ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Celsunax 74 MBq/mL solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL of solution contains 74 MBq of ioflupane (^{123}I) at reference time (0.07 to 0.13 µg/mL of ioflupane).

Each 2.5 mL single dose vial contains 185 MBq ioflupane (^{123}I) (specific activity range 2.5 to 4.5 x 10^{14} Bq/mmol) at reference time.
Each 5 mL single dose vial contains 370 MBq ioflupane (^{123}I) (specific activity range 2.5 to 4.5 x 10^{14} Bq/mmol) at reference time.

Iodine-123 has a physical half-life of 13.2 hours. It decays emitting gamma radiation with a predominant energy of 159 keV and X-rays of 27 keV.

Excipient with known effect

This medicinal product contains 39.5 g/L ethanol, resulting in a maximum of 197 mg of ethanol in 5 mL solution.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

Celsunax is indicated for detecting loss of functional dopaminergic neuron terminals in the striatum:

- In adult patients with clinically uncertain parkinsonian syndromes, for example those with early symptoms, in order to help differentiate essential tremor from parkinsonian syndromes related to idiopathic Parkinson's disease, multiple system atrophy and progressive supranuclear palsy. Celsunax is unable to discriminate between Parkinson's disease, multiple system atrophy and progressive supranuclear palsy.
- In adult patients, to help differentiate probable dementia with Lewy bodies from Alzheimer's disease.
  Celsunax is unable to discriminate between dementia with Lewy bodies and Parkinson's disease dementia.

4.2 Posology and method of administration

Prior to administration appropriate resuscitation equipment should be available.

Celsunax should only be used in adult patients referred by physicians experienced in the management of movement disorders and/or dementia. Celsunax should only be used by qualified personnel with the appropriate government authorisation for the use and manipulation of radionuclides within a designated

clinical setting.

Posology

Clinical efficacy has been demonstrated across the range 110 to 185 MBq. Do not exceed 185 MBq and do not use when the activity is below 110 MBq.

Patients must undergo appropriate thyroid blocking treatment prior to injection to minimise thyroid uptake of radioactive iodine, for example by oral administration of approximately 120 mg potassium iodide 1 to 4 hours prior to injection of Celsunax.

Special populations

Renal and hepatic impairment
Formal studies have not been carried out in patients with significant renal or hepatic impairment. No data are available (see section 4.4).
Careful consideration of the activity to be administered is required since an increased radiation exposure is possible in these patients.

Paediatric population
The safety and efficacy of Celsunax in children aged 0 to 18 years has not been established. No data are available.

Method of administration

For intravenous use.

Vial for single use.

For patient preparation, see section 4.4.

Precautions to be taken before handling or administering the medicinal product

Celsunax should be used without dilution. To minimise the potential for pain at the injection site during administration, a slow intravenous injection (not less than 15 to 20 seconds) via an arm vein is recommended.

Image acquisition

SPECT imaging should take place between three and six hours post-injection. Images should be acquired using a gamma camera fitted with a high-resolution collimator and calibrated using the 159 keV photopeak and a ± 10% energy window. Angular sampling should preferably be not less than 120 views over 360 degrees. For high resolution collimators the radius of rotation should be consistent and set as small as possible (typically 11-15 cm). Experimental studies with a striatal phantom, suggest that optimal images are obtained with matrix size and zoom factors selected to give a pixel size of 3.5-4.5 mm for those systems currently in use. A minimum of 500k counts should be collected for optimal images. Normal images are characterised by two symmetrical crescent-shaped areas of equal intensity. Abnormal images are either asymmetric or symmetric with unequal intensity and/or loss of crescent.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Pregnancy (see section 4.6).

4.4 Special warnings and precautions for use

Potential for hypersensitivity or anaphylactic reactions

If hypersensitivity or anaphylactic reactions occur, the administration of the medicinal product must be discontinued immediately and, if necessary, intravenous treatment initiated. The necessary resuscitative medicinal products and equipment (e.g. endotracheal tube and ventilator) have to be readily available, to enable immediate action in emergencies.

