

VOLUMEX- iodinated I-131 albumin injection, solution
Iso-Tex Diagnostics, Inc.

Volumex

R_x Only

DESCRIPTION

Volumex (Iodinated I 131 Albumin Injection) is a diagnostic radiopharmaceutical containing iodinated I 131 albumin for intravenous use. Each mL of sterile, nonpyrogenic, aqueous, colorless to very pale yellow solution provides approximately 10 mg protein (albumin human), 16 mg dibasic sodium phosphate, 1.6 mg monobasic sodium phosphate, not more, than 0.4 mg guanidine hydrochloride, sodium chloride for isotonicity, and 9 mg benzyl alcohol as a preservative. The stabilizer acetyltryptophanate and sodium caprylate have a concentration of less than 0.0089M. The pH has been adjusted to 7.2-7.8 with sodium hydroxide or hydrochloric acid.

Volumex was prepared from blood that was nonreactive when tested for hepatitis B surface antigen (HB_sAg). The structure of the complex is unknown.

PHYSICAL CHARACTERISTICS

Iodine 131 decays by beta and gamma emissions with a physical half-life of 8.08 days.¹

Photons that are useful for detection and imaging studies are listed in Table 1.

TABLE 1

Principal Radiation Emission Data		
Radiation	Mean % per Disintegration	Mean Energy (keV)
Beta-4 (average)	89.3	191.6
Gamma-14	81.2	364.5

¹Evaluated Nuclear Structure Data File of the Oak Ridge Nuclear Data Project DOE (1985).

EXTERNAL RADIATION

The specific gamma ray constant for iodine 131 is 2.2R/hour-millicurie at 1 cm. The first half-value layer is 0.24 cm lead (Pb). A range of values for the relative attenuation of the radiation emitted by this radionuclide that result from interposition of various thicknesses of Pb is shown in Table 2. To facilitate control of the radiation exposure from this radionuclide, the use of a 2.55 cm thickness of Pb will attenuate the radiation emitted by a factor of about 1,000.

TABLE 2

Radiation Attenuation by Lead Shielding	
Shield Thickness (Pb) cm	Attenuation Factor
0.24	0.5
0.89	10^{-1}
1.6	10^{-2}
2.55	10^{-3}
3.7	10^{-4}

To correct for physical decay of iodine 131, the fractions that remain at selected intervals after the time of calibration are shown in Table 3.

TABLE 3

Physical Decay Chart: Iodine 131 half-life 8.08 days					
Days	Fraction Remaining	Days	Fraction Remaining	Days	Fraction Remaining
0*	1.000	11	.388	21	.164
1	.918	12	.356	22	.151
2	.842	13	.327	23	.138
3	.773	14	.300	24	.127
4	.709	15	.275	25	.116
5	.651	16	.253	26	.107
6	.597	17	.232	27	.098
7	.548	18	.213	28	.090
8	.503	19	.195	29	.083
9	.461	20	.179	30	.076
10	.423				

*Calibration Time

CLINICAL PHARMACOLOGY

Following intravenous injection, radioiodinated albumin human is uniformly distributed throughout the intravascular pool within 10 minutes; extravascular distribution takes place more slowly. Iodinated I 131 albumin also can be detected in the lymph and in certain body tissues within 10 minutes after injection, but maximum distribution of radioactivity throughout the extravascular space does not occur until two to four days after administration. The time at which extravascular activity is maximal has been designated as the "equilibrium time." When this point has been reached, the radioactivity remaining in the intravascular and extravascular spaces decreases slowly and exponentially in parallel fashion.

The administered radioactivity is eliminated almost entirely in the urine, only about 2 percent of the total dose ultimately appearing in the feces.

The biologic half-life of iodinated I 131 albumin is dependent upon a number of factors, and published studies have varied considerably in their reporting of this figure. It has ranged, in the literature, from below 10 days to over 20 days. One important factor affecting the biologic half-life is the initial rate of excretion, and this depends in part on the quality of the iodinated I 131 albumin. With Volumex, the biologic half-life in normal individuals has been reported to be approximately 14 days.

INDICATIONS AND USAGE

Volumex (Iodinated I 131 Albumin injection) is indicated for use in determinations of total blood and plasma volumes and in protein turnover studies

CONTRAINDICATIONS

None known.

WARNINGS

A few instances of hyperpyrexia and aseptic (chemical) meningeal irritation have been reported

with the use of iodinated I 131 albumin in cisternography. Iodinated I 131 Albumin Injection is not approved for use in cisternography.

PRECAUTIONS

General

In the use of any radioactive material, care should be taken to insure minimum radiation exposure to the patient and occupational workers 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.

Carcinogenesis, Mutagenesis, Impairment of Fertility

No long-term animal studies have been performed to evaluate carcinogenic potential or whether iodinated I 131 albumin affects fertility in males or females.

