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

MEGATOPE

Rx only.

DESCRIPTION

Chemical Characteristics

MEGATOPE (iodinated I 131 albumin) injection is a sterile, nonpyrogenic, radioactive diagnostic agent for intravenous use. Each mL contains albumin human (approximately 10 mg), dibasic sodium phosphate (16 mg), guanidine hydrochloride (not more than 0.4 mg), monobasic sodium phosphate (1.6 mg), sodium chloride for isotonicity, and benzyl alcohol (9 mg) as a preservative. The stabilizers acetyltryptophanate and sodium caprylate have a concentration of less than 0.89 mM. The pH has been adjusted to 7.2 to 7.8 with sodium hydroxide or hydrochloric acid. Each vial contains 37 MBq/mL (1,000 microCi/mL) of radioactivity as iodinated I 131 albumin at time of calibration (see HOW SUPPLIED).

Physical Characteristics Iodine-131 decays by beta and gamma emissions with a physical half-life of 8.02 days. Photons that are useful for detection and imaging studies are listed in Table 1.

Table 1. Principal Radiation Emission Data[1]

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 8.02 days

Days	Fraction Remaining	Days	Fraction Remaining	Days	Fraction Remaining
0*	1	11	0.386	21	0.163
1	0.917	12	0.354	22	0.149
2	0.841	13	0.325	23	0.137
3	0.772	14	0.298	24	0.126
4	0.708	15	0.274	25	0.115
5	0.649	16	0.251	26	0.106
6	0.595	17	0.23	27	0.097
7	0.546	18	0.211	28	0.089
8	0.501	19	0.194	29	0.082
9	0.459	20	0.178	30	0.075
10	0.421				

* Calibration time

CLINICAL PHARMACOLOGY

Following intravenous injection, iodinated I 131 albumin is 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 appears 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 MEGATOPE, the biologic half-life in normal individuals has been reported to be approximately 14 days.

INDICATIONS AND USAGE

MEGATOPE is indicated in adults for use in determinations of total blood and plasma volumes.

CONTRAINDICATIONS

None Known.

WARNINGS

Aseptic meningitis and pyrogenic reactions have been reported following cisternography with MEGATOPE. The safety and effectiveness of MEGATOPE for cisternography have not been established. MEGATOPE is **not approved** for this use.

PRECAUTIONS

General

In the use of any radioactive material, care should be taken to minimize radiation exposure to the patient and healthcare providers consistent with proper patient management.

Radiopharmaceuticals should be used by or under control of healthcare providers who are qualified by specific 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

Iodine-131 crosses the placenta and can permanently impair fetal thyroid function. MEGATOPE should be administered to a pregnant woman only if clearly needed. Administration of an appropriate thyroid blocking agent is recommended before use of MEGATOPE in a pregnant woman to protect the woman and fetus from accumulation of iodine-131 (see DOSAGE AND ADMINISTRATION).

There are no data on iodinated I 131 albumin use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes. Animal reproduction studies have not been conducted. All radiopharmaceuticals have the potential to cause fetal harm depending on the fetal stage of development and the magnitude of the radiation dose.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 - 4% and 15 - 20%, respectively.

Nursing Mothers

Iodine-131 is present in human milk. There are no data on the effect of iodinated I 131 albumin on the breastfed infant or milk production. Because of the potential for serious adverse reactions in the breastfed infant, including transient hypothyroidism, advise women not to breastfeed during treatment with MEGATOPE and for 80 days after the final dose.

Pediatric Use

Safety and effectiveness of MEGATOPE in pediatric patients have not been established.

Geriatric Use

Clinical studies of MEGATOPE did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the

elderly and younger patients.

ADVERSE REACTIONS

The following adverse reactions have been identified with the use of radioiodinated albumin products. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Immune System Disorders: Hypersensitivity

DOSAGE AND ADMINISTRATION

Premedication

Administer 10 drops of Strong Iodine Solution, USP (e.g., Lugol's Solution) three times daily, beginning at least 24 hours before administration of MEGATOPE and continue for 1 week or 2 weeks thereafter to minimize the uptake of iodine-131.