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 the appropriate licences of the local competent official organisations.

Individual benefit/risk justification

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 dose is as low as reasonably achievable bearing in mind the need to obtain the intended diagnostic result.

Renal impairment/hepatic impairment

Formal studies have not been carried out in patients with significant renal or hepatic impairment. In the absence of data, Celsunax is not recommended in cases of moderate to severe renal or hepatic impairment.
Careful consideration of the benefit risk ratio in these patients is required since an increased radiation exposure is possible.

Patient preparation

The patient should be well hydrated before the start of the examination and urged to void as often as possible during the first hours after the examination in order to reduce radiation.

Specific warnings

This medicinal product contains up to 197 mg of alcohol (ethanol) in each dose which is equivalent to 39.5 mg/mL (5% by volume). The amount in 5 mL of this medicinal product is equivalent to 5 mL beer or 2 mL wine. The small amount of alcohol in this medicinal product will not have any noticeable effects.

Precautions with respect to environmental hazard see section 6.6.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed in humans.

Ioflupane binds to the dopamine transporter. Active substances that bind to the dopamine transporter with high affinity may therefore interfere with Celsunax diagnosis. These include:
- amfetamine,
- benzatropine,
- buproprion,
- cocaine,
- mazindol,
- methylphenidate,
- phentermine,
- sertraline.

Active substances shown during clinical studies not to interfere with Celsunax imaging include:

- amantadine,
- trihexyphenidyl,
- budipine,
- levodopa,
- metoprolol,
- primidone,
- propranolol,
- selegiline.

Dopamine agonists and antagonists acting on the postsynaptic dopamine receptors are not expected to interfere with Celsunax imaging and can therefore be continued if desired. Medicinal products shown in animal studies not to interfere with Celsunax imaging include pergolide.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Where 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 satisfactory imaging. Alternative techniques which do not involve ionising radiation should be considered.

Pregnancy

Animal reproductive toxicity studies have not been performed with this product. Radionuclide procedures carried out on pregnant women also involve radiation doses to the foetus. Administration of 185 MBq of ioflupane (^{123}I) results in an absorbed dose to the uterus of 3.0 mGy. Celsunax is contraindicated in pregnancy (see section 4.3).

Breast-feeding

It is not known whether ioflupane (^{123}I) is excreted in human milk. Before administering a radioactive medicinal product to a breast-feeding mother, consideration should be given as to whether the investigation could be reasonably delayed until 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 radioactivity in breast milk. If administration is considered necessary, breast-feeding should be interrupted for 3 days and substituted by formula feeding. During this time, breast milk should be expressed at regular intervals and the expressed feeds should be discarded.

Fertility

No fertility studies have been performed. No data are available.

4.7 Effects on ability to drive and use machines

Celsunax has no known influence on the ability to drive and use machines.

4.8 Undesirable effects

The following undesirable effects are recognised for ioflupane (^{123}I):

Tabulated summary of adverse reactions

The frequencies of adverse reactions are defined as follows:
Very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000) and not known (cannot be estimated from the available data).
Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

MedDRA system organ classification (SOC)	**Adverse reaction**	**Frequency**
Immune system disorders	Hypersensitivity	Not known
Metabolism and nutrition disorders	Appetite increased	Uncommon
Nervous system disorders	Headache	Common
	Dizziness, formication (paraesthesia), dysgeusia	Uncommon
Ear and labyrinth disorders	Vertigo	Uncommon
Vascular disorders	Blood pressure decreased	Not known
Respiratory, thoracic and mediastinal disorders	Dyspnea	Not known
Gastrointestinal disorders	Nausea, dry mouth	Uncommon
	Vomiting	Not known
Skin and subcutaneous tissue disorders	Erythema, pruritus, rash, urticaria, hyperhidrosis	Not known
General disorders and administration site conditions	Injection site pain (intense pain or burning sensation following administration into small veins)	Uncommon
	Feeling hot	Not known

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose is 4.63 mSv when the maximal recommended activity of 185 MBq is administered these adverse events are expected to occur with a low probability.

