

# Chondro-Gide<sup>®</sup> AMIC<sup>®</sup> in the Knee

Up

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More than 10 Years of Clinical Success

#### **About Geistlich Surgery**

Geistlich Surgery produces innovative bio-derived matrix products for bone and cartilage, including Orthoss<sup>®</sup>, Orthoss Collagen<sup>®</sup>, and Chondro-Gide<sup>®</sup>. Our products leverage the body's own healing potential to regenerate bone and cartilage. Our focus is on helping people maintain and regain their quality of life.

Geistlich Surgery is a business unit of Geistlich Pharma AG, which is headquartered in Switzerland. Entirely family owned since 1851, the company develops, produces, and markets medical devices for regenerative medicine and pharmaceuticals. From research and development to marketing, our operations are fully integrated under one roof, which enables us to oversee and optimize all levels of our business.

#### **Geistlich and Collagen**

Geistlich was among the first pharmaceutical companies to apply collagen for medical use in the 1990s. With more than 160 years experience with bioderived bone and collagen products, we applied our extensive knowledge of collagen and its biofunctionality to develop the first collagen membrane to foster regeneration by providing a protective environment for the cells and nutrients that are essential for regrowth.

As experts in bone and tissue regeneration, we see tremendous potential for collagen in the future of regenerative medicine. That is why we have dedicated a team of biochemists, materials scientists, process engineers and other experts at our headquarters in Switzerland to focus exclusively on collagen, and to explore its other possible therapeutic applications. Through close relationships with the medical and scientific community, we continue to share our knowledge and optimize our collagen-derived products. Finding ways to improve peoples' quality of life remains our larger goal.

Several studies report articular defects in 60–66% of knees undergoing arthroscopy for pain. 55% of these were larger than 2 cm<sup>2</sup> in size.<sup>1</sup>

#### CONTENTS

- 1 AMIC<sup>®</sup> for Knee Cartilage Regeneration
- 2 Developed to Support Regeneration: Chondro-Gide<sup>®</sup> and AMIC<sup>®</sup>
- 4 Chondro-Gide<sup>®</sup> AMIC<sup>®</sup>
- 6 Mini-Open Surgery
- 8 Arthroscopic Surgery
- 10 Clinical Summaries
- 12 Rehabilitation and Follow-up Treatment
- 13 Geistlich Surgery

# AMIC<sup>®</sup> for Knee Cartilage Regeneration

### Your Challenge

As an orthopedic surgeon today, you face a growing number of treatment challenges. Patients are now living longer and are more physically active than previous generations. While many are staying active as they age, some are overweight.

With these changes in longevity and lifestyle, patients are using the major joints of their bodies more than ever. As a result, the number of patients with knee cartilage damage is rising. But with developments in diagnostic arthroscopy and Magnetic Resonance Imaging (MRI), early and precise detection and treatment is now possible.

#### **The Solution**

Chondro-Gide<sup>®</sup>, a bio-derived collagen membrane, combined with Autologous Matrix-Induced Chondrogenesis (AMIC<sup>®</sup>) is a 1-step treatment for repairing cartilage lesions. Developed by Geistlich Surgery in collaboration with leading surgeons, AMIC<sup>®</sup> uses enhanced microfracturing (MFx) in combination with Chondro-Gide<sup>®</sup> to support the body's own healing potential to regenerate cartilage tissue.

### The Results

Backed by more than 10 years of clinical success, Chondro-Gide<sup>®</sup> AMIC<sup>®</sup> is an effective and cost-effective<sup>2,3</sup> treatment for repairing cartilage lesions, alleviating or preventing pain, and slowing the progression of damage.



GEISTLICH CHONDRO-GIDE® AMIC®

1

### Developed to Support Regeneration: Chondro-Gide<sup>®</sup>

Geistlich Pharma is a leader in the field of regenerative orthopedics, which leverages the body's own ability to repair bone and cartilage.

