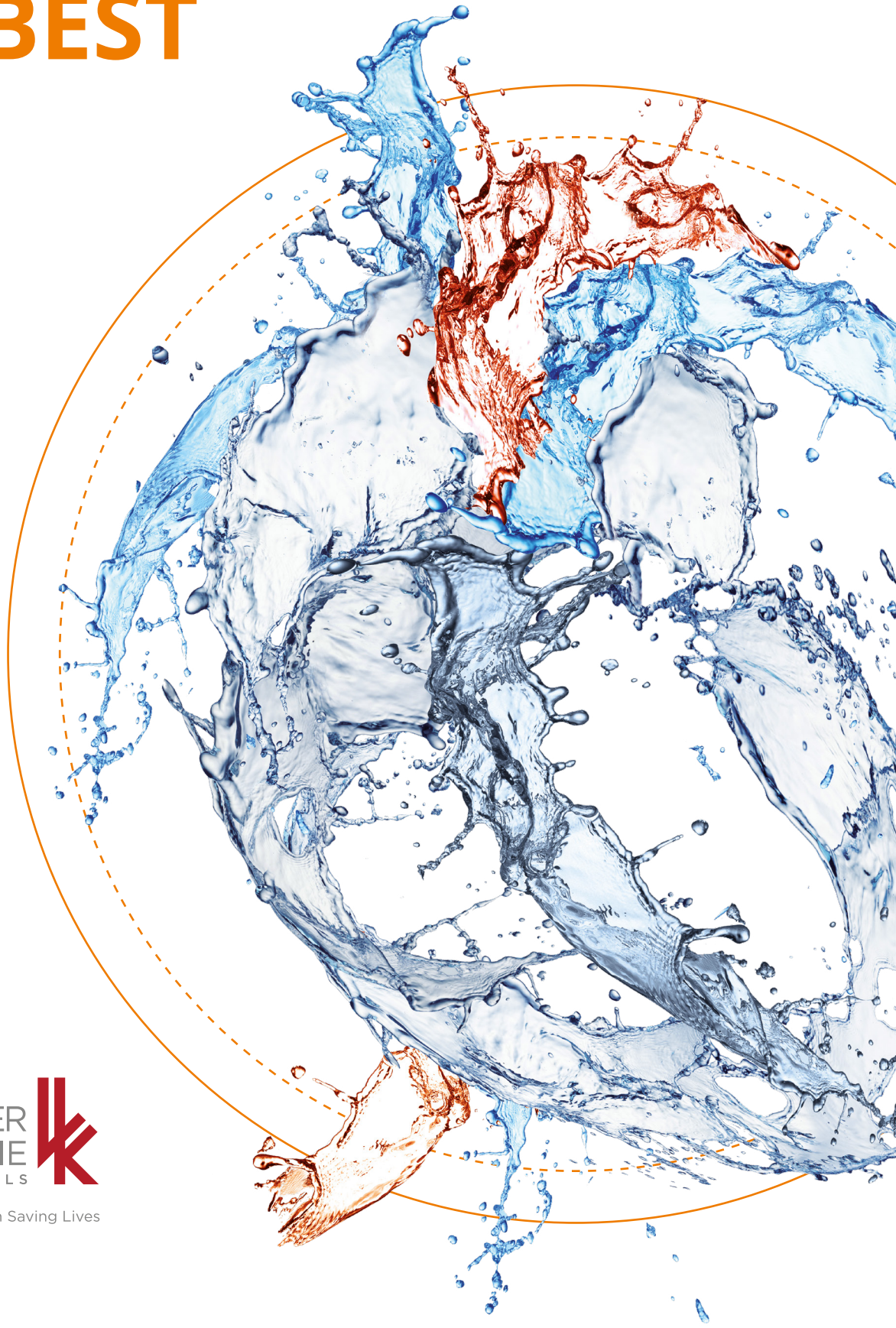


CUSTODIOL®

HTK - Bretschneider®

Every **HEART** deserves
the **BEST**

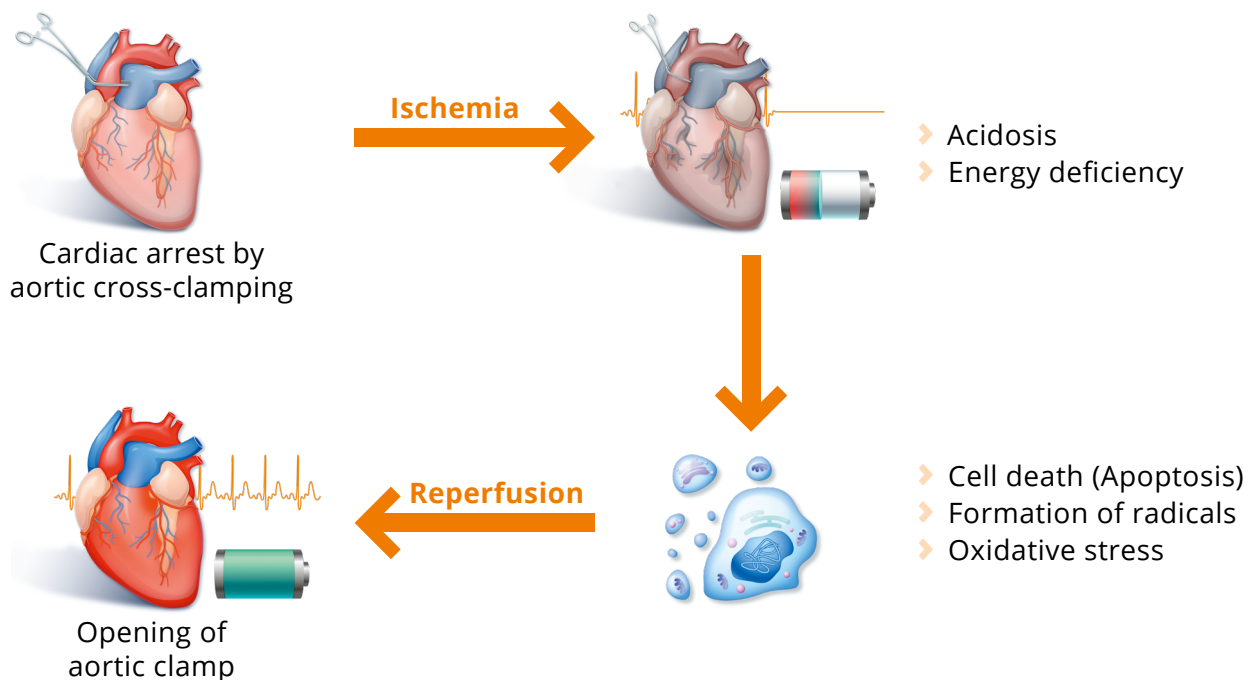


DR. F. KÖHLER
CHEMIE
PHARMACEUTICALS



Your Dedicated Partner in Saving Lives

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 Cardioplegia¹⁻⁴

CLINICAL REQUIREMENTS