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 listed in Appendix V.

4.9 Overdose

In cases of administration of a radiation overdose, frequent micturition and defaecation should be

encouraged in order to minimise radiation dose to the patient. Care should be taken to avoid contamination from the radioactivity eliminated by the patient using such methods.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Diagnostic radiopharmaceuticals, central nervous system,
ATC code: V09AB03

At the chemical concentrations used for diagnostic examinations, Celsunax does not appear to have any pharmacodynamic activity.

Mechanism of action

Ioflupane is a cocaine analogue. Studies in animals have shown that ioflupane binds with high affinity to the presynaptic dopamine transporter and so radiolabelled ioflupane (^{123}I) can be used as a surrogate marker to examine the integrity of the dopaminergic nigrostriatal neurons. Ioflupane also binds to the serotonin transporter on 5-HT neurons but with lower (approximately 10-fold) binding affinity.

There is no experience in types of tremor other than essential tremor.

Clinical efficacy

Clinical studies in patients with dementia with Lewy bodies

In a pivotal clinical study including evaluation of 288 subjects with dementia with Lewy bodies (DLB) (144 subjects), Alzheimer's disease (124 subjects), vascular dementia (9 subjects) or other (11 subjects), the results of an independent, blinded visual assessment of the ioflupane (^{123}I) images were compared to the clinical diagnosis as determined by physicians experienced in the management and diagnosis of dementias. Clinical categorisation into the respective dementia group was based on a standardised and comprehensive clinical and neuropsychiatric evaluation. The values for the sensitivity of ioflupane (^{123}I) in determining probable DLB from non-DLB ranged from 75.0% to 80.2% and specificity from 88.6% to 91.4%. The positive predictive value ranged from 78.9% to 84.4% and the negative predictive value from 86.1% to 88.7%. Analyses in which both possible and probable DLB patients were compared with non-DLB dementia patients demonstrated values for the sensitivity of ioflupane (^{123}I) ranging from 75.0% to 80.2% and specificity from 81.3% to 83.9% when the possible DLB patients were included as non-DLB patients. The sensitivity ranged from 60.6% to 63.4% and specificity from 88.6% to 91.4% when the possible DLB patients were included as DLB patients.

5.2 Pharmacokinetic properties

Distribution

Ioflupane (^{123}I) is cleared rapidly from the blood after intravenous injection; only 5% of the administered activity remains in whole blood at 5 minutes post-injection.

Organ uptake

Uptake in the brain is rapid, reaching about 7% of injected activity at 10 minutes post-injection and decreasing to 3% after 5 hours. About 30% of the whole brain activity is attributed to striatal uptake.

Elimination

At 48 hours post-injection, approximately 60% of the injected radioactivity is excreted in the urine, with faecal excretion calculated at approximately 14%.

5.3 Preclinical safety data

Non-clinical data for ioflupane reveal no special hazard for humans based on conventional studies of safety pharmacology, single and repeated dose toxicity and genotoxicity.

Studies on reproductive toxicity and to assess the carcinogenic potential of ioflupane have not been performed.

Environmental Risk Assessment (ERA)

After use, all materials associated with the preparation and administration of radiopharmaceuticals, including any unused medicinal 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 material must be disposed of as radioactive waste via an authorised route.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Acetic acid, glacial (E260)
Sodium acetate trihydrate (E262)
Ethanol (96%) (E1510)
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf-life

24 hours from the end of the synthesis (EOS) time stated on the label.

6.4 Special precautions for storage

Do not store above 25°C. Do not freeze.
Store in the original lead shielding.

Storage of radiopharmaceuticals should be in accordance with national regulation on radioactive materials.

