICATIONS AND CLINICAL USE**

Gallium (Ga 67) Citrate Injection may be useful to demonstrate the presence and extend of Hodgkin’s disease, lymphoma, and bronchogenic carcinoma. Positive gallium (Ga 67) uptake in the absence of prior symptoms warrants follow-up as an indication of a potential disease state. Gallium (Ga 67) Citrate Injection may be useful as an aid in detecting some acute inflammatory lesions.

### **CONTRAINDICATIONS**

None known.

However, for patients who are hypersensitive to this drug or to any ingredient in the formulation or component of the container, please see **DOSAGE FORMS, COMPOSITION AND PACKAGING** for a complete listing,

### **WARNINGS AND PRECAUTIONS**

#### **Serious Warnings and Precautions**

Radiopharmaceuticals should be used under the supervision of physicians who are qualified by training and experience in the safe use and handling of radionuclides and whose experience and training have been approved by the appropriate government agency authorized to license the use of radionuclides.

## **General**

The product should be administered under the supervision of a physician who is experienced in the use of radiopharmaceuticals. Appropriate management of therapy and complications is only possible when adequate diagnostic and treatment facilities are readily available.

A thorough knowledge of the normal distribution of intravenously administered Gallium (Ga 67) Citrate Injection is essential in order to accurately interpret pathologic states. The finding of an abnormal gallium (Ga 67) citrate concentration usually implies the existence of underlying pathology, but further diagnostic studies should be done to distinguish benign from malignant lesions. Gallium Citrate (Ga 67) Injection is intended for use as an adjunct in the diagnosis of certain neoplasms as well as focal areas of infection. Certain pathologic conditions may yield up to 40 percent false negative gallium (Ga 67) studies. Therefore, a negative study cannot be definitely interpreted as ruling out the presence of disease.

Lymphocytic lymphoma frequently does not accumulate Gallium (Ga 67) sufficiently for unequivocal imaging and the use of gallium with this histologic type of lymphoma is not recommended at this time.

Gallium (Ga 67) localization cannot differentiate between tumor and acute inflammation, and other diagnostic studies must be added to define the underlying pathology.

## **Carcinogenesis and Mutagenesis**

No long-term animal studies have been performed to evaluate carcinogenic potential, mutagenic potential, or whether this drug affects fertility in males or females.

## **Contamination**

The following measures should be taken after receiving the radiopharmaceutical product: Toilet should be used instead of urinal. Toilet should be flushed several times after use.

Special precautions such as bladder catheterization should be taken following administration to incontinent patients to minimize the risk of radioactive contamination of clothing, bed linen and the patient's environment.

## **Special Populations**

### **Pregnant Women**

Ideally, examinations using radiopharmaceuticals, especially those elective in nature of women of childbearing capability, should be performed during the first few (approximately ten) days following the onset of menses.

Animal reproductive studies have not been conducted with gallium (Ga 67) citrate. It is also not known whether gallium (Ga 67) citrate can cause fetal harm when administered to a pregnant

woman or can affect reproduction capacity. Gallium (Ga 67) citrate should be given to a pregnant woman only if clearly needed.

### **Nursing Women**

This drug is known to be excreted in human milk during lactation, therefore, formula feedings should be substituted for breastfeedings for four (4) weeks following the administration of Gallium Citrate (Ga 67) Injection. Breast milk expressed within that time should be discarded.

### **Pediatrics (0 - 16 years of age)**

Safety and effectiveness in pediatric patients below the age of 18 have not been established.

### **Geriatrics (> 65 years of age)**

No data available.

## **ADVERSE REACTIONS**

Rare occurrences of allergic reactions, skin rash and nausea have been reported in association with gallium (Ga 67) citrate use.

## **DRUG INTERACTIONS**

No data available.

## **DOSAGE AND ADMINISTRATION**

The recommended adult (70 kg) dose of Gallium (Ga 67) Citrate Injection is 74 to 185 megabecquerels (2 to 5 millicuries). Gallium (Ga 67) Citrate Injection is intended for intravenous administration only.

Approximately 10 percent of the administered dose is excreted in the feces during the first week after injection. Daily laxatives and/or enemas are recommended from the day of injection until the final images are obtained in order to cleanse the bowel of radioactive material and minimize the possibility of false positive studies.

Studies indicate the optimal tumor to background concentration ratios are obtained 48 hours post injection. However, considerable biological variability may occur in individuals and acceptable images may be obtained as early as 6 hours and as late as 120 hours after injection.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. Do not use if contents are turbid.

### Administration

The patient dose should be measured by a suitable radioactivity calibration system immediately prior the administration.

