SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Octreoscan 111 MBq/mL, kit for radiopharmaceutical preparation

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Octreoscan is supplied as two vials which cannot be used separately.

Vial A with 1.1 mL solution contains at activity reference time:
Indium(^{111}In)chloride 122 MBq (111 MBq/mL)
Vial B contains:
Pentetreotide 10 micrograms
After reconstitution and labelling the obtained solution contains indium(^{111}In)pentetreotide 111 MBq/ mL.

Indium(^{111}In) decays with a half-life of 2.83 days to stable cadmium(^{111}Cd).
Emission characteristics:
Gamma-rays 172 keV (90 % abundance)
Gamma-rays 247 keV (94 % abundance)
X-rays 23-26 keV

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Kit for radiopharmaceutical preparation. The kit consists of two vials:

Vial A: Radiopharmaceutical precursor. Clear and colourless solution.
Vial B: Powder for solution for injection. White lyophylised powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.
Indium(^{111}In)pentetreotide specifically binds to receptors for somatostatin.
After radiolabelling pentetreotide with indium(^{111}In)chloride, the solution obtained is indicated for use as adjunct in the diagnosis and management of receptor bearing gastro-entero-pancreatic neuroendocrine (GEP) tumours and carcinoid tumours, by aiding in their localisation. Tumours which do not bear somatostatin receptors will not be visualised.
In a number of patients suffering from GEP or carcinoid tumours the receptor density is insufficient to allow visualisation with Octreoscan. Notably in approximately 50% of patients suffering from insulinoma the tumour cannot be visualised.

4.2 Posology and method of administration

Posology

Adults and elderly population

The activity to be administered for single photon emission tomography (SPECT) depends on the available equipment. In general for an adult of 70 kg, an activity of 110 to 220 MBq in one single intravenous injection should be sufficient. Other activities should be justifible.

Renal impairment

Careful consideration of the activity to be administered is required since an increased radiation exposure is possible in these patients. In patients with significant renal failure administration of ^{111}In-pentetreotide is not advisable because the reduced or absent function of the principal route of excretion will lead to delivery of an increased radiation dose, see section 4.4.

Paediatric population

The decision to administer pentetrotide (^{111}In) to a child must be taken by a nuclear medicine specialist familiar with somatostatin receptor scintigraphy, after considering using alternative radiopharmaceuticals with a lower radiation burden (PET in particular). Pentetreotide (^{111}In) should only be administered to a child when alternative radiopharmaceuticals are not available or they do not yield a satisfactory performance in the clinical setting of the child.

Method of administration

The medicinal product is for single use. Administration by intravenous injection.

Careful administration is necessary to avoid paravasal deposition of activity.

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

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

For patient preparation see section 4.4.

Image acquisition

Images can be acquired at 4 and 24 hours, or 24 and 48 hours post-injection. 4 hours images may be useful for comparison and evaluation of abdominal activity imaged at 24 hours. When activity in the abdomen is observed at 24 hours which cannot be interpreted with certainty as uptake in tumour or activity in bowel contents, scintigraphy should be repeated at 48 hours. It is important to acquire two sets of images with at least one SPECT (or SPECT/CT) acquisition. Spot views may be repeated at 48 hours, 72 hours and/or 96 hours p.i. to allow clearance of interfering bowel radioactivity.

Physiologic uptake occurs in spleen, liver, kidneys and bladder. Thyroid, pituitary and intestines are visible in most patients.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

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 immediately available.

Individual benefit/risk justification

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

Renal impairment
Careful consideration of the activity to be administered is required since an increased radiation exposure is possible in these patients. In patients with significant renal failure administration of ^{111}In-pentetreotide is not advisable because the reduced or absent function of the principal route of excretion will lead to delivery of an increased radiation dose. Administration should be considered only when the possible damage from radiation is outweighed by the potential diagnostic information. Interpretable scintigrams may be obtained after haemodialysis during which the high background activity can at least partially be removed. Prior to dialysis images are non-diagnostic because of activity in the circulation. After dialysis a higher than usual uptake in liver, spleen and intestinal tract, and a higher than usual activity in circulation, were observed.

Peadiatric population
Because of the potential hazard of the ionizing radiation ^{111}In-pentetreotide should not be used in children under 18 years of age, unless the value of the expected clinical information is considered to outweigh the possible damage from radiation.
For information on the use in the paediatric population see Section 4.2.
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 radiation.

Administration of a laxative is necessary in patients not suffering from diarrhoea, to differentiate stationary activity accumulations in lesions in, or adjacent to, the intestinal tract from moving accumulations in the bowel contents.

