GLOFIL-125- iothalamate sodium, i-125 injection
QOL Medical

GLOFIL®-125
Sodium Iothalamate I-125 Injection, USP

DESCRIPTION

General

GLOFIL®-125 (Sodium Iothalamate I-125 Injection) is a sterile, nonpyrogenic aqueous injection containing approximately 1 mg sodium iothalamate per mL, and 0.9 percent benzyl alcohol as a preservative. The radioactive concentration of the material is 250-300 µCi/mL as of the calibration date. Sodium bicarbonate and hydrochloric acid are present for pH adjustment.

Physical Characteristics

Iodine-125 decays by electron capture with a physical half-life of 60.14 days. Photons that are useful for detection are listed in Table 1.

Table 1. Principal Radiation Emission Data*

Radiation	Mean Number Per Disintegration	Mean Energy (keV)
Gamma-1	0.067	35.5
$K\alpha_1$ X-ray	0.741	27.5
$K\alpha_2$ X-ray	0.398	27.2
$K\beta_1$ X-ray	0.140	31.0
$K\beta_2$ X-ray	0.043	31.7
$K\beta_3$ X-ray	0.072	30.9

* ICRP Publication 38: *Radionuclide Transformations - Energy and Intensity of Emissions.* Published for the International Commission on Radiological Protection by Pergamon Press, New York, 1983, p. 446.

The specific gamma ray constant for I-125 is 1.43 R/mCi-hr at 1 cm. The first half value thickness of lead (Pb) for I-125 is 0.017 mm. A range of values for the relative attenuation of the radiation emitted by this radionuclide resulting from interposition of various thicknesses of Pb is shown in Table 2. For example, the use of 0.28 mm of Pb will decrease the external radiation exposure by a factor of 10,000.

Table 2. Radiation Attenuation by Lead Shielding*

Shield Thickness (Pb), mm	Coefficient of Attenuation
0.017	0.5
0.058	0.1
0.12	0.01
0.2	0.001
0.28	0.0001

* Data supplied by Oak Ridge Associated Universities, Radiopharmaceutical Internal Dose Information Center, Oak Ridge, TN 1989.

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

Table 3. Physical Decay Chart; I-125, half-life 60.14 days

Days	Fraction Remaining	Days	Fraction Remaining	Days	Fraction Remaining
0*	1.000	15	0.841	30	0.707
1	0.989	16	0.831	31	0.699
2	0.977	17	0.822	32	0.691
3	0.966	18	0.812	33	0.683
4	0.955	19	0.803	34	0.675
5	0.944	20	0.794	35	0.667
6	0.933	21	0.785	36	0.660
7	0.922	22	0.776	37	0.652
8	0.912	23	0.767	38	0.645
9	0.901	24	0.758	39	0.637
10	0.891	25	0.749	40	0.630
11	0.881	26	0.740	41	0.623
12	0.871	27	0.732	42	0.616
13	0.861	28	0.724	43	0.608
14	0.851	29	0.715	44	0.601
				45	0.595

* Calibration Date

CLINICAL PHARMACOLOGY

The renal clearance of sodium iothalamate in man closely approximates that of inulin. The compound is cleared by glomerular filtration without tubular secretion or reabsorption. Following infusion administration of I-125 iothalamate, the effective half-life is about 0.07 days.

INDICATIONS AND USAGE

GLOFIL®-125 (Sodium Iothalamate I-125 Injection) is indicated for evaluation of glomerular filtration in the diagnosis or monitoring of patients with renal disease.

CONTRAINDICATIONS

GLOFIL®-125 should not be administered via a central venous line.

WARNINGS

None known.

PRECAUTIONS

General

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

Radiopharmaceuticals should be used only by physicians who are qualified by training and experience in the safe use and handling of radionuclides.

Rapid or bolus-like injections should be avoided.

Carcinogenesis, Mutagenesis, Impairment of Fertility

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

Pregnancy Category C

Animal reproduction studies have not been conducted with GLOFIL®-125. It is also not known whether GLOFIL®-125 can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. GLOFIL®-125 should be given to a pregnant woman only if clearly needed.

Nursing Mothers

Radioiodine is excreted in human milk during lactation. It is not known whether GLOFIL®-125 is excreted in human milk. Therefore, formula feedings should be substituted for breast feedings.

Pediatric Use

Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

None reported.

