Gallium Citrate Ga 67 Injection
Rx Only.

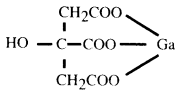
Diagnostic—For Intravenous Use

DESCRIPTION

Gallium Citrate Ga 67 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 chloride Ga 67, 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 to between 5.5 to 8.0 with hydrochloric acid and/or sodium hydroxide solution.

Gallium Ga 67, with a half-life of 78.26 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% 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 78.26 hours[1] 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[1]

Radiation	Mean % Per Disintegration	Energy (keV)
Gamma-2	2.9	91.3
Gamma-3	35.7	93.3
Gamma-4	19.7	184.6
Gamma-5	2.2	209.0
Gamma-6	16.0	300.2
Gamma-7	4.5	393.5

EXTERNAL RADIATION

The specific gamma ray constant for Gallium Ga 67 is 1.6 R/mCi-hour at 1 cm. The first half-value thickness of lead (Pb) is 0.066 cm. A range of values for the relative attenuation of the radiation emitted by this radionuclide that results from interposition of various thicknesses 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

Shield Thickness (Pb), cm	Coefficient of Attenuation
0.066	0.5
0.41	10^{-1}
1.2	10^{-2}
2.5	10^{-3}
4.8	10^{-4}

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.

[1] Kocher, D.C., Radioactive Decay Tables, Health and Safety Research Division, National Technical Information Service, DOE/TIC-11026, pg. 80, 1981.

Table 3. Physical Decay Chart; Gallium Ga 67 Half-Life 78.26 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 PHARMACOLOGY

Gallium Citrate Ga 67, 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.

INDICATIONS AND USAGE

Gallium Citrate Ga 67 Injection may be useful to demonstrate the presence and extent 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 Citrate Ga 67 Injection may be useful as an aid in detecting some acute inflammatory lesions.

CONTRAINDICATIONS

None.

WARNINGS

None known.

PRECAUTIONS

General

A thorough knowledge of the normal distribution of intravenously administered Gallium Citrate Ga 67 Injection is essential in order to accurately interpret pathologic states. The finding of an abnormal Gallium Ga 67 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.

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

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

Radiopharmaceuticals should be used only by physicians who are qualified by training and experience in the safe use and handling of radionuclides produced by nuclear reactor or particle accelerator and whose experience and training have been approved by the appropriate government agency authorized to license the use of radionuclides.

Carcinogenesis, Mutagenesis, Impairment of Fertility

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

Pregnancy Category C

Animal reproductive studies have not been conducted with Gallium Citrate Ga 67. It is also not known whether Gallium Citrate Ga 67 can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Gallium Citrate Ga 67 should be given to a pregnant woman only if clearly needed.

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.

Nursing Mothers

This drug is known to be excreted in human milk during lactation, therefore, formula feedings should be substituted for breast feedings.

Pediatric Use

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

ADVERSE REACTIONS

Rare occurrences of allergic reactions, skin rash and nausea have been reported in association with Gallium Citrate Ga 67 use.

DOSAGE AND ADMINISTRATION

The recommended adult (70 kg) dose of Gallium Citrate Ga 67 Injection is 74 to 185 megabecquerels (2 to 5 millicuries). Gallium Citrate Ga 67 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 often 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.

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

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

Instructions for the handling of Gallium Citrate Ga 67:

1. Waterproof gloves should be used during the entire handling and administration procedure.
2. Using proper shielding, the vial containing the Gallium Citrate Ga 67 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 estimated absorbed radiation doses[2] from an intravenous injection of 185 megabecquerels (5 millicuries) of Gallium Citrate Ga 67 are shown in Table 4.

Table 4. Absorbed Radiation Doses

Tissue	mGy/ 185MBq	rads/ 5mCi
Whole Body	13.0	1.30
Skeleton	22.0	2.20
Liver	23.0	2.30
Bone Marrow	29.0	2.90
Spleen	26.5	2.65
Kidney	20.5	2.05
Ovaries	14.0	1.40
Testes	12.0	1.20
Gastrointestinal Tract		
Stomach	11.0	1.10
Small Intestine	18.0	1.80
Upper Large Intestine	28.0	2.80
Lower Large Intestine	45.0	4.50

HOW SUPPLIED

Catalog Number 180.

Gallium Citrate Ga 67 Injection is supplied sterile and non-pyrogenic for intravenous use. Each milliliter contains 74 megabecquerels (2 millicuries) of Gallium Ga 67 on the calibration date, as a complex formed from 8.3 nanograms gallium chloride Ga 67, 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 to between 5.5 to 8.0 with hydrochloric acid and/or sodium hydroxide solution.

Gallium Citrate Ga 67 Injection is available in vials containing 111 MBq, 222 MBq and 444 MBq (3 mCi, 6 mCi and 12 mCi) on the calibration date.

STORAGE AND HANDLING
The contents of the vial are radioactive, and adequate shielding and handling precautions must be maintained. Store at controlled room temperature 20-25°C (68-77°F) [see USP].

Storage and disposal of Gallium Citrate Ga 67 Injection should be controlled in a manner that is in compliance with the appropriate regulations of the government agency authorized to license the use of this radionuclide.

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Mallinckrodt Inc.
St. Louis, MO 63134

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[2] MIRD Dose Estimate Report No. 2, J. Nucl. Med. 14; 755-6 (1973).