SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Strontium chloride $^{89}SrCl_2$ POLATOM

37.5 MBq/ml solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Strontium-89 chloride 37.5 MBq/ml.
Strontium-89 is a pure beta emitter with an energy of 1.492 MeV and a half-life of 50.5 days.
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear, colourless solution.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Strontium chloride $^{89}SrCl_2$ POLATOM is indicated for the palliation of pain from bone metastases. The best documented use of strontium chloride-89 is in case of osteoblastic or mixed metastases from prostate cancer and breast cancer, it can also be used in cases of other tumorus resulting in osteoblastic (scintigraphicaly “hot”) metastases to the bone.
Bone scintigraphy is recommended prior to Strontium-89 chloride therapy.
Most common indication for strontium chloride is the treatment of pain in patients with multiple disseminated metastases (chemotherapy, hormonal therapy, treatment with analgesics including narcotic drugs), who have not responded to previous conventional therapies).

4.2. Posology and method of administration

Strontium chloride $^{89}SrCl_2$ POLATOM is administered as a single inravenous injection in a dose of 150 MBq activity in about 4 ml of the solution.
Alternatively in particularly heavy or light framed patients a dose of 2 MBq/kg ‘fat-free’ body weight may be used. This dosage is suitable for the elderly.
Patient’s hospitalisation is not necessary.
In case of recurrent pain a repeated administration of the radiopharmaceutical may be applied. Repeat administrations should not be performed within 3 months of the previous injection to reduce the risk of cumulative effects. Further administrations are not indicated in patients who have not responded to the previous administration. The product is not for administration to children.
The instructions for preparation of radiopharmaceutical are given in section 12.

4.3. Contraindications

Absolute contraindications
Strontium chloride $^{89}SrCl_2$ POLATOM must not be used:
- In patients with hypersensitivity to the active substance or any of the excipients,
- In woman in established or suspected pregnancy or when pregnancy has not been excluded (see section 4.6),
- In breastfeeding women.

Relative contraindications
Blood morphology parameters below: Hb - 90 g/l, leukocytosis total - 3.5 x 10^9/l, thrombocytosis - 100 x 10^9/l is a relative contraindication for the use of strontium-89 chloride because of its possible myelotoxic effect. However in certein cases, the administration of strontium-89 chloride can be considered in patients with leukocytopenia > 2.4 x 10^9/l and (or) thrombocytopenia > 60 x 10^9/l, after previous exclusion of chronic disseminated intravascular coagulation syndrome (DIC).
Other restrictions
Impaired renal function may lead to decreased excretion of strontium strontium-89 chloride by kidneys, increased whole-body exposure to radiation and increased myelotoxicity strontium-89 chloride. In patients with renal failure (creatinine > 180 µmol/l, GFR < 30 ml/min) the administration of strontium-89 chloride should be refrained.
It is also recommended to reduce the administered activity of strontium-89 chloride to 50%, in patients with creatinine clearance < 50 ml/min.
Strontium-89 chloride should not be used as a primary treatment for cord compression secondary to spinal metastases where more rapid treatment may be necessary nor in pathological fractures.

4.4. Special warnings and precautions for use

Pregnancy, see section 4.6.
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 therapeutic effect.
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. Use of the product in patients with evidence of seriously compromised bone marrow, particularly low neutrophil and platelet counts, is not recommended unless the potential benefit of the treatment is considered to outweigh the risk. Special precautions, such as urinary catheterisation, should be taken following administration of Strontium chloride $^{89}SrCl_2$ POLATOM to patients who are significantly incontinent to minimise risks of radioactive contamination. The catheter should be kept at least 5 days.
Urine excreted during this time contains radioactive substances, and therefore containers (bags) must be emptied with special caution. All activities must be carried out in hygienic rubber gloves, to avoid skin contact with radioactive urine. It is recommended that the blood parameters are monitored. If case of repeated administration of Strontium chloride $^{89}SrCl_2$ POLATOM, the patient’s haematological response to the initial dose as well as current platelet levels and any other evidence of marrow depletion should all be carefully considered. A cytotoxic agent may be administered to a patient who has previously received Strontium chloride $^{89}SrCl_2$ POLATOM provided that his haematological parameters are stable and within the normal range. An interval of 12 weeks is recommended between administrations of the two therapies. The expected time of onset of pain relief (10 to 20 days following administration of Strontium chloride $^{89}SrCl_2$ POLATOM) should be taken into account in patient management. It is not recommended that Strontium chloride $^{89}SrCl_2$ POLATOM is administered to patients with very short life expectancies. Care should be exercised in the pre-treatment assessment of the haematological status of patients who, for the same cause, have previously received extensive bone radiation and/or another injectable bone-seeking isotope. It is important that written information concerning this treatment and the associated safety precautions are given to the patient, relatives and hospital staff. Users should refer to the accompanying Patient Information.

