ChondroFiller liquid®

Surgical technique

meidrix

Improving Collagen. Improving Life.

Introduction

Every year, more than 50 million people worldwide are affected by joint pain, half of them have articular cartilage damage. A topic in which everyone will be increasingly interested in the near future.

Today, the focus on articular cartilage regeneration and joint preservation is based on state-of-the-art growth factors, scaffolds and biological matrices, cells and other joint maintenance techniques for traumatic defects and degenerative osteoarthritis. There are several types of improved techniques and modern treatments for cartilage repair and regeneration. New techniques and concepts are developed and designed not only to treat damaged or diseased joint cartilage by filling the defect with biological repair tissue, but also to receive processes of achieving regeneration to normal cartilage that gains long-lasting improvements and return to a fully active lifestyle.

Larger defects can be treated by autologous chondrocyte transplantation or autologous chondrocyte implantation (ACI). Smaller defects can be treated by other techniques like biological matrices and scaffolds. The choice of treatment depends on the size and localisation of the defect.

The ACI was first adopted in 1987 by Brittberg et al. However, this first generation technique had several disadvantages, such as periosteal hypertrophy, the loss of cells and the complexity of the surgical technique. Therefore, in the second generation carrier substances were designed, the cells were transplanted in a 3-dimensional matrix, mostly collagen-based. The matrix induced autologous chondrocyte implantation (MACI) was created.

Despite the promising clinical results of ACI/MACI, one of the serious disadvantages of this techniques are, that those are two-step procedures. A first surgery is needed to harvest a cartilage biopsy and a second surgery to implant the cultered cells with the support matrix into the defect. These methods are time-consuming and imply high costs.

Therefore, there have been increasing efforts to develop a cartilage repair treatment based on a single-step, cell-free technique. A new approach is the use of a collagen gel, which is already well established as a cell-based method

(Andereya et al. 2006, Schneider et al. 2011, Rackwitz et al. 2012). Further animal studies showed that cells migrate into the collagen gel and differentiate into cartilage-like cells over the time (Gavenis et al. 2010). This results in a well-integrated and differentiated cartilage tissue, that is very close to embryonic cartilage tissue (Schneider et al. 2011). First clinical applications of these cell-free matrices showed very good clinical and MRI results in the treatment of small local cartilage defects (Efe et al. 2012, Schüttler et al. 2013, Rössler et al. 2015). However, this technique still uses an arthrotomy of the joint in order to insert the implant into the defect.

The further development and modification of this cell-free collagen gel matrix allows an arthroscopic application of the patented and unique ChondroFiller liquid and the individual adaptation of the implant to the defect directly in the joint (Schneider et al. 2016, Jerosch et al. 2016, Beck 2018). Meidrix focuses with ChondroFiller liquid on arthroscopic articular cartilage treatment, which enables individual restoration of damaged hyaline cartilage in joints.

What is ChondroFiller liquid®?

ChondroFiller liquid is the only patented injectable 3-dimensional chondro-conductive collagen matrix in a two chamber-syringe ready to use. The CE marked implant is a medical device class III, produced under GMP conditions.

By arthroscopically filling of articular cartilage defects ChondroFiller liquid provides an easy and fast treatment of traumatic or degenerative arthrosis defects of individual defect size and all grades. The liquid collagen implant allows the application in a single-step procedure by standard arthroscopy without opening the joint and without microfracturing and fibrin glue. Directly inside the defect ChondroFiller liquid changes its stabilisation state within a few minutes into a 3-dimensional matrix which provides an excellent cell scaffold and encourages new cartilage growth. The operation can be performed outpatient or inpatient. An outpatient rehab for about 6 weeks depending on the location of the defect is recommended.

ChondroFiller liquid technology also allows regions to be reached that are normally difficult or impossible to reach like posterior tibia plateau, retropatellar defects and ankle joint. Our product contains highly purified, native collagen type I and buffer, the final concentration of collagen is 8 mg / mL. The sterile implant is supplied in 3 sizes of 2.3 mL, 1.5 mL and 1.0 mL.

