Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Indium (111In) DTPA 37MBq/ml Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition per ml at activity reference time and date:
Indium [^{111}In] pentetate 37 MBq
Pentetic acid 0.1 mg

Summary of the physical characteristics of the radioactive isotope in the active substance: ^{111}In.
Physical half-life 2.8 days.
Most important radiation emitted
Energy level Abundance (%)
171 keV 90.9%
245 keV 94 %

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.

Clear, colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.
Cisternoscintigraphy:

- Detection of obstructions in cerebrospinal flow.
- Differentiation between normal pressure hydrocephalus and other forms of hydrocephalus.
- Detection of leaks of cerebrospinal fluid (rhinorrhoea or otorrhoea).

4.2 Posology and method of administration

Posology
Adults and elderly population: 9 - 20 MBq (250-500 microCi
Paediatric population: 0.4 - 0.6 MBq/kg body weight (10-15 microCi/kg)

Method of administration
Indium [^{111}In]-pentetate is administered by intrathecal injection (lumbar or suboccipital).

Image acquisition
A first visualisation of the skull area should preferably be done 1 to 1.5 hrs after injection. Further imaging is done at 3, 6 and 24 hrs and sometimes 48 or 72 hours after administration, depending on the diagnostic information required.

Ten to 15 minutes after lumbar puncture a control scan should be performed at the puncture level to exclude extra-arachnoidal activity, which might cause false-negative results.

In case of suboccipital injection scintigraphy should preferably be started as early as 15 minutes after injection. The time points given above, for obtaining the subsequent images, should be advanced by 1 or more hours.

In otorrhoea or rhinorrhoea leakage may be so minimal that it can not be seen on the scintigraphic images. Leakage through the nose or ear can be detected by introducing cotton wool plugs in the outer ear or in the nasal cavity, which are subsequently measured for radioactivity.

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
- Haemorrhagic tendency.
- Increased intracranial pressure.

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, 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 result.

Paediatric population
For information on the use in the 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 radiation.

Interpretation of images
In a high percentage of patient studies extra-arachnoidal activity is seen due to failed lumbar puncture or to puncture leaks. This might cause false-negative results to occur. A control scan at the injection site for detecting extra-arachnoidal activity is recommended.

Specific warnings
This medicinal product contains less than 1 mmol sodium (23 mg) per milliliter solution for injection, i.e. it is essentially 'sodium- free'.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential
When an administration of radioactive medicinal products to women 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 doses to the foetus. Only imperative investigations should be carried out during pregnancy, when likely benefit exceeds the risks incurred by mother to foetus.

Breastfeeding

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 activity in breast milk. If the administration is considered necessary, breast-feeding should be interrupted for two days and the expressed feeds discarded. Breast-feeding can be restarted when the level in the milk will not result in a radiation dose to a child greater than 1 mSv.

4.7 Effects on ability to drive and use machines

Indium [^{111}In] Pentetate has no influence on the ability to drive or to use machines.

4.8 Undesirable effects

Performing a lumbar or occipital puncture may cause adverse reactions which are usually of a mild nature. The symptoms include headache and signs of meningism, which as a rule improve within 48 hours. Aseptic meningitis and pyrexia have been reported.

If, in the case of suboccipital administration, the radiopharmaceutical is deposited in the immediate vicinity of those places where cerebral nerves exit from the brainstem, the n. oculomotoris, the n. facialis and the n. vestibulocochlearis may be activated causing transitory effects like ptosis of the eyelid, tinnitus or facial paresis.

Exposure to ionising radiation is linked with induction of malignant neoplasms and a potential for development of hereditary disorders. 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. As the effective dose is 2.8 mSv when the maximal recommended activity for adults of 20 MBq is administered these adverse reactions are expected to occur with a low probability. 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 HPRA Pharmacovigilance, Website: www.hpra.ie

4.9 Overdose

The dose form of Indium [^{111}In] Pentetate Injection contains so little material that overdosing with pharmacological effects is not probable.

The dangers of overdose to be expected are those relating to the inadvertent administration of excess of radioactivity. The radiation dose may be reduced by promoting diuresis and frequent voiding of urine. It might be helpful to estimate the effective dose that was applied.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other central nervous system diagnostic radiopharmaceuticals
ATC code: V09A X01.