Indium(^{111}In)-pentetreotide not bound to receptors, and non-peptide bound indium(^{111}In), are rapidly eliminated through the kidneys. To enhance the process of excretion, in order to reduce background noise and to reduce the radiation dose to kidneys and bladder, a liberal fluid intake (at least 2 litres) is required for 2 or 3 days following administration.

Regarding patients on octreotide therapy it is recommended to withdraw this therapy temporarily to avoid a possible blockade of somatostatin receptors. This recommendation is given on empirical grounds, the absolute need for such measure has not been demonstrated. In some patients the withdrawal of therapy might be not tolerated and may cause rebound effects. This is notably the case in insulinoma patients, where the danger of sudden hypoglycaemia must be considered, and in patients suffering from the carcinoid syndrome. If the clinician responsible for the patients therapeutic management considers withdrawal of octreotide therapy tolerable a three days withdrawal period is recommended.

Interpretation of images
Positive scintigraphy with indium(^{111}In)-pentetreotide reflects the presence of an increased density of tissue somatostatin receptors rather than a malignant disease. Furthermore positive uptake is not specific for GEP- and carcinoid-tumours. Positive scintigraphic results require evaluation of the possibility that another disease, characterised by high local somatostatin receptor concentrations, may be present. An increase in somatostatin receptor density can also occur in the following pathological conditions: tumours arising from tissue embryologically derived from the neural crest, (paragangliomas, medullary thyroid carcinomas, neuroblastomas, pheochromocytomas), tumours of the pituitary gland, endocrine neoplasms of the lungs (small-cell carcinoma), meningiomas, mammary carcinomas, lympho-proliferative disease (Hodgkin's disease, non-Hodgkin lymphomas), and the possibility of uptake in areas of lymphocyte concentrations (subacute inflammations) must be considered.

After the procedure
Close contact with infants and pregnant women should be restricted during the first 36 hours after administration.

Specific warnings
In diabetic patients, receiving high doses of insulin, the administration of pentetreotide may cause paradoxical hypoglycaemia via a temporary inhibition of glucagon secretion.

This medicinal product contains less than 1 mmol 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 products and other forms of interaction
No interactions have been described to date.

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
There is no experience with the use of Octreoscan in pregnant women.

Radionuclide procedures carried out on pregnant women also involve radiation dose to the foetus. The administration of the maximal diagnostic activity of 220 MBq to the patient results in an absorbed dose to the uterus of 8.6 mGy. In this dose range lethal effects and the induction of malformations, growth retardations and functional disorders are not to be expected; however the risk for the induction of cancer and hereditary defects may be increased. Only essential investigations should therefore be carried out during pregnancy, when the likely benefit exceeds the risk incurred by the mother and foetus.

Breast-feeding
Before administering radiopharmamaceuticals to a mother who is breast-feeding 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, it is not necessary to discontinue breast-feeding. However, close contact with infants should be restricted during the first 36 hours after administration.

4.7 Effects on ability to drive and use machines
Octreoscan has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects
Adverse effects attributable to the administration of Octreoscan are uncommon (≥1/1000 to <1/100). Specific effects have not been observed. The symptoms reported are suggestive of vasovagal reactions or of anaphylactoid drug effects.

The withdrawal of octreotide therapy as a preparatory step to scintigraphy might provoke severe adverse effects, generally of the nature of a return of the symptoms seen before this therapy was started. Exposure to ionising radiation is linked with cancer induction and a potential for the development of hereditary defects. As the effective dose is 12 mSv, when the maximal recommended activity of 220 MBq is administered, these adverse events 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
The pharmaceutical form (monodose injection) makes inadvertent overdosing improbable. In the event of administration of a radiation overdose with indium(^{111}In)pentetreotide, the absorbed dose by 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: Diagnostic radiopharmaceuticals for tumour detection
ATC code: V09I B 01

Mechanism of action
Octreoscan attaches to somatostatin receptors (mainly subtype 2 and subtype 5) in tissues where, as consequence of disease, the cell-surfaces contain these receptors in a more than physiologic density. In individual patients, where the disease did not lead to an increased receptor density, scintigraphy will not be successful.

In carcinoids and GEP-tumours the prevalence of increased receptor density in the tumour-tissue in general is rather high.

Pharmacodynamic effects
Only limited studies of pharmacodynamic effects have been performed. The in vitro biological activity is approximately 30% of the biological activity of natural somatostatin. The in vivo biological activity, measured in rats, is less than that of equal amounts of octreotide. Intravenous administration of 20 µg of pentetreotide resulted in some patients in a measurable but very limited decrease of serum gastrin and serum glucagon levels of less than 24 hours duration.

