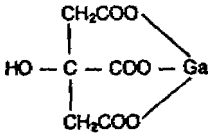
Neoscan®
Gallium Citrate Ga 67
DIAGNOSTIC FOR INTRAVENOUS USE

DESCRIPTION: The Medi-Physics, Inc., Amersham Healthcare Neoscan,® Gallium Citrate Ga 67 Kit for intravenous administration, is supplied as a sterile, pyrogen-free, aqueous solution, with no carrier added. Each milliliter of the solution contains 74 MBq,2 mCi of Gallium Ga 67 at calibration time, 2 5% sodium citrate and 1% benzyl alcohol as a preservative. The pH is 4.5-7.5, Gallium Ga 67, with a half-life of 78 3 hours, is cyclotron produced by the proton irradiation of Zinc Zn 68 enriched metal. The radionuclidic composition at calibration time is not less than 99 0% Gallium Ga 67, less than 0.9% Gallium Ga 66 and less than 0.1 % due to Zinc Zn 65 and other radiocontaminants, each expressed as a percentage of total activity. The radionuclidic composition at expiration time is not less than 99.6% Gallium Ga 67, less than $2x10^{-5}$ % Gallium Ga 66 and less than 0.4% due to Zinc Zn 65 and other radiocontaminants, each expressed as a percentage of total activity.

The chemical names are: 1. 1,2,3-Propanetricarboxylic acid, 2-hydroxy-, gallium^{67}- Ga(1:1)salt; and 2. Gallium^{67}-Ga Citrate (1:1).

Structural Formula:



PHYSICAL CHARACTERISTICS: Gallium Ga 67 decays to stable Zinc Zn 67 by electron capture with a physical half-life of 78.3 hours[1]. The principal photons are listed in Table 1.

Table 1. Principal Radiation Emission Data[1]

Radiation	Mean %/Disintegration	Mean Energy (keV)
Gamma-3	35.7	93.3
Gamma-4	19.7	184.6
Gamma-6	16.0	300.2

' Kocher, David C., "Radioactive Decay Data Tables " DOE/TIC 11026, 80,(1981).

EXTERNAL RADIATION: The specific gamma ray constant for Gallium Ga 67 is 1.6 R/hr-mCi at 1 cm. The first half-value thickness of lead (Pb) is 0.066 cm. To facilitate control of the radiation, exposure from rnegabecquerel (millicurie) amounts of this radionuclide, a range of values for the relative attenuation of the radiation emitted by this radionuclide that results from the interposition of various thicknesses of Pb is shown in Table 2. For example, the use of a 1.2 cm thickness of Pb will attenuate the radiation emitted by a factor of about 100.

Table 2 Radiation Attenuation by Lead (Pb) 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.

Table 3 Physical Decay Chart. Gallium Ga 67, half-life 78 3 hours

Hours	Fraction Remaining	Hours	Fraction Remaining	Hours	Fraction Remaining
0*	1.00	48	0.65	96	0.43
6	0.95	54	0.62	108	0.38
12	0.90	60	0.59	120	0.35
18	0.85	66	0.56	132	0.31
24	0.81	72	0.53	144	0.28
30	0.77	78	0.50	156	0.25
36	0.73	84	0.48	168	0.23
42	0.69	90	0.45		

•Calibration Time

CLINICAL PHARMACOLOGY: Essentially, 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 nine percent in the stools.

INDICATIONS AND USAGE: Gallium Citrate Ga 67 may be useful in demonstrating the presence and extent of the following malignancies: Hodgkin's disease, lymphomas 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 may also be useful as an aid in detecting some acute inflammatory lesions.

CONTRAINDICATIONS: None known.

WARNINGS. None known

PRECAUTIONS:

General

A thorough knowledge of the normal distribution of intravenously administered Gallium Ga 67 is essential in order to accurately interpret pathological 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. Neoscan is intended for use as an adjunct in the diagnosis of certain neoplasms as well as focal areas of infection. Certain pathological conditions may yield up to 40 percent false negative Gallium Ga 67 studies. Therefore, a negative study can not 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 Ga 67 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.

Neoscan, as well as other radioactive drugs, must be handled with care. Appropriate safety measures should be used to minimize external radiation to clinical occupational personnel. Care should also be taken to minimize radiation exposure to patients in a manner consistent with proper patient management.

Radiopharmaceuticals should be used only by 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.

Do not use after the expiration time and date (7 days after calibration time and date) stated on the label.

Carcinogenesis, Mutagenesis, Impairment of Fertility

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

Pregnancy Category C
Animal reproduction 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, in a woman of childbearing capability should be performed during the first few (approximately 10) days following the onset of menses.

Nursing Mothers
Gallium Ga 67 is excreted in human milk during lactation. Therefore, formula feedings should be substituted for breast feedings.

Pediatric Use
Safety and effectiveness in children below the age of 18 have not been established.

ADVERSE REACTIONS: The rare occurrence of allergic reactions, skin rash, and nausea has been reported in association with Gallium Ga 67 use.

DOSAGE AND ADMINISTRATION: The recommended adult (70 kg) dose of Neoscan is 74-185 MBq, 2 5 mCi. Neoscan 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 after 48 hours post injection. However, considerable biological variability may occur in individuals and acceptable images may be obtained as early as six 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.

Use contents of vial up to seven (7) days after calibration time and date. Thereafter, discard the vial with its contents. Aseptic procedures, in addition to a shielded syrige and waterproof gloves, should be employed in the withdrawal of the dose for administration to the patient.

RADIATION DOSIMETRY: The estimated absorbed radiation doses[2] to an average adult (70 kg) from an intravenous injection of 185 MBq, 5 mCi of Neoscan are shown in Table 4.

Table 4. Absorbed Radiation Dose[2]

Organ	mGy/185 MBq	Rads/5 mCi
GI 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
Gonads		
Ovaries	14.0	1.40
Testes	12.0	1.20
Kidneys	2.05	2.05
Liver	23.0	2.30
yarrow	29.0	2.90
Bone	22.0	2.20
Spleen	26.5	2.65
Total Body*	13.0	1.30

[2]MIRD Dose Estimate Report No. 2, J Nucl Med 14(10): 755-6(1973)
*Assuming a uniform distribution of radioactivity in total body.

HOW SUPPLIED: Neoscan is supplied as a sterile, pyrogen-free, aqueous solution, with no carrier added. Each vial contains 222 MBq, 6.0 mCi in 3 mL or 444 MBq**,** 12.0 mCi in 6 mL at calibration time. Each milliliter contains 74 MBq, 2 mCi ± 10% Gallium Ga 67 at the time of calibration in 2.5% sodium citrate. Benzyl alcohol 1% is present as a preservative.

The contents of the vial are radioactive and adequate shielding and handling precautions must be maintained.

Waterproof gloves should be worn during the handling procedures.

Using proper shielding, the vial containing the Gallium Citrate Ga 67 solution should be visually inspected prior to administration to insure that it is clear and free of particulate matter. With a shielded sterile syringe, aseptically withdraw the material for use.

Disposal
The residual materials may be discarded in ordinary trash provided the vials and syringes read no greater than background with an appropriate low-range survey meter. All identifying labels should be destroyed before discarding.

This radiopharmaceutical is licensed by Illinois Department of Nuclear Safety for distribution to persons licensed pursuant to 32 Ill Adm Code 330.260(a) and Part 335, Subpart E, 335.4010, or under equivalent licenses of an Agreement State or a Licensing State.

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