6.5 Nature and contents of container

Sterile 10 mL glass vial (Type I) with a rubber stopper and a flip cap.
The vial is placed into a lead container for protective shielding.

Pack size of 1 vial containing 2.5 mL or 5 mL of solution.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

General warning

Normal safety precautions for handling radioactive materials should be observed.

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.

If at any time in the preparation of this product the integrity of this vial is compromised it should not be used.

Administration procedures should be carried out in a way to minimise risk of contamination of the medicinal product and irradiation of the operators. Adequate shielding is mandatory.

The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spill of urine, vomiting etc. Radiation protection precautions in accordance with national regulations must therefore be taken.

7. MARKETING AUTHORISATION HOLDER

Pinax Pharma GmbH
Lausitz Mühlenweg 5
04924 Bad Liebenwerda
Germany

8. MARKETING AUTHORISATION NUMBERS

EU/1/21/1560/001 (2.5 mL)
EU/1/21/1560/002 (5 mL)

9. DATE OF FIRST AUTHORISATION

Date of first authorisation:

10. DATE OF REVISION OF THE TEXT

11. DOSIMETRY

The estimated absorbed radiation doses to an average adult patient (70 kg) from intravenous injection of ioflupane (^{123}I) are listed in the table below. The values are calculated assuming urinary bladder emptying at 4.8-hour intervals and appropriate thyroid blocking (Iodine-123 is a known Auger electron emitter). Frequent bladder emptying should be encouraged after dosing to minimise radiation exposure.

The biokinetic model for ioflupane (^{123}I) adopted by the International Commission on Radiological Protection (ICRP) publication 128 (2015) assumes initial uptake of 31% of the administered activity in the liver, 11% in the lungs, and 4% in the brain. The rest is assumed to be distributed uniformly in the remaining organs and tissues. For all organs and tissues, 80% is assumed to be excreted with a biological half-time of 58 h, and 20% with a half-time of 1.6 h. It is further assumed that 60% of the injected activity is excreted to the urine, and 40% is excreted to the gastrointestinal tract for all organs and tissues. Activity in the liver is excreted according to the ICRP publication 53 gallbladder model (1987), where 30% is eliminated via the gallbladder and the remainder passes directly into the small

intestine.

Target organ	**Absorbed radiation dose µGy/MBq**
Adrenals	17.0
Bone surface	15.0
Brain	16.0
Breast	7.3
Gallbladder wall	44.0
Gastrointestinal tract	
Stomach wall	12.0
Small intestine wall	26.0
Colon wall	59.0
(Upper large intestine wall	57.0)
(Lower large intestine wall	62.0)
Heart wall	32.0
Kidneys	13.0
Liver	85.0
Lungs	42.0
Muscles	8.9
Oesophagus	9.4
Ovaries	18.0
Pancreas	17.0
Red marrow	9.3
Salivary glands	41.0
Skin	5.2
Spleen	26.0
Testes	6.3
Thymus	9.4
Thyroid	6.7
Urinary bladder wall	35.0
Uterus	14.0
Remaining organs	10.0
Effective dose (µSv/MBq)	**25.0**

Ref.: Publication 128 of the annals of ICRP (Radiation dose to patients from radiopharmaceuticals: a compendium of current information related to frequently used substances), 2015.

The effective dose (E) resulting from administration of 185 MBq of Celsunax injection is 4.63 mSv (per 70 kg individual). The above data are valid in normal pharmacokinetic behaviour. When renal or hepatic function is impaired, the effective dose and the radiation dose delivered to organs might be increased.

For an administered activity of 185 MBq the typical radiation dose to the target organ (brain) is 3 mGy and the typical radiation doses to the critical organs: liver and colon wall are 16 mGy and 11 mGy, respectively.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Any unused medicinal product or waste material should be disposed of in accordance with local requirements. See also section 6.6.

