SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Iodinated (\(^{125}\)I) human albumin injection CIS bio international
Reference : SERALB-125

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Iodinated (\(^{125}\)I) human albumin: 320 kBq at calibration date for 1.7 mL

This product contains an antimicrobial preservative.

Iodine (\(^{125}\)I) (atomic number 53; atomic weight 125) has a physical half-life of 60.14 days. It decays by electron capture (100%) to stable tellurium (\(^{125}\)Te). Only 7% of the iodine (\(^{125}\)I) disintegrations result in an elevated state of nuclear energy and the emission of gamma radiation with a mean energy of 35.5 KeV. Iodine (\(^{125}\)I) is therefore a poor gamma emitter and yet it is efficiently detected because of the (\(^{125}\)Te) X-rays (\(K_{\alpha} = 27\) keV; \(K_{\beta} = 31\) keV) produced in the decay process.

Excipient: benzyl alcohol
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear, colourless or slightly yellow solution with a pH ranging between 5.0 and 9.0.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

This medicinal product is for diagnostic use only.

Determination of plasma volume and total blood volume.
Examination of albumin turnover.
4.2. Posology and method of administration

The adult administered activities are:
- determination of plasma volume: 0.185 MBq - 0.2 MBq
- albumin turnover: 1 MBq

For the determination of plasma volume, blood samples are taken ten and twenty minutes after injection. If equilibrium is likely to be delayed by a sluggish circulation such as in cardiac failure or shock, then a third sample at forty minutes is advisable.

The dose to be administered in children should be a fraction of the adult dose and should be calculated according to the following equation:

\[
\text{Pediatric dose (MBq)} = \frac{\text{Adult dosage (MBq)} \times \text{Child weight (kg)}}{70 \text{ kg}}
\]

Although body weight is the more useful factor on which to base the adjustment of the activity administered, in a limited number of cases the body surface area may be considered to be more appropriate.

\[
\text{Pediatric dose (MBq)} = \frac{\text{Adult dose (MBq)} \times \text{Child surface (m²)}}{1.73}
\]

In order to block the possible accumulation of free radioiodine in the thyroid gland resulting from the catabolism of radiolabelled human albumin, oral administration of potassium iodate (140 mg/day), beginning 24 hours before the test and continuing for 1 week thereafter, or potassium perchlorate (200 mg/day) beginning 1 hour before the test and continuing 7-10 days after, is recommended. Significant hypersensitivity to iodide should contraindicate use of this product.

4.3. Contraindications

Due to the presence of benzyl alcohol, this medicinal product is contraindicated in Premature babies or neonates.

4.4. Special warnings and precautions for use

The product is prepared from batches of human serum albumin but has been screened for hepatitis B surface antigen (HBsAg), antibodies for human immunodeficiency virus (anti-HIV) and antibodies for hepatitis C virus (anti-HCV).

If the patient has received other radioactive materials recently, the blood background should be determined and the dose injected should be increased in order to exceed the blood background by a factor of 4.

The preparation must not be used intrathecally.

Radiopharmaceuticals should be administered only by authorised persons. Their receipt, use, transfer and disposal are subject to national licensing regulations.

Radiopharmaceuticals should be prepared by the user in a manner which satisfies both radiological safety and pharmaceutical quality requirements.

This medicine contains 0.016 mL of benzyl alcohol per vial. It may cause toxic reactions and anaphylactoid reactions in infants and children up to 3 years old.
4.5. Interaction with other medicinal products and other forms of interaction

None have been described.

4.6. Pregnancy and lactation

**Pregnancy**

When it is necessary to administer radioactive medicinal products to women of childbearing potential, information should always be sought about pregnancy. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. Where uncertainty exists it is important that radiation exposure should be the minimum consistent with achieving the desired clinical information. Alternative techniques which do not involve ionising radiation should be considered.

Radionuclide procedures carried out on pregnant women also involve radiation doses to the fetus. Only imperative investigations should be carried out during pregnancy, when the likely benefit exceeds the risk incurred by the mother and the foetus. Administration of 0.185 MBq and 1 MBq iodinated \(^{125}\text{I}\) human albumin to a patient results in an absorbed dose to the uterus of \(3.7 \times 10^{-2}\) and \(2.0 \times 10^{-1}\) mGy respectively. Doses above 0.5 mGy would be regarded as a potential risk to the fetus.

**Lactation**

Before administering a radioactive medicinal product to a mother who is breast feeding consideration should be given as to whether the investigation could be reasonably delayed until the mother has ceased breast feeding and as to whether the most appropriate choice of radiopharmaceutical has been made, bearing in mind the secretion of radioactivity in breast milk. If the administration is considered necessary, breast feeding should be interrupted and not restarted until the level in the milk will not result in a radiation dose to the child greater than 1 mSv.

4.7. Effect on ability to drive and use machines

None known to date.

4.8 Undesirable effects

With the administration of iodinated human albumin, allergic and febrile reactions have been reported. Manifestations include fever, dizziness, nausea, vomiting, tachycardia, hypotension and urticaria.

For each patient, exposure to ionising radiation must be justifiable on the basis of likely benefit. The activity administered must be such that the resulting radiation dose is as low as reasonably achievable bearing in mind the need to obtain the intended diagnostic or therapeutic result.

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. For diagnostic nuclear medicine investigations the current evidence suggests that these adverse effects will occur with low frequency because of the low radiation doses incurred.