### Instructions for Preparation and Use

The vial contents are sterile and pyrogen-free. It is essential that the user follow the directions carefully and adhere to strict aseptic procedures.

### Instructions for the Handling of Gallium (Ga 67) Citrate

1. Waterproof gloves should be used during the entire handling and administration procedure.
2. Using proper shielding, the vial containing the gallium (Ga 67) citrate should be visually inspected to insure that it is free of particulate matter and discoloration prior to use.
3. Maintain adequate shielding during the life of the product and use a sterile, shielded syringe for withdrawing and injecting the preparation.

### RADIATION DOSIMETRY

The absorbed radiation dose<sup>3</sup> from an intravenous injection of 185 megabecquerels (5 millicuries) of gallium (Ga 67) citrate are shown in Table 4. The estimated fetal absorbed radiation dose<sup>4</sup> from an intravenous injection of 190 megabecquerels (5 millicuries) of gallium (Ga 67) citrate are shown in Table 5.

**Table 4. Absorbed Radiation Doses for Ga 67 Citrate Injection<sup>3</sup>**

Organ	Dose (mGy/185 MBq)	Dose (rad/5 mCi)
Adrenals	2.4E+01	2.4E+00
Bladder	1.5E+01	1.5E+00
Bone surfaces	1.2E+02	1.2E+01
Brain	1.1E+01	1.1E+00
Breast	8.7E+00	8.7E-01
Gall bladder	1.5E+01	1.5E+00
Stomach	1.3E+01	1.3E+00
Small Intestines (SI)	1.1E+01	1.1E+00
Colon	3.0E+01	3.0E+00
Upper Large Intestines (ULI)	2.2E+01	2.2E+00
Lower Large Intestines (LLI)	3.9E+01	3.9E+00
Heart	1.3E+01	1.3E+00
Kidneys	2.2E+01	2.2E+00



Organ	Dose (mGy/185 MBq)	Dose (rad/5 mCi)
Liver	2.2E+01	2.2E+00
Lungs	1.2E+01	1.2E+00
Muscles	1.1E+01	1.1E+00
Oesophagus	1.1E+01	1.1E+00
Ovaries	1.5E+01	1.5E+00
Pancreas	1.5E+01	1.5E+00
Red marrow	3.9E+01	3.9E+00
Skin	8.3E+00	8.3E-01
Spleen	2.6E+01	2.6E+00
Testes	1.0E+01	1.0E+00
Thymus	1.1E+01	1.1E+00
Thyroid	1.1E+01	1.1E+00
Uterus	1.4E+01	1.4E+00
Remaining organs	1.1E+01	1.1E+00
Effective dose	1.9E+01 mSv/ 185 MBq	1.9E+00 rem/ 5 mCi

**Table 5. Fetal Absorbed Radiation Doses Estimates from a 190MBq (5mCi) dose of Ga 67 Citrate Injection<sup>4</sup>**

Stage of Gestation	Fetal Dose mGy/MBq (rad/mCi)	Fetal dose mGy (rad)
Early	0.093 (0.34)	18 (1.7)
3 months	0.2 (0.74)	38 (3.7)
6 months	0.18 (0.67)	34 (3.35)
9 months	0.13 (0.48)	25 (2.4)

## OVERDOSAGE

No data available.

## ACTION AND CLINICAL PHARMACOLOGY

Gallium (Ga 67) citrate, with no carrier added, has been found to concentrate in certain viable primary and metastatic tumors as well as focal sites of infection. The mechanism of concentration is unknown, but investigational studies have shown that gallium (Ga 67) accumulates in lysosomes and is bound to a soluble intracellular protein.

It has been reported in the scientific literature that following intravenous injection, the highest tissue concentration of gallium (Ga 67) – other than tumors and sites of infection – is the renal

cortex. After the first day, the maximum concentration shifts to bone and lymph nodes and after the first week, to liver and spleen. Gallium (Ga 67) is excreted relatively slowly from the body. The average whole body retention is 65 percent after seven days, with 26 percent having been excreted in the urine and 9 percent in the stools.

## **STORAGE AND STABILITY**

The contents of the vial are radioactive, and adequate shielding and handling precautions must be maintained. Store at controlled room temperature 20° to 25°C (68° to 77°F).

## **SPECIAL HANDLING INSTRUCTIONS**

As in the use of any other radioactive material, care should be taken to minimize radiation exposure to patients consistent with proper patient management, and to minimize radiation exposure to occupational workers.

Gallium (Ga 67) Citrate Injection may be received, used and administered only by authorized persons in designated clinical settings. Its receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licenses of local competent official organizations.