Recommended Dosage

The recommended dose of MEGATOPE for total blood or plasma volume determination in adult patients is from 0.185 MBq to 1.85 MBq (5 microCi to 50 microCi) administered intravenously.

When a procedure such as a blood volume is to be repeated, do not exceed 7.4 MBq (200 microCi) in any 1 week.

Administration Instructions

• Measure the patient dose using a suitable dose calibrator immediately prior to administration.
• Use a shielded syringe for withdrawing and injecting MEGATOPE.
• Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. MEGATOPE is a colorless to very pale yellow solution. Do not use MEGATOPE if excessive coloration is present.
• The expiration date given on the MEGATOPE vial label pertains to the stability of MEGATOPE and not to the radioactivity level.

Blood Volume Determination

Preparation of Reference Solution

1. Remove the amount from the vial to be used in the procedure identical in volume to the dose to be administered to the patient.
2. Prepare a reference solution using 0.9% Sodium Chloride Injection, USP as a diluent. The recommended dilution is 1:4,000 [Dilution Factor (DF) = 4,000].
3. Determine the radioactivity concentration (net cpm/mL) of the reference solution.
4. Assay the reference solution and the blood samples (Step 3 of Administration of Dose) using the same geometric configuration.

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. Do not reuse the syringe. Dispose the syringe in accordance with the US Nuclear Regulatory Commission or Agreement State regulations pertaining to the disposal of

radioactive waste.
3. At 5 minutes and 15 minutes after injecting the dose, withdraw blood samples **from the patient's other arm** with a sterile heparinized syringe.

Calculation of Blood Volume
1. Take a known aliquot from each blood sample and determine radioactivity concentration in net cpm/mL.
2. Plot the 5-minute and 15- minute sample counts (net cpm/mL) on semilog graph paper using the average count value of each sample and determine the radioactivity concentration at injection time (zero time) by drawing a straight line through the 15-minute and 5-minute points to zero time. The x ordinate of the graph is the sample withdrawal time and the logarithmic y ordinate is radioactivity concentration in net cpm/mL.
3. Calculate patient's blood volume (in mL) using the following formula:

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

*DF: Dilution factor of reference solution

Sample Blood Volume Calculations

Volume of blood sample aliquot =	1 mL
Volume of reference solution aliquot =	1 mL
Net counts at zero time =	48,100
Net counts obtained from reference solution aliquot =	52,430

Using the formula above gives $\frac{52,430}{48,100} \times 4,000 = 4,360$ mL

Serial Blood Volume Determinations
• Use a low dose of MEGATOPE to permit repetitions as often as required by clinical circumstances.
• In each determination after the first dose, correct the background radioactivity remaining in the blood from former determinations by subtracting the radioactivity concentration of a blood sample obtained **before** the injection of MEGATOPE (i.e., background blood sample) from the radioactivity concentration of a post-injection blood sample.

Background Blood Sample
1. Prior to injecting MEGATOPE, 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 radioactivity concentration in net cpm/mL of aliquots taken from background and post-injection blood samples, and from the reference solution.

Calculation of Blood Volume
Subtract the radioactivity concentration (net cpm/mL) per aliquot of the background blood sample from the radioactivity concentration per aliquot of the blood sample obtained **after** the injection of MEGATOPE. The formula for calculating each blood volume determination after the first one thus becomes:

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

*DF: Dilution Factor of reference solution

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:

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

*DF: Dilution factor of reference solution

Radiation Dosimetry
The estimated absorbed radiation doses to an adult patient from an intravenous injection of 1.85 MBq (50 microCi) of MEGATOPE are shown in Table 4.