Pregnancy Category C

Animal reproduction studies have not been conducted with Iodinated I 131 Albumin Injection. It is also not known whether this agent can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity.

Iodinated I 131 Albumin Injection should be administered to a pregnant woman only if clearly needed.

Ideally, examinations using radiopharmaceuticals, especially those elective in nature, of a woman of childbearing capability should be performed during the first few

(approximately 10) days following the onset of menses.

Nursing Mothers

Since iodine 131 is excreted in human milk during lactation, formula feedings should be substituted for breast feedings.

Pediatric use

Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Although the immunological properties of albumin human are believed to be virtually unaltered by the iodination process, there is a theoretical possibility that allergic reactions may occur in patients receiving additional doses a number of weeks after an initial dose.

DOSAGE AND ADMINISTRATION

Volumex (Iodinated I 131 Albumin Injection) is administered intravenously.

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

Volumex (Iodinated I 131 Albumin Injection) may be colorless to very pale yellow. Solutions with excessive coloration should not be used.

When a procedure such as a blood volume or a circulation time determination is to be repeated, the total dosage administered in any one week should not exceed 200 microcuries.

To minimize the uptake of radioactive iodine by the thyroid, prior administration of Lugol's Solution (Strong Iodine Solution USP) may be used. Ten drops of Lugol's Solution three times daily, beginning at least 24 hours before administration of Volumex and continuing for one or two weeks thereafter, is a suitable dose. Complete assay data for each single unit dose are provided on the container.

Note: The expiration date given on the container pertains to the biologic properties of the material and not to the radioactivity level. It is important to make certain that the radioactivity in the dose at the time of administration is sufficient for the intended use.

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

Note: A shielded syringe may be used for withdrawing and injecting the iodinated I 131 albumin.

Total Blood and Plasma Volumes

Dosage may range from 5 to 50 microcuries.

Blood Volume Determination

A. Reference Solution

Reference solution is provided with each single unit dose of Volumex. Determine the

radioactivity concentration (net cpm/mL) of the reference solution. Care must be taken to assure that the reference solution and the blood samples (Step B3) are assayed using the same geometric configuration.

B. Administration of Dose

1. After withdrawing a background blood sample as described below, insert an intravenous (IV) line into a large vein in patient's arm. Inject the entire Volumex dose (one milliliter) through the IV line for immediate delivery. Measure the residual radioactivity in the syringe and needle.
2. Destroy syringe after injecting. Do not attempt to resterilize. CAUTION: The syringe should be disposed of in accordance with the US Nuclear Regulatory Commission or Agreement State regulations pertaining to the disposal of radioactive waste.
3. At 12, 18, 24, 30 and 36 minutes after injecting the dose, withdraw blood samples from the patient with a sterile syringe or evacuated sample tube containing anti-coagulant.

C. Calculation of Blood Volume

1. Take a known aliquot from each blood sample and determine radioconcentration in net cpm/mL.
2. Plot the 12, 18, 24, 30 and 36 minute sample counts (net cpm/mL) on semilog graph paper using the average count value of each sample and determine the radioconcentration at injection time (zero time) by drawing a straight line through the 12, 18, 24, 30 and 36 minute points to zero time. The x ordinate of the graph is the sample withdrawal time and the logarithmic y ordinate is radioconcentration in net cpm/mL.
3. Calculate patient's blood volume (in mL) using the following formula:

$$\frac{\text{Net cpm/mL reference solution}}{\text{Net cpm/mL patient's blood sample}} \times \text{DF} = \frac{\text{blood volume}}{\text{(in mL)}}$$

Sample Blood Volume Calculations

$$\begin{aligned} \text{Volume of Blood sample aliquot} &= 1.0 \text{ mL} \\ \text{Volume of Reference Solution aliquot} &= 1.0 \text{ mL} \\ \text{Net counts at zero time} &= 48,100 \\ \text{Net counts obtained from reference solution aliquot} &= 52,430 \\ \text{If, for example, DF, dilution factor of the reference solution} &= 4000 \\ \text{Using the above formula gives} &= \frac{52,430}{48,100} \times 4000 = 4360 \text{ mL} \end{aligned}$$

Serial Blood Volume Determinations

Iodinated I 131 Albumin Injection is administered in sufficiently low dosage to permit repetitions as often as required by clinical circumstances. It must be remembered that it

is always necessary to correct for background radioactivity remaining in the blood from former determinations. Therefore, for each determination after the first one, a background blood sample must be taken just **before** the iodinated I 131 albumin is injected.

