

## Indications

For cardioplegia in cardiac surgery and preservation of organs for transplantation.<sup>17</sup>

**This includes all Cardiac Surgical Procedures with Cardiopulmonary Bypass,<sup>8,15</sup> such as:**

- Minimally invasive cardiac surgery (MICS)
- Coronary artery bypass (CABG)
- Pediatric heart surgery
- Heart transplantation

## Single-Shot Protection for up to 180 minutes<sup>17</sup>

### Superior Myocardial Protection<sup>20</sup>

- Prevents acidosis with organic buffer<sup>9</sup>
- High antioxidant effect with mannitol and histidine<sup>8</sup>
- Prevents hypercalcemia and intracellular edema<sup>4,9,10</sup>
- Ketoglutarate and magnesium ensure energy provision<sup>8,21</sup>
- Low level of cardiac enzyme release compared to blood cardioplegia<sup>20,22-24</sup>

### ➤ Reduced hospital stay and faster recovery<sup>20,25-27</sup>

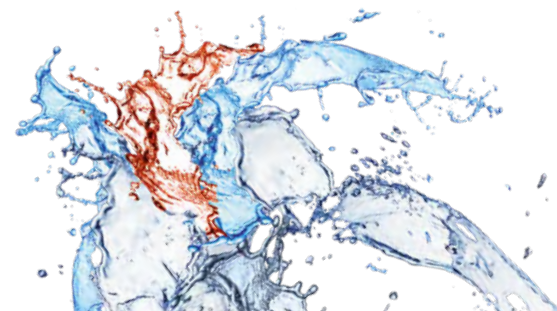
### Practical and Economical Benefits

- Safe, simple and ready to use<sup>28</sup>
- Standardized formulation<sup>30</sup>, manufactured to GMP
- Bloodless surgical field
- Less intraoperative time compared to traditional repetitive cardioplegia<sup>30,31</sup>
- Cost-effective when compared with blood cardioplegia<sup>31</sup>



## Safety and Efficacy proven in

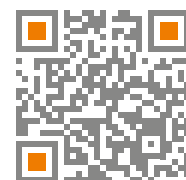
- Over 1000 scientific publications
- More than 3 million procedures worldwide
- Authorized for cardioplegia in Europe and many countries worldwide



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**Composition:** 1,000 ml of the solution contain: 0.8766 g sodium chloride (15.0 mmol), 0.6710 g potassium chloride (9.0 mmol), 0.8132 g magnesium chloride x 6 H<sub>2</sub>O (4.0 mmol), 27.9289 g histidine (180.0 mmol), 3.7733 g histidine hydrochloride monohydrate (18.0 mmol), 0.4085 g tryptophan (2.0 mmol), 5.4651 g mannitol (30.0 mmol), 0.0022 g calcium chloride x 2 H<sub>2</sub>O (0.015 mmol), 0.1842 g potassium hydrogen 2-ketoglutarate (1.0 mmol), potassium hydroxide solution, water for injection. **Indication:** Cardioplegia in connection with cardio-surgical operations, organ protection during operations under ischemia (heart, kidney, liver), preservation of organ transplants (heart, kidney, liver, pancreas), together with venous or arterial segments, multi-organ protection. **Contraindications:** Hypersensitivity to the active substances or to any of the excipients. **Side effects:** If CUSTODIOL® is not stored properly, the two components histidine and ketoglutaric acid can convert to mikimopine, which could block the angiotensin II receptors and thus might lead to a drop of blood pressure. **Warning:** CUSTODIOL® is not intended for systemic intravenous or intra-arterial administration, but only for selective perfusion of the relevant organs and for surface cooling and preservation of the donor organ en route from donor to recipient. CUSTODIOL® must therefore not be used for systemic infusion. **Presentation and pack sizes:** Bags of 1,000 ml, 2,000 ml and 5,000 ml. Prescription Drug. **Manufacturer:** Dr. Franz Köhler Chemie GmbH, Werner-von-Siemens-Str. 14-28, 64625 Bensheim, Germany. Sept 2024