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

Calcium may reduce the of strontium-89 in metastatic lesions.
Calcium therapy should be discontinued at least two weeks before strontium chloride-89 administration.

4.6. Pregnancy and lactation

Strontium-89 chloride is contraindicated during pregnancy and breastfeeding. When it is necessary to administer a radioactive medicinal product 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. Before administering a radioactive medicinal product to a mother who is breastfeeding consideration should be given as to whether the therapy could be reasonably delayed until the mother has ceased breastfeeding. Breastfeeding should be discontinued before strontium-89 chloride administration.

4.7. Effects on ability to drive and use machines

No data.

4.8. Undesirable effects

In some patients an exacerbation of pain within the first few days (mostly within 72 hours) is an early adverse effect after administration of strontium-89. This symptom may be an indication of good response to therapy. This effect was usually mild, temporary and controlled with analgesics.
Some degree of haematological toxicity, including thrombocytopenia and leucopenia, is to be expected following administration of Strontium chloride $^{89}SrCl_2$ POLATOM. Typically platelets will be depressed by about 30% within 4 – 6 weeks of therapy, compared to pre-administration levels. After 3 – 6 weeks number of platelets returns to the output value, though this process depends on the extent of neoplastic changes during therapy. More severe depression of platelet levels may be observed in some patients.
The radiation dose resulting from therapeutic exposure may result in higher incidence of cancer and mutations. In all cases it is necessary to ensure that the risks of the radiation are less than from the disease itself.

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 Pharmacovigilance Department of the Office for Registration of Medicinal Products, Medical Devices and Biocidal Products:
Al. Jerozolimskie 181C
02-222 Warszawa
Tel.: + 48 22 49 21 301
Fax: + 48 22 49 21 309
e-mail: ndl@urpl.gov.pl

Adverse reactions may be reported to marketing authorization holder.

4.9. Overdose
Radioactivity of the dose administered to patients should always be considered in relation to its diagnostic and therapeutic value.
Any cases of overdose of strontium-89 chloride understood as the administration of excessive amounts of radioactivity are not known.
Radiopharmaceutical Strontium chloride $^{89}SrCl_2$ POLATOM should be administered under strict medical control only in nuclear medicine facilities and by qualified personnel, hence the risk of overdose is extremely low.
In the event of administration of a radiation overdose, the absorbed dose to the patient should be reduced where possible by increasing the elimination of the radionuclide from the body by administering large amounts of fluids, by forced diuresis and frequent bladder voiding.

5. PHARMACOLOGICAL PROPERTIES
5.1. Pharmacodynamic properties
Pharmacotherapeutic group: Therapeutic radiopharmaceuticals, pain palliation,
ATC code: V10B X01
The chemical properties of strontium enable it to imitate calcium *in vivo*, rapidly localising in proliferating bone. The average range of β-particles emitted by ^{89}Sr in tissue is 2.4 cm.

5.2. Pharmacokinetic properties
The extent of uptake and retention of strontium-89 will depend on the metastatic involvement of the skeleton. Strontium is retained in lesions with a long biological half-life compared to the physical half-life of strontium-89, whilst strontium taken up into normal bone exhibits a halflife of about 14 days. The longer retention of strontium-89 in metastatic lesions enables the isotope to deliver a larger radiation dose to metastases whilst delivering a relatively small dose to bone marrow. Strontium-89 which is not localised in the skeleton is excreted mainly via the urine with a small amount via the faeces.