Indication

Cartilage repair and regeneration is recommended for joints that have damaged cartilage but are otherwise healthy. The ChondroFiller liquid technique is suitable for patients with cartilage damage or deterioration caused by traumata or injury, including sports injuries, repetitive strong stress of the joint, degenerative cartilage development like osteoarthritis and osteochondritis.

- Preserved cartilage shoulder
- Intact surrounding cartilage
- Outerbridge classification grade III and IV
- Intact corresponding surface (damage up to outerbridge grade II permitted)
- Intact meniscus (partial resection up to max. ⅓ is possible)
- Intact ligaments
- free joint mobility < 5°
- Free joint mobility
- Patient age from 18 to 65 years and more (biological age of the joint is criteria)
- Defect size up to 3 cm^2

Contraindications

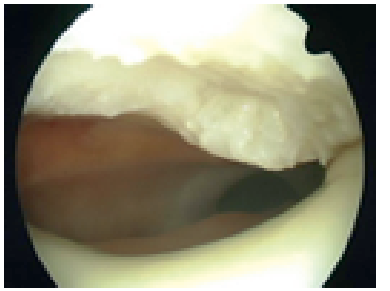
Following exclusion criteria are contraindications for the use of ChondroFiller liquid:

- Hypersensitivity or allergy to collagen or rat protein
- Multi compartmental arthrosis
- Arthrofibrosis
- Hematopoetic or malignant disorders
- Increased risk of bleeding
- Neurological or metabolic diseases
- Pregnant or breast feeding woman
- Leg malalignment of > 5°
- Depending on location: cartilage defect size larger than 3 cm^2

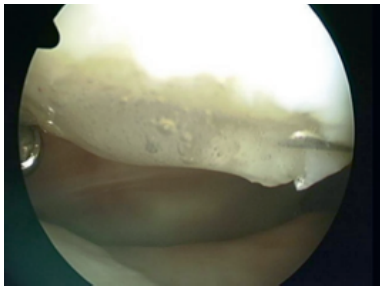
Surgical technique ChondroFiller liquid®

Patient positioning

The positioning of the limb during the operation depends on the location of the defect zone in the joint. Before injecting ChondroFiller liquid the affected limb must be positioned in a way that prevents the primary liquid collagen from draining to the side. Thus, the positioning is highly dependent on the location of the defect. If for example the defect is located in the main loading area of the femoral chondyle, debridement can be performed in the standard position. In femoral defects it is usually enough to fix the leg with 90° hip and knee flexion. Defects of the trochlea and the tibia usually require no special bedding position. Retropatellar defects can be treated in face-down position or otherwise, with more experience, ChondroFiller liquid also works in standard position, that means application of ChondroFiller liquid against gravity.



cartilage defect knee



defect filling with ChondroFiller liquid against gravity

Arthroscopy

As first part of the arthroscopy of the joint the indication and applicability of ChondroFillerliquid should be checked again due to the indications and contraindications. Accompanying joint pathologies such as meniscal damage, ligament insufficiency, false position of the leg axis can be treated first in the same session.

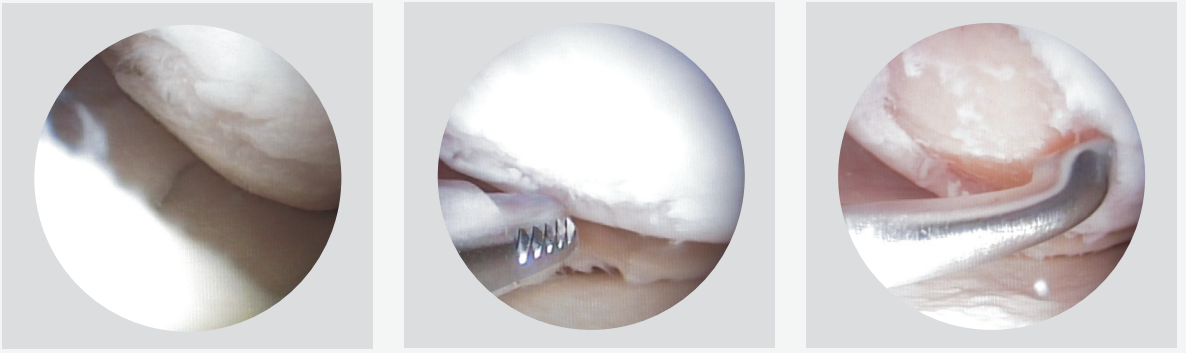
Alternatively to the liquid arthroscopy the surgery can be carried out with gas arthroscopy (CO_2). This has the advantage, that the cartilage defect is much better accessible and the defect zone is dry for better adhesion of the matrix, which is not always possible with conventional irrigation fluid-based arthroscopy.