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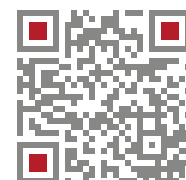


Download of the brochure  
and more scientific data  
available at:

[www.custodiol-college.com/cardioplegia/](http://www.custodiol-college.com/cardioplegia/)

### Manufacturer

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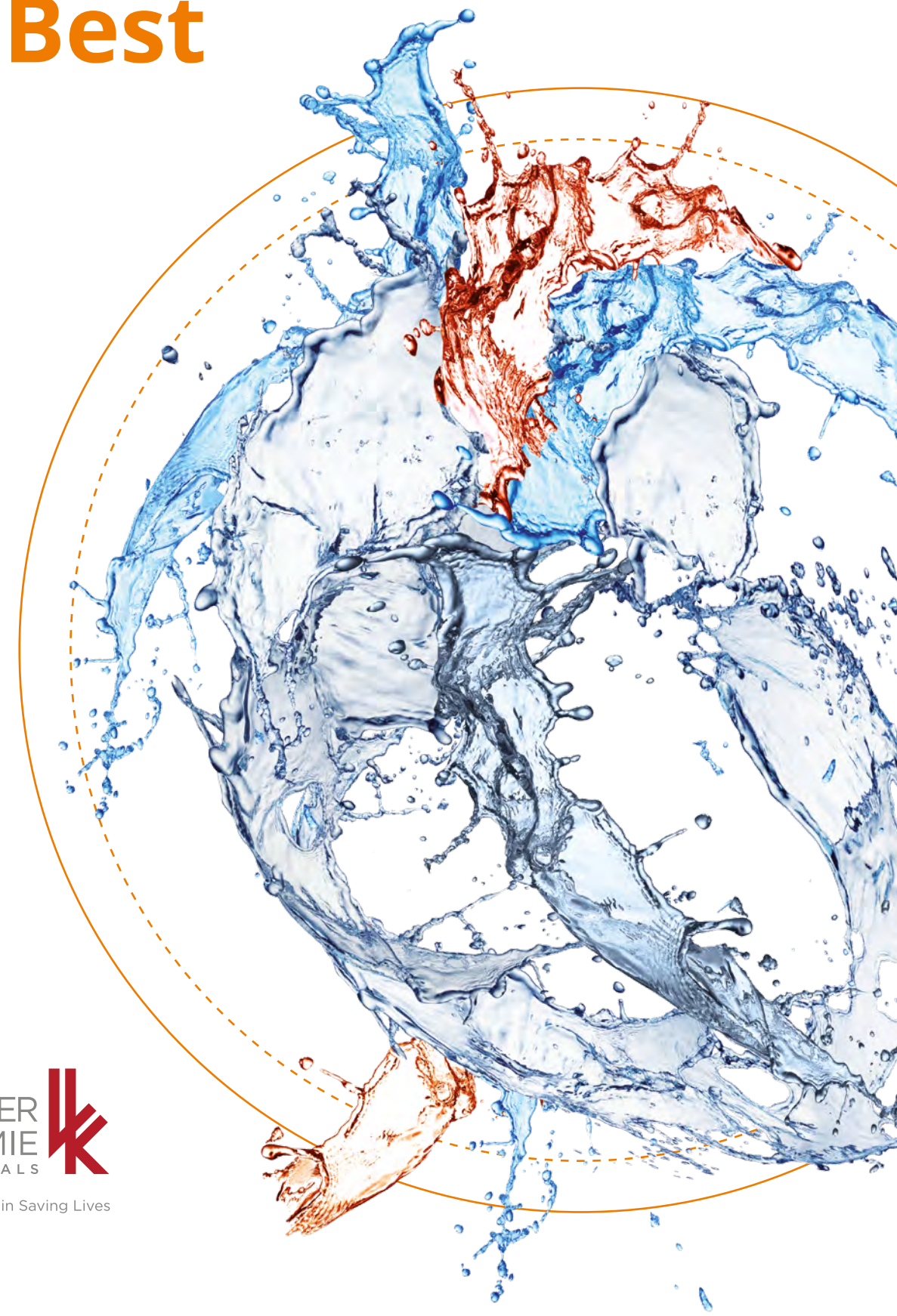


