# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

KryptoScan, [81m Kr] Radionuclide generator

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Rubidium ($^{81}$Rb) bound as ion to a cation exchange resin is in equilibrium with the daughter-product Krypton ($^{81m}$Kr) and serves as a generator for Krypton ($^{81m}$Kr) gas.

The generator is available with activities ranging between 74-740 MBq (DRN 3633).

**Physical characteristics**
Rubidium ($^{81}$Rb) decays with a physical half-life of 4.58 hours to its metastable daughter-product Krypton ($^{81m}$Kr) thus generating the short-lived radionuclide with a half life of 13 seconds. Krypton ($^{81m}$Kr) decays by isometric transition to Krypton ($^{81}$Kr), emitting pure gamma radiation of 0.190 MeV which is internally converted. $^{81}$Kr decays to stable $^{81}$Br with a half life of $t_{1/2}$ = 2.1 x $10^5$ years.

For a full list of excipients see section 6.1.

## 3 PHARMACEUTICAL FORM

Radionuclide generator.

The product is a shielded Radionuclide generator producing a colourless, odourless, inert gas for inhalation.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

- Investigation of pulmonary ventilation. This product can be especially recommended for paediatric examination because of the low radiation dose.
- Combined with a pulmonary perfusion scintigraphy for diagnosis of pulmonary embolism.
- Pulmonary ventilation ($^{81m}$Kr)/perfusion ($^{99m}$Tc-macroaggregation) studies are possible because of the different spectrometric windows of $^{81m}$Kr and $^{99m}$Tc.

### 4.2 Posology and method of administration

Krypton images are acquired during the continuous inhalation of the short lived and otherwise inert radioactive gas, krypton [$^{81m}$Kr]. This is eluted with humidified air from a rubidium generator and administered to the patient through a face mask or airway.

In general adequate imaging is achieved when 200,000-350,000 counts are accumulated per gamma camera image. This corresponds to approx. 18 MBq/kg body weight.

Most investigations require a number of views (4 to 6). The activities for children may be calculated according to the following equation:

$$\text{Paediatric dose (MBq)} = \frac{\text{Adult dose (MBq) x child weight (kg)}}{\text{70 kg}}$$

Continuous inhalation is stopped upon acquisition of approx. 300,000 counts per gamma camera image.

### 4.3 Contraindications

None known.

**4.4 Special warnings and precautions for use**

Radiopharmaceutical agents should only be used by qualified personnel with the appropriate government authorisation for the use and manipulation of radionuclides. They 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 licence of the local competent official organisations.

**4.5 Interaction with other medicinal products and other forms of interaction**

Diazepam in sedative doses and general anaesthetic agents may affect the distribution of radioactive gases in the lung by slightly shifting the activity to the lung apex and reducing basal accumulation.

**4.6 Fertility, pregnancy and lactation**

Elective exposure to diagnostic radiation should be restricted in so far as possible to the first 10 days of the ovulation cycle.

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.

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 an as to whether the most appropriate choice of radiopharmaceutical has been made, bearing in mind the secretion of activity in breast milk. If administration of Krypton [$^{81m}$Kr] gas is considered necessary, however, breast feedingneed not be specifically interrupted.

**4.7 Effects on ability to drive and use machines**

Effects on the ability to drive or to operate machines have not been described.

**4.8 Undesirable effects**

For each patient, exposure to ionising radiation must be justifiable on the basis of likely clinical 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 or therapeutic 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 negligible frequency because of the low radiation dose incurred.

For more diagnostic investigations using a nuclear medicine procedure the radiation dose delivered (EDE) is less than 20 mSv. Higher doses may be justified in some clinical circumstances.

No adverse/undesirable effects have been reported for this agent.

**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; Earlsfort Terrace; IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517; Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

**4.9 Overdose**

In the unusual event of radiation overdose caused by an unrequired but prolonged period of krypton gas inhalation due to the rapid washout from the lungs during normal ventilation, patients need only be removed from the source of radiation to a fresh and uncontaminated atmosphere.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

ATC code: V09 EX 01 (Other respiratory system diagnostic radiopharmaceuticals)

Krypton is an inert gas which is not metabolized and, in the concentrations applied, [$^{81m}$ Kr] Krypton shows no pharmacodynamic effects.

### 5.2 Pharmacokinetic properties

[$^{81m}$Kr] Krypton is an inert gas with a short biological half-life. Due to its rapid decay the effective half-time of lung elimination is equal to the physical half-life of 13 seconds. Peripheral [81m] Kr Krypton-activity is exhaled after the first passage.

### 5.3 Preclinical safety data

No data available.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

PTFE membrane with immobilised poly (styrenedivinylbenzene) cation exchange resin, with sulphonic acid functional groups.

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

The shelf life for this product is 20 hours after the activity reference date.

### 6.4 Special precautions for storage

Store below 25ºC and in accordance with national regulations for radioactive materials.

