SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Iodinated (^{125}I) human albumin CIS bio international 320 kBq solution for injection
Reference: SERALB-125

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains 320 kBq Iodinated (^{125}I) human albumin at calibration date.

Iodinated (^{125}I) human albumin CIS bio international is prepared from human serum albumin derived from human blood donations tested according to the EEC Regulations.

Iodine (^{125}I) has a physical half-life of 59,4 days. It decays by electron capture (100%) to stable tellurium (^{125}Te). Only 6,7% 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 with known effect:

benzyl alcohol (16,6 mg per vial).

For the 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.

It is indicated in adults and children over one month in:

- Determination of plasma volume
- Examination of albumin turnover.

4.2 Posology and method of administration

Posology

Adults

In adults of average body weight of 70 kg, the recommended average activity is:

determination of plasma volume	: 0.2 MBq
albumin turnover	: 1 MBq

Renal impairment

Careful consideration of the activity to be administered is required since an increased radiation exposure is possible in these patients.

Paediatric population

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

$$\text{Pediatric activity (MBq)} = \frac{\text{Adult activity (MBq) x Child weight (kg)}}{\text{70 kg}}$$

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:

$$\text{Pediatric activity (MBq)} = \frac{\text{Adult activity (MBq) x Child surface (m}^2\text{)}}{1.73}$$

Method of administration

Single dose vial.

Intravenous use.

Precautions to be taken before administration of the medicinal product

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.

For patient preparation, see section 4.4.

Determination of plasma volume

For the determination of total blood/plasma volumes, 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 radioactive concentrations in total blood/plasma samples are plotted on a logarithmic scale and extrapolation back to zero time allows estimation of the virtual activity at this time. Total blood/plasma volume is the ratio of the injected activity to the activity in 1 mL total blood/plasma at zero time.

For determination of albumin turnover, blood samples are taken daily for 7 days and the radioactive concentrations are plotted on a logarithmic scale and extrapolated to zero time. The half-live is calculated on the graph.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Premature babies or neonates due to the presence of benzyl alcohol (see section 4.4).

4.4 Special warnings and precautions for use

Potential for hypersensitivity or anaphylactic reactions
If hypersensitivity or anaphylactic reactions occur, the administration of the medicinal product must be discontinued immediately and intravenous treatment initiated, if necessary. To enable immediate action in emergencies, the necessary medicinal products and equipment such as endotracheal tube and ventilator must be immediately available.

Individual benefit/risk justification
For each patient, the radiation exposure must be justifiable by the likely benefit. The activity administered should in every case be as low as reasonably achievable to obtain the required diagnostic information.

Renal impairment
Careful consideration of the benefit risk ratio in these patients is required since an increased radiation exposure is possible.

Paediatric population
For information on the use in paediatric population, see section 4.2.
Careful consideration of the indication is required since the effective dose per MBq is higher than in adults (see section 11).

Patient preparation
Thyroid blockade before administration of iodine albumin solution (^{125}I) helps prevent possible accumulation of free radioactive iodine in the thyroid resulting from the catabolism of labeled human albumin (see section 4.2).

The patient should be well hydrated before the start of the examination and urged to void as often as possible during the first hours after the examination in order to reduce radiation.

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

This product contains human albumin.
Standard measures to prevent infections resulting from the use of medicinal products prepared from human blood or plasma include selection of donors, screening of individual donations and plasma pools for specific markers of infection and the inclusion of effective manufacturing steps for the inactivation/removal of viruses. Despite this, when medicinal products prepared from human blood or plasma are administered, the possibility of transmitting infective agents cannot be totally excluded.
This also applies to unknown or emerging viruses and other pathogens.
There are no reports of virus transmissions with albumin manufactured to European Pharmacopoeia specifications by established processes.

Traceability
In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

This medicine contains 16.6 mg benzyl alcohol in each vial which is equivalent to 9.8 mg/mL.

Benzyl alcohol may cause allergic reactions. Intravenous administration of benzyl alcohol has been associated with serious adverse events and death in neonates ("gasping syndrome"). The minimum amount of benzyl alcohol at which toxicity may occur is not known.

This medicinal product contains less than 1 mmol sodium (23 mg) per injection, that is to say essentially 'sodium- free'.

Precautions with respect to environmental hazard see section 6.6.

4.5 Interaction with other medicinal products and other forms of interaction

None have been described.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential
When an administration of radiopharmaceuticals to a woman of childbearing potential is intended, it is important to determine whether or not she is pregnant. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. If is doubt about her potential pregnancy (if the woman has missed a period, if the period is very irregular, etc.), alternative techniques not using ionising radiation (if there are any) should be offered to the patient.

Pregnancy
Radionuclide procedures carried out on pregnant women also involve radiation dose to the foetus. Only essential investigations should therefore be carried out during pregnancy, when the likely benefit far exceeds the risk incurred by the mother and foetus. Administration of 0.2 MBq and 1 MBq iodinated (^{125}I) human albumin to a patient results in an absorbed dose to the uterus of 0.04 and 0.20 mGy respectively.

Lactation
Before administering radiopharmaceuticals to a mother who is breastfeeding consideration should be given to the possibility of delaying the administration of radionuclide until the mother has ceased breastfeeding, and to what is the most appropriate choice of radiopharmaceuticals, bearing in mind the secretion of activity in breast milk. If the administration is considered necessary, breast feeding should be interrupted and the milk expressed should be discarded.

Fertility
No studies on fertility have been performed.

4.7 Effects on ability to drive and use machines

Iodinated (^{125}I) human albumin CIS bio international has no or negligible influence on the ability to drive and use machines.