Debridement of the defect

The debridement of the cartilage defect can be done purely arthroscopic either with a sharp spoon or with appropriately sized curettes. It is important that all diseased cartilage is removed, leaving stable cartilage shoulder on all sides (Fig. 1). During the preparation of the defect it is important to ensure that the subchondral plate is not damaged.

It has been proven to undermine the cartilage margins with a small sharp spoon, so that a good anchoring of the implant in the defect can be achieved. For a better documentation the debrided defect should be measured accurately. The preparation of ChondroFiller liquid should take place at the same time as the debridement (see preparation and application of ChondroFiller liquid).

Arthroscopy with irrigation fluid



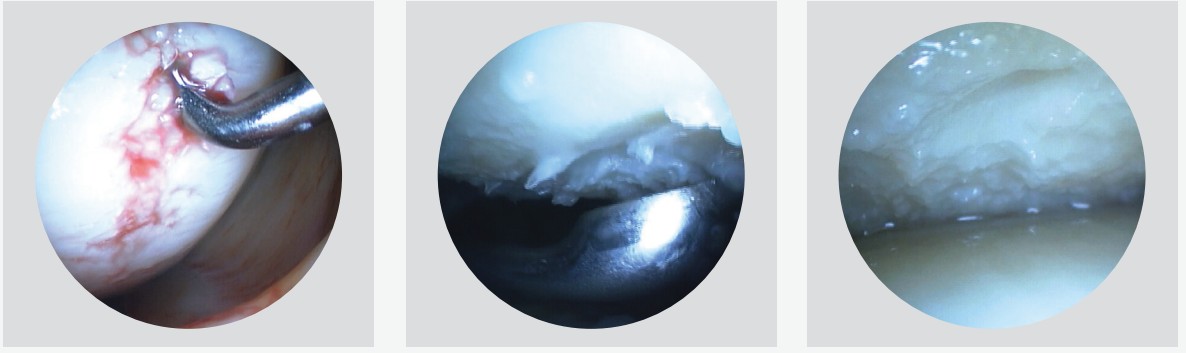
1 Defect

2 Debridement

3 Debrided defect

Fig. 1
Defect and debridement

Arthroscopy with gas (CO_2)



1 Defect

2 Debridement

3 Debrided defect

Drying of the defect prior to application of **ChondroFiller** liquid®

Before applying ChondroFiller liquid the cartilage defect area should be as dry as possible. When using irrigation fluid for arthroscopy it should be completely drained. Then the cartilage area should be dried separately. The aspiration of the fluid with an aspirator does not usually suffice. Using a cannula which is positioned right in front of the defect combined with intraluminal insertion of an extended compress into this cannula using a forceps has paid off. The compresses wicking action normally allows for sufficient drying of the defect.

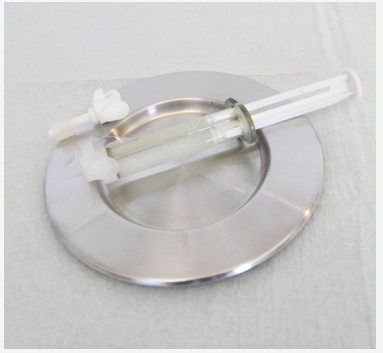
Alternatively, a CO_2 arthroscopy can be performed. In this case, usually no additional drying of the defect is necessary.