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Seibersdorf Labor GmbH
Grundstück Nr. 482/2 EZ 98 KG
2444 Seibersdorf
Austria

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

LEAD CONTAINER –5 mL presentation

1. NAME OF THE MEDICINAL PRODUCT

Celsunax 74 MBq/mL solution for injection
Ioflupane (^{123}I)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Ioflupane (^{123}I): 74 MBq/mL at reference time (0.07 to 0.13 µg/mL of ioflupane)

3. LIST OF EXCIPIENTS

E1510 (see leaflet for further information), E260, E262, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
1 vial

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Intravenous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP: 24 h post EOS
EOS: dd/mm/yy, hh:mm CET
Ref.: 370 MBq/5 mL at dd/mm/yy, hh:mm CET

9. SPECIAL STORAGE CONDITIONS

Do not store above 25°C. Do not freeze.
Store in the original lead shielding.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Handling and disposal – see package leaflet.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Pinax Pharma GmbH
Lausitz Mühlenweg 5
04924 Bad Liebenwerda
Germany

12. MARKETING AUTHORISATION NUMBER(S)

5 mL EU/1/21/1560/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

GLASS VIAL – 5 mL presentation

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Celsunax 74 MBq/mL solution for injection
Ioflupane (^{123}I)
Intravenous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP: 24 h post EOS (see out packaging)

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

370 MBq/5 mL at ref. (see outer packaging)

6. OTHER

Manufacturer name address
Seibersdorf Labor GmbH
2444 Seibersdorf, Austria

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

LEAD CONTAINER – 2.5 mL presentation

1. NAME OF THE MEDICINAL PRODUCT

Celsunax 74 MBq/mL solution for injection
Ioflupane (^{123}I)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Ioflupane (^{123}I): 74 MBq/mL at reference time (0.07 to 0.13 µg/mL of ioflupane)

3. LIST OF EXCIPIENTS

E1510 (see leaflet for further information), E260, E262, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
1 vial

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Intravenous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP: 24 h post EOS
EOS: dd/mm/yy, hh:mm CET
Ref.: 185 MBq/2.5 mL at dd/mm/yy, hh:mm CET

9. SPECIAL STORAGE CONDITIONS

Do not store above 25°C. Do not freeze.
Store in the original lead shielding.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Handling and disposal – see package leaflet.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Pinax Pharma GmbH
Lausitz Mühlenweg 5
04924 Bad Liebenwerda
Germany

12. MARKETING AUTHORISATION NUMBER(S)

2.5 mL EU/1/21/1560/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

GLASS VIAL – 2.5 mL presentation

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Celsunax 74 MBq/mL solution for injection
Ioflupane (^{123}I)
Intravenous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP: 24 h post EOS (see out packaging)

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

185 MBq/2.5 mL at ref. (see outer packaging)

6. OTHER

Manufacturer name address
Seibersdorf Labor GmbH
2444 Seibersdorf, Austria

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Celsunax 74 MBq/mL solution for injection
Ioflupane (^{123}I)

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your nuclear medicine doctor who will supervise the procedure.
- If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Celsunax is and what it is used for

This medicine is a radiopharmaceutical product for diagnostic use only. It is used only to identify illness.
Celsunax contains the active substance ioflupane (^{123}I) which is used to help identify (diagnose) conditions in the brain. It belongs to a group of medicines called "radiopharmaceuticals", which contain a small amount of radioactivity.

- When a radiopharmaceutical is injected, it collects in a specific organ or area of the body for a short time.
- Because it contains a small amount of radioactivity it can be detected from outside the body using special cameras.
- A picture, known as a scan, can be taken. This scan will show exactly where the radioactivity is inside the organ and the body. This can give the doctor valuable information about how that organ is working.

When Celsunax is injected into an adult, it is carried around the body in the blood. It collects in a small area of your brain. Changes in this area of the brain occur in:
- parkinsonism (including Parkinson's disease) and
- dementia with Lewy bodies.

