Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Celsior solution for organ preservation

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each bag with 1 litre solution contains

Glutathione 0.921 g (3 mmol)
Mannitol 10.930 g (60 mmol)
Lactobionic acid 28.664 g (80 mmol)
Glutamic acid 2.942 g (20 mmol)
Sodium hydroxide 4.000 g (100 mmol)
Calcium chloride dihydrate 0.037 g (0.25 mmol)
Potassium chloride 1.118 g (15 mmol)
Magnesium chloride hexahydrate 2.642 g (13 mmol)
Histidine 4.650 g (30 mmol)

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for organ preservation.

Clear, colourless (or slightly yellow) solution.

pH = 7.3
Osmolality: 320 mosmol/kg

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Solution for the preservation of thoracic organs (heart and lung) and abdominal organs (kidney, liver, and pancreas) during transplantation:From removal from the donor as well as during storage, transportation and until transplantation into the recipient.

4.2 Posology and method of administration

Restricted to hospital use only.

Posology
The volume of flushing solution depends on the organ(s).

Suggested Minimum Volumes:

- Heart: Adult: 1-2 litres
- Infants: 30 ml/kg
- Liver: 6-8 litres
- Lung: 4-6 litres
- Kidney: 4-5 litres
- Pancreas: 4 litres.
- Multi-organ: in accordance with the appropriate organs.

Paediatric population
There have been no adequate clinical studies of the use of Celsior for organ transplantation in children.

Method of administration:
Precautions to be taken before handling or administering the medicinal product

- The bag in the aluminium-protected outer container contains oxygen-absorber substances. The contents of this bag should not be mixed with the solution.
- Only intact containers (bag and aluminium packaging) should be used.
- There is no need to filter the solution before use.
- For single use only. Do not reuse.
- A careful visual inspection of the solution for turbidity should be carried out. Only clear and colourless or slightly yellow solutions should be used. If any turbidity, precipitates or contamination is evident, the solution must be discarded.
- Not suitable for continuous machine perfusion.

The solution may turn yellow during storage. This does not impair the quality and effectiveness of Celsior.

After removal from cold storage (2-8°C), the cooled solution should be used immediately.

Flushing of the organ
The exact flushing method depends on the centre and on whether or not several organs are to be removed at the same time. Flushing is often carried out in two stages: the 1st flush while the organ is still *in situ* and the 2nd flush once the organ has been removed.

The organ is flushed via a cannula inserted into an artery, while maintaining sufficient pressure to obtain a steady stream of solution in order to produce adequate flushing. In the case of liver transplantation the biliary tree is usually flushed out after explantation, before placing in the storage and transport container.

Flushing should be continued until the organ is uniformly pale and the effluent is relatively clear.

Storage under cold conditions
The organ is stored at 5 ± 3 °C in a sterile container appropriately sized for the organ. The organ must be **completely covered** by thecooled solution. The organ storage container must be aseptically sealed.

The container should then be placed in at least a second container. This should be filled with ice, but no ice must enter the organ storage container, where the ice could come into direct contact with the organ. Care must be taken to ensure that the organ is aseptically stored in its container, i.e. the inside of the organ storage container and its contents must remain sterile.

The additional container(s) must be securely sealed.

The organ storage containers must then be maintained within a well-insulated transport container. The organ storage containers should be surrounded by ice.

Transport times must be as short as possible.

4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

- Not suitable for direct injection or for intravenous use in the recipient.
- Exclusively for use in the flushing and cold storage of solid organs.
- Theoretical possibility of residual Celsior being released into the general circulation of the recipient on declamping, which could provoke cardiac arrythmias or hypotension. Impaired cardiac function in the event of non-optimal heart preservation in the early post-transplantation phase cannot be ruled out.

4.5 Interaction with other medicinal products and other forms of interaction

There are no known interactions when used as directed.

