



## **VASCULOCIS 10 mg kit for radiopharmaceutical preparation**

### **SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE MEDICINAL PRODUCT

VASCULOCIS 10 mg kit for radiopharmaceutical preparation.

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains 10 mg of human serum albumin (HSA)

The radionuclide is not part of the kit.

Excipient with known effect: 3.6 mg of sodium

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Kit for radiopharmaceutical preparation.

White powder.

## 4. CLINICAL PARTICULARS

### 4.1. Therapeutic indications

This medicinal product is for diagnostic use only.

After labelling with sodium pertechnetate ( $^{99m}\text{Tc}$ ) solution, the solution of technetium ( $^{99m}\text{Tc}$ ) human albumin is indicated for blood pool imaging, angiocardiology and ventriculography.

### 4.2. Posology and method of administration

#### Posology

##### *Adults:*

The recommended activity administered to an adult weighing 70 kg depends on the indication:

- Static blood pool imaging: 111-185 MBq.
- Radionuclidic angiocardiology: 370-740 MBq.
- Circulation and blood flow studies: 18.5-185 MBq.
- Ventriculography 185-925 MBq.

### *Paediatric population*

The use in paediatric children and adolescents has to be considered carefully, based upon clinical needs and assessing the risk/benefit ratio in this patient group.

For the ventriculography and the angiocardiology, the activities to be administered to children and to adolescents may be calculated according to the paediatric Task Group of the EANM (2008). This activity can be calculated from the formula below using a multiplying coefficient based on the patient's body mass (table 1).

$$\text{Recommended activity [MBq]} = 56.0 \text{ MBq} \times \text{Factor (Table 1)}$$

**Table 1**

Body weight	factor	Body weight	factor	Body weight	factor
3 kg	= 1*	22 kg	= 5.29	42 kg	= 9.14
4 kg	= 1.14*	24 kg	= 5.71	44 kg	= 9.57
6 kg	= 1.71	26 kg	= 6.14	46 kg	= 10.00
8 kg	= 2.14	28 kg	= 6.43	48 kg	= 10.29
10 kg	= 2.71	30 kg	= 6.86	50 kg	= 10.71
12 kg	= 3.14	32 kg	= 7.29	52-54 kg	= 11.29
14 kg	= 3.57	34 kg	= 7.72	56-58 kg	= 12.00
16 kg	= 4.00	36 kg	= 8.00	60-62 kg	= 12.71
18 kg	= 4.43	38 kg	= 8.43	64-66 kg	= 13.43
20 kg	= 4.86	40 kg	= 8.86	68 kg	= 14.00

\*In very young children (up to 1 year) a minimum dose of 80 MBq is necessary in order to obtain images of sufficient quality.

For the blood pool imaging and the circulation and blood flow studies, the activity to be administered in children should be a fraction of the adult dose and should be calculated according to the following equation:

$$\text{Paediatric dose (MBq)} = \frac{\text{Adult dose (MBq)} \times \text{Child weight (kg)}}{70}$$

Although body weight is the more used 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.

$$\text{Paediatric dose (MBq)} = \frac{\text{Adult dose (MBq)} \times \text{Child body surface (m}^2\text{)}}{1.73}$$

### **Method of administration**

This medicinal product should be reconstituted before administration to the patient.

The radiolabelled solution should be administered by intravenous injection, whatever the indication.

For the radionuclidic angiocardigraphy, the technetium ( $^{99m}\text{Tc}$ ) human albumin solution should be administered via a rapid intravenous bolus (1-2 mL) of 370 to 740 MBq.

For instructions on extemporaneous preparation of the medicinal product before administration, see section 12.

For patient preparation, see section 4.4.

### **Image acquisition**

In the course of ventriculography or angiocardigraphy, the image acquisition starts during the injection of the medicinal product (first-pass images) and continues during 10 to 15 minutes (equilibrium images).

In the course of the blood pool imaging and the circulation and blood flow studies, the image acquisition can start immediately after injection and be repeated at regular intervals until 24 hours after injection.

## **4.3. Contraindications**

Hypersensitivity to the active substance, to any of the excipients listed in section 6.1 or to any of the components of the radiolabelled radiopharmaceutical.

## **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.

### 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

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 the radiation.

### Specific warnings

This product is not indicated to be administered in the spinal and cerebral fluid for myeloscintigraphy and cisternography.