A scan will give your doctor information about any changes in this area of your brain. Your doctor may feel that the scan would help in finding out more about your condition and deciding on possible treatment.

When Celsunax is used, you are exposed to small amounts of radioactivity. This exposure is less than in some types of X-ray investigation. Your doctor and the nuclear medicine doctor have considered that the clinical benefit of this procedure with the radiopharmaceutical outweighs the risk of being exposed to these small amounts of radiation.

2. What you need to know before Celsunax is used

Celsunax must not be used
- if you are allergic to ioflupane or any of the other ingredients of this medicine (listed in section 6).
- if you are pregnant.

Warnings and precautions
Talk to your nuclear medicine doctor before using this medicine if you have a **moderate or severe problem** with your kidneys or liver.

Before you are given Celsunax you should drink plenty of water before the start of the examination in order to urinate as often as possible during the first hours after the study.

Children and adolescents
Celsunax is not recommended for children and adolescents below 18 years.

Other medicines and Celsunax
Tell your nuclear medicine doctor if you are taking or have recently taken any other medicines.
Some medicines or substances can affect the way that this medicine works.
These include:
- buproprion (used to treat depression (sadness)),
- benzatropine (used to treat Parkinson's disease),
- mazindol (reduces appetite, as a means to treat obesity),
- sertraline (used to treat depression (sadness)),
- methylphenidate (used to treat hyperactivity in children and narcolepsy (excessive sleepiness)),
- phentermine (reduces appetite, as a means to treat obesity),
- amfetamine (used to treat hyperactivity in children and narcolepsy (excessive sleepiness); also a substance of abuse),
- cocaine (sometimes used as an anaesthetic for nose surgery; also a substance of abuse).

Some medicines may reduce the quality of the picture obtained. The doctor may ask you to stop taking them for a short time before you receive Celsunax.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your nuclear medicine doctor for advice before you are given this medicine.

Do not use Celsunax if you are pregnant or think you may possibly be pregnant. This is because the child may receive some of the radioactivity. Alternative techniques which do not involve radioactivity should be considered.

If you are breast-feeding, your nuclear medicine doctor may delay the use of Celsunax, or ask you to stop breast-feeding. It is not known whether ioflupane (^{123}I) is passed into breast milk.

- You should not breast-feed your child for 3 days after Celsunax is given.
- Instead use formula feed for your child. Express your breast milk regularly and throw away any breast milk you have expressed.
- You will need to continue to do this for 3 days, until the radioactivity is no longer in your body.

Driving and using machines
Celsunax has no known influence on the ability to drive and use machines.

Celsunax contains alcohol (ethanol): up to 197 mg of alcohol in each dose which is equivalent to 39.5 mg/mL (5% by volume). The amount in 5 mL of this medicine is equivalent to 5 mL beer or 2 mL wine. The small amount of alcohol in this medicine will not have any noticeable effects.

3. How Celsunax is used

There are strict laws on the use, handling and disposal of radiopharmaceutical medicines. Celsunax will always be used in a hospital or a similar place. It will only be handled and given to you by people who are trained and qualified to use it safely. They should tell you anything you need to do for the safe use of this medicine.

Your nuclear medicine doctor will decide which dose of Celsunax is best for you. It will be the smallest quantity necessary to get the desired information.

Before you receive Celsunax, your nuclear medicine doctor will ask you to take some tablets or liquid that contain iodine. These stop the radioactivity building-up in your thyroid gland. It is important that you take the tablets or liquid as the doctor tells you.

Administration of Celsunax and conduct of the procedure
Celsunax is given to you as an injection, usually into a vein in your arm. The recommended radioactivity given by injection is between 110 to 185 MBq (megabequerel or MBq is a unit used to measure radioactivity). A single injection is enough.

Duration of the procedure
The camera pictures are usually taken 3 to 6 hours after the injection of this medicine. Your nuclear medicine doctor will inform you about the usual duration of the procedure.