Preparation and application of **ChondroFiller** liquid®

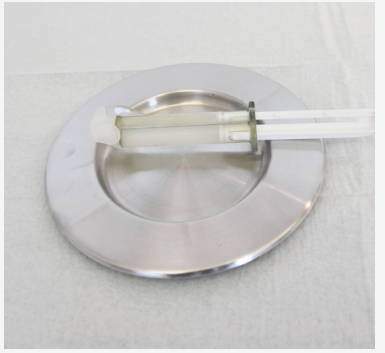
If the indication for the use of ChondroFiller liquid is given, the dual-chamber syringe should be defrosted. It can be thawed within 24 h at 2–10 °C (e.g. in the refrigerator) or within approximately 30 min at 25–30 °C (e.g. in a incubator or in the warm hands). Right before the application the ChondroFiller liquid syringe must be warmed up to 30–33 °C (e.g. in the warm hand, but only for a short time < 15 min).

Warming temperatures of 30–33 °C for longer than 15 min and temperatures higher than 33 °C lead to irreversible collagen damage and as a consequence to no matrix stabilisation!

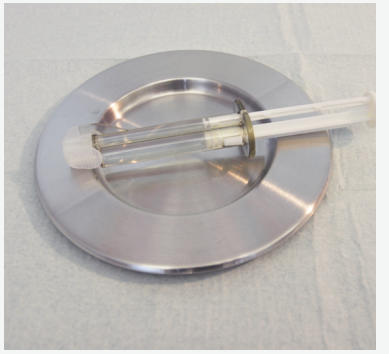
The Luer lock mixing adapter is only possible to place in one position („nose to nose“ – click sound). Before the actual injection the first few microliters of the liquid matrix have to be discarded after placing an injecting needle on the Luer lock mixing adapter (Fig. 2).



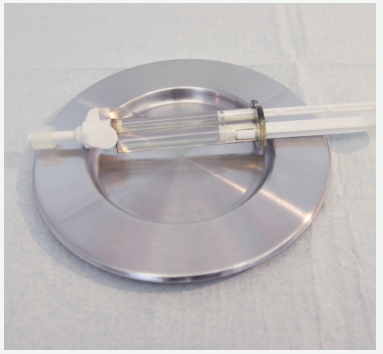
1 ChondroFiller liquid-Set



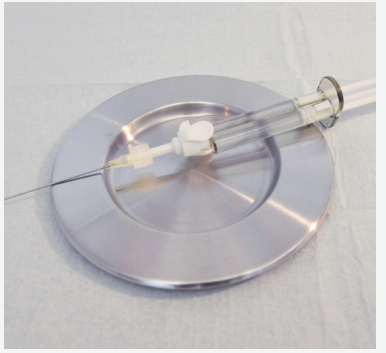
2 Frozen



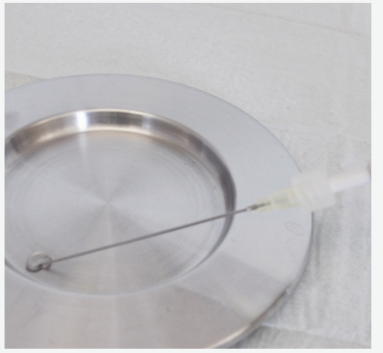
3 Defrosted and temperature 30–33 °C



4 + Luer lock mixing adapter



5 + Injection cannula



6 Discarding a few microliter

Fig.2
Preparation of ChondroFiller liquid 1–6

Preparation and application of **ChondroFiller** liquid®

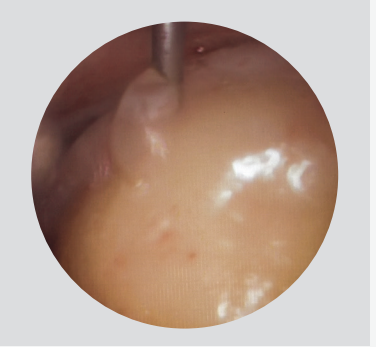
Subsequently, the defect should be filled with a continuous, rapid emptying of the syringe (< 20 sec) and without interruptions because of the immediate reaction of the two components. For a homogeneous matrix it is not recommended to apply layer by layer. The cartilage defect is filled completely and minimally beyond the height of the surrounding cartilage with the liquid matrix (Fig. 3). The matrix stabilisation takes approx. 3–5 min at an optimal processing temperature of approx. 30–33 °C. This stabilisation is optically visible, the gel changes from transparent to milky white.