Table 4. Estimated Absorbed Radiation Doses

Tissue	Rads
Blood	0.25 to 1
Thyroid (blocked)	1.25 to 2.5
Liver	0.06
Gonads	0.1 to 0.45
Whole-body	0.05

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

HOW SUPPLIED

MEGATOPE (iodinated I 131 albumin) injection is a colorless to very pale yellow solution available in multiple-dose vials containing the following amounts of radioactivity on the date of calibration:

Total Radioactivity	Concentration	NDC
296 MBq/ 8 mL (8,000 microCi/ 8 mL)	37 MBq/mL (1,000 microCi/mL)	50914-7731-4

Complete radioassay data for each vial are provided on the MEGATOPE vial label.

Store refrigerated at 2º to 8ºC (36° to 46°F) in suitable lead shield.

This radiopharmaceutical is licensed for distribution to facilities and persons licensed by the U.S. Nuclear Regulatory Commission or under an equivalent license issued by an Agreement State.

Iso-Tex Diagnostics, Inc. • U.S. License No. 2189
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(281) 482-1231 • FAX: (281) 482-1070

Revised 7/2023
Code 95-1731/Rev.002

Packaging

Vial

NDC: 50914-7731-4 Rx only

Iodinated I 131 Albumin
MEGATOPE
Injection

Dosage: See Package Insert Multiple-dose vial

LOT: _____ EXP: _____
As of: _____ 6 PM/CST Total mL: __
Total activity: _____ MBq (_____ microCi)
Concentration: _____ MBq/mL (_____ microCi/mL)
Iso-Tex Diagnostics, Inc. 1511 County Road 129, Alvin, Texas 77511
U.S. License No. 2189 PL010 / Rev.002

Lead shield

NDC 50914-7731-4
Rx only

CAUTION:
RADIOACTIVE
MATERIAL

Iodinated I 131 Albumin
MEGATOPE
Injection
For Intravenous Use Only
Dosage: See Package Insert Multiple-dose Vial

LOT NO: EXP DATE:
As of: _____6 PM/CST Total mL: _____
Total activity: _____ MBq (___ microCi)
Concentration: _____ MBq/mL (___ microCi/mL)

Store refrigerated at 2°C to 8°C (36°F to 46°F) in suitable lead shield

Iso-Tex Diagnostics, Inc. 1511 County Road 129, Alvin, Texas 77511
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Plastic container

NDC: 50914-7731-4
Rx only

CAUTION RADIOACTIVE MATERIAL

Iodinated I 131 Albumin
MEGATOPE
Injection
For Intravenous Use Only
Dosage: See Package Insert
Multiple-dose vial
Store refrigerated at 2°C to 8°C (36°F to 46°F) in suitable lead shield

LOT NO: EXP DATE:
As of: _____6 PM/CST Total mL: _____
Total activity: _____ MBq (___ microCi)
Concentration: _____ MBq/mL (___ microCi/mL)

Each mL contains albumin human (approximately 10 mg), dibasic sodium phosphate (16 mg), guanidine hydrochloride (not more than 0.4 mg), monobasic sodium phosphate (1.6 mg), sodium chloride for isotonicity and benzyl alcohol (9 mg) as a preservative. The stabilizers acetyltrytophanate and sodium caprylate have a concentration of less than 0.89 mM. The pH has been adjusted to 7.2 to 7.8 with sodium hydroxide or hydrochloric acid.

CAUTION: This drug contains radioactive material which must be handled only by qualified personnel in conformity with United States Nuclear Regulatory Commission or Agreement State (USA) regulations. Care must be taken to avoid excessive exposure to its radiation. Shielding or equivalent radiation protective measures must be used.

Manufactured by:
Iso-Tex Diagnostics, Inc. 1511 County Road 129 Alvin, Texas 77511
U.S. License No. 2189 PL010 / Rev.002

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**
HUMAN SERUM ALBUMIN I-131 (UNII: ACH35131L1) (HUMAN SERUM ALBUMIN I-131 - UNII:ACH35131L1)	HUMAN SERUM ALBUMIN I-131	1 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:50914-7731-4	8 mL in 1 VIAL, MULTI-DOSE; Type 0: Not a Combination Product	05/21/1996	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA017837	05/21/1996	

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

Establishment

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

Revised: 9/2023 Iso-Tex Diagnostics, Inc.