MEGATOPE- iodinated i-131 albumin injection, solution
Iso-Tex Diagnostics, Inc.

Megatope

CAUTION

Federal (USA) law prohibits dispensing without prescription

DESCRIPTION

Megatope (Iodinated I 131 Albumin Injection) is a diagonostic radiopharmaceutical containing iodinated I 131 albumin for intravenous use. Each mL of sterile, nonpyrogenic, aqueous, colorless to very pale yellow solution provides approximate 10 mg protein (albumin human), 16 mg dibasic sodium phosphate, 1.6 mg monobasic sodium phosphate, not more than 0.4 guanidine hydrochloride, sodium chloride for isotonicity, and 9 mg benzyl alcohol as a preservative. The pH has been adjusted to 7.2 to 7.8 with sodium hydroxide or hydrochloric acid.
Megatope was prepared from blood that was nonreactive when tested for hepatitis B surface antigen (HBsAg).
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

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

External Radiation

The specific gamma ray constant for iodine 131 is 2.2 R/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 can also 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 biological half-life is the initial rate of excretion, and this depends in part on the quality of the Iodinated I 131 albumin. With Megatope, the biologic half-life in normal individuals has been reported to be approximately 14 days.`

INDICATIONS AND USAGE

Megatope (Iodinated I 131 Albumin Injection) is indicated for use in determinations of total blood and plasma volumes, cardiac output, cardiac and pulmonary blood volumes and circulation times, and in protein turnover studies, heart and great vessel dilineation, localization of the placenta, and localization of celebral neospasms.

CONTRAINDICATIONS

None Known.

WARNINGS

A few instances of hyperpyrexia and aseptic (chemical) meningeal irritation have been reported with the use of iodinated I 131 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 iodinate I 131 albumin affects fertility in males and 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

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

When a procedure such as 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 Megatope and continuing for one or two weeks thereafter, is a suitable dose.

Complete assay data for each vial 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 should 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. Preparation of Reference Solution

Remove an aliquot of the contents of the vial to be used in the procedure identical in volume to the dose to be administered to the patient. Prepare a reference solution using normal saline as a diluent. The recommended dilution is 1:4000 [Dilution Factor (DF) = 4000]. 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.

A. Administration of Dose

1. Inject the dose into a large vein in patient's arm. Measure the residual radioactivity in the syringe and needle.
2. Destroy the 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 5 and 15 minutes after injecting the dose, withdraw blood samples **from the patient's other arm** with a sterile heparinized syringe.

B. Calculation of Blood Volume

1. Take a known aliquot from each blood sample and determine radioconcentration in net cpm/mL.
2. Plot the 5- and 15-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 15- and 5- minute points to zero time. The x ordinate iof the graph is the sample withdrawal time and the logarithmic y ordinate is radioconcentration in net cpm/mL.
3. Calculate the patient's blood volume (in mL) using the following formula:

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

Sample Blood Volume Calculations

Volume of blood sample aliquot = 1.0 mL

Volume of reference solution aliquot = 1.0 mL

Net counts at zero time = 48,100

Net counts obtained from reference solution aliquot = 52,430

Using the formula above gives $\frac{52,430}{48,100}$ x 4000 = 4360 mL

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 arm with a sterile heparinized syringe.
2. Leaving needle in patient's vein, detach syringe containing blood sample.
3. Attach syringe containing the dose of Megatope to the indwelling needle 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.

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:

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

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:

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

Cardiac Output

Dosage generally ranges from 3 to 50 microcuries.

Cardiac and Pulmonary Blood Volumes; Circulation Times

Dosages used have generally been 75 to 130 microcuries.

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.

Heart and Great Vessel Delineation

The suggested dosage is 5 microcuries per kg of body weight, although doses up to 750 microcuries have been used, depending on the instrumentation available and the scanning technique employed.

Localization of the Placenta

For localization of the placenta in the differential diagnosis of placenta praevia, a 3 to 5 microcurie dose is recommended; this dose has proved adequate for excellent localization, and the fetal total body radiation is a fraction of that received during x-ray placentography. While fetal thyroid irradiation is higher with Iodinated I 131 Albumin Injection than with x-ray placentography, the administration of Lugol's Solution is reported to eliminate this hazard.

Localization of Celebral Neospasms

The suggested dosage is 5 microcuries per kg of body weight. Although doses as large as 500 microcuries of Iodinated I 131 Albumin Injection have been used, the dose should be kept as small as possible. Dosage is administered six hours before the initial examination, and scans are repeated at periodic intervals.

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

HOW SUPPLIED

Megatope (Iodinated I 131 Albumin Injection USP) is available in multiple dose vials

containing the following amounts of activity on the date of calibration: 500 microcuries and 1.0 millicurie. Complete assay data for each vial are provided on the container.

The maximum concentration of Iodinated I 131 Albumin Injection does not exceed one millicurie per milliliter at a time of calibration.

Storage

Store between 2° and 8° C.

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.

Iso-Tex Diagnostics, Inc.

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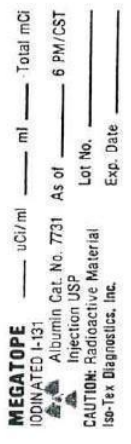
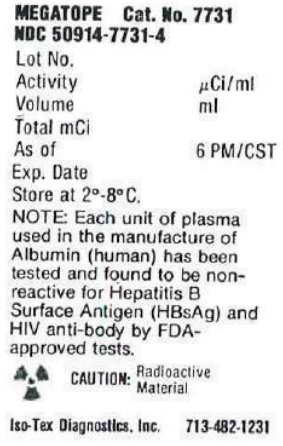
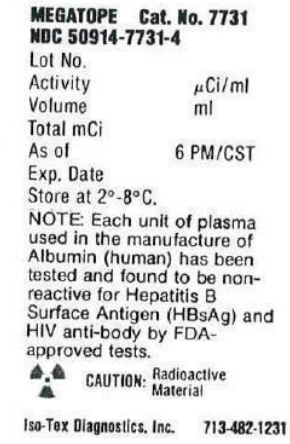
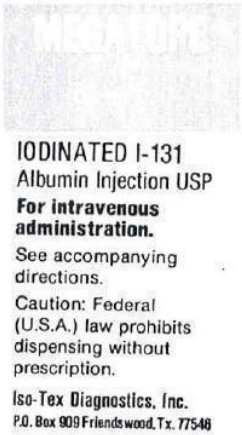
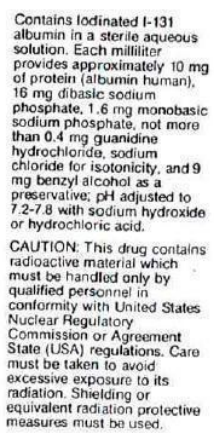
Packaging











MEGATOPE

iodinated i-131 albumin injection, solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:50914-7731
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
IODINATED I-131 SERUM ALBUMIN (UNII: ACH35131L1) (IODINATED I-131 SERUM	IODINATED I-131 SERUM	1 mCi

ALBUMIN - UNII:ACH35131L1)	ALBUMIN	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:50914-7731-4	8 mL in 1 VIAL, MULTI-DOSE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA017837	06/01/1990	

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

Establishment

Name	Address	ID/FEI	Business Operations
Iso-Tex Diagnostics, Inc.		181202995	manufacture(50914-7731)

Revised: 4/2014 Iso-Tex Diagnostics, Inc.