Product class: Diagnostic radiopharmaceuticals, central nervous system.

The pharmacology of pentetate has not been studied. However, pentetate is a complexing agent. Since sufficient Ca/Mg ions are included in the preparation to fill the complexing capacity of the fraction of pentetate that is not complexed with ^{111}In, no pharmacodynamic effects are expected to occur.

5.2 Pharmacokinetic properties

Distribution/Organ uptake
After injection into the subarachnoidal space at lumbar level Indium [^{111}In]-pentetate moves upwards into the cervical subarachnoidal space and usually accumulates in the posterior fossa after 1 to 1.5 hours. 3 hours after injection activity is observed in the Sylvian and interhemispheric fissures. After 6 hours the tracer has reached the convexity of the hemispheres. At this point it passes from the cerebrospinal fluid into the blood.

Elimination
Subsequently after Indium [^{111}In]-pentetate is quickly excreted by glomerular filtration. 24 hours after administration the highest activity can be found in the resorption sites along the superior sagittal sinus.
In the case of a pathological impairment of the cerebrospinal flow this characteristic distribution pattern disappears, which yields diagnostic information.

5.3 Preclinical safety data

Acute toxicity studies with Indium [^{111} In]-pentetate have not been performed. Ytterbium-pentetate intrathecally administered in dogs (up to 300 mg) did not produce toxic effects. Studies of the toxicity after multiple administrations were not performed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Calcium chloride
Sodium hydroxide
Sodium chloride
Disodium phosphate dodecahydrate
Hydrochloric acid
Water for injections

6.2 Incompatibilities

No incompatibilities are known to exist, but to safeguard the sterility and the non-pyrogenicity of the injectate no attempts should be made to dilute the product prior to administration.

6.3 Shelf life

The product expires 24 hours after activity reference time and date.
If multi-dose use is intended, each aliquot should be removed under aseptic conditions, and used within one working day. The vial should be stored between 2°C - 8 °C after first opening.

6.4 Special precautions for storage

Store below 25°C in a radiation shielding and in the original, unopened container.
For storage conditions after first opening of the medicinal product, see section 6.3.
Storage should take place in accordance with national regulations for radioactive materials.

6.5 Nature and contents of container

10 ml (Type 1 Ph. Eur.) clear, colourless, borosilicate glass vial closed with a butyl rubber stopper sealed with an aluminium crimp cap. Each vial is packed within a radiation shielding container of lead metal.

Pack sizes: 18.5 MBq (0.5 mCi) in 0.5 ml
37 MBq (1 mCi) in 1 ml

6.6 Special precautions for disposal

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.

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 to other persons, from external radiation or contamination from spills or urine, vomiting, etc. Radiation protection precautions in accordance with national regulations must therefore be taken.

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

7 MARKETING AUTHORISATION HOLDER

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

8 MARKETING AUTHORISATION NUMBER

PA0690/009/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 31 March 2004
Date of last renewal : 31 March 2009

10 DATE OF REVISION OF THE TEXT

April 2024

11 DOSIMETRY

Data from ICRP publication 53 (Vol. 18-No 1-4, 1987)

"Radiation dose to patients from radiopharmaceuticals"

The list includes only those organs which are also used in the calculation for the effective (whole body) dose equivalent. These are the seven standard organs and the additional five with the highest absorbed dose (marked with *).

Absorbed dose per unit activity administered (mGy/MBq)

Adult

* Spinal cord	0.95
* Adrenals	0.16
* Bladder wall	0.20
* Brain	0.13
* Kidneys	0.13
Gonads	
Ovaries	0.039
Testes	0.011
Breast	0.010

Red marrow	0.24
Lungs	0.033
Thyroid	0.021
Bone surface	0.072

Effective dose equivalent (mSv/MBq) 0.14

The effective dose equivalent resulting from the administration of a (maximal recommended) of 20 MBq of ^{111}In for an adult weighing 70 kg is about 2.8 mSv .

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

12 INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

During handling adequate radiation shielding must be used. After decay of the radioactivity the contents of the vial may be disposed of as nontoxic chemical waste.

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.