IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PA0240/005/003
Case No: 2064486

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

GE Healthcare Limited

Amersham Place, **Little Chalfont**, **Buckinghamshire**, **HP7 9NA**, **United Kingdom**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Indium Chloride Sterile, 370 MBq/ml

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **16/04/2009** until **02/03/2010**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Indium (^{111}In) Chloride 370MBq/ml radiopharmaceutical precursor, solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Indium-111 chloride:
(no carrier added) (370 MBq/ml)
at the activity reference date
The formulation contains <0.2 µg In/ml. Indium-111 disintegrates by electron capture with a half-life of approximately 67 hours (2.8 days) and emits gamma radiation with principal energies of 171 keV (91%) and 245 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, solution
Clear colourless solution

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

This medicinal product is for diagnostic use only.

Indium -111 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 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 chloride has also been used as the radiolabelling ingredient in injectable preparations such as indium-111-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 chloride required for radiolabelling and the quantity of indium-111-labelled pharmaceutical that is subsequently administered will depend on the pharmaceutical being labelled and its intended use.

Information on recommended activity 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 or to any of the excipients.
Information on contraindications to particular indium-111-labelled pharmaceuticals prepared by radiolabelling with indium-111 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-labelled pharmaceuticals prepared by radiolabelling with indium-111 chloride will be supplied by the manufacturer of the pharmaceutical to be radiolabelled.

4.5 Interaction with other medicinal products and other forms of interaction

Information concerning interactions associated with the use of indium-111-labelled pharmaceuticals prepared by radiolabelling with indium-111 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-labelled pharmaceuticals, prepared by radiolabelling with indium -111 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 foetus. Only imperative investigations should be carried out during pregnancy, when the likely benefit exceeds the risk incurred by the mother and the foetus.

The absorbed dose to the uterus following administration of indium -111-labelled pharmaceuticals prepared by radiolabelling with indium -111 chloride will be dependent on the specific pharmaceutical being radiolabelled and information will be available from the manufacturer of the pharmaceutical to be labelled. Doses above 0.5mGy should be regarded as a potential risk for the foetus.

Advice on avoidance of pregnancy until the calculated dose to the uterus is below 0.5mGy should be given to women of child-bearing 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 a radiation dose to the child greater than 1 mSv.

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-labelled pharmaceutical preparation in which the radiolabelling agent is indium-111 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 effective dose is less than 20mSv. However, with indium -111-labelled pharmaceutical preparations this level may be exceeded. Higher doses may be justified in 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-labelled pharmaceutical will be available from the manufacturer of the pharmaceutical to be radiolabelled.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: diagnostic pharmaceuticals, tumour detection, ATC code: V09I B01

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-labelled radiopharmaceuticals, prepared by radiolabelling with indium-111 chloride prior to administration, will be dependent on the nature of the pharmaceutical to be labelled.

5.3 Preclinical safety data

Indium-111 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 1mg/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 (0.04M)

6.2 Incompatibilities

Radiolabelling of macromolecules such as monoclonal antibodies with indium -111 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 shelf-life for this product is not more than 9 days from the date of release.
The reference date of the product is 3 days before expiry.

Once opened, store in refrigerator (2 °C – 8 °C) and use within 8 hours.

Multidose vial, contains no antimicrobial preservative.

6.4 Special precautions for storage

Store below 25^{o}C. Do not freeze.
Storage should take place in accordance with national regulations for radioactive materials.

6.5 Nature and contents of container

The product is supplied in a 1.0ml, clear, borosilicate, Ph. Eur. Type 1, glass vial sealed with an FEP-faced butyl rubber closure and aluminium overseal. The vial is packed into a lead shielded container.
Pack sizes: 74, 130 and 185 MBq (2, 3.5 and 5 mCi).

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

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 MARKETING AUTHORISATION HOLDER

GE Healthcare Limited
Amersham Place
Little Chalfont
Buckinghamshire
HP7 9NA
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 0240/005/003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 03 March 2000
Date of last renewal: 03 March 2005

10 DATE OF REVISION OF THE TEXT

February 2009

11 DOSIMETRY

The radiation dose received by the various organs following intravenous administration of an indium-111-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-labelled pharmaceuticals will be of the order of 10^{-1} mSv/MBq.

Administration of indium-111-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-labelled pharmaceuticals prepared by radiolabelling with indium-111 chloride should not be administered later than 4 days from the reference date of the indium-111 chloride in order to ensure that the level of indium-114m present is less than 0.2%.

12 INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

This radiopharmaceutical may 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 local competent official organisations (see section 6.6).

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. Storage procedures and the disposal of waste should be in accordance with national guidelines.