1. NAME OF THE MEDICINAL PRODUCT

Indium (In111) Chloride

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Per ml at activity reference date:
Indium-111 370 MBq

^{111}In disintegrates by electron capture with a half-life of approximately 67 hours (2.8 days) and emits gamma radiation with principal energies of 172 keV (91%) and 246 keV (94%). By internal conversion X radiations of 23 and 26 keV are also emitted.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Radiopharmaceutical precursor.
Clear, colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

Indium (^{111}In) chloride is used as an ingredient for the radiolabelling of certain suitably derivatised proteins which are subsequently administered intravenously for a variety of investigative purposes using appropriate imaging procedures.

Indium (^{111}In) chloride is used extensively for the radiolabelling of monoclonal antibodies. The nature of the disease state to be investigated will be determined by the particular monoclonal antibody to be labelled.

Indium (^{111}In) chloride has also been used as the radiolabelling ingredient in injectable preparations such as Indium (^{111}In)-labelled proteins.

4.2 Posology and method of administration

The vial contains a sterile aqueous solution for the in-vitro radiolabelling of suitable conjugated proteins such as monoclonal antibodies, which are subsequently administered intravenously.

The quantity of Indium (^{111}In) chloride required for radiolabelling and the quantity of Indium (^{111}In)-labelled pharmaceutical that is subsequently administered will depend on the pharmaceutical being labelled and its intended use. Information on recommended dosage and administration will be provided by the manufacturer of the pharmaceutical to be radiolabelled.

The activity to be administered to children may be calculated approximately by correcting on a weight, body surface area or age basis the activity to adults. For the newborn and children under about one year of age, the target organ size in relation to the whole body must also be taken into consideration.

4.3 Contraindications

Hypersensitivity to the active substance, to any of the excipients or to any of the components of the labelled radiopharmaceutical.

Information on contra-indications to particular Indium (^{111}In)-labelled pharmaceuticals prepared by radiolabelling with Indium (^{111}In) chloride will be supplied by the manufacturer of the pharmaceutical to be radiolabelled.

4.4 Special warnings and precautions for use

The contents of the vial of Indium (^{111}In) Chloride are not to be administered directly to the patient.

Information concerning special warnings and precautions for use of Indium (^{111}In)-labelled pharmaceuticals prepared by radiolabelling with Indium (^{111}In) chloride will be supplied by the manufacturer of the pharmaceutical to be radiolabelled.

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
Paediatric population, see section 4.2.

4.5 Interaction with other medicinal products and other forms of interaction

Information concerning interactions associated with the use of Indium (^{111}In)-labelled pharmaceuticals prepared by radiolabelling with Indium (^{111}In) chloride will be supplied by the manufacturer of the pharmaceutical to be radiolabelled.

4.6 Fertililty, pregnancy and lactation

The availability of data on the use of indium (^{111}In)-labelled pharmaceuticals, prepared by radiolabelling with indium (^{111}In) chloride, in pregnancy and lactation will be specified by the manufacturer of the pharmaceutical to be radiolabelled.

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 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 be carried out during pregnancy, when likely benefit exceeds the risks incurred by 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 after 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. Breast-feeding can be restarted when the level in the milk will not result in radiation dose to the child greater than 1 mSv.

Fertility
There is some evidence from animal experiments of teratogenicity of indium in very high doses compared with the maximal possible concentration of free indium chloride in a labeled pharmaceutical.

4.7 Effects on 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

Possible side effects following the intravenous administration of an Indium (^{111}In)-labelled pharmaceutical preparation in which the radiolabelling agent is indium (^{111}In) chloride will be dependent on the specific pharmaceutical being used. Such information should be available from the manufacturer of the pharmaceutical to be radiolabelled.