If the processing temperature of 30-33 °C is not reached, the matrix stabilisation time can increase significantly (e.g. 25–30 °C → > 10 min). If the stabilisation time is prolonged, the extremity should not be moved. Vibrations can inhibit the matrix stabilisation. During this time the treated extremity should not be moved. Vibrations can inhibit the matrix stabilisation.

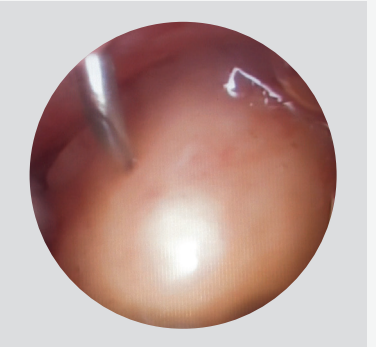
The height of the implant can be adapted to the height of the surrounding cartilage either manually or automatically through the pressure of the corresponding articular surface. Subsequently, the extremity is carefully transferred to the stretched position and surgical access channels can be closed. Inserting a drainage is usually not necessary. As far as possible, a checking of the defect filling should be avoided as the bleeding into the joint prevents a clear view of the implant. A renewed swelling of the joint carries the risk of implant detachment. After applying a bandage, the treated joint should be immobilized for 48 hours with an orthosis in neutral position.

Filling of the defect with ChondroFiller liquid after drying the defect zone processing temperature 30–33 °C

Arthroscopy with irrigation fluid



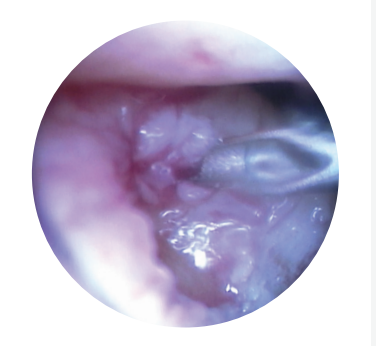
Filling of the defect with ChondroFiller liquid



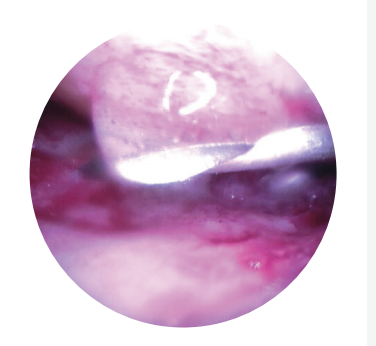
Filling of the defect with ChondroFiller liquid

Fig. 3
Application ChondroFiller liquid

Arthroscopy with gas (CO_2)



Filling of the defect with ChondroFiller liquid



Filling of the defect with ChondroFiller liquid

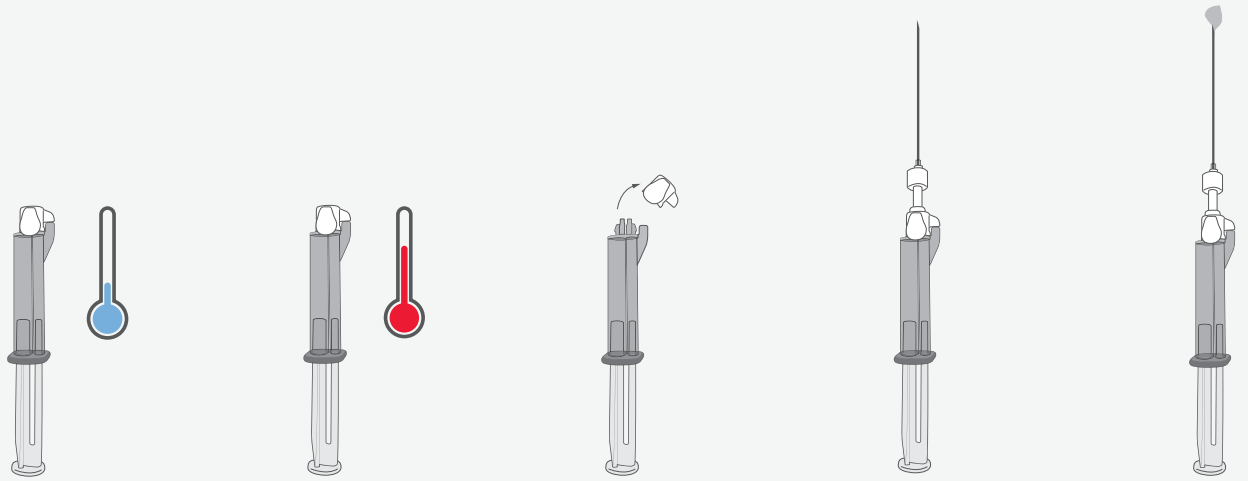
Chart surgical technique ChondroFiller liquid®