Vasculocis contains human serum 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.

It is strongly recommended that every time that Vasculocis is administered to a patient, the name and batch number of the product are recorded in order to maintain a link between the patient and the batch of the product.

This medicinal product contains less than 1 mmol of sodium (23 mg) per dose, i.e. essentially "sodium-free".

Precautions with respect to environmental hazard, see section 6.6.

## **4.5. Interaction with other medicinal product and other forms of interaction**

None known.

#### **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 in 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 the foetus.

##### Breast-feeding:

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 for 12 hours and the expressed feeds discarded.

#### **4.7. Effects on the ability to drive and use machines**

No studies on the effects on the ability to drive and use machines have been performed.

#### **4.8. Undesirable effects**

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

Adverse Reactions sorted by System Organ Class and frequency:

Immune system disorders:

Frequency unknown: hypersensitivity, face oedema.

Nervous system disorders:

Frequency unknown: vertigo

Cardiac disorders:

Frequency unknown: tachycardia

Vascular disorders:

Frequency unknown: circulatory collapse, vasodilatation, hypotension, flushing

Respiratory, thoracic and mediastinal disorders:

Frequency unknown: dyspnoea

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose is 5.6 mSv when the maximal recommended activity of 925 MBq is administered these adverse reactions are expected to occur with a low probability.

#### **4.9. Overdose**

In the event of administration of a radiation overdose with the technetium ( $^{99m}\text{Tc}$ ) human albumin solution, the absorbed dose to the patient should be reduced where possible by increasing the elimination of the radionuclide from the body by forced diuresis and frequent bladder voiding.

### **5. PHARMACOLOGICAL PROPERTIES**

#### **5.1. Pharmacodynamic properties**

Pharmacotherapeutic group: Radiopharmaceuticals preparation for diagnostic use, cardiovascular system.

ATC code: V09GA04.

At the chemical concentrations used for diagnostic examinations, technetium ( $^{99m}\text{Tc}$ ) human albumin does not appear to have any pharmacodynamic activity.

## **5.2. Pharmacokinetics properties**

Human serum albumin is a naturally occurring component of blood. It remains within the blood stream for at least four hours.

No significant concentration of technetium ( $^{99m}\text{Tc}$ ) human albumin outside the vascular space is observed, except in excretory organs (kidney, bladder).

## **5.3. Preclinical safety data**

The product used in preclinical studies contained 10 mg of human serum albumin and 0.02 mg of stannous chloride dihydrate.

Doses equivalent to approximately 900 times the human dose of 0.14 mg/kg (126 mg/kg) cause no deaths or adverse reactions in mice and rats injected intravenously with heterologous protein.

Repeated dose toxicity studies performed in rats show no detectable variations in the general behaviour of the animals and in haematological and biochemical parameters taken into consideration after intravenous administration during 14 days of doses equivalent to approximately 50 and 100 times the human dose of 0.14 mg/kg (7.15 mg/kg and 14.3 mg/kg per day). No evidence of pathological changes in the main organs are detected.

This medicinal product is not intended for regular or continuous administration.

Mutagenicity and long-term carcinogenicity studies have not been carried out.

# **6. PHARMACEUTICAL PARTICULARS**

## **6.1. List of excipients**

Stannous chloride dihydrate  
Sodium chloride  
Under nitrogen atmosphere



## 6.2. Incompatibilities

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

## 6.3. Shelf life

1 year from the manufacturing date.

The expiry date is indicated on the outer packaging and on each vial.

Do not store the labelled product above 25°C, and use within 8 hours.

## 6.4. Special precautions for storage

Store the kit in a refrigerator (between 2°C and 8° C).

For storage conditions of the radiolabelled medicinal product, see section 6.3.

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

## 6.5. Nature and contents of container

15 mL, brown coloured, European Pharmacopoeia type I, drawn glass vials, closed with chlorobutyl rubber stoppers and aluminium capsules.

Pack size: 5 multidose vials.

## 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 licences 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.

Contents of the vial are intended only for use in the preparation of the technetium ( $^{99m}\text{Tc}$ ) human albumin and are not administered directly to the patient without first undergoing the preparative procedure.

For instructions on extemporaneous solution of the medicinal product before administration, see section 12.

