SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF MEDICINAL PRODUCT

Trade name: Indium (In111) Chloride
(Curium Netherlands catalogue number: DRN 4901)

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 excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Radiopharmaceutical precursor.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

This product is for diagnostic use only.

Indium (In111) 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 (In111) 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 (In111) 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

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 special precautions for use

The contents of the vial of Indium (In111) Chloride are not to be administered directly to the patient.

Radiopharmaceutical agents should only be used by qualified personnel with the appropriate government authorization for the use and manipulation of radionuclides.

They may be received, used and administered only by authorized persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or the appropriate licences of the local competent official organisations.

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.

4.5 Interactions with other medicinal products and other forms of interactions

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 Pregnancy and lactation

There is some evidence from animal experiments of teratogenicity of indium. 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.

When it is necessary to administer radioactive medicinal products to women of childbearing potential, information should always be sought about pregnancy. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. Where uncertainty exists it is important that radiation exposure should be the minimum consistent with achieving the desired clinical information. Alternative techniques which do not involve ionising radiation should be considered. Radionuclide procedures carried out on pregnant women also involve radiation doses to the fetus. Only imperative investigations should be carried out during pregnancy, when likely benefit exceeds the risks incurred by mother and fetus. The absorbed dose to the uterus following administration of indium (^{111}In)-labelled pharmaceuticals prepared by radiolabelling with indium (^{111}In) chloride will be dependent on the spe-

cific pharmaceutical being radiolabelled and information will be available from the manufacturer of the pharmaceutical to be labelled. Doses above 0.5 mGy should be regarded as a potential risk for the fetus. Advice on avoidance of pregnancy until the calculated dose to the uterus is below 0.5 mGy should be given to women of childbearing potential.

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.

4.7 Effects on ability to drive and use machines

None known.

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.

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.

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

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.

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

ATC-code: V 09 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 (In111) 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.

5.4 Radiation 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.

Indium-114m may be present as a radionuclidic impurity in indium-111. This isotope has a longer half-life (49.5 days) than indium-111 (2.8 days) and will therefore make an increasing contribution to the radiation dose with time. Indium (^{111}In)-labelled pharmaceuticals prepared by ra-

diolabelling with indium (^{111}In) chloride should not be administered later than 24 hours from the reference date of the indium (^{111}In) chloride in order to ensure that the level of indium-114m present is less than 0.2%.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydrochloric acid.

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 Special precautions for storage

Refer to outer label for storage temperature before use and after removal of first aliquot.

The product in unpreserved. If multi-dose use is intended, each aliquot should be removed under aseptic conditions, and within one working day.

Storage should be in accordance with national regulations for radioactive material.

6.4 How supplied

Indium (In111) Chloride is supplied in the following activity amounts at activity reference time:
111 MBq in 0.3 ml per vial

6.5 Instructions for use and handling and disposal

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.

Radiopharmaceuticals intended for administration to patients should be prepared by the user in a manner which satisfies both radiological safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken, complying with the requirements of Good Pharmaceutical Manufacturing Practice, in order to maintain sterility throughout the labelling procedures and to maintain the sterility of the indium (^{111}In) chloride.

A maximal dilution of 1 ml until 6 ml with saline solution is possible.

Because of the small mass of chemical substances present, no special handling precautions are recommended other than those necessary because of the radioactive and pharmaceutical nature of the product. The

normal precautions for handling radioactive materials should be observed. After use, all materials associated with the preparation and administration of radiopharmaceuticals, including any unused product and its container, should be decontaminated or treated as radioactive waste and disposed of in accordance with the conditions specified by the local competent authority. Contaminated materials must be disposed of as radioactive waste via an authorised route.

7 PRODUCT OWNER

Manufactured and released by:
Curium Netherlands B.V.
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1755 LE PETTEN
The Netherlands

Marketing Authorisation Holder:
QT Instruments (S) Pte Ltd
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8 DATE OF (PARTIAL) REVISION OF THE TEXT

10 July 2023