- Controlled diastolic cardiac arrest
- Myocardial protection
- Reversible restoration to normal function
- Reduced energy consumption during ischemic phase
- Optimal osmolarity 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



CUSTODIOL®

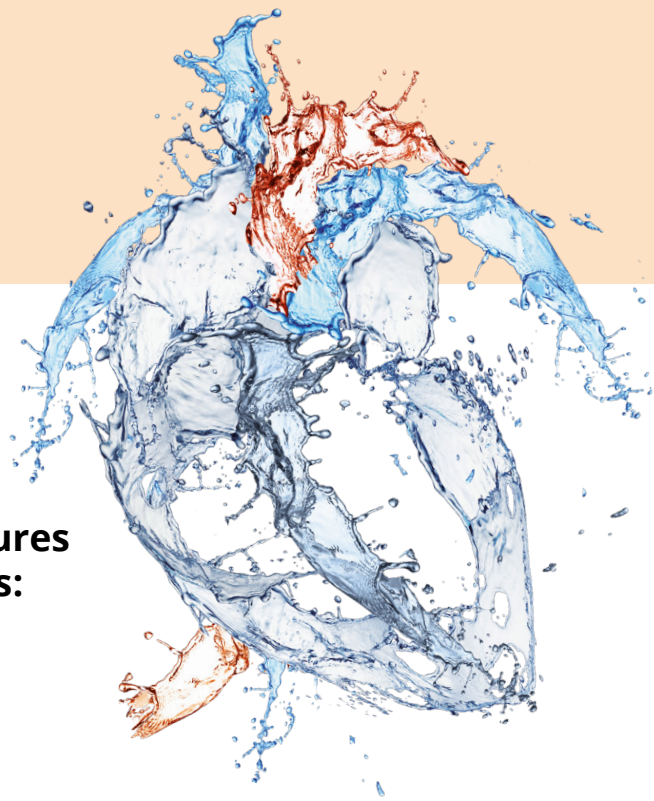
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Indications