For most diagnostic investigations using a nuclear medicine procedure the radiation dose delivered \((E)\) is less than 20 mSv. Higher doses may be justified in some clinical circumstances.
Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

4.9. Overdose

With a diagnostic radiopharmaceutical classical overdosage is not relevant. In general, the dangers to be expected are those relating to the inadvertent administration of excess activity. If overdosage of radioactivity occurs, frequent voiding urine should be encouraged in order to minimize radiation exposure to the patient.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: diagnostic radiopharmaceuticals.

ATC code: V09GB02

\(^{125}\text{I}\) human albumin, administered at the recommended dose, shows no detectable pharmacodynamic effects in patients.

5.2. Pharmacokinetic properties

Analysis of radioactivity indicates that administered iodinated human albumin will distribute from the blood to produce a disappearance curve which could be described as the sum of three exponential components, having half-times of 6.8 hours (0.40), 1.29 days (0.22) and 19.4 days (0.38). Gradual metabolism of iodinated human albumin suggests that some free \(^{125}\text{I}\) will be available and may be taken up by the thyroid. Blockade of thyroid uptake diverts radioactivity into urinary excretion.

5.3. Preclinical safety data

No studies of toxicity in animals models of radiiodinated human albumin have been reported.

The human albumin is a natural component of human blood and the labelling process does not alter the biological behaviour in vivo when no more than one atom of iodine for each molecule of albumin is present.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Human albumin, benzyl alcohol, sodium chloride, water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.
6.3. Shelf-life

49 days from the date of manufacture. The expiry date is indicated on the outer packaging and on each vial.

6.4. Special precautions for storage

Store in a refrigerator (2°C – 8°C) in its original packaging.

Storage procedures should be in accordance with national regulations for radioactive materials.

6.5. Nature and contents of container

5 mL, colourless, European Pharmacopoeia type I, drawn glass vials, closed with rubber stoppers and aluminium capsules.

Pack size: 4 single dose vials containing 320 kBq at calibration date (1,7 mL)

6.6. Special precautions for disposal and other handling

Usual precautions regarding sterility and radioprotection should be respected.

Before use, packaging, pH, radioactivity and spectrum will be checked.

The vial should never be opened and must be kept inside its lead shielding.

The product should be aseptically withdrawn through the stopper using sterilized single use needle and syringe after desinfection of the stopper.

The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spills of urine, vomiting, etc. Radiation protection precautions in accordance with national regulations must therefore be taken.

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

CIS bio international
R.N. 306- Saclay
B.P. 32
91192 GIF-SUR-YVETTE CEDEX
FRANCE

8. MARKETING AUTHORISATION NUMBER

Country specific

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION
11. DOSIMETRY

According to ICRP 53 and 60 the radiation doses absorbed by the patients, with thyroid blocking are the following:

<table>
<thead>
<tr>
<th>Organ</th>
<th>ABSORBED DOSE PER UNIT OF ADMINISTERED ACTIVITY (mGy/MBq)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adult</td>
</tr>
<tr>
<td>Adrenals</td>
<td>3.0 x 10^{-1}</td>
</tr>
<tr>
<td>Bladder wall</td>
<td>2.0 x 10^{-1}</td>
</tr>
<tr>
<td>Bone surfaces</td>
<td>3.2 x 10^{-1}</td>
</tr>
<tr>
<td>Breast</td>
<td>2.0 x 10^{-1}</td>
</tr>
<tr>
<td>Gastrointestinal tract</td>
<td></td>
</tr>
<tr>
<td>Stomach wall</td>
<td>2.1 x 10^{-1}</td>
</tr>
<tr>
<td>Small intestine</td>
<td>2.1 x 10^{-1}</td>
</tr>
<tr>
<td>Upper large intestine wall</td>
<td>2.1 x 10^{-1}</td>
</tr>
<tr>
<td>Lower large intestine wall</td>
<td>2.0 x 10^{-1}</td>
</tr>
<tr>
<td>Heart</td>
<td>6.9 x 10^{-1}</td>
</tr>
<tr>
<td>Kidneys</td>
<td>3.3 x 10^{-1}</td>
</tr>
<tr>
<td>Liver</td>
<td>3.0 x 10^{-1}</td>
</tr>
<tr>
<td>Lungs</td>
<td>5.7 x 10^{-1}</td>
</tr>
<tr>
<td>Ovaries</td>
<td>2.0 x 10^{-1}</td>
</tr>
<tr>
<td>Pancreas</td>
<td>2.3 x 10^{-1}</td>
</tr>
<tr>
<td>Red marrow</td>
<td>3.7 x 10^{-1}</td>
</tr>
<tr>
<td>Spleen</td>
<td>5.9 x 10^{-1}</td>
</tr>
<tr>
<td>Testes</td>
<td>1.6 x 10^{-1}</td>
</tr>
<tr>
<td>Thyroid</td>
<td>2.6 x 10^{-1}</td>
</tr>
<tr>
<td>Uterus</td>
<td>2.0 x 10^{-1}</td>
</tr>
<tr>
<td>Other tissue</td>
<td>1.9 x 10^{-1}</td>
</tr>
<tr>
<td>Effective dose (mSv/MBq)</td>
<td>3.0 x 10^{-1}</td>
</tr>
</tbody>
</table>

For this product the effective dose (E) resulting from an administered activity of 1 MBq is typically $3.0 \times 10^{-1}$ mSv (per 70 kg individual) with thyroid blockade.
12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Any unused product or waste material should be disposed of in accordance with local requirements.