SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Hippurate-^{131}I for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Sodium 2-[^{131}I]iodohippurate 3.7 - 74 MBq/ml
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Hippurate-^{131}I is a radiopharmaceutical used in diagnostics of kidneys dysfunction and urinary tract obstructions (dynamic renal scintigraphy, renoscintigraphy). Renal scintigraphy utilizing this radiopharmaceutical allows the evaluation of:

- kidney blood flow resolution (effective renal plasma flow – ERPF),
- renal tubular function,
- urine outflow from the pyelocalyceal system,
- vesico-ureteral reflux (examination during miction),
- renal function impairment in transplanted kidney

and can be used in the diagnostics of renovascular hypertension (particularly in the captopril enhanced renal scintigraphy). The preparation accumulates in the kidneys where it concentrates and is later excreted.

4.2 Posology and method of administration

Hippurate-^{131}I for injection is administered in a single dose corresponding to activity of 0.185-1.295 MBq for adult patient (70 kg). Depending on the diagnostic indication, the administration is by intravenous infusion or injection.
After intravenous administration, Hippurate-^{131}I for injection accumulates over 2-5 minutes in the kidneys, where it is concentrated and then excreted.

4.3 Contraindications

Pregnancy and breastfeeding are absolute contraindications.

4.4 Special warnings and precautions for use

The radiopharmaceutical may only be used in authorized facilities and by authorized persons. Safety precautions for careful handling this radiopharmaceutical should be observed.
Ensure protection of the staff and patients against unnecessary exposure to ionising radiation. Permit to store and administer radiopharmaceuticals depends on specified local standards and regulations for radioactive materials.
Diagnosis of kidney function usually requires the administration of fluids, in order to ensure appropriate and constant diuresis.

4.5 Interactions with other medicinal products and other forms of interaction

Furosemid, a diuretic agent, alleviates functional obstruction of excretory phase of Hippurate-^{131}I for injection. It's not recommended to take any diuretic drugs prior the examination.

4.6 Pregnancy and lactation

Hippurate-^{131}I for injection should not be administered to pregnant and breastfeeding women. Alternative diagnostic methods, which do not utilize ionising radiation, should always be considered. When it is necessary to administer Hippurate-^{131}I for injection to women of childbearing potential, information should always be sought about pregnancy. Pregnancy should be excluded in any women who has had menstrual cycle disturbances.
Any women who has missed a period should be assumed to be pregnant until proven otherwise. Examinations using radiopharmaceuticals in women of childbearing potential should be carried out during the first (about 10) days following the onset of menses.

Breastfeeding should be interrupted following administration of the first dose of radiopharmaceutical product due to potential risk for the child. It can be restarted when radiation dose potentially received by the child during breastfeeding and contact with mother is within the range of approved standards.

4.7 Effects on ability to drive and use machines

No affects to the ability to drive or to use machines have been reported.

4.8 Undesirable effects

No significant side effects caused by Hippurate-^{131}I for injection are known, however according to literature data (J.Nucl. Med. **37**, 185-192, 1064-1067, 1996), in some patients the following symptoms have been reported: nausea, vomiting, rash, itch, nettle-rash and hypotension.

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. Adverse reactions may be reported to Marketing Authorisation Holder.

4.9. Overdose

The activity of the radiopharmaceutical dose administered to patients should always be considered in relation to its diagnostic value. Any cases of Hippurate-^{131}I for injection overdose understood as administration of an excess of radioactive substance are known. In case of overdose, a diuretic should be administered in order to accelerate urination and reduce the patient's radiation dose.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:
diagnostic radiopharmaceutical
ATC: V 09C X02
Hippurate-^{131}I for injection in diagnostic dose is not inducing any pharmacological effects.

5.2 Pharmacokinetic properties

After intravenous administration, sodium iodohippurate (^{131}I) is rapidly excreted by the renal system. The maximum renal uptake occurs normally within 2-5 minutes of intravenous administration, depending on the patient hydration, extent of renal impairment, the nature of the kidneys disease and medication. Approximately two thirds of the compound binds reversibly with plasma proteins. The compound easily crosses cell membranes, renal excretion is mainly by tubular secretion (80%) and glomerular filtration (20%). The renal transit time and distribution of radiopharmaceutical depend on renal flow and the excretory ability of kidney tubules.
Maximum tubular excretion of sodium iodohippurate (^{131}I) is around 76 mg/min or approximately 0.2/ml of plasma flow.

More than 90% of sodium iodohippurate (^{131}I) is taken up by the kidneys and instantly transferred to the bladder along with the urine. Approximately 50-75% is excreted within 25 minutes, 90-95% within 8 hours. Hepatobiliary excretion is less than 0.4%. However in case of severe renal impairment, hepatobiliary excretion may increase to 5%. Sodium iodohippurate (^{131}I) is secreted in breast milk.

5.3 Preclinical safety data
Hippurate-^{131}I for injection does not linger in the system and is quickly excreted. It is not toxic.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
benzyl alcohol
sodium chloride
water for injections

6.2 Incompatibilities
If the obstruction is noted in the excretory phase, often furosemide is administered intravenously a few minutes after peak of renal activity is reached. Furosemide is a diuretic agent and therefore alleviates functional obstruction, whereby the renogram showing excretory obstruction becomes normal. On the other hand, if the obstruction is mechanical little change in the renogram will occur after furosemide administration.