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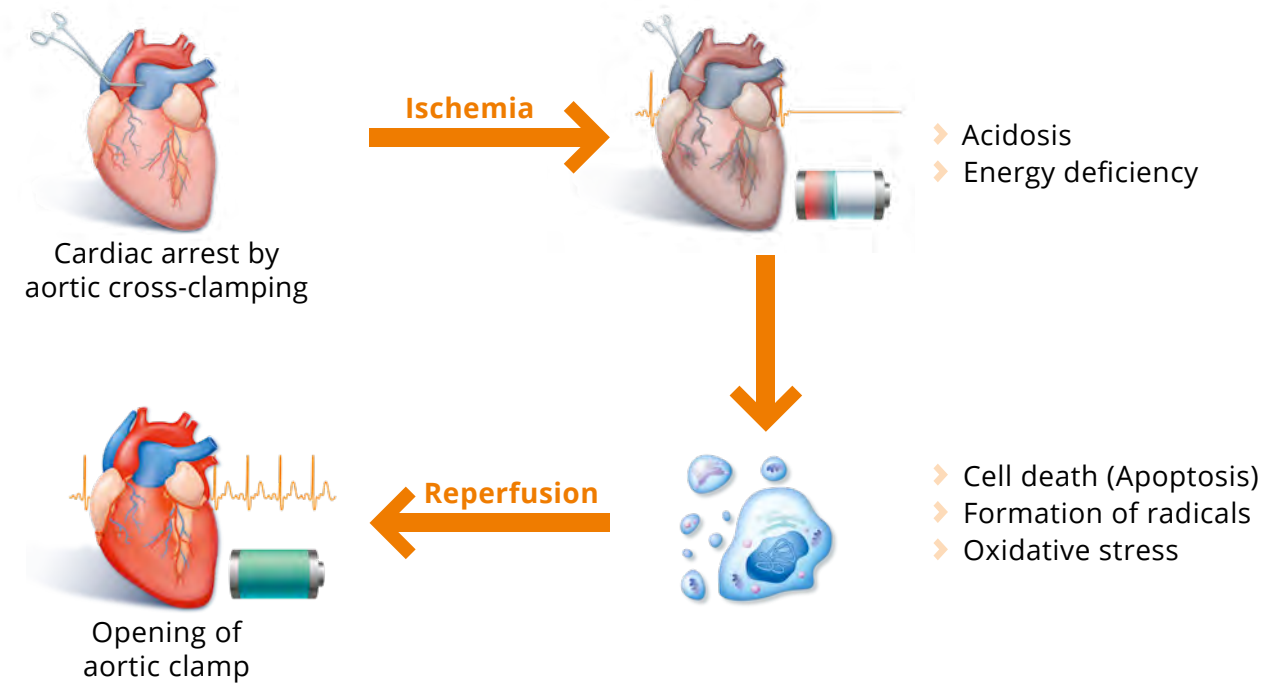
# Every Heart deserves the Best



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## THE PROBLEM: Ischemia-Reperfusion Injury



Max. natural ischemic tolerance of the heart is 20 min

Need for advanced ischemic protection strategies in cardiac surgery

## THE REQUIREMENT: Effective Cardioplegia<sup>1-4</sup>

### CLINICAL REQUIREMENTS

- Controlled diastolic cardiac arrest
- Myocardial protection
- Reversible restoration to normal function
- Reduced energy consumption during ischemic phase
- Optimal osmolality to prevent edema
- Buffering to prevent ischemia-induced acidosis
- Uniform distribution throughout the entire organ
- Minimal or no side effects

### PRACTICAL REQUIREMENTS

- User-friendly handling
- Optimal visibility for the surgeon
- Limited interruption of procedural workflow



## THE SOLUTION: CUSTODIOL®

CUSTODIOL® is a cardioplegic solution specifically formulated to protect the heart from ischemia/reperfusion damage during cardiac surgery.<sup>5,6</sup>

