CoolGard 3000 / Alsius Icy Heat Exchange Catheter

Thermal Regulating System

510(k) Summary

Pre-Market Notification K040429

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510(k) SUMMARY FOR ALSIUS CORPORTATION'S COOLGARD AND CATHETER THERMAL REGULATION SYSTEM

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2 Name of Device

The Alsius CoolGard And Catheter Thermal Regulation System.

2.1 Common or Usual Name

Central Venous Catheter (short term) and Thermal Regulating System.

2.2 Classification Name

FDA has classified the Alsius CoolGard/Catheter system for various indications as a Class II device under 21 C.F.R. § 870.5900.

3 Indications for Use

The Alsius CoolGard 3000/Icy™ Catheter Heat Exchange System is indicated for use in the induction, maintenance and reversal of mild hypothermia in the treatment of unconscious adult patients with spontaneous circulation after out-of-hospital cardiac arrest when the initial rhythm was ventricular fibrillation (VF).

4 Technical Characteristics

The CoolGard and Catheter Thermal Regulation System consists of the CoolGard® 3000, a disposable Start Up Kit used in the CoolGard® for interface with the cooling bath and patient catheter and the Intravascular Catheter. The Alsius CoolGard® 3000 is an integrated electro-mechanical heater/cooler that consists of a temperature monitor, a temperature controller unit, a heat exchanger unit, and roller pump. It supplies temperature controlled sterile saline to the indwelling Catheter that is placed percutaneously in the patient.

The technical characteristics of the Catheter are essentially identical to those of widely used multi-lumen central venous catheters except for the dedicated closed

loop fluid path through the heat exchange balloons. The Alsius Catheter materials are biocompatible polyurethanes and PET.

Likewise, the CoolGard® 3000 heater/cooler has the same technical features as the medical heater/cooler unit identified as the predicate device. These common technical features include connections for re-circulating coolant to and intravascular catheter and all or combinations of the following: redundant safety controls and alarms, patient monitoring and control and temperature displays for the clinician users.

The ICY™ catheter is multi lumen intravascular catheter. Two of the catheter's lumens are used to circulate sterile saline to exchange heat with the central venous blood supply. When the heat exchange feature of the catheter is in use, heated/chilled saline is pumped through the heat exchange lumen, expanding the diameter of the distal portion of the catheter to a nominal 8mm where the heating/cooling membranes interface with the patient's circulating blood. The inflow lumen/outflow lumen forms a closed-loop system through which the heated/chilled saline circulates. The chilled saline is not infused into the patient.

Additional lumens of the Icy™ Catheters consist of a standard guide wire lumen that can be used as a primary infusion lumen.

The Catheter blood contact surfaces are coated with Duraflo® Treatment, a heparin coating manufactured by Edwards Lifesciences Corporation.

The Alsius Catheters are supplied sterile for single-use only.

5 Principles of Operation

The CoolGard® 3000 system automatically adjusts the temperature of the heater/chiller saline bath to achieve the patient target temperature that has previously been set by the attending physician. This is done via data from a temperature probe in the patient that interfaces with the temperature controller. This principle of operation is identical to currently marketed devices.

6 Summary of the Basis for Finding of Substantial Equivalence

Hypothermia is recommended in the treatment of comatose survivors of out of hospital VF arrest. The CoolGard 3000 / Icy catheter system provides this therapy. There are two predicates upon which to base the finding of substantial equivalence.

Under Pre-market Notification K030421 the CoolGard System is cleared for use in providing the induction, maintenance and reversal of hypothermia in neurosurgical patients. The system provides its own predicate.

In addition, the CoolGard System is substantially equivalent to external heat exchange systems that are pre-amendment devices such as the Thermorite HC-83.

Thermorite Model HC-83 Hypo/Hyperthermia Unit
Thermorite Inc, El Cajon, CA
Pre-market notification K854856, S.E. 06-02-1985

7 Clinical Experience

Sudden cardiac arrest (SCA) is a major killer. The benefits of hypothermia in the treatment of comatose survivors of SCA, due to ventricular fibrillation (VF-SCA), have been established in randomized controlled trials. The use of hypothermia is standard of care for these patients.