6.3 Shelf life
Hippurate-^{131}I for injection expires 21 days from manufacturing date.

6.4 Storage precautions for storage
Store in refrigerator (2°C - 8°C). During transportation (not longer than 7 days after production date) up to 25°C.

6.5 Nature and contents of the container
10 ml glass vial sealed with a rubber stopper and an aluminum crimp cap, placed in a lead shielding container. The vial contains a volume of the solution corresponding to the activity determined on the calibration day.

6.6 Special precautions for disposal
This radiopharmaceutical may be received, used and administered only by authorized persons in designated clinical settings. Its receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licenses of the local competent official organizations. Any unused products and material waste should be disposed of in accordance with regulations for radioactive materials.

7. MARKETING AUTHORISATION HOLDER
Narodowe Centrum Badań Jądrowych
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05-400 Otwock, Poland
Tel.: +48 22 7180700
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8. MARKETING AUTHORISATION NUMBER
R/3272

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
18.06.1976/22.12.1999/05.02.2005/16.12.2008/12.08.2013

10. DATE OF APPROVAL/REVISION OF THE TEXT
04.2016

11. DOSIMETRY
As a result of nuclear decay, iodine-131 emits beta radiation with a maximum energy of 606 keV, as well as gamma radiation quanta with energies of 248 keV, 365 keV, 637 keV and 723 keV. The half-life of iodine-131 is 8.02 days.
After intravenous administration of Hippurate-^{131}I for injection, the doses absorbed by the various organs depend on the patient's age, as described in ICRP 80: Radiation Dose to Patients from Radiopharmaceuticals, 1998, p. 78, and are presented in the table below.

Absorbed dose per unit administered activity [mGy/MBq]

Organ	Adult	15 years	10 years	5 years	1 year
Adrenals	2.5E-03	3.2E-03	5.0E-03	7.7E-03	1.5E-02
Bladder	9.2E-01	1.2E+00	1.5E+00	1.4E+00	2.7E+00
Bone surfaces	3.5E-03	4.4E-03	6.1E-03	7.7E-03	1.5E-02
Brain	1.3E-03	1.7E-03	2.8E-03	4.7E-03	9.0E-03
Breast	1.3E-03	1.8E-03	2.9E-03	4.6E-03	9.3E-03
Gall bladder	3.1E-03	4.2E-03	7.0E-03	8.4E-03	1.5E-02
Gastrointestinal tract					
Stomach	2.4E-03	3.0E-03	5.0E-03	7.1E-03	1.4E-02
Small intestine	7.7E-03	1.0E-02	1.4E-02	1.6E-02	2.8E-02
Colon	1.1E-02	1.4E-02	1.8E-02	2.0E-02	3.2E-02
ULI	6.2E-03	8.4E-03	1.2E-02	1.4E-02	2.4E-02
LLI	1.8E-02	2.2E-02	2.7E-02	2.7E-02	4.3E-02
Heart	1.7E-03	2.2E-03	3.6E-03	5.6E-03	1.1E-02
Kidneys	3.1E-02	3.7E-02	5.2E-02	7.7E-02	1.4E-01
Liver	2.2E-03	2.8E-03	4.7E-03	7.1E-03	1.3E-02
Lungs	1.5E-03	2.1E-03	3.3E-03	5.2E-03	1.0E-02
Muscles	5.3E-03	6.5E-03	8.8E-03	1.0E-02	1.8E-02
Oesophagus	1.5E-03	2.0E-03	3.2E-03	5.1E-03	9.9E-03
Ovaries	1.6E-02	2.1E-02	2.6E-02	2.5E-02	4.3E-02
Pancreas	2.5E-03	3.1E-03	3.3E-03	7.7E-03	1.5E-02
Red marrow	4.0E-03	5.2E-03	6.9E-03	7.7E-03	1.3E-02
Skin	2.5E-03	3.1E-03	4.6E-03	6.3E-03	1.2E-02
Spleen	2.4E-03	3.1E-03	4.9E-03	7.2E-03	1.4E-02
Testes	1.2E-02	1.7E-02	2.7E-02	2.7E-02	4.9E-02
Thymus	1.5E-03	2.0E-03	3.2E-03	5.1E-03	9.9E-03
Thyroid	1.4E-03	1.9E-03	3.1E-03	5.2E-03	1.0E-02
Uterus	3.6E-02	4.3E-02	5.6E-02	5.4E-02	9.1E-02
Remaining organs	5.4E-03	6.7E-03	8.9E-03	1.0E-02	1.8E-02
Effective dose [mSv/MBq]	**5.2E-02**	**6.7E-02**	**8.6E-02**	**8.3E-02**	**1.6E-01**
Bladder walls contributes 88% of the effective dose					
Effective dose if bladder is emptied 1 or 0.5 hours after administration					
1 hour	2.0E-02	2.6E-02	3.6E-02	4.7E-02	8.9E-02
30 minutes	2.6E-02	3.4E-02	4.5E-02	4.7E-02	9.0E-02

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS
Radiopharmaceutical is delivered in a ready-to-use form.

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