### Histidine (180 mmol)<sup>4,7,8</sup>

- Strong organic buffer
- Prevents myocardial acidosis
- Scavenger of reactive oxygen species (ROS)

### Tryptophan (2 mmol)<sup>4,8</sup>

- Stabilizes the cell membranes

### α-Ketoglutarate (1 mmol)<sup>4,8</sup>

- Essential part of the Krebs cycle
- Energy substrate with a particular significance for the post-ischemic phase

### Mannitol (30 mmol)<sup>4,8</sup>

- Osmotic diuretic (metabolically inert), prevents the formation of cell edema
- Scavenger of reactive oxygen species (ROS)

### "Intracellular solution"<sup>8,9</sup>

- Low sodium (15 mmol) and calcium (0.015 mmol), moderate potassium (9 mmol) and magnesium (4 mmol)
- Cardiac arrest via hyperpolarization
  - Significant reduction of myocardial oxygen consumption

The "water like" **viscosity** guarantees an optimal perfusion of the microvasculature.<sup>10</sup> The isotonic **osmolality** mitigates cell swelling and edema formation.<sup>4,11</sup>

## The Science behind CUSTODIOL®

### Controlled diastolic cardiac arrest

CUSTODIOL®'s intracellular electrolyte composition induces electrophysiological decoupling by blocking sodium influx, causing myocyte membrane hyperpolarization and diastolic cardiac arrest. Equilibration across the extracellular space and interstitium is crucial and **requires 6-8 minutes.**<sup>8,9,12</sup>

### Myocardial protection

Hyperpolarized arrest by CUSTODIOL® significantly lowers the myocardial oxygen consumption, especially in conjunction with hypothermia. This leads to reduced energy consumption, and hence improved protection.<sup>9,13</sup>

➤ **The powerful combination of saving energy and buffering against myocardial acidosis allows a safe cold ischemia time of up to 180 minutes with a single shot.**<sup>8,14</sup>

### Intracellular crystalloid solution containing:

Histidine  
Tryptophan  
α-Ketoglutarate

Mannitol

Sodium  
Calcium  
Potassium  
Magnesium

## CUSTODIOL® Administration

### 1. Aortic Cross-Clamping

Placement of the aortic cross-clamp

### 2. CUSTODIOL® Perfusion<sup>14-17</sup>

CUSTODIOL® is typically administered **antegrade** in a **single-shot**

**Perfusion Pressure:** 80-110 mmHg (equivalent to 110-140 cm above the thorax) until cardiac arrest, typically within 2-3 minutes, then at 40-60 mmHg (equivalent to 50-70 cm above the thorax)

**Perfusion Duration:** 6-8 minutes in total to guarantee full equilibration

### OPTIONAL

#### Retrograde application<sup>14,15,17</sup>

Apply at a lower pressure of 30 mmHg

#### Redosing<sup>16,17</sup>

A second administration of CUSTODIOL® is only required in case of myocardial activity (200-400 ml over 1-2 minutes)

## Specific Patient Groups



### PEDIATRIC PATIENTS Perfusion:<sup>16,17</sup>

Initial perfusion pressures: 80-90 mmHg (equivalent to 110-120 cm above the thorax), then 30-40 mmHg (equivalent to 40-50 cm above the thorax)

Perfusion Duration: 4-6 minutes

Perfusion Volume: *Depends on age*  
1 month: 50 ml/kg bodyweight  
2 months to 1 year: 30 ml/kg bodyweight  
Over 1 year: 20 ml/kg bodyweight



### HEART TRANSPLANTATION Perfusion:<sup>17-19</sup>

The heart should be perfused and preserved at 2-4 °C

Infusion Process: Begin with a root perfusion pressure of 80-110 mmHg, which can be reduced after cardiac arrest to 40-50 mmHg

Perfusion Volume: Superior results have been achieved, with a perfusion rate of approximately 3500 ml administered within 10 min<sup>18,19</sup>