

1. NAME OF THE MEDICINAL PRODUCT

Indium (^{111}In) DTPA 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.

pH: 7.0-7.6.

Osmolality: 280-320 mosmol/kg.

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 μCi)
Paediatric population:	0.4-0.6 MBq/kg body weight (10-15 $\mu\text{Ci/kg}$)

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.

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Style Definition: Header: Font: 10 pt, English (United Kingdom), Widow/Orphan control, Tab stops: 1 cm, Left

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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

A control scan at the injection site for detecting extra arachnoidal activity is recommended 10-15 minutes after lumbar puncture.

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.

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 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 doses to the fetus. Only essential investigations should therefore be carried out during pregnancy, when the likely benefit far exceeds the risks incurred by the mother and fetus.

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(¹¹¹In) Pentetate has no or negligible 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 meningeal irritation, which as a rule improve within 48 hours. Aseptic meningitis and fever 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 drooping of a corner of the mouth.

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. 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 authorization of the medical 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:

www.legemiddelverket.no/meldeskjema

4.9 Overdose

The dose form of Indium(¹¹¹In) Pentetate Injection contains so little material that overdosing with pharmacological effects is not probable.

The danger 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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

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 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

Sodium chloride
Disodium phosphate dodecahydrate
Calcium chloride dihydrate
Sodium hydroxide (for pH-adjustment)
Hydrochloric acid (for pH-adjustment)
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 within one working day. The vial should be stored between 2°C - 8 °C after removal of the first aliquot.

6.4 Special precautions for storage

Store below 25°C, 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 material.

6.5 Nature and contents of container

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

Indium (^{111}In) DTPA Injection is supplied in the following activity amounts at activity reference time:

18.5 MBq (0.5 mCi) in 0.5 ml

37 MBq (1 mCi) in 1.0 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 medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

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

8. MARKETING AUTHORISATION NUMBER

MT 8230

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

31 January 1995/ 10 May 2012

10. DATE OF REVISION OF THE TEXT

08 September 2021

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	0.14 (mSv/MBq)

The effective dose resulting from the administration of a (maximal recommended) activity of 20 MBq for an adult weighing 70 kg is about 2.8 mSv.