### A Better Alternative to Standard MFx

Standard MFx is commonly used in cartilage repair surgeries to recruit mesenchymal stem cells and other key bone marrow components to the site of the defect to support the regeneration of cartilage tissue. In larger lesions<sup>10</sup>, the blood clot resulting from MFx is not stable enough to withstand shear forces in the joint. "Enhanced" MFx addresses this problem by combining standard MFx with the use of a collagen membrane, which covers and protects not only the super clot but also the repair tissue." Chondro-Gide® is a biocompatible and fully resorbable porcine collagen membrane developed by Geistlich for use in Chondro-Gide® AMIC®, a onestep enhanced MFx procedure that is backed by more than 10 years of positive clinical results.<sup>7</sup>

# Effective for Both Large and Small Defects

Chondro-Gide<sup>®</sup> AMIC<sup>®</sup> was developed specifically to treat cartilage lesions in articular joint surfaces. While standard MFx is generally recommended for small chondral defects (<2 cm<sup>2</sup>), Chondro-Gide<sup>®</sup> AMIC<sup>®</sup> is an effective solution for larger defects<sup>6,11,12</sup>.

What Makes Chondro-Gide® Unique<sup>13</sup>

- > Bio-derived, bilayer Collagen I/III membrane<sup>13</sup>
- > Biocompatible and naturally resorbed<sup>13</sup>
- > Easy to handle: supple and tear-resistant<sup>13</sup>
- > Can be glued or sutured<sup>11</sup>
- > Compatible with a range of tissue regeneration techniques<sup>17</sup>
- > One-step procedure<sup>13</sup>

# Bioengineered to Leverage the Body's Own Healing Potential

Chondro-Gide<sup>®</sup> is a porcine Collagen I/III bilayer membrane. It has a unique structure, being compact and smooth on one side and rough and porous on the other. This provides a protective environment for the stabilization of tissue repair.<sup>13,14</sup>

#### CHONDRO-GIDE® IS AVAILABLE IN THREE SIZES:

The top layer of the membrane is marked with the word "UP" in one corner.

UP			
20 × 30 m	ım (30890.3	3)	

30 × 40 mm (30915.5)

40 × 50 mm (30939.9)

A STERILE ALUMINUM TEMPLATE FOR CUTTING THE MEMBRANE IS INCLUDED

38×48 mm

A Barrier to Prevent Cell Diffusion<sup>15,16</sup> The smooth, compact top layer is also sturdy enough to protect the cells and newly forming cartilage from shear stress in the joint while the cartilage regenerates and patients undergo rehabilitation.

A Rough, Porous Bottom Layer This layer adheres to the defect, keeping the membrane in place. Cells that are released through microfracturing or other marrow stimulation techniques attach themselves to this layer, where they proliferate and produce new tissue.<sup>17,18</sup>



## Chondro-Gide<sup>®</sup> AMIC<sup>®</sup>

Chondro-Gide<sup>®</sup> AMIC<sup>®</sup> is a minimally-invasive 1-step procedure that can be performed either by mini-open surgery, or in an arthroscopic manner.

Developed by Geistlich Surgery in collaboration with leading surgeons in Europe, this technique has been effective in repairing chondral or osteochondral defects in the knee, talus, and hip.<sup>11,12,21</sup>

### The Benefits of Using Chondro-Gide<sup>®</sup> AMIC<sup>®</sup>

With both mini-open and arthroscopic techniques, the unique advantage of Chondro-Gide<sup>®</sup> AMIC<sup>®</sup> is that it supports the body's own potential to heal itself. Damaged cartilage is removed, and then the subchondral bone is microfractured (MFx) or drilled to release supply of fresh, viable mesenchymal stem cells.

The membrane covers the defect and serves as a protective shield that contains the cells and minimizes the impact of shear forces on the delicate superclot. At the same time, it functions as the roof of a biological chamber that forms over the defect. The biocompatible collagen material provides an environment for cell growth and is replaced by new cartilage tissue over time.<sup>13,14</sup>

INDICATIONS FOR CHONDRO-GIDE<sup>® 19</sup>



#### INDICATIONS<sup>20</sup>

Chondro-Gide<sup>®</sup> is used to cover:

- cartilage defects treated with autologous chondrocyte implantation (ACI);
- cartilage defects treated with bone marrow stimulation techniques (e.g., AMIC<sup>®</sup>); and
- > meniscal defects.

Defects can be caused by falls, accidents, or other traumatic events and located at articular joint surfaces, including the knee, hip, ankle, foot, and shoulder.