For cardioplegia in cardiac surgery and preservation of organs for transplantation.¹⁷

This includes all Cardiac Surgical Procedures with Cardiopulmonary Bypass,^{8,15} such as:

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



Single-Shot Protection for up to 180 minutes¹⁷

Superior Myocardial Protection²⁰

- Prevents acidosis due to organic buffer⁹
- High antioxidant effect with mannitol and histidine⁸
- Prevents hypercalcemia and intracellular edema^{4,9,10}
- Ketoglutarate and magnesium ensure energy provision^{8,21}
- Low level of cardiac enzyme release compared to blood cardioplegia^{20,22-24}

➤ **Reduced hospital stay and faster recovery^{20,25-27}**

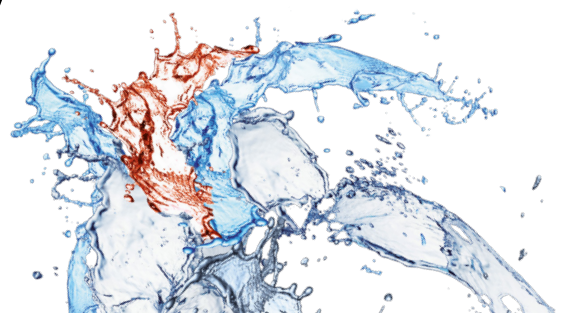
Practical and Economical Benefits

- Safe, simple and ready to use²⁸
- Standardized formulation²⁹, manufactured to GMP
- Bloodless surgical field
- Less intraoperative time compared to traditional repetitive cardioplegia^{30,31}
- Cost-effective when compared with blood cardioplegia³¹



Safety and Efficacy proven by

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



THE SOLUTION: CUSTODIOL®

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

Histidine (180 mmol)^{4,7,8}

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

Tryptophan (2 mmol)^{4,8}

- Stabilizes the cell membranes

α-Ketoglutarate (1 mmol)^{4,8}

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

Mannitol (30 mmol)^{4,8}

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

“Intracellular solution”^{8,9}

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.¹⁰
The isotonic **osmolarity** mitigates cell swelling and edema formation.^{4,11}

Intracellular crystalloid solution containing:

Histidine
Tryptophan
α-Ketoglutarate

Mannitol

Sodium
Calcium
Potassium
Magnesium

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**.^{8,9,12}

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.^{9,13}

➤ **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.**^{8,14}



CUSTODIOL® Administration

1. Aortic Cross-Clamping

Placement of the aortic cross-clamp

2. CUSTODIOL® Perfusion¹⁴⁻¹⁷

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 ensure full equilibration

OPTIONAL

Retrograde administration^{14,15,17}

Apply at a lower pressure of 30 mmHg

Redosing^{16,17}

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:^{16,17}

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:¹⁷⁻¹⁹

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^{18,19}

CUSTODIOL®

HTK - Bretschneider®

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 H₂O (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 H₂O (0.015 mmol), 0.1842 g potassium hydrogen 2-ketoglutarate (1.0 mmol), potassium hydroxide solution, water for injection. **Indications:** Cardioplegia in cardiac surgery 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 in 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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available at:**

www.custodioli-college.com/cardioplegia/

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