Patient

A Result arthroscopy: Indication for ChondroFiller liquid treatment given

B Debridement of the defect; if necessary change the position of the patient

C Drying of the defect zone



Start preparing ChondroFiller liquid

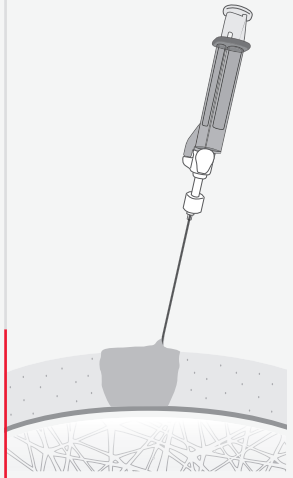
1 Thawing within 24 h prior to surgery at 2–10 °C (e.g. in a refrigerator) or approx. 30 min at 25–30 °C (e.g. in a incubator)

2 Warming to optimal processing temperature 30–33 °C for a short time < 15 min (e.g. in the warm hand)

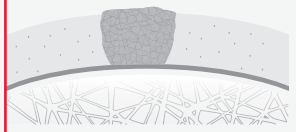
3 Removal of the closing cap

4 Placing of the Luer lock mixing adapter and the injection cannula

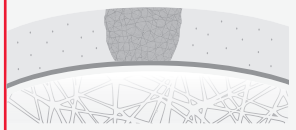
5 Discarding a few microliters of the primary liquid matrix



6/ D Filling of the defect as quickly as possible (< 20 sec)



7/ E Matrix stabilisation within 3–5 min without vibrations and at optimal processing temperature of 30–33 °C



8/ F Adjustment of the implant height via the pressure of the corresponding joint; manual adaptation is possible

G Transferring of the extremity to the stretched position

H Closure of the surgically access channels

After treatment

Post-operative treatment

The treatment is mainly determined by the anatomic location of the defect in the concerned joint. There are two basic ways:

1. defects located in the main load-carrying area of the joint and thus loaded axially and 2. defects are located on the patella or on the corresponding joint surface, e.g. on the femoral trochlea, and are only loaded during flexion of the joint. In both cases the rehabilitation program is based on the respective recommendations of the professional societies for trauma surgery DGU and orthopedics DGOOC (Pietschmann, 2012).

Main load zone of the femoral condyles/talus:

- Mobilization at day 2 postoperative
- 20 kg partial load on the operated limb for 6 weeks
- At least twice a day exercise bar (CPM) for one hour
- From the 7th week load build up to 30 kg, 2 weeks until full load
- After reaching full loading capability, cycling and swimming are allowed, careful muscle building through isometric training
- Jumping, running and contact sports are allowed after 1 year

Patella and retropatellar bearing

- Mobilization at day 2 postoperative
- The knee flexion is limited to 0–0–30° by an IROM-splint for 3 weeks
- 20 kg partial partial load on the operated limb for 1 week
- Full load allowed after the 2nd week
- After the 3rd week increase the flexion by 30° every 2 weeks, from 90° flexion the IROM-splint can be removed
- After reaching 90° flexion, cycling and swimming are allowed, careful muscle building through isometric training
- Sports with a high risk of falling only allowed after 1 year