## **DOSAGE FORMS, COMPOSITION AND PACKAGING**

Catalog Number: 180G0 / 180M0

Gallium (Ga 67) Citrate Injection is supplied in a 10 milliliter vial as an isotonic, sterile, non-pyrogenic solution. Each milliliter of the isotonic solution contains 74 megabecquerels (2 millicuries) of gallium (Ga 67) on the calibration date as a complex formed from 8.3 nanograms gallium (Ga 67) chloride, 1.9 milligrams of sodium citrate dihydrate, 7.8 milligrams of sodium chloride and 0.9 percent benzyl alcohol (v/v) as a preservative. The pH is adjusted between 5.5 and 8.0 with hydrochloric acid and/or sodium hydroxide solution.

Gallium (Ga 67) Citrate Injection is available in vials containing 222 MBq and 444 MBq (6 mCi and 12 mCi) on the calibration date.

## PART II: SCIENTIFIC INFORMATION

### PHARMACEUTICAL INFORMATION

#### Drug Substance

Proper name: Gallium (Ga 67) Citrate

Chemical name: Not applicable

Molecular formula and molecular mass: Not applicable

Structural formula: Not applicable

Physicochemical properties: Gallium (Ga 67) with a physical half-life of 78.3 hours decays by electron capture to stable Zinc (Zn 67).

#### Product Characteristics

Gallium (Ga 67) with a physical half-life of 78.3 hours<sup>1</sup> decays by electron capture to stable Zinc (Zn 67). Photons that are useful for imaging studies are listed in the table below.

#### Principal Radiation Emission Data<sup>1</sup>

Radiation	Mean % Per Disintegration	Energy (keV)
Gamma-2	3.2	91.3
Gamma-3	39.2	93.3
Gamma-4	21.2	184.6
Gamma-5	2.4	209.0
Gamma-6	16.8	300.2
Gamma-7	4.7	393.5

#### External Radiation

The specific gamma ray constant for Gallium (Ga 67) is 0.8 R\*cm<sup>2</sup>/mCi\*hour. The first half-value thickness of lead (Pb) is 0.086 cm. A range of values for the relative attenuation of the radiation emitted by this radionuclide that results from interposition of various thickness of lead is shown in the following table. For example, the use of 1.2 cm of lead will decrease the radiation exposure by a factor of about 100.

## Radiation Attenuation by Lead Shielding<sup>2</sup>

Shield Thickness (Pb), cm	Coefficient of Attenuation
0.086	0.5
0.48	$10^{-1}$
1.4	$10^{-2}$
3.4	$10^{-3}$

To correct for physical decay of this radionuclide, the fractions that remain at selected time intervals after the time of calibration are shown in the table below.

### Physical Decay Chart; Gallium (Ga 67) Half-Life 78.3 Hours

Hours	Fraction Remaining	Hours	Fraction Remaining
0*	1.000	72 (3d)	0.529
6	0.948	78	0.501
12	0.899	84	0.475
18	0.853	90	0.451
24 (1d)	0.809	96 (4d)	0.427
30	0.767	108	0.384
36	0.727	120 (5d)	0.345
42	0.689	132	0.311
48 (2d)	0.654	144 (6d)	0.279
54	0.620	156	0.251
60	0.588	168 (7d)	0.226
66	0.557		

\*Calibration Time

### CLINICAL TRIALS

No data available.

### DETAILED PHARMACOLOGY

See ACTION AND CLINICAL PHARMACOLOGY in PART I of the Product Monograph.

### TOXICOLOGY

No long-term animal studies have been performed to evaluate carcinogenic or mutagenic potential or whether Gallium (Ga 67) Citrate Injection affects fertility in males or females.

As with other radiopharmaceuticals which distribute intracellularly, there may be increased risk of chromosome damage from Auger electrons if nuclear uptake occurs.

## **REFERENCES**

1. Stabin MG, da Luz CQPL. Decay Data for Internal and External Dose Assessment, Health Physics. 83(4):471-475, 2002.
2. Smith David S., Stabin MG. Exposure Rate Constants and Lead Shielding Values for Over 1,100 Radionuclides, Health Physics. 102(3):271-291, March 2012.
3. International Commission on Radiological Protection. ICRP Publication 80, Radiation Dose to Patients from Radiopharmaceuticals: Addendum 2 to ICRP Publication 53, Ann. ICRP 28(3), 1998.
4. Russell JR, Stabin MG, Sparks RB and Watson EE. Radiation Absorbed Dose to the Embryo/Fetus from Radiopharmaceuticals, Health Physics. 73(5):756-769, 1997.