#### LIMITATIONS AND PRECAUTIONS

Chondro-Gide<sup>®</sup> should not be used in patients with:

- > a known allergy to porcine collagens;
- > infected wounds; and
- > arthritis and inflammatory joint reactions.

Chondro-Gide<sup>®</sup> should not be used on pregnant or breastfeeding women, as studies have not been performed on women who are pregnant or lactating.

Allergic reactions to collagen may not be totally excluded. Please refer to the IFU for detailed information.

### **Mini-Open Surgery**











#### Prepare the Surgical Site

Using a standard, minimally invasive anterior approach, open the knee joint. Remove damaged and unstable cartilage with a scalpel, curette, and spoon until a stable, perpendicular shoulder surrounds the defect.



Measure defect

Place the sterile aluminum template included with the Chondro-Gide<sup>®</sup> in the defect to obtain an exact impression of the defect. Cut out the imprint and transfer it onto the membrane. The side that was facing the defect must be placed on the smooth layer of the Chondro-Gide<sup>®</sup>.



Trim the Chondro-Gide<sup>®</sup>

When trimming the Chondro-Gide<sup>®</sup>, remember to cut it 10-15% smaller than the template, as the area of the Chondro-Gide<sup>®</sup> will expand once moistened. Supple and soft when wet, the membrane can be easily wrapped to conform to defects of various shapes. If needed, use a sterile pen to lightly mark the smooth (top) layer that will face the joint cavity. The "UP" sign might not be visible any more once you have cut or hydrated the membrane.



#### Perforate

Use a sharp awl or drill to perforate the subchondral bone at the base of the lesion. Start at the periphery of the lesion and then move toward the center at intervals of 4-5 mm.<sup>21</sup> With adequate cooling, antegrade drilling is also possible.

Prior to surgery during diagnostic arthroscopy, carefully assess the size and classification of the defect. If necessary, carry out concomitant interventions, e.g., meniscal repair, alignment or stabilization.











Remove Residual Tissue

Carefully remove residual tissue and check for adequate subchondral bleeding.



Secure the Chondro-Gide<sup>®</sup>

Apply fibrin glue directly to the subchondral bone plate around the perforations.



### Position and Glue

Place the Chondro-Gide<sup>®</sup> into the defect with the rough (bottom) layer facing the bone surface. Moisten the membrane until fully saturated.

Check the position of the membrane and close. Once the glue has set, after about 5 minutes, use a sharp scalpel to remove the excess fibrin glue carefully. To prevent delamination of the membrane, make sure the Chondro-Gide<sup>®</sup> is sitting flush inside the defect.



# Suturing Instead of Gluing

Using a TF-plus needle (inside-out technique, single stitches every 5 mm), adhering the Chondro-Gide<sup>®</sup> with Vicryl or PDS 6/o sutures is also possible.

Check to make sure the membrane is positioned properly and stable by bending and extending the knee 10 times. To complete the surgery, carefully stop the bleeding, and suture the wound. If applying a drain, use a non-suction drain.

### **Arthroscopic Surgery**



Prepare the Surgical Site

Use a sharp curette to remove cartilage fragments and create smooth vertical defect walls.



Measure the Defect Size

Using a probe, measure the defect size. Turn the probe in different directions to determine the diameter and shape of the defect. Transfer the measurement in the same way onto the Chondro-Gide<sup>®</sup>.



Prepare the Chondro-Gide<sup>®</sup>

Once the Chondro-Gide<sup>®</sup> has been cut, moistened and is inside the joint, distinguishing the smooth from the rough layer might be difficult. Use a sterile pen to lightly mark the smooth (top) layer of the Chondro-Gide<sup>®</sup> that will face the joint cavity.

When trimming the Chondro-Gide<sup>®</sup>, remember to cut it 10–15% smaller than the defect itself, as the area of the Chondro-Gide<sup>®</sup> will expand once moistened.



### Microfracturing

Using a 1.2 mm K-wire, perforate the subchondral bone at the base of the lesion. Working from the periphery of the lesion towards the center, insert holes at intervals of 3–4 mm. With a shaver, carefully remove tissue fragments. Alternatively, you can use an awl or nanofracturing to perforate the subchondral bone.