Literature

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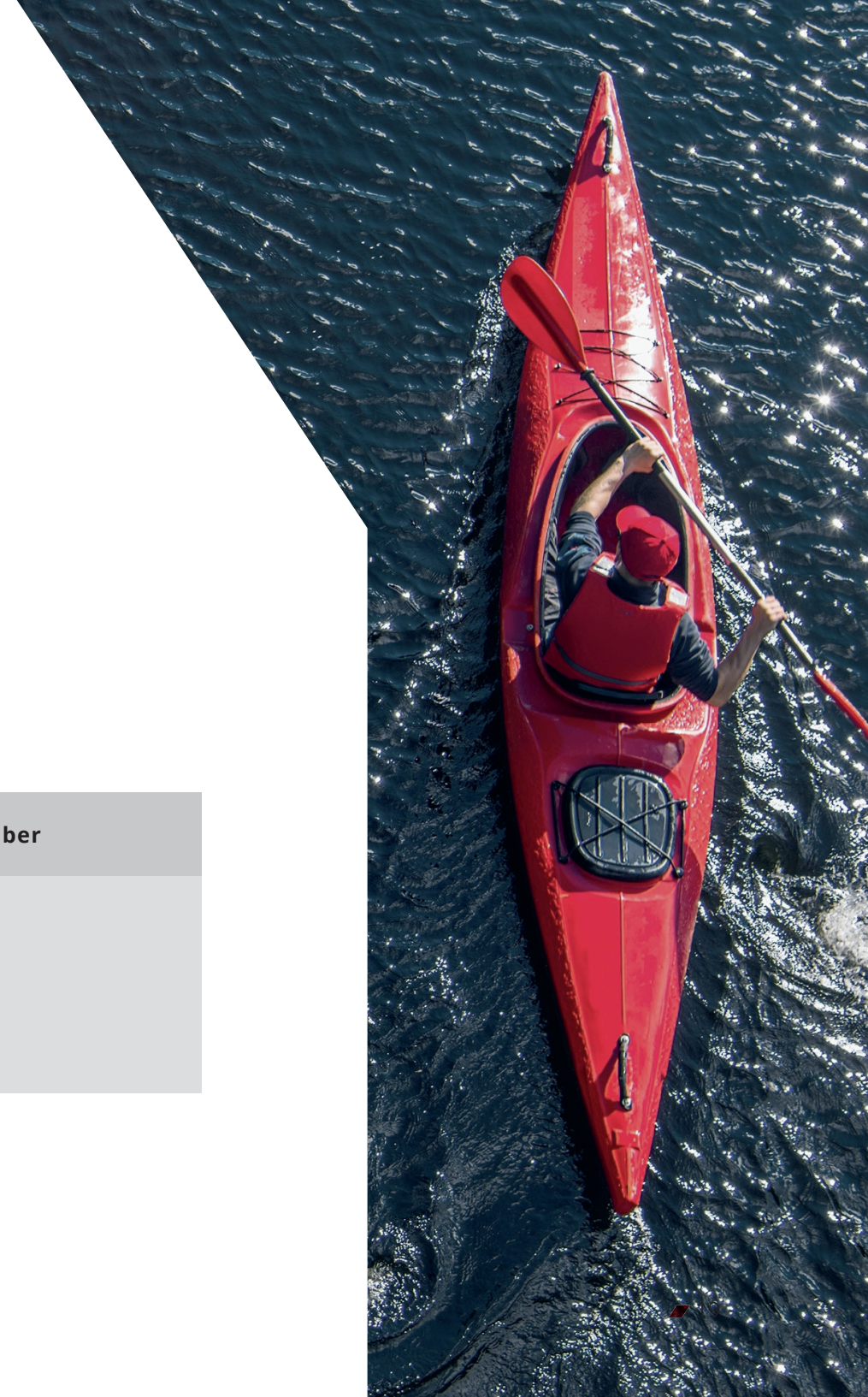
Order information

This surgical instruction serves as an educational tool of the clinical support of medical professionals to use specific Meidrix products. Finally medical professionals decide about the technique and how to use the product. Medical professionals should act corresponding to their education and experience and refer to medical literature or the instruction for use.

Product	Description	Order number
ChondroFiller liquid®	volume 2.3 ml	HCFL -23
ChondroFiller liquid®	volume 1.5 ml	HCFL -15
ChondroFiller liquid®	volume 1.0 ml	HCFL -10



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