**PART III: CONSUMER INFORMATION**

**Gallium (Ga 67) Citrate Injection**  
Gallium (Ga 67) Citrate

This leaflet is part III of a three-part "Product Monograph" published when Gallium (Ga 67) Citrate Injection was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about Gallium (Ga 67) Citrate Injection. Contact your doctor or pharmacist if you have any questions about the drug.

**ABOUT THIS MEDICATION**

What the medication is used for:

Gallium (Ga 67) Citrate Injection is an imaging agent used to detect certain types of cancers or lesions.

What it does:

Gallium (Ga 67) Citrate Injection is a radioactive tracer that is injected in the vein and collects in areas of the body where there are certain types of tumors or infections. After the tracer is injected, pictures (scans) can be taken with a special camera to show the areas where the radioactivity collects. These pictures will help your doctor make the diagnosis.

What the medicinal ingredient is:

Gallium (Ga 67) Citrate

What the important non-medicinal ingredients are:

Benzyl alcohol, Sodium chloride, Sodium citrate dihydrate.

For a full listing of non-medicinal ingredients see Part 1 of the product monograph.

**WARNINGS AND PRECAUTIONS**

Since Gallium (Ga 67) Citrate Injection is a radiopharmaceutical, it can only be given by a healthcare professional who is specially trained and experienced in the safe use and handling of radionuclides, and whose experience and training have been approved by the appropriate government agency authorized to license the use of radionuclides.

BEFORE you receive Gallium (Ga 67) Citrate Injection talk to your doctor or pharmacist if:

- You had any allergic reaction to this radiopharmaceutical in the past or its ingredients.
- There is a possibility that you may be pregnant. If there is a need to consider Gallium (Ga 67) Citrate Injection during your pregnancy, your doctor will discuss the benefits and risks of giving it to you.
- Gallium (Ga 67) Citrate is excreted in human milk during lactation; therefore, for four (4) weeks after

administration of Gallium (Ga 67) Citrate Injection, formula feedings should be substituted for breastfeeding and breast milk expressed within that time should be discarded.

Safety precautions to be followed after receiving Gallium (Ga 67) Citrate Injection:

- Men should use toilet instead of urinal.
- Toilet should be flushed several times after use.
- Wash hands thoroughly after using toilet.

If you have difficulty with bladder control, special precautions may be used to minimize the risk of radioactive contamination of clothing, bed linen and your surroundings.

**INTERACTIONS WITH THIS MEDICATION**

No interactions are known, however, your doctor should be informed about all the prescribed or over-the-counter products you use.

**PROPER USE OF THIS MEDICATION**

Gallium (Ga 67) Citrate Injection will be administered under the supervision of a health professional who is trained and experienced in the safe use of radiopharmaceuticals.

**SIDE EFFECTS AND WHAT TO DO ABOUT THEM**

Rarely, allergic reactions, skin rash and nausea may occur with Gallium (Ga 67) Citrate Injection.

This is not a complete list of side effects. If you have any unexpected effects after receiving Gallium (Ga 67) Citrate Injection, contact your doctor or pharmacist.

DIN: 02327813

Artwork revision: 02/2019

### **REPORTING SUSPECTED SIDE EFFECTS**

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at [www.healthcanada.gc.ca/medeffect](http://www.healthcanada.gc.ca/medeffect)
- Call (toll-free) at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
  - Fax (toll-free) to 1-866-678-6789, or
  - Mail to: Canada Vigilance Program  
Health Canada  
Postal Locator 1908C  
Ottawa, ON, K1A 0K9

You can also report suspected adverse reactions directly to Curium Canada Inc. by one of the following 2 ways:

- Call (toll-free) to 1-866-789-2211
- Mail to: Curium Canada Inc.  
c/o Pharmacovigilance Department  
2572 boul. Daniel-Johnson, suite 248  
Laval, QC, H7T-2R3

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at [www.healthcanada.gc.ca/medeffect](http://www.healthcanada.gc.ca/medeffect)

*NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.*

### **MORE INFORMATION**

This document plus the full product monograph, prepared for health professionals can be obtained by contacting the sponsor, Curium Canada Inc., at 1-866-885-5988.

Curium and the Curium logo are trademarks of a Curium company.

© 2018 Curium Canada Inc. All rights reserved.

This leaflet was prepared by Curium Canada Inc.

Last revised: April 26<sup>th</sup>, 2019

Distributed by:  
Curium Canada Inc.  
Laval, QC, H7T-2R3  
CANADA

**CURIUM™**