5.2 Pharmacokinetic properties
Organ uptake
Indium(^{111}In)pentetreotide is taken up by the following organs: liver (approximately 2% at 24 hours) and spleen (approximately 2.5% at 24 hours). Uptake in thyroid and pituitary occurs but not reproducibly. The uptake in kidneys is partly a reflection of ongoing elimination through the urine and partly due to delayed excretion by the kidney.

Elimination
Indium(^{111}In)pentetreotide not bound to receptors, and non-peptide bound indium(^{111}In), is rapidly eliminated through the kidneys. Within 24 hours after intravenous administration, approximately 80% of the radiolabelled pentetreotide is eliminated through the urinary system. After 48 hours 90% is excreted.

The elimination via the gallbladder and subsequently the faeces is approx. 2% of the administered activity in patients with normal intestinal function.

Up to 6 hours post-administration radioactivity in urine is predominantly intact indium(^{111}In)pentetreotide. Thereafter, increasing amounts of non-peptide-bound activity are excreted.
Half life
^{111}In decays with a half-life of 2.83 days to stable cadmium.

5.3 Preclinical safety data
Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use. No testing has been done on carcinogenic potential nor of the influence of pentetreotide on fertility or on embryotoxicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Vial A
Hydrochloric acid
Water for injections
Ferric chloride hexahydrate.

Vial B
Sodium citrate dihydrate
Citric acid monohydrate
Inositol
Gentisic acid.

6.2 Incompatibilities
This medicinal product must not be mixed with other medicinal products except those mentioned in section 12.

6.3 Shelf life
Vial A and vial B expire 24 hours after the activity reference time/date of the indium(^{111}In).
After reconstitution : 6 hours. Store below 25 °C.

6.4 Special precautions for storage
Store below 25 °C.
For storage conditions of the reconstituted 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
Octreoscan is supplied as one pack containing two vials:

- vial A: a 10 ml quartz-coated, type I glass vial with a teflon-coated bromobutyl rubber stopper and shielded with lead containing 1.1. ml of indium(^{111}In)chloride solution corresponding to 122 MBq at activity reference time.
- vial B: 10 ml type I glass vial closed with a bromobutyl rubber stopper and orange flip off cap, containing 10 micrograms of pentetreotide.

The vials cannot be used separately. Both vials are sealed with an aluminium crimp cap and packed in a closed, folded tin. Enclosed in the tin is a Sterican Luer Lock 0.90 x 70 mm / 20 G x 2 3/4 needle to be used for the labelling procedure.

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 is subject to the regulations and/or appropriate licences of the local 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.

The contents of both vials are intended only for use in the preparation of indium(^{111}In)pentetreotide solution for injection and are not to be administered directly to the patient without first undergoing the preparative procedure.

For instructions on reconstitution of the medicinal product before administration, section 12.

If at any time in the preparation of this product the integrity of the vials is compromised they should not be used.

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

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

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

7. MANUFACTURED AND RELEASED BY

Curium Netherlands B.V.
Westerduinweg 3
1755 LE Petten
The Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

13 April 2026

11. DOSIMETRY

Indium(^{111}In) is cyclotron produced and decays with the emission of gamma radiation with an energy as shown in the table below and a half-life of 2.83 days to cadmium-111 (stable).

Gamma-rays	172 keV	(90% abundance)
Gamma-rays	247 keV	(94% abundance)
X-rays	23-26 keV	

The following radiation dosimetry is calculated according to the MIRD system. The data listed below are from ICRP publication 106 and are calculated according to the following assumptions:

According to the biokinetic model described in ICRP 106 intravenously injected indium(^{111}In)pentreotide is assumed to be immediately taken up in liver, spleen, kidneys and thyroid, while the rest is assumed to be homogeneously distributed in the remainder of the body. The experimentally found retention data is best described by mono- or bi-exponential functions. The biokinetic data come from patients with carcinoid tumours and endocrine tumours in the GI-tract. Uptake in tumour tissue present in any given organ may therefore be included in the published organ uptake values. The main route of excretion is via the kidneys and less than 2 % is excreted in faeces. An observed excretion of 85 % via urine after 24 h fits well with the model. The small excretion via the GI tract is not included in the model, since its contribution to the absorbed dose in normal circumstances is negligible.

Organ(s)	F_s	$T_{1/2}$	a	$\tilde{A}_s/A_0$
Liver	0.06	2 h	0.40	2.59 h
		2.5 d	0.30	
		70 d	0.30	
Spleen	0.05	2.5 d	1.00	2.30 h
Kidney	0.06	2.5 d	1.00	2.76 h
Thyroid	0.001	2.5 d	1.00	2.76 min
Other organs and tissues	0.829	3 h	0.90	6.90 h
		2.5 d	0.10	
Bladder	1.00			
Adults and 15 years				1.65 h
10 years				1.40 h
5 years and 1 year				54.3 min

F_s fractional distribution to organ or tissue

$T_{1/2}$ biological half-time for uptake or elimination

a fraction of F_s taken up or eliminated with the corresponding half-time. A minus sign indicates uptake.