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose is 10^{-1} mSv/MBq is administered these adverse events are expected to occur with a low probability. For most diagnostic investigations using a nuclear medicine procedure the radiation dose delivered (EDE) is less than 20 mSv. However, with indium (^{111}In)-labelled pharmaceutical preparations this level may be exceeded. Higher doses may be justified under 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 the national reporting system: www.legemiddelverket.no/meldeskjema

4.9 Overdose

In the event of administration of an overdose of a radiopharmaceutical, the absorbed radiation dose to the patient should be reduced where possible by increasing the elimination of the radionuclide from the body. Action to be taken in the event of administration of an overdose of an indium (^{111}In)-labelled pharmaceutical will be available from the manufacturer of the pharmaceutical to be radiolabelled.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: diagnostic radiopharmaceuticals, tumour detection, Indium(^{111}In) compounds, ATC code: V09 IB
At the activities normally administered for diagnostic procedures indium-111 labelled pharmaceuticals do not generally appear to exert pharmacological effects.

5.2 Pharmacokinetic properties

The pharmacokinetic properties of indium (^{111}In)-labelled radiopharmaceuticals, prepared by radiolabelling with indium (^{111}In) chloride prior to administration, will be dependent on the nature of the pharmaceutical to be labelled.

5.3 Preclinical safety data

Indium (^{111}In) chloride is supplied with no added carrier and the specific activity of the indium-111 is high. Consequently the chemical concentration of the indium chloride is very low (less than 1 μg/ml). No data are

available from animal studies on the mutagenic or carcinogenic potential of indium chloride. However, there is some evidence of teratogenicity from animal experiments.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydrochloric acid, water for injections.

6.2 Incompatibilities

Radiolabelling of macromolecules such as monoclonal antibodies with indium (^{111}In) chloride is very susceptible to the presence of trace metal impurities. It is important that all glassware, syringe needles etc, used for the preparation of the radiolabelled product are thoroughly clean to ensure freedom from such trace metal impurities. Only syringe needles (for example, non-metallic) with proven resistance to dilute acid should be used to minimise trace metal impurity levels.

6.3 Shelf life

The product expires 24 hours after activity reference date and time.

6.4 Special precautions for storage

Do not store the preparation above 25°C.

6.5 Nature and contents of container

10 ml glass vial (Type I, Ph.Eur.) closed with a bromobutyl rubber stopper, sealed with an aluminium crimpcap. Indium Chloride (In111) is supplied in the following activity amounts at activity reference time:
111 MBq in 0.3 ml
185 MBq in 0.5 ml
370 MBq in 1.0 ml
555 MBq in 1.5 ml
740 MBq in 2.0 ml

6.6 Special precautions for disposal

General warnings
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 radiolabelling and are not to be administered directly to the patient without first undergoing the preparative procedure.

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

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.

Any unused 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 8237

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

1 October 1996/ 31 January 2005

10. DATE OF REVISION OF THE TEXT

15.05.2019

11. DOSIMETRY

The radiation dose received by the various organs following intravenous administration of an indium (^{111}In)-labelled pharmaceutical preparation will be dependent on the specific pharmaceutical being radiolabelled. Information on radiation dosimetry of each different pharmaceutical following administration of the radiolabelled preparation will be available from the manufacturer of the pharmaceutical to be radiolabelled.

In view of the energies of the electromagnetic transitions associated with the decay of indium-111, it is anticipated that Effective Dose Equivalents resulting from the intravenous administration of indium (^{111}In)-labelled pharmaceuticals will be of the order of 10^{-1} mSv/MBq. Administration of indium (^{111}In)-labelled pharmaceutical preparations frequently results in relatively high exposure which may exceed 20 mSv and sometimes may even exceed 50 mSv.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Instructions for radiolabelling of the pharmaceutical with Indium-111 by means of Indium(In-111)chloride together with methods to determine the labelling efficiency and radiochemical purity of the radiolabelled pharmaceutical will be provided by the manufacturer of the pharmaceutical to be radiolabelled.

The use of meticulously clean glassware is essential to avoid the introduction of trace impurities, which may interfere with the labelling procedure. Some plastics may interfere by absorbing excessive amounts of ^{111}In activity.