If at any time in the preparation of this product the integrity of the vial is compromised, it should not be used.

Administration procedures should be carried out in a way to minimise risk of contamination of the medicinal product and irradiation of the operators.

The content of the kit before reconstitution is not radioactive. However, after technetium ( $^{99m}\text{Tc}$ ) human albumin solution is added, adequate shielding of the final preparation must be maintained.

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

## **7. MARKETING AUTHORIZATION HOLDER**

CIS bio international  
RN 306 - Saclay  
BP 32 - 91192 Gif sur Yvette Cedex  
FRANCE

## **8. MARKETING AUTHORISATION NUMBER**

Country specific.

## **9. DATE OF FIRST AUTHORISATION / RENEWAL OF AUTHORISATION**

Country specific.

## **10. DATE OF REVISION OF TEXT**

12/2012

## 11. DOSIMETRY

Technetium ( $^{99m}\text{Tc}$ ) is produced by means of a ( $^{99}\text{Mo}/^{99m}\text{Tc}$ ) generator and decays with the emission of gamma radiation with a mean energy of 140 keV and a half-life of 6.02 hours to technetium ( $^{99}\text{Tc}$ ) which, in view of its long half-life of  $2.13 \times 10^5$  years can be regarded as quasi stable.

According to ICRP 53, 60 and 80 the radiation doses absorbed by the patients are the following:

ORGAN	ABSORBED DOSE PER ACTIVITY ADMINISTERED (mGy/MBq)				
	Adult	15 years	10 years	5 years	1 year
Adrenals	8.3E-03	1.0E-02	1.6E-02	2.5E-02	4.7E-02
Bladder wall	4.0E-03	5.8E-03	8.1E-03	1.1E-02	2.1E-02
Bone surfaces	8.9E-03	1.2E-02	2.2E-02	3.6E-02	7.1E-02
Breast	4.6E-03	4.7E-03	7.4E-03	1.1E-02	2.0E-02
Gastrointestinal tract					
Stomach wall	5.1E-03	6.5E-03	1.0E-02	1.4E-02	2.5E-02
Small intestine	4.8E-03	5.8E-03	8.8E-03	1.3E-02	2.4E-02
Upper large intestine wall	4.7E-03	6.0E-03	8.6E-03	1.4E-02	2.3E-02
Lower large intestine wall	4.2E-03	5.6E-03	8.6E-03	1.2E-02	2.3E-02
Heart	2.0E-02	2.5E-02	3.6E-02	5.4E-02	9.2E-02
Kidneys	8.1E-03	9.7E-03	1.5E-02	2.4E-02	4.4E-02
Liver	7.3E-03	8.7E-03	1.4E-02	2.1E-02	3.7E-02
Lungs	1.3E-02	1.6E-02	2.6E-02	4.1E-02	7.6E-02
Ovaries	4.4E-03	5.7E-03	8.5E-03	1.3E-02	2.3E-02
Pancreas	6.4E-03	7.7E-03	1.2E-02	1.7E-02	3.0E-02
Red marrow	7.5E-03	9.0E-03	1.3E-02	2.0E-02	3.5E-02
Spleen	1.4E-02	1.6E-02	2.6E-02	4.0E-02	7.6E-02
Testes	2.9E-03	3.9E-03	5.7E-03	8.8E-03	1.6E-02
Thyroid	4.9E-03	7.3E-03	1.2E-02	1.9E-02	3.5E-02
Uterus	4.8E-03	5.7E-03	8.5E-03	1.3E-02	2.3E-02
Other tissue	4.0E-03	4.7E-03	6.9E-03	1.1E-02	2.0E-02
Effective dose (mSv/MBq)	6.1E-03	7.7E-03	1.2E-02	1.8E-02	3.3E-02

The effective dose resulting from the administration of a maximal activity of 925 MBq for an adult weighing 70 kg is about 5.6 mSv.

For an administered activity of 925 MBq the typical radiation dose to the target organ, heart is 18.5 mGy and the typical radiation doses to the critical organs adrenals, kidneys, liver and spleen are 7.7, 7.5, 6.8 and 13 mGy.

## 12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Withdrawals should be performed under aseptic conditions. The vials must not be opened before 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.

If the integrity of this vial is compromised, the product should not be used.

Vasculocis is a kit for the preparation of technetium ( $^{99m}\text{Tc}$ ) human albumin injection, containing a sterile, pyrogen-free, freeze-dried product under nitrogen.