$\tilde{A}_s/A_0$ cumulated activity in organ or tissue per unit of administered activity

Organ	Absorbed dose per unit activity administered (mGy/MBq)				
	Adult	**15 Years**	**10 Years**	**5 Years**	**1 Year**
Adrenals	0.058	0.075	0.11	0.17	0.29
Bladder	0.20	0.25	0.37	0.46	0.56
Bone surfaces	0.027	0.033	0.050	0.075	0.14
Brain	0.0096	0.012	0.020	0.032	0.057
Breast	0.012	0.015	0.023	0.037	0.067
Gall bladder	0.052	0.063	0.092	0.14	0.22
GI- tract					
Stomach	0.043	0.050	0.077	0.11	0.18
SI	0.029	0.037	0.059	0.090	0.15
Colon	0.029	0.035	0.055	0.086	0.14
(ULI	0.030	0.037	0.058	0.094	0.15
(LLI	0.027	0.033	0.052	0.075	0.12
Heart	0.025	0.032	0.048	0.070	0.12
Kidneys	0.41	0.49	0.67	0.96	1.6
Liver	0.10	0.13	0.20	0.27	0.48
Lungs	0.023	0.030	0.044	0.067	0.12
Muscles	0.020	0.026	0.038	0.056	0.10
Oesophagus	0.014	0.018	0.027	0.043	0.077
Ovaries	0.027	0.035	0.053	0.080	0.13
Pancreas	0.072	0.088	0.13	0.20	0.32
Red marrow	0.022	0.026	0.039	0.053	0.085
Skin	0.011	0.013	0.021	0.032	0.059
Spleen	0.57	0.79	1.2	1.8	3.1
Testes	0.017	0.022	0.037	0.054	0.087
Thymus	0.014	0.018	0.027	0.043	0.077
Thyroid	0.075	0.12	0.18	0.37	0.68
Uterus	0.039	0.049	0.077	0.11	0.16
Remaining organs	0.024	0.032	0.049	0.080	0.13
Effective dose (mSv/MBq)	**0.054**	**0.071**	**0.11**	**0.16**	**0.26**

The effective dose resulting from the administration of a (maximal recommended) activity of 220 MBq for an adult weighing 70 kg is about 12 mSv.

Indium(^{111}In)pentetreotide specifically binds to somatostatin receptors, so a target organ cannot be defined. For an administered activity of 220 MBq the typical radiation doses to the critical organs – kidneys, liver and spleen – are 90, 22 and 125 mGy respectively.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Do not use Octreoscan if you notice visible signs of deterioration.

Method of preparation:

Instructions for labelling

1. Add the contents of vial A (indium(^{111}In)chloride) to vial B (lyophilised pentetreotide) to obtain the product Indium (^{111}In) pentetreotide; only the Sterican (0.90 x 70) needle supplied with the shipped patient dose should be used to remove the indium chloride from its vial.
2. Observe an incubation period of 30 minutes following the reconstitution.
3. The preparation may be diluted with 2-3 mL of 0.9% sodium chloride solution if a larger volume is desired for easier handling in the syringe.
4. The solution must be clear and colourless, this can be checked behind a lead wall containing a lead glass window. If the solution does not comply it should be discarded.
5. Use a tiny sample of this (diluted or not) volume for the quality control, which is described in the following paragraph.
6. The solution is ready for use. The solution must be used within 6 hours.

Note: For the reconstitution do not use any other indium(^{111}In)chloride solution than the one supplied in the same container that holds the lyophilised pentetreotide.
After reconstitution and labelling the pH of the aqueous solution is 3.8-4.3.

Quality control:

Analysis of indium(^{111}In)bound peptides versus indium(^{111}In)bound non-peptide compounds may be done on silicagel impregnated glass fibre strips. Prepare a thoroughly dried strip, approx. 10 cm long and 2.5 cm wide by marking a starting line at 2 cm, with additional marks at 6 and 9 cm. Apply 5 to 10 µl of the reconstituted and labelled solution to the starting line and develop in freshly prepared sodium citrate solution 0.1M, adjusted with HCl to pH 5. In approximately 2-3 min the front will have reached the 9 cm mark. Cut the strip at the 6 cm mark and measure the activity of both halves. Non-peptide bound ^{111}In moves with the front. Requirement: The lower end of the chromatogram should contain ≥ 98% of the applied activity.