Prior to surgery during diagnostic arthroscopy, carefully assess the size and classification of the defect. If necessary, carry out concomitant interventions, e.g., meniscal repair, alignment or stabilization.



#### Position the Chondro-Gide®

Use forceps or a clamp to place the membrane in the defect. To prevent delamination of the membrane, make sure the Chondro-Gide<sup>®</sup> is sitting flush inside the defect.



Apply Glue

Inject fibrin glue into the space between the Chondro-Gide<sup>®</sup> and the defect. Apply the glue at the top of the lesion and then let it flow to the lower part.



Secure the Chondro-Gide<sup>®</sup>

Using an arthroscopic probe, tap the membrane into place.



**Remove Excess Glue** 

With a probe or a shaver, remove the excess fibrin glue.

#### NOTE

In addition to the wet arthroscopic technique illustrated above,<sup>22</sup> AMIC<sup>®</sup> can also be performed using a dry approach. The successful use of the dry technique has been described by different surgeons.<sup>23,24</sup> The choice between wet or dry AMIC<sup>®</sup> depends on the preference of the surgeon.

Check to make sure the membrane is positioned properly and stable by bending and extending the knee 10 times. To complete the surgery, carefully stop the bleeding, and suture the wound. If applying a drain, use a non-suction drain.

## Consistently Positive Results at 10 Years

## Mini-Open Surgery

A 10-year follow-up study by Kaiser et al.<sup>9</sup> investigated the use of AMIC<sup>®</sup> in the treatment of isolated chondral and osteochondral defects in the knee. Key scores remained constant from the 2-year to the 10-year follow up, with Visual Analogue Scores (VAS) at 2.0±1.6 and Lysholm scores at 86±13. These 10-year scores clearly show the longterm durability of the regenerated tissue and significant improvement over the preoperative status.

#### 5-Year Results of a Randomized, Controlled Study

In a randomized, controlled 3-arm study of 47 patients in 2 centers, a significant degradation in results was seen after 2 years following MFx alone (without Chondro-Gide<sup>®</sup>).

### AMIC<sup>®</sup> Shows Better Performance Than MFx Alone After Two Years

All treatment groups in the 3-arm study showed significant improvement in the first year, followed by stabilization at 2 years. However, at 5 years, results of the AMIC<sup>®</sup> Chondro-Gide<sup>®</sup> patients were different from those of the MFx-only patients.

Pain and function scores (ICRS and modified Cincinnati scores) remained stable or even improved with AMIC, while pain and function scores for the MFx group decreased after 2 years (figure 1).

Overall, the results of the 3-arm Volz et al.<sup>11</sup> study are consistent with the body of other published studies that show positive mid-to long-term clinical results for AMIC<sup>®</sup>, while clinical results for surgeries performed with MFx alone show a decline in performance over time.<sup>4,5,25,26</sup>

### 7-Year Results

A retrospective analysis by Schiavoni Panni et al.<sup>2</sup> found that Chondro-Gide<sup>®</sup> AMIC<sup>®</sup> was effective when treating full-thickness knee cartilage defects larger than 2 cm<sup>2</sup>. Over an average 7-year follow-up, patients consistently showed significant clinical and functional improvement, based on their International Knee Documentation Committee (IKDC), MRI, and Lysholm scores.



# Arthroscopic Surgery

### Results of Arthoscopic Technique Equally Positive as Arthroscopy and Mini-Arthrotomy with Chondro-Gide<sup>®</sup> AMIC<sup>®</sup>

In a retrospective study, Schagemann et al.<sup>22</sup> compared the clinical outcomes of Chondro-Gide<sup>®</sup> AMIC<sup>®</sup> procedures that were performed as arthroscopic or mini-open surgeries. The study followed patients up to 2 years. According to the patients' Visual Analog Scale (VAS), Lysholm scores, and Knee injury and Osteoarthrithis Outcome Scores KOOS), both surgical approaches yielded equally positive results.

# Reparing Patellar Cartilage Lesions with Chondro-Gide<sup>®</sup> AMIC<sup>®</sup>

In another 2017 study, Sadlik et. al.<sup>24</sup> analyzed 12 patients who had undergone arthroscopic surgery using Chondro-Gide® AMIC® to repair patellar catilage lesions. The Sadlik study assessed patients before surgery and at an average follow-up time of 38 months. Both clinical and radiological results improved significantly, according to criteria including KOOS, International Knee Documentation Committee (IKDC), Visual Analog Scale (VAS), Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) scores, and MRI.