DOSAGE AND ADMINISTRATION

Dosage

The suggested dose range employed in the average patient (70 kg) is as follows:
Continuous intravenous infusion: 20 to 100 µCi (0.74-3.7 megabecquerels) (Sigman, et al (1) method).
Single intravenous injection: 10 to 30 µCi (0.37-1.11 megabecquerels) (Cohen, et al (2) method).
The patient dose should be measured by a suitable radioactivity calibration system immediately prior to administration.

Technique

Continuous intravenous infusion

Sigman (1) **method**

I. Preparation:

1. Adequate diuresis (a urine flow exceeding 3 mL/min.) is established, preferably by an oral water load of 1,500 mL two hours prior to the beginning of the clearance study.
2. It is not necessary to withhold breakfast or admit the patient the night before.

II. Procedure:

1. After the establishment of adequate diuresis, a number 14 or 16 French Foley catheter is aseptically inserted into the bladder.
2. An intravenous infusion of Lactated Ringer's (Hartmann's) solution is started in each arm, one to maintain a site for injection of the GLOFIL®-125, the other to serve as a site for serial withdrawal of blood. A two-way stopcock connects the needle and intravenous tubing of each arm.
3. The dose is equally divided into (1) an intravenous priming dose to be injected as is and (2) a sustaining dose to be diluted in 30 to 60 mL of isotonic sodium chloride, depending on how many collection periods are anticipated.
4. The priming dose is slowly injected into one arm. This is immediately followed by infusion of the sustaining solution through the same site, usually at the rate of 0.5 mL/min., by means of an automatic pump. During this infusion, the Lactated Ringer's solution in the same arm is discontinued, and 40 to

45 minutes are allowed for equilibration in order to reach a state of constant plasma concentration of radioactivity.

5. After attaining equilibrium, consecutive 15 minute collection periods are started. From the arm opposite the injection site, 5 mL of blood (allowing duplicate plasma counting volumes) is drawn six minutes prior to the midpoint of each collection period, placed in heparinized tubes, mixed, and centrifuged. The blood samples may be obtained through the two-way stopcock after discarding the first 30 mL aspirated into the syringe. This 30 mL contains the contents of the tubing, including infusion fluid, and must be cleared in order to obtain an undiluted blood sample. If desired, this step may be eliminated and blood samples obtained by direct venipuncture.
6. During each collection period, total urine must be accurately collected and the volume accurately measured. Three such consecutive collection periods are sufficient for most clinical studies.

III. Clearance Calculations:

1. Aliquots (1 mL each) of plasma and urine from each collection period are counted in a standard gamma-ray scintillation well detector.
2. All counts are corrected for background activity.
3. Glomerular filtration rate is calculated by the formula C=UV/P, in which:
   C = glomerular filtration rate in mL/min
   U= urinary concentration of radioactivity in net counts/min/mL
   V= urinary flow rate in mL/min
   P = plasma concentration of radioactivity in net counts/min/mL
4. Average glomerular filtration rate (GFR) is calculated from the rates for the individual collection periods. GFR can be expressed in terms of body weight (mL/min/kg) or body surface area ($mL/min/m^2$).
5. Unilateral glomerular filtration rates can be determined by the same technique by utilizing ureteral catheterization.

Single intravenous injection

Cohen (2) **method:**

The method of Cohen, et al (2) requires little preparation, few and small blood samples, no bladder catheterization, and no constant intravenous infusion. It is simple to perform, rapid, and utilizes equipment which is readily available in most modern laboratories.

I. Preparation:

1. Lugol's solution, 3 drops orally, three times a day, is administered for one or two days prior to the test.
   No diet or water restriction is necessary.
2. Oral water load is begun one hour before starting the test. Start with 20 mL/kg and force any clear liquids (unless contraindicated) until the test is complete.

II. Procedure: Record actual times for the collection of the blood and urine samples.

1. Empty the bladder and label the urine *Urine control.*
2. Inject 10-30 µCi GLOFIL®-125 intravenously; wait 30 to 60 minutes.
3. Collect the entire urine and label *Urine discard.*
4. Draw 4 to 5 mL of blood into a heparinized syringe. Label *Plasma #1.*
5. After another 30 to 60 minutes, collect the entire urine and label *Urine #1.*
6. Immediately draw another blood specimen. Label *Plasma #2.*
7. After final 30 to 60 minute wait, collect the urine. Label *Urine #2.*
8. Draw the last blood specimen immediately. Label *Plasma #3.*

III. Clearance Calculations:

1. Radioactivity of one mL aliquots of both urine and plasma are determined using a well-scintillation

detector with a single channel pulse-height analyzer. Sufficiently reproducible counts are usually obtained with time settings of 2 minutes for urine samples and 20 minutes for the plasma samples. Calculations of the clearance rates are made by using the formula:(1)

C = UV/P + 1.73/SA where

C = glomerular filtration rate in mL/min/1.73 m^2
U = urine radioactivity in counts/min/mL
V = urine flow rate in mL/min
P= mean plasma radioactivity in counts/min/mL
SA= body surface area in m^2

Radiation Dosimetry

The estimated absorbed radiation doses to an average (70 kg) patient from an intravenous dose of 100 µCi (3.7 megabecquerels) of GLOFIL®-125 are shown in Table 4. Calculations assume that there is 1% free iodide in the preparation and that the thyroid uptake of the iodine is 25%.