4.6 Fertility, pregnancy and lactation

No data are available. Since Celsior is not administered systemically to organ recipients themselves, no solution-specific effects are to be expected.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

- Since Celsior is not administered to organ recipients themselves, no solution-specific side effects are to be expected.
- Hypersensitivity reactions to the active substances or to any of the excipients can occur.
- There is a theoretical possibility of residual Celsior being released into the general circulation of the recipient on declamping, which could provoke cardiac arrhythmias or hypotension. Impaired cardiac function in the event of non-optimal heart preservation in the early post-transplantation phase cannot be ruled out.
- If relatively large volumes enter the systemic circulation as a result of improper use, this may lead to volume overload or electrolyte abnormalities, particularly in patients with cardiac defects or renal failure. In such cases, intensive care should be instituted.

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

Not applicable when used as directed.

If relatively large volumes enter the systemic circulation as a result of improper use, this may lead to volume overload or electrolyte abnormalities, particularly in patients with cardiac defects or renal failure. In such cases, intensive care should be instituted.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Solvent and diluting agents, incl. irrigating solutions.
ATC code: V07AB.

Celsior is suitable for thoracic organ (heart and lung) and abdominal organ (kidney, liver and pancreas) transplant preservation.

Administration of the solution at the recommended temperature effectively cools the organ, and its metabolic requirements and associated energy consumption are reduced. In particular, Celsior reduces ischaemic reperfusion damage due to the following properties:

- Prevention of oxidative damage caused by free radicals due mainly to the use of reduced glutathione as the antioxidant.
- Prevention of hypothermia-induced cellular swelling and oedema due to the use of membrane-impermeable substances mannitol and lactobionic acid which hold water in the extracellular compartment due to their osmotic effect.

- Reduction of calcium loading by use of a suitable solution, e.g. low calcium concentration, moderately high potassium concentrations which is also slightly hyperkalaemicand high sodium and magnesium concentrations comparable to the extracellular environment.
- Regeneration of high-energy substances by supplying them with glutamate, a high-energy substrate, which allows energy to be produced in anaerobic situations.
- Provision of a buffering capacity due to the use of histidine, which prevents tissue acidosis caused by lactic acid accumulation.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injection
Sodium hydroxide 4% (for pH adjustment).

6.2 Incompatibilities

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

6.3 Shelf life

10 months After opening: 24 hours.

6.4 Special precautions for storage

In order to protect from light store in original aluminium protected overwrap. Store and transport refrigerated (2°C – 8°C).

Do not freeze.

6.5 Nature and contents of container

Celsior is a sterile ready-to-use solution stored in an ethylene vinylacetate copolymer bag in an outer aluminium bag containing oxygen-absorber.

The bag in contact with the solution is manufactured from an ethylene vinylacetate copolymer (EVA type).

Celsior is available in multipacks containing 4 bags. Each bag contains 1 litre of solution.

6.6 Special precautions for disposal and other handling

Although the packaging materials are produced under aseptic conditions, the outside of the Celsior bag is not sterile. The outside of the bag should be decontaminated if Celsior is to be poured out of it.

The aluminium outer packaging and the oxygen-absorber bag should be removed before use. As soon as the outer packaging has been removed, the container should be checked for any leaks by squeezing the bag. If a leak is found, the solution must not be used.

The labelled side of the bag should be visible in front in preparation for use. The 3 exit ports should be extended from the bag. The tab on the left port should be pulled, and the protective cap removed completely from the opening. The spike on a

standard cystoscopy infusion set should be inserted into the left port with a twisting motion. The infusion line should be clamped until the start of the infusion.

The bag of solution should be placed inside an appropriately sized pressure cuff. The cuff should be inflated to apply sufficient pressure to express the fluid. Before infusion, the solution container should be suspended from a sufficient height to guarantee a steady stream of the solution.

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

7 MARKETING AUTHORISATION HOLDER

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Parc Tertiaire du Bois Dieu
RN6 - 1 allee des Chevreuils
F-69380 Lissieu
France

8 MARKETING AUTHORISATION NUMBER

PA1996/001/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 1st April 2011Date of last renewal: 25th November 2012

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