5.3. Preclinical safety data
LD_{50} value determined for strontium chloride in mice is 147.6 mg/kg. No immunization of patients was observed.

6. PHARMACEUTICAL PARTICULARS
6.1. List of excipients
Strontium chloride
Sodium chloride
Water for injections

6.2. Incompatibilities
No data.

6.3. Shelf life
28 days after reference date.

6.4. Special precautions for storage
Store below 25ºC. Do not freeze.
Store in accordance with national regulation on radioactive materials.

6.5. Nature and contents of container
The immediate packaging is a glass vial 10 ml of volume closed with a rubber stopper and aluminium cap placed in a lead container. The vial contains solution in a volume corresponding to the activity determined on the day of the calibration.

6.6. Special precautions for disposal and other handling
The radiopharmaceutical product is delivered in portions of required activity (radioactivity is calculated at 12:00 CET on reference day).
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. Any unused products and material waste should be disposed of accordance with regulations for radioactive materials.

7. MARKETING AUTHORISATION HOLDER
National Centre for Nuclear Research
Andrzej Sołtan 7
05-400 Otwock, Poland
Tel.: +48 22 7180700
Fax: +48 22 7180350
e-mail: polatom@polatom.pl

8. MARKETING AUTHORISATION NUMBER
R/6807

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
20.09.1996 / 21.09.2001/17.09.2008/03.06.2011

10. DATE OF REVISION OF THE TEXT
April 2016

11. DOSIMETRY
The estimated radiation doses that would be received by normal healthy adults from the intravenous administration of strontium-89 are given in the table below. Data are taken from the ICRP Publication 53 of the ICRP (International Commission on Radiological Protection, Radiation Dose to Patients from Radiopharmaceuticals, Pergamon Press 1987).

Radiation doses to normal adults from the intravenous injection of strontium-89

	Organ	Absorbed radiation dose [mGy/MBq]
1.	Bone surfaces	17.0
2.	Red bone marrow	11.0
3.	LLI wall	4.7
4.	ULI wall	1.8
5.	Bladder wall	1.3
6.	Breast	0.96
7.	Stomach wall	0.78
8.	Adrenals	0.78
9.	Kidneys	0.78
10.	Liver	0.78
11.	Lungs	0.78
12.	Ovaries	0.78
13.	Pancreas	0.78
14.	Spleen	0.78
15.	Testes	0.78
16.	Thyroid	0.78
17.	Uterus	0.78
18.	Other tissue	0.78
19.	Small intest	0.023

When osseous metastases are present significantly enhanced localisation of the radiopharmaceutical will occur with correspondingly higher doses to the metastases relative to other organs.
The absorbed dose to vertebral metastases has been measured in a group of 10 patients with widely varying extent of disease. The minimum, maximum and mean doses in this group are listed below (Blake, G M *et al* Strontium-89 therapy: Measurement of absorbed dose to skeletal metastases. J Nucl Med 1988; **29**(4), 549-557).

Radiation dose to vertebral metastases from intravenous injection of strontium-89

	Absorbed radiation dose [mGy/MBq]
Minimum	60
Maximum	610
Mean	230

The effective dose (ED) for strontium-89 is 465 mSv per 150 MBq (ICRP **80**, 1998; p. 116).

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS
This radiopharmaceutical is delivered in ready-to-use form.
Before administration of the radiopharmaceutical to the patient it is necessary to check solution appearance and whether the packaging/vial is not damaged. The solution should be clear and colourless.

Instruction for opening the radiopharmaceutical product:
Take off the lid of the lead container. Using forceps tear off the central part of the aluminium cap without removing the vial from the lead container.
Using the syringe with the needle pierce the rubber septum and draw the vial content.
The product can be slowly administered intravenously to the patient (within about 30 seconds).
This radiopharmaceutical may be received, used and administered only by authorised persons in designated clinical settings. Its receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the local competent official organisations.

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