The product is to be used after reconstitution by the addition of sterile, pyrogen-free, isotonic sodium pertechnetate ( $^{99m}\text{Tc}$ ) allowing the preparation of technetium ( $^{99m}\text{Tc}$ ) human albumin injection ( $^{99m}\text{Tc}$  HSA).

### Method of preparation

Sodium pertechnetate ( $^{99m}\text{Tc}$ ) injection should comply with European Pharmacopoeia specifications.

Use freshly eluted sodium pertechnetate ( $^{99m}\text{Tc}$ ) solution (**less than two hours**), obtained from generators previously eluted **within the last 24 hours**.

Take a vial from the kit and put it in an appropriate lead shielding.

Using a hypodermic syringe, introduce through the rubber stopper 1 to 8 mL of sterile pyrogen-free sodium pertechnetate ( $^{99m}\text{Tc}$ ) injection, activity varying as a function of the volume from 90 MBq to maximum 2200 MBq.

**Do not use a breather needle as the contents are under nitrogen.**

After introduction of the volume of sodium pertechnetate ( $^{99m}\text{Tc}$ ) injection, without removing the needle, withdraw an equivalent volume of nitrogen in order to avoid excess pressure in the vial.

Shake the vial carefully several times in order to dissolve the dried product, then allow to stand for about 20 minutes.

The obtained preparation is a clear and colourless solution, with a pH ranging between 2.0 and 6.5.

Before use, limpidity of the solution after preparation, pH, radioactivity and and radiochemical purity should be checked.

The vial should never be opened and must be kept inside its lead shielding. The solution should be removed aseptically through the stopper with a sterile lead protected syringe.

#### Quality control

The quality of labelling (radiochemical purity) could be checked according to the following procedure.

#### **Method**

Ascending paper chromatography

#### **Materials and reagents**

- 1 Chromatographic paper  
Whatman 1 strip of sufficient length and not less than 2.5 cm wide.  
Trace two fine lines parallel to the ends of the strips, the one being called "deposit line" at 2.5 cm, the other one being called "solvent line" at 15 cm from the "deposit line".
- 2 Mobile phase  
methanol/water (80/20)
- 3 Glass tank  
Glass tank of suitable size for the chromatographic paper used, ground at the top to take a closely fitting lid. In the top of the tank is a device which suspends the chromatographic paper and is capable of being lowered without opening the chamber.
- 4 Miscellaneous  
Forceps, scissors, syringes, needles, appropriate counting assembly.

## Procedure

- 1 Place into the glass tank a layer 2 cm deep of the mobile phase.
- 2 Apply a spot of the preparation to the "deposit line" of the paper strip using a syringe and needle and dry in air.
- 3 Using forceps, insert the paper strip into the tank and close the lid. Lower the paper into the mobile phase and allow the solvent to migrate to the "solvent line".
- 4 Remove the paper strip with forceps and dry in air.
- 5 Determine distribution of radioactivity with an appropriate detector. Identify each radioactive spot by calculating the Rf. The Rf of technetium ( $^{99m}\text{Tc}$ ) human albumin is 0, and that of pertechnetate ion (free ( $^{99m}\text{Tc}$ ) technetium) is 0.6.  
Measure the radioactivity of each spot by integration of the peaks.
- 6 Calculations  
Calculate the percentage of technetium ( $^{99m}\text{Tc}$ ) human albumin (radiochemical purity)

$$\% \text{ technetium } (^{99m}\text{Tc}) \text{ human albumin} = \frac{\text{Radioactivity of the spot at Rf 0}}{\text{Total radioactivity of the paper strip}} \times 100$$

Calculate the percentage of free ( $^{99m}\text{Tc}$ ) technetium

$$\% \text{ free } (^{99m}\text{Tc}) \text{ technetium} = \frac{\text{Radioactivity of the spot at Rf 0.6}}{\text{Total radioactivity of the paper strip}} \times 100$$

- 7 The percentage of technetium ( $^{99m}\text{Tc}$ ) human albumin (radiochemical purity) should be at least 95 % and the percentage of free ( $^{99m}\text{Tc}$ ) technetium should be no greater than 5 %.

Do not use the radiolabeled solution if the radiochemical purity is less than 95 %.

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