Table 4. Absorbed Radiation Doses*

	Absorbed radiation doses for 100 µCi (3.7 megabecquerels)			
	2 hour bladder voiding interval		4.8 hour bladder voiding interval	
Organ	rads	mGy	rads	mGy
Lower Large Intestine Wall	0.00065	0.0065	0.0012	0.012
Small Intestine	0.00044	0.0044	0.00050	0.0050
Stomach	0.00047	0.0047	0.00047	0.0047
Upper Large Intestine Wall	0.00040	0.0040	0.00044	0.0044
Kidneys	0.0064	0.064	0.0064	0.064
Liver	0.0018	0.018	0.0018	0.018
Ovaries	0.00054	0.0054	0.00085	0.0085
Testes	0.0019	0.019	0.0021	0.021
Urinary Bladder Wall	0.022	0.22	0.06	0.6
Red Marrow	0.00033	0.0033	0.00034	0.0034
Thyroid	0.78	7.8	0.78	7.8
Total Body	0.00096	0.0096	0.0011	0.011

* Data supplied by Oak Ridge Associated Universities, Radiopharmaceutical Internal Dose Information Center, Oak Ridge, TN, 1988.

Visual Inspection

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

HOW SUPPLIED

Identity

No. 1000, GLOFIL®-125 is a clear, colorless, sterile, and nonpyrogenic solution available as a 4 mL vial. It is supplied in a concentration of approximately 1 mg/mL sodium iothalamate (range is 0.5–2.0 mg sodium iothalamate per mL), with a radioactivity concentration of 250 to 300 µCi/mL at the time of calibration. Benzyl alcohol 0.9%, is added as a preservative. Sodium bicarbonate and hydrochloric acid are added for pH adjustment. The calibration and expiration dates are shown on the label.

Storage

Refrigerate the product upon receipt at 2°C to 8°C.

Dose Volume Calculation

Table 3 provides the required factors for the determination of activity per mL post calibration date for GLOFIL®-125 sterile solution.

To determine the dose volume, locate the decay factor (fraction remaining) which corresponds to the day that the dose is to be administered. The following equation is then utilized to determine the dose volume:

(activity of desired dose) /[(decay factor) x (amount of activity/mL on calibration day)] = dose volume (mL) (information on label)

REFERENCES

1. Sigman EM, Elwood CM, Reagan ME, Morris AM, Catanzaro A. The renal clearance of ^{131}I labeled sodium iothalamate in man. *Invest Urol* 1965; 2:432.
2. Cohen ML, Smith FG Jr., Mindell RS, Vernier RL. A simple reliable method of measuring glomerular filtration rate using single low dose sodium iothalamate ^{131}I.*Pediatrics* 1969; 43:407.

ADDITIONAL REFERENCES

3. Maher FT, Nolan NG, Elveback LR. Comparisons of simultaneous clearances of ^{125}I-labeled sodium iothalamate (Glofil) and of Inulin. *Mayo Clin Proc* 1971; 46: 690-691.
4. Skov PE. Glomerular filtration rate in patients with severe and very severe renal insufficiency. *Acta Med Scand* 1970; 187: 419-428.

Manufactured by Iso-Tex Diagnostics, Inc. for QOL Medical

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No. 1000

NDC 67871-772-92

GLOFIL-125

iothalamate sodium, i-125 injection

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:67871-772
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
Iothalamate sodium, I-125 (UNII: 31J5U3Q9ZN) (Iothalamate sodium, I-125 - UNII:31J5U3Q9ZN)		1 mg

Inactive Ingredients	
Ingredient Name	**Strength**
benzyl alcohol (UNII: LKG8494WBH)	
sodium bicarbonate (UNII: 8MDF5V39QO)	
hydrochloric acid (UNII: QTT17582CB)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:67871-772-92	4 mL in 1 VIAL		

Labeler - QOL Medical

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