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4.8 Undesirable effects

For safety information with respect to transmissible agents, see section 4.4.

The table below reports adverse reactions by MedDRA system organ classes.
The frequency listed below is defined using the following convention: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data)

MedDRA System Organ Classes	**Adverse reactions**	**Frequency**
Immune system disorders	Anaphylactoid reactions (e.g. hypersensitivity, dizziness, nausea, vomiting, tachycardia, hypotension and urticaria)	Not known
General disorders and administration site conditions	Fever	Not known

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose is 0.2 mSv when the maximal recommended activity of 1 MBq is administered these adverse reactions are expected to occur with a low probability.

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

In the event of administration of a radiation overdose with Iodinated (^{125}I) human albumin CIS bio international, there is no immediate applicable measure to be taken to reduce tissues radiation exposure, as the labelled product is not significantly eliminated by urine or faeces.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: diagnostic radiopharmaceuticals for cardiovascular system, iodine (^{125}I) compounds, ATC code: V09GB02

Pharmacodynamic effect
Iodinated (^{125}I) human albumin, at recommended activities and at the chemical concentrations used for diagnostic examinations, does not appear to have any pharmacodynamic activity.

5.2 Pharmacokinetic properties

Distribution
Following intravenous injection, the blood disappearance curve can be described as the sum of three exponential components, having half-times of 6.8 hours, 1.29 days and 19.4 days.

Organ uptake
Gradual metabolism of iodinated human albumin suggests that some free ^{125}I may be released and taken up by the thyroid gland. Blockade of thyroid uptake diverts radioactivity into urinary excretion.

Elimination
The iodinated human albumin is a substance which is identical from a chemical, biological and immunological point of view to the albumin in the organism. The liver, despite its high rate of protein metabolism, degrades 15% or less of the total; the kidneys are responsible for about 10%, while another 10% leaks through the stomach wall into the gastrointestinal tract.

Insuffisance rénale/hépatique
In patients with renal impairment, even slight, considerable retention of radioiodine in the body (due to the reduced renal clearance of iodine) is present.

5.3 Preclinical safety data

No studies of toxicity in animals models of radioiodinated human albumin have been performed.

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.

This medicinal product is not intended for regular or continuous administration.
Mutagenicity studies und long-term carcinogenicity studies have not been carried out.

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

Do not store above 25°C. Store in the original package.

Storage of radiopharmaceuticals should be in accordance with national regulations on radioactive materials.

6.5 Nature and contents of container

5 mL, colourless, European Pharmacopoeia type I, drawn glass vials, closed with EFTE coated chlorobutyl stopper and polypropylene lid welded to an aluminium crimp capsule.

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

6.6 Special precautions for disposal and other handling

General warning
Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licenses of the competent official organisation.
Radiopharmaceuticals should be prepared in a manner which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken.

Administration procedures should be carried out in a way to minims risk of contamination of the medicinal product and irradiation of the operators. Adequate shielding is mandatory.

Before use, packaging, radioactivity and spectrum should be checked.
Withdrawals should be performed under aseptic conditions. The vial must never be opened. After disinfecting the stopper, the solution should be withdrawn via the stopper using a single dose syringe fitted with suitable protective shielding and a disposable sterile needle or using an authorised automated application system. If the integrity of this vial is compromised, the product should not be used.

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

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

7. MARKETING AUTHORISATION HOLDER

Country specific

8. MARKETING AUTHORISATION NUMBER(S)

Country specific

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Country specific

10. DATE OF REVISION OF THE TEXT

10/2026

11. DOSIMETRY

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

Organ	ABSORBED DOSE PER UNIT OF ADMINISTERED ACTIVITY (mGy/MBq)				
	Adult	15 years	10 years	5 years	1 year
Adrenals	0.3	0.39	0.67	1.1	2.3
Bladder wall	0.2	0.25	0.38	0.65	1.4
Bone surfaces	0.32	0.42	0.73	1.2	2.6
Breast	0.2	0.21	0.32	0.54	1.1
Gastrointestinal tract					
Stomach wall	0.21	0.26	0.4	0.7	1.4
Small intestine	0.21	0.25	0.42	0.69	1.4
Upper large intestine wall	0.21	0.25	0.42	0.67	1.4
Lower large intestine wall	0.2	0.24	0.38	0.63	1.3
Heart	0.69	0.8	1.3	2.0	3.6
Kidneys	0.33	0.41	0.68	0.11	2.2
Liver	0.3	0.35	0.6	0.98	1.9
Lungs	0.57	0.72	1.2	1.9	3.8
Ovaries	0.2	0.25	0.42	0.69	1.4
Pancreas	0.23	0.27	0.46	0.78	1.6
Red marrow	0.37	0.46	0.78	1.3	2.6
Spleen	0.59	0.69	1.1	1.8	3.6
Testes	0.16	0.21	0.33	0.54	1.1
Thyroid	0.26	0.33	0.56	0.93	1.8
Uterus	0.2	0.25	0.42	0.68	1.4
Other tissue	0.19	0.23	0.37	0.6	1.2
Effective dose (mSv/MBq)	**0.3**	**0.36**	**0.6**	**0.98**	**2.0**

According to ICRP 80, the effective dose resulting from the administration of a (maximal recommended) activity of 1 MBq for an adult weighting 70 kg with thyroid blockade, is about 0.2 mSv.
For an administered activity of 1 MBq the typical radiation dose to the target organ, heart, is 0.7 mGy and the typical radiation dose/doses to the critical organs, spleen and lungs, are both 0,6 mGy.