The CoolGard 3000™ / Icy™ Catheter system is safe and effective in providing mild hypothermia to the comatose survivors of VF-SCA. The use of this system to provide mild hypothermia for these patients does not pose unanswered new questions of safety or efficacy.

The therapeutic value of hypothermia in the immediate treatment of resuscitated but comatose patients suffering out of hospital cardiac arrest has been recognized. The International Liaison Committee on Resuscitation (ILCOR[1]) have recommended that:

- Unconscious adult patients with spontaneous circulation after out-of-hospital cardiac arrest should be cooled to 32°C to 34°C for 12 to 24 hours when the initial rhythm was ventricular fibrillation (VF).

This recommendation was based upon two randomized controlled trials: the HACA study[2] in Europe and the Bernard Study[3] in Australia. Significant improvements in mortality and morbidity were obtained using hypothermia.

A meta analysis of the results of these and other trials is reported in this submission[2][3][4]. This meta analysis provides clear evidence that the use of mild hypothermia is beneficial in the comatose survivors of cardiac arrest. The number needed to treat (NNT) for survival is 7.0 (95% confidence interval 4.2 to 20.8). The NNT for survival and favorable neurological recovery is 6.1 (95% confidence interval 3.9 to 14.5).

The Alsius CoolGard 3000™ / Icy™ Catheter thermal regulation system (CoolGard System) is already cleared for intravascular temperature control applications. One of these, K030421, relates to the induction, maintenance and reversal of hypothermia and covers the use of the system in the post-operative period (i.e. the immediate 24 hours after surgery).

The utility of the CoolGard 3000™ / Icy™ Catheter System in the treatment of out of hospital cardiac arrest has been studied in a USA IDE Clinical Study (G000207). This feasibility IDE demonstrated the basic utility of the device within the context of US clinical practice.

Study data collected in a ninety-six patient series has demonstrated the safety and efficacy of the CoolGard 3000™ / Icy™ Catheter System. This study included a comparison of the results obtained with the System, with concurrent controls using propensity scores and Bayesian statistical methods.

From the data collected in this study, the CoolGard System was demonstrated to be effective in reducing mortality and morbidity in the comatose survivors of out-of-hospital cardiac arrest. The analysis was conducted using propensity scores and case matched controls. Odds ratios of the benefit of the Icy were determined and from these estimates were obtained of Number Needed to Treat (NNT) score (see Table 1). The NNT, to obtain one life saved, is 5.6 (95% confidence interval 3.4 to 18.0, p=0.007) and the NNT for good neurological outcome is 4.3 (95% confidence interval 2.8 to 9.8, p<0.001). This results compare favourably with the results of the meta analysis described above that relates to hypothermia using surface cooling techniques.

Table 1 Outcomes CoolGard 3000/Icy v Normothermia

Univariate and propensity score matched analysis: absolute risk difference between hypothermia using CoolGard and normothermia treatment

Model	Risk ratio	95% confidence interval (bootstrapped)	p-value	NNTB for hypothermia	95% confidence interval (bootstrapped)
Survival					
Univariate risk difference (%)	11.0	-0.8 to 22.8	0.086	9.1	NNTB 4.4 to ∞ to NNTH 125
Adjusted risk difference (%) (matched for propensity score)	17.7	5.5 to 29.5	0.007	5.6	NNTB 3.4 to 18.0
Survival and good neurology					
Univariate risk difference (%)	10.7	-2.0 to 22.3	0.099	9.3	NNTB 4.5 to ∞ to NNTH 50
Adjusted risk difference (%) (matched for propensity score)	23.3	10.1 to 35.7	<0.001	4.3	2.8 to 9.8

A Bayesian analysis, using a skeptical prior, produced a log odds ratio of 1.61, as an estimate of System efficacy, which is “statistically” significant when looking at the 95% credible interval of the posterior probability (1.06 to 2.44). Further analysis was undertaken using an empirical prior based on a meta-analysis of the three RCT of other hypothermia devices. The log odds ratio of System efficacy obtained was 1.72 which indicates a clinically relevant increase in survival (1.27 to 2.34). The Bayesian interpretation of the data is that the effect of the CoolGard data is robust when discounting that the effect of hypothermia is,

in itself, generally robust. The Icy catheter is an effective means of improving survival and survival with good outcome in the post-resuscitative care of the comatose survivors of cardiac arrest.

