DRN 3103 Gallium Citrate (Ga-67) Injection

Description

Gallium Citrate (Ga-67) Injection is a clear, colourless, sterile, isotonic, aqueous solution with pH of 5.0-8.0. At activity reference time the product has the following composition:

- gallium-67 (as gallium citrate)	37	MBq (1 mCi)
- sodium chloride	6.9	mg
- sodium citrate	2.0	mg
- benzyl alcohol	9.0	mg
- sodium hydroxide (pH adjustment)	q.s	
- hydrochloric acid 37% (pH adjustment)	q.s	
- water for injections .	q.s	

Gallium-67 is carrier free. It contains at reference time less than 0.2% of gallium-66.

Storage

Store below 25°C. If multi-dose use is intended, each aliquot should be removed under aseptic conditions. Store below 30°C after removal of the first aliquot.

Stability

Gallium (Ga-67) Citrate Injection expires 16 days after production. The expiry date and time is provided on the outer packaging and on each vial.
After opening of the vial, the shelf-life of the product is 8 hours.

Action

Upon intravenous injection carrier-free gallium-67 initially binds to serum proteins. The mechanism of concentration in various tissues is unknown, but intracellular accumulation in lysosomes has been reported. In the first day 10-15% of the administered dose is excreted by the kidneys, thereafter the liver becomes the main route of excretuibm resyktubg ub ekunubatuib if another 15-20% with the faeces.
The normal non-pathological pattern of distribution always shows uptake in the liver and spleen and in parts of the skeleton, including marrow. Further accumulation with a variable degree of intensity may be observed in the orbita, the nasopharynx and the salivary glands, the sternum and the sternoclavicular joints and in the large joints of the body. Accumulation in mammary tissue nearly always occurs in lactation but is also occasionally found in apparently normal breasts. This non-pathological distribution distinguishes itself from pathological accumulation by its symmetry. In children the thymus or remnants of thymic tissue may accumulate considerable amounts of gallium-67.
Pathological uptakes occur in certain primary and metastatic tumours, as well as in inflammatory lesions and abscesses. Uptake in lymph nodes must generally be interpreted as being pathologic. It must be recognized that the incidence of false-negative results may be high. Therefore, Gallium Citrate (Ga-67) Injection must be used as an adjunct to other diagnostic procedures.

Indications

Scintigraphy with gallium-67 is indicated in:
- the clinical evaluation of patients suspected of neoplastic diseases, notably Hodgkin's disease, other malignant lymphomas, soft tissue sarcomas and most bronchogenic carcinomas,
- the localisation of metastases of malignant melanomas.
- the differentiation of hepatoma and liver metastases, and pleural and peritoneal mesotheliomas.
- determining the extent of involvement of malignancy.
- the follow-up of tumour therapy and screening for recurrent tumour.
- the localisation of focal inflammatory lesions and the evaluation of fever of unknown origin.

Contraindications
Gallium Citrate (Ga-67) Injection is contraindicated in lactating mothers unless the child is formula-fed for a period of at least three weeks after the injection.
No other contraindications are known.

Precautions
Radiopharmaceuticals should not be administered to patients under 18 years or during pregnancy unless the information to be gained outweighs the potential radiation hazards. Examinations with radiopharmaceuticals of women of child bearing capability should preferably be done during the first 10 days following the onset of menses.

Warnings
Radiopharmaceuticals must be used by persons qualified by the appropriate government authorities. These persons have followed a specific training in the use and handling of radionuclides.
All unnecessary exposure to radiation, either of personnel or of patients, should be avoided.

Adverse reactions
An occasional mild adverse cutaneous reaction to the use of gallium-67 has been published in literature.

Dosage and administration
Usual dose 74-111 MBq (2-3mCi) by intravenous injection.

Procedure

Screening procedure are usually started 48 hours after administration. However, depending on the type of lesion to be detected and the region of the body to be visualized, acceptable images may be obtained as early as 6 hours and as late as 120 hours after administration. When abdominal studies are included in the diagnostic procedure it is strongly advised to start a bowel-cleansing regimen upon injection, until the last scanning takes place. By this regimen the accumulated activity within the bowel lumen may be removed. Otherwise, this activity may influence the interpretation of the scan.

Physical characteristics
Gallium-67 is a carrier-free cyclotron-produced radionuclide, obtained by proton irradiation of zinc. Its half-life is 78 hours. It decays by electron capture, followed by the emission of gamma-rays of 91 + 93, 185, 209, 300 and 394 keV.
The irradiation procedure also yields limited amounts of gallium-66

Gallium-67 decay

Time before reference		Time after reference		Time after reference	
Time	Factor	Time	Factor	Time	Factor
4 days	2.34	1 day	0.81	6 days	0.28
3 days	1.89	2 days	0.65	7 days	0.23
2 days	1.53	3 days	0.53	8 days	0.18
1 day	1.24	4 days	0.43	9 days	0.15
		5 days	0.35	10 days	0.12

Radiation dosimetry
Estimated absorbed dose of gallium-67 (J, Nucl, Med, 14, 755-756, 1973):

	mGy/MBq	rad/mCi
Bone marrow	0.16	0.58
Gonads	0.07	0.26
Kidneys	0.11	0.41
Liver	0.12	0.46
Skeleton (bone + marrow)	0.12	0.44
Spleen	0.14	0.53
Total body	0.07	0.26

Incompatibilities
Incompatibilities are not known to exist.

Interaction with other medicaments and other forms of interaction
The biodistribution of gallium (^{67}Ga) may be affected by a wide range of pharmacological substances including cytotoxic agents, immunosuppressant (including steroids), radiocontrast agents, phenothiazines, tricyclic antidepressants, metoclopramide, reserpine, methyl dopa, oral contraceptives and stilboestrol.
Pre-treatment with some cytotoxic agents may lead to an increased uptake of radiogallium in the bony skeleton, accompanied by a reduced accumulation in the liver, in soft tissues and also in tumour.
Non-specific, non-pathological ^{67}Ga lung uptake has been described in patients who have received contrast media for contrast-enhanced radio lymphangiography, who have undergone chemotherapy and radiotherapy. This is non-pathological and is as a consequence of secondary hyperplasia.
Drugs causing increases in plasma prolactin levels may lead to increased bone gallium uptake in the mammary tissues.
Alteration in ^{67}Ga radiokinetics and tissue binding may occur after iron therapy.
Therefore, the possibility of false positive results should always be born in mind.

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