Background Blood Sample

1. Withdraw background blood sample from large vein in patient's sampling arm with a sterile syringe or evacuated sampling tube containing anti-coagulant.
2. Leaving needle in patient's vein, detach syringe containing blood sample.
3. Attached syringe containing the dose of Volumex to the indwelling IV line and administer (see instructions under **Blood Volume Determination, Administration of Dose**).
4. Determine radioconcentration in net cpm/mL of aliquots taken from background and postinjection blood samples, and from the reference solution.
5. The radioconcentration (net cpm/mL) per aliquot of the **background** blood sample must be subtracted from the radioconcentration per aliquot of the blood sample obtained after the injection of iodinated I 131 albumin. The formula for calculating each blood volume determination after the first one thus becomes:

$$\frac{\text{Net cpm/mL reference solution blood}}{\text{Net cpm/mL postinjection blood sample} \text{ minus } \text{Net cpm/mL background blood sample}} \times \text{DF} = \text{blood volume (in mL)}$$

Plasma Volume Determination

The procedure is essentially the same as that for blood volume determination, except that the blood sample drawn from the patient is centrifuged, the red blood cells are removed, and net cpm/mL of the plasma is determined. The formula for calculation of plasma volume, therefore is:

$$\frac{\text{Net cpm/mL reference solution}}{\text{Net cpm/mL patient's plasma sample}} \times \text{DF} = \text{plasma volume (in mL)}$$

Protein Turnover Studies

Dosages used have ranged from 10 to 150 microcuries. After injection, a period of seven days should be allowed before determinations are made to permit the elimination of any degraded protein in the dose.

Radiation Dosimetry

The estimated absorbed radiation doses to an average patient (70 kg) from an intravenous injection of 50 microcuries of Iodinated I 131 Albumin Injection USP are shown in Table 4.

TABLE 4

Estimated Absorbed Radiation Doses	
Tissue	Rads
Blood	0.25-1.0
Thyroid (blocked)	1.25-2.5
Liver	0.06
Gonads	0.1-0.45
Whole-body	0.05

Method of Calculation: Hine GJ, Johnston RE: Absorbed Doses from Radionuclides, J. Nucl Med 11:468-469, 1970.

For doses of 10, 25, 75, 150, 500 and 750 microcuries, the estimated absorbed doses are 0.2, 0.5, 1.5, 3, 10 and 15 times the number of rads given, respectively.

HOW SUPPLIED

Volumex (Iodinated I 131 Albumin Injection USP) is available in single unit dose syringes containing 25 microcuries of activity in one milliliter per syringe on the date of calibration. Each single unit dose syringe is supplied with reference solution. Complete assay data for each single unit dose syringe and reference solution are provided on their respective containers. The maximum concentration of a single unit dose syringe of Volumex does not exceed 26.3 microcuries per milliliter at time of calibration

Storage

Store in a refrigerator, 2-8°C (36-46°F)

This radiopharmaceutical is licensed by the Texas Department of Health, Bureau of Radiation Control for distribution to persons licensed

pursuant to 41.26 (b) and Appendix 41-C, Group I and Group II, "Texas Regulations for Control of Radiation," or under equivalent licenses of the

U.S. Nuclear Regulatory Commission, an Agreement State, or a Licensing State.

Manufactured for **Daxor Corporation**

350 Fifth Avenue, Suite 7120 · New York, NY 10118 · 212-244-0804

by Iso-Tex Diagnostics, Inc., Friendswood, Texas 77546

Packaging

VOLUMEX 25 uCi/ml 1 ml/syringe 25 uCi Total
 Single Unit Dose As of: 6 PM/CST
 IODINATED I-131 Albumin Injection USP
 For intravenous administration
 Rx only Lot No:
 Caution: Radioactive Material Exp. Date:
 Manufactured for Daxor Corp. NY, NY (212)244-0555
 By: Iso-Tex Diagnostics, Inc. 101615A



VOLUMEX

iodinated i-131 albumin injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:50914-7720
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
HUMAN SERUM ALBUMIN I-131 (UNII: ACH35131L1) (HUMAN SERUM ALBUMIN I-131 - UNII:ACH35131L1)	HUMAN SERUM ALBUMIN I-131	0.025 mCi in 1 mL

Inactive Ingredients

Ingredient Name	Strength
ALBUMIN HUMAN (UNII: ZIF514RVZR)	
BENZYL ALCOHOL (UNII: LKG8494WBH)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:50914-7720-8	1 mL in 1 SYRINGE, PLASTIC; Type 3: Prefilled Biologic Delivery Device/System (syringe, patch, etc.)	08/01/1993	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA017837	08/01/1993	

Labeler - Iso-Tex Diagnostics, Inc. (181202995)

Establishment

Name	Address	ID/FEI	Business Operations
Iso-Tex Diagnostics, Inc.		181202995	manufacture(50914-7720)

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Iso-Tex Diagnostics, Inc.