### 6.5 Nature and contents of container

The generator containing Kr81m is placed in a lexan housing and then in tungsten shielding. The shielding, together with the other shielding-and packing components, is fixed in a heavy blue synthetic housing and equipped with a synthetic cover with a carry handle at the top and a stopper at the bottom. This complex is hermetically sealed and, together with packaging material, packed in transport packaging.

Pack size: 74-740MBq.

### 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

*Preparation for elution*
1. Remove the Krypton [$^{81m}$ Kr] generator from the transport packaging.
2. Remove the stopper from the bottom and store it in the special cut-away in the transport packaging.
3. Place the generator in the ventilation device.
4. Close the cover of the Krypton ventilation device.
5. Take the krypton supply cable from the ventilation tubing set and connect it to the Krypton ventilation device.

6. Connect the other side of the tubing set to the face mask.
7. Put the plug into a socket.
8. Adjust flow rate to maximum volume.

*Administration*

1. Position the patient in front of the gamma camera (equipped with a $^{99m}$Tc collimator).
2. Put the face mask on face of patient; make sure there is no leakage.
3. Switch on power manually or by remote control.
4. Start accumulation of counts and continue until the required number is reached.
5. Switch power off.

*Handling of expired generator*

1. Replace the stop that was removed earlier.
2. Store the generator in a suitable place for decay until a level of activity acceptable for return transport is reached.
3. Prepare the generator for return transport following the return procedure.

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. Waste must be disposed of in accordance with national regulations for radioactive materials.

## 7 MARKETING AUTHORISATION HOLDER

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

## 8 MARKETING AUTHORISATION NUMBER

PA0690/007/001

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26 May 2006

Date of last renewal: 26 May 2011

## 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. Absorbed dose per unit activity administered (mGy/MBq) ICRP 53.

| **Organ** | Absorbed dose per unit activity administered (mGy/MBq) | | | | |
|---|---|---|---|---|---|
| | Adult | 15 year | 10 year | 5 year | 1 year |
| Adrenals | 3.4E-06 | 5.7E-06 | 8.3E-06 | 1.3E-05 | 2.1E-05 |
| Bladder wall | 6.8E-08 | 7.6E-08 | 2.0E-07 | 4.7E-07 | 1.2E-06 |
| Bone surface | 1.7E-06 | 2.2E-06 | 1.3E-06 | 4.8E-06 | 9.3E-06 |
| Breast | 4.6E-06 | 4.6E-06 | 8.9E-06 | 1.3E-05 | 1.8E-05 |
| Intestinal tract | | | | | |
| Stomach wall | 2.5E-06 | 3.2E-06 | 4.4E-06 | 6.7E-06 | 1.1E-05 |
| Small intestine | 2.7E-07 | 4.7E-07 | 8.6E-07 | 1.6E-06 | 3.4E-06 |
| ULI wall | 3.2E-07 | 5.5E-07 | 1.2E-06 | 1.9E-06 | 3.5E-06 |
| LLI wall | 1.4E-07 | 1.5E-07 | 3.0E-07 | 8.0E-07 | 2.0E-06 |

| | | | | | |
|---|---|---|---|---|---|
| Kidneys | 1.2E-06 | 1.9E-06 | 2.9E-06 | 4.5E-06 | 8.4E-06 |
| Liver | 3.4E-06 | 4.8E-06 | 6.6E-06 | 9.5E-06 | 1.6E-05 |
| Lungs | 2.1E-04 | 3.1E-04 | 4.4E-04 | 6.8E-04 | 1.3E-03 |
| Ovaries | 1.7E-07 | 1.7E-07 | 4.1E-07 | 8.0E-07 | 1.9E-06 |
| Pancreas | 3.5E-06 | 4.4E-06 | 6.4E-06 | 9.8E-06 | 1.8E-05 |
| Red marrow | 2.1E-06 | 3.3E-06 | 4.2E-06 | 5.3E-06 | 8.2E-06 |
| Spleen | 3.1E-06 | 4.1E-06 | 6.0E-06 | 9.2E-06 | 1.6E-05 |
| Testes | 1.7E-08 | 2.3E-08 | 7.4E-08 | 1.3E-08 | 5.6E-07 |
| Thyroid | 1.2E-06 | 2.1E-06 | 3.7E-06 | 6.0E-06 | 1.1E-05 |
| Uterus | 1.3E-07 | 1.8E-07 | 3.5E-07 | 7.2E-07 | 1.8E-06 |
| Other tissue | 1.8E-06 | 2.3E-06 | 3.2E-06 | 4.7E-06 | 8.5E-06 |
| Dose effective dose equivalent (mSv/MBq) | 2.7E-05 | 4.0E-05 | 5.7E-05 | 8.8E-05 | 1.7E-04 |

**11.1** For this product the effective dose equivalent resulting from an administered activity of 3000-9000 MBq, (range of actual exposure) expected activities in adults, is 0.08-0.24 mSv.

Due to the difference in half-lives, the amount of $^{81}$Kr per 37MBq (1 mCi) of $^{81m}$Kr is about 2nCi (2uBq/MBq). Thus the contribution of $^{81}$Kr to the total radiation burden of the patient is negligible.

**12 INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS**

*See Section 6.6*