After administration of Celsunax, you should urinate frequently in order to eliminate the medicine from your body.

The nuclear medicine doctor will inform you if you need to take any special precautions after receiving this medicine. Contact your nuclear medicine doctor, if you have any questions.

If you are given more Celsunax than you should
Since Celsunax is given by a doctor under controlled conditions, it is unlikely that you will get an overdose. Your nuclear medicine doctor will suggest that you drink plenty of fluids to help the body get rid of the medicine. You will need to be careful with the water (urine) that you pass - your doctor will tell you what to do. This is normal practice with medicines like Celsunax. Any ioflupane (^{123}I) which remains in your body will naturally lose its radioactivity.

If you have any further questions on the use of this medicine, ask your nuclear medicine doctor who supervises the procedure.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The frequency of side effects is:

Common: may affect up to 1 in 10 people

- Headache

Uncommon: may affect up to 1 in 100 people

- Increased appetite
- Dizziness
- Taste disturbance
- Nausea

- Dry mouth
- Vertigo
- A brief irritating feeling similar to ants crawling over your skin (formication)
- Intense pain (or burning sensation) at the injection site. This has been reported among patients receiving Celsunax into a small vein.

Not known: frequency cannot be estimated from the available data

- Hypersensitivity (allergic)
- Shortness of breath
- Redness of the skin
- Itching
- Rash
- Hives (urticaria)
- Excessive sweating
- Vomiting
- Low blood pressure
- Feeling hot

The amount of radioactivity in the body from Celsunax is very small. This low amount of ionising radiation is associated with the least risk of cancer and hereditary abnormalities. It will be passed out of the body in a few days without need for you to take special precautions.

Reporting of side effects
If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How Celsunax is stored

You will not have to store this medicine. This medicine is stored under the responsibility of the specialist in appropriate premises. Storage of radiopharmaceuticals will be in accordance with national regulation on radioactive materials. Hospital staff will ensure that the product is stored and thrown away correctly and not used after the expiry date stated on the label.

The following information is intended for the specialist only:
- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date, which is stated on the carton and vial after EXP and is 24 hours from the end of the synthesis (EOS) time stated on the label.
- Do not store above 25 °C.
- Do not freeze.
- Store in the original lead shielding. Store in accordance with national regulation on radioactive materials.
-

6. Contents of the pack and other information

What Celsunax contains
- The active substance is ioflupane (^{123}I). Each mL of solution contains 74 MBq of ioflupane (^{123}I) at reference time (0.07 to 0.13 µg/mL of ioflupane).
  Each 2.5 mL single dose vial contains 185 MBq ioflupane (^{123}I) (specific activity range 2.5 to 4.5 x 10^{14} Bq/mmol) at reference time.
  Each 5 mL single dose vial contains 370 MBq ioflupane (^{123}I) (specific activity range 2.5 to 4.5 x 10^{14} Bq/mmol) at reference time.

Iodine-123 has a physical half-life of 13.2 hours. It decays emitting gamma radiation with a predominant energy of 159 keV and X-rays of 27 keV.

- The other ingredients are acetic acid, glacial (E260), sodium acetate trihydrate (E262), ethanol (96%) (E1510) and water for injections.

What Celsunax looks like and contents of the pack
Celsunax is a 2.5 or 5 mL colourless solution for injection, supplied in a 10 mL glass vial (Type I) with a rubber stopper and a flip cap.

Marketing Authorisation Holder
Pinax Pharma GmbH
Lausitz Mühlenweg 5
04924 Bad Liebenwerda
Germany

Manufacturer
Seibersdorf Labor GmbH
Grundstück Nr. 482/2 EZ 98 KG
2444 Seibersdorf
Austria

This leaflet was last revised in

Other sources of information
Detailed information on this medicine is available on the European Medicines Agency website: http://www.ema.europa.eu.