



CELSIOR®

Flushing and Cold Storage Solution for Heart Preservation

COMPOSITION

Celsior® is a clear to slightly yellow, sterile, non-pyrogenic solution for hypothermic flushing and storage of hearts. The solution is slightly acidic (approximate pH 7.3 at 20°C), slightly hypertonic (approximate calculated osmolarity 320–360 mOsmol/L) with low viscosity (1.15 cSt), and has a high buffering capacity (acidic approximately 11 mmol, alkaline approximately 7 mmol).

INGREDIENT	AMOUNT
Mannitol	60 mmol
Lactobionic Acid	80 mmol
Glutamic Acid	20 mmol
Histidine	30 mmol
Calcium Chloride	0.25 mmol
Potassium Chloride	15 mmol
Magnesium Chloride	13 mmol
Sodium Hydroxide	100 mmol
Reduced Glutathione	3 mmol
Water for Injection	Up to 1 liter

MECHANISM OF ACTION

Celsior® is intended for flushing and cold storage of hearts at the time of their removal from the donor in preparation for storage, transportation, and eventual transplantation into a recipient. Administration of Celsior® cools the organ, and therefor reduces its metabolic requirements and associated energy consumption. Celsior® is specially formulated for optimal preservation of heart organs.

ANTIOXIDANTS	Glutathione (in a stable reduced form)	0,921 g/L
	Histidine	4,650g/L
	Lactobionic acid	28,664 g/L
	Mannitol	10,930 g/L

Celsior® guarantees the antioxidant action, with permanently reduced glutathione, histidine, lactobionate and mannitol.

IONIC COMPOSITION	Sodium hydroxide	4,000 g/L
	Potassium chloride	1,118 g/L
	Calcium chloride	0,037 g/L
	Magnesium chloride	2,642 g/L

With a low potassium, low calcium and high magnesium content, Celsior® can be used for the heart organs, protecting against calcium overload.

IMPERMEANTS AND MEMBRANE STABILIZERS	Lactobionic acid	28,664 g/L
	Mannitol	10,930 g/L

Celsior®'s composition of impermeants helps to avoid the swelling of cells during cold ischaemic storage.

BUFFER	Histidine	4,650 g/L
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Celsior® contains histidine, which has an excellent capacity for hydrogen ion buffering¹ thereby protecting grafts from acidosis.

HIGH-ENERGY SUBSTRATES	Gluthathione	0,921 g/L
	Glutamic acid	2,942 g/L

Celsior® contains substrates that help the production of energy in anaerobic conditions.

CLINICAL BENEFITS

CELSIOR® IS ASSOCIATED WITH SUPERIOR OUTCOMES IN GRAFT FUNCTION VS HTK.

Table 1. Clinical cardiac outcomes following heart transplantation. Prospective, open-label study²

OUTCOME	CELSIOR® (n=16)	UW (n=17)	HTK (n=15)	P-VALUE
Spontaneous sinus rhythm	12 (75,0%)	5 (29,4%)	5 (33,3%)	0,01
Cardiac output (L/min)	6,49 ± 1,02	6.16 ± 0,93	5,57 ± 0,87	0,03

Table 2. Clinical outcomes following heart transplantation. Preliminary single-centre data from a prospective, randomised, multicentre study³

OUTCOME	CELSIOR® (n=24)	HTK (n=24)
Acute graft failure	1/24	2/24
Spontaneous sinus rhythm	19/24	9/24
Donor heart dysfunction	2/24	7/24
Adrenaline equivalent for weaning from extracorporeal circulation	0,054 ± 0,17	0,085 ± 0,066

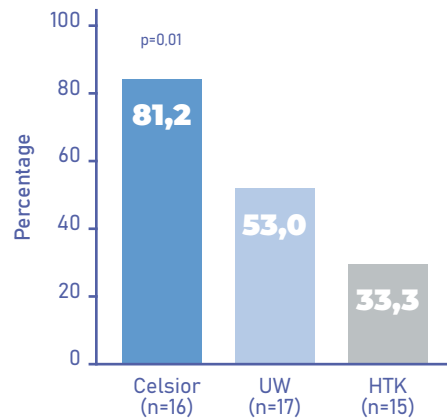
PERFUSION VOLUMES ARE LOW WITH CELSIOR®.

A volume of 1-2L of Celsior® solution is recommended for perfusion of an adult donor heart.

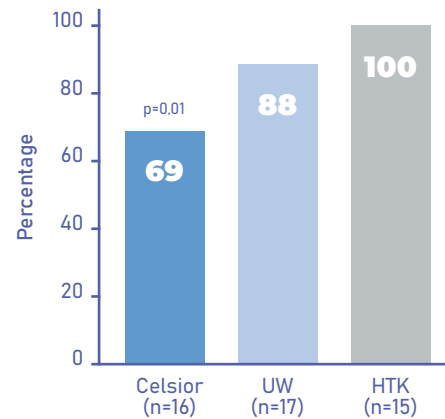
1. Menasche P, Termignon JL, Pradier F, et al. Experimental evaluation of Celsior®, a new heart preservation solution. Eur J Cardiothorac Surg 1994;8(4):207-13.
2. Gartlicki M. May preservation solution affect the incidence of graft vasculopathy in transplanted heart? Ann Transplant 2003;8(1):19-24.
3. Wieselthaler GM, Chevitchik O, Konetschny R, et al. Improved graft function using a new myocardial preservation solution: Celsior. Preliminary data from a randomized prospective study. Transplant Proc 1999;31(5):2067-8.

CELSIOR® IS ASSOCIATED WITH A REDUCED INCIDENCE OF GRAFT REJECTION.

FIGURE A AND B. Graft rejection and vasculopathy rates following heart transplantation. Prospective, open-label study comparing Celsior, HTK and UW showed significantly reduced acute rejection and vasculopathy for Celsior ($p=0.01$ for both outcomes)².



A/ FREEDOM FROM ACUTE REJECTION



B/ VASCULOPATHY (>0.5 MM)

BENEFITS OF CELSIOR® :

- Specially formulated for Heart Preservation
- Superior outcomes compared to HTK^{1,2}
- Easy to transport and stock due to low required perfusion volumes
- Low viscosity leading to lower perfusion pressure and safety for smaller blood vessels
- Ready to use: no additives required, no filtering required
- Two-year shelf life for convenient inventory management
- Available in 1000ml bag equipped with easy perfusion spike port and additive port
- EVA bag, free from PVC, latex and phthalates, to guaranty excellent biocompatibility properties
- Oxygen absorber in packaging to reduce degradation of the solution components
- EVA bag overwrapped with an aluminium-protected bag to protect from light
- Manufactured to FDA GMP, by ISO 13485 certified company



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