The safety of the CoolGard 3000™ / Icy™ Catheter System was assessed. The Frequency of adverse events in the patients using the system (Endovascular cooling) are listed in Table 2 .

Table 2 Complications during and after endovascular cooling

Adverse event within the first 32 hours	Endovascular cooling (n=96)
Arrhythmia	
• Atrial fibrillation; n, (%)	4 (14)
• Ventricular tachycardia; n, (%)	15 (16)
• Ventricular fibrillation; n, (%)	6 (6)
• Narrow complex tachycardia; n, (%)	0
• Bradycardia; n, (%)	14 (15)
Bleeding	
• Any Bleeding; n, (%)	23 (24)
• Gusto Bleeding mild; n, (%)	21 (22)
• Gusto Bleeding moderate; n, (%)	2 (2)
Bleeding Site; n, (%)	
• Catheter Insertion; n, (%)	13 (14)
• Mucosal; n, (%)	6 (6)
• Respiratory tract; n, (%)	2 (2)
• Gastrointestinal; n, (%)	4 (2)
Within the first 7 days	
• Pneumonia; n, (%)	28 (29)
• Elevation of pancreatic enzymes; n, (%)	4 (4)
• Sepsis; n, (%)	0
• Acute renal failure; n, (%)	11 (11)

Frequency matching was used to select controls from patients treated conventionally to make the groups comparable. Matching criteria were witnessed out of hospital ventricular cardiac arrest of presumed cardiac cause with a duration of cardiac arrest > 1 minute; 341 patients were dropped because

they did have an in-hospital arrest, 201 patients had a presumed cause other than cardiac, 129 did not have ventricular fibrillation and 11 had resuscitation times ≤ 1 minute. There were no statistically significant differences in adverse events between the groups except for the occurrence of transient bradycardia (Table 3). In most cases the rate of adverse events was comparable; pneumonia occurred more often in the hypothermia group but this was not statistically significant.

Table 3 Complications - Icy vs Control

Adverse event within the first 32 hours	Endovascular cooling (n=62)	Control (n=104)	P
Arrhythmia			
• Atrial fibrillation; n, (%)	2 (3)	2 (3)	0.987
• Ventricular tachycardia; n, (%)	14 (23)	9 (14)	0.231
• Ventricular fibrillation; n, (%)	6 (10)	6 (10)	0.977
• Narrow complex tachycardia; n, (%)	0	3 (5)	0.082
• Bradycardia; n, (%)	9 (15)	2 (3)	0.025
Bleeding			
• Any Bleeding	16 (26)	27 (26)	0.982
• Gusto Bleeding			0.796
○ Gusto Bleeding mild; n, (%)	14 (23)	12 (19)	
○ Gusto Bleeding moderate; n, (%)	2 (3)	3 (5)	
Bleeding Site			0.796
• Catheter Insertion; n, (%)	7 (11)	0	
• Mucosal; n, (%)	5 (8)	6 (10)	
• Respiratory tract; n, (%)	2 (3)	3 (5)	
• Gastrointestinal; n, (%)	2 (3)	6 (10)	
Within the first 7 days			
• Pneumonia; n, (%)	17 (27)	20 (19)	0.233
• Elevation of pancreatic enzymes; n, (%)	1 (2)	0	0.194
• Sepsis; n, (%)	0	0	-
• Acute renal failure; n, (%)	4 (6)	4 (4)	0.448

8 Conclusion

In summary, descriptive information and performance data demonstrate that the Alsius CoolGard and Catheter Thermal Regulation System characteristics do not

raise questions of safety and effectiveness that are different from those of the predicate devices. Where appropriate, performance data demonstrate equivalence. The CoolGard system is substantially equivalent to the predicate devices.

9 References

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2. Bernard SA, Gray TW, Buist MD, et al. Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. N Engl J Med 2002;346:557-563.
3. The Hypothermia after Cardiac Arrest Study Group. Mild therapeutic hypothermia to improve neurologic outcome in cardiac arrest. N Engl J Med 2002;346:549-556.
4. Hachimi-Idrissi S, Corne L, Ebinger G, Michotte Y, Huyghens L. Mild hypothermia induced by a helmet device: a clinical feasibility study. Resuscitation 2001;51:275-281