Using augmented MFx in combination with Chondro-Gide<sup>®</sup> either arthroscopic or mini-open has been shown to be a successful treatment for more than 10 years. Using augmented MFx with Chondro-Gide<sup>®</sup> makes this technique even more effective, with enhanced healing and stability.

#### FIGURE 2: CARTILAGE DEFECT REPAIR AFTER AMIC®



MRI (1.5T) follow-up at 1,2, and 5 years after AMIC<sup>®</sup> shows progressive defect filling (20 × 20 mm, see arrows).<sup>11</sup> Image from Volz et al. CC BY 4.0

# Beyond Microfracture

Designed to be used in combination with MFx and Autologous Chondrocyte Implantation (ACI), Chondro-Gide<sup>®</sup> is equally well-suited to be used with other bone marrow stimulation techniques.<sup>27, 28</sup> The unique bilayer structure of the membrane is key. With 1 porous and 1 cell-occlusive layer, Chondro-Gide<sup>®</sup> acts as both a cover or wrapper that encloses cell-rich material while also providing a protected environment for regeneration.

A review by Lee et al.<sup>29</sup> on AMIC<sup>®</sup> and related techniques in the knee also documents the trend to add concentrated bone marrow-derived mesenchymal stem cells MSCs and Platelet-rich plasma, alone or in combination.

Bone marrow has been shown to be a possible source of multipotent stem cells with chondrogenic potential and can be harvested during the same surgical procedure. In a recent study, Gobbi et al.<sup>30</sup> used bone marrow-derived MSCs and Chondro-Gide<sup>®</sup> for large full-thickness chondral lesions of the knee. They demonstrated lasting post-operative results up to 3 years.

Another approach, presently in Phase II, uses nasal chondrocytes. They can be easily accessed and demonstrated their capacity to support articulate cartilage repair.<sup>16</sup> Cells from a nose biopsy are seeded and expanded on the Chondro-Gide<sup>®</sup>, the structure of which is perfect for this tissue culture approach. It allows a simple loading of the cells on the rough layer, while the smooth cell occlusive layer keeps the cells in place. The cultured tissue is then sutured into the cartilage lesion site. First clinical results showed statistically significant improvements in all categories.<sup>16</sup>

At Geistlich, we continue to share our knowledge and optimize our collagenderived products through close relationships with the medical and scientific community. As experts in bone and tissue regeneration, we see tremendous potential for collagen in the future of regenerative medicine. That is why we have dedicated a team of biochemists, materials scientists, process engineers and other experts at our headquarters in Switzerland to focus exclusively on collagen, and to explore its other possible therapeutic applications.

## Rehabilitation and Follow-Up Treatment

Within a few days after surgery, patients can begin partial weight-bearing, supporting a small amount of weight (up to 50%) using the operated leg. However, they should not try full weight-bearing for approximately 6 weeks. Patients should take a gradual approach to increasing activity, but by 6 months after surgery, most should be able to resume their regular sports activities.

Key factors in determining whether a patient has recovered and can return to sports activities are whether the patient's state of healing has been accurately assessed, and whether the patient is ready to resume an active lifestyle. As objective and subjective measures of healing often yield contradictory results, using both presents challenges in managing patient expectations.

In 2016, researchers correlated the results of subjective assessments, such as International Knee Documentation Committee (IKDC) and Lysholm scores, with objective isokinetic tests in patients who had undergone arthroscopic AMIC<sup>®</sup> in the knee. The results showed that while both objective and subjective measures were useful in monitoring a patient's overall rehabilitation progress, the IDKC and Lysholm tests were particularly useful in determining a patient's general state of recovery and readiness to return to sports activities.<sup>31</sup>

# Postoperative Rehabilitation after Cartilage Repair in the Knee

### **Stationary Phase**

- Prior to first mobilization, position the knee post-op in full extension in a splint and foam splint.
- Mobilization on the first day by a physiotherapist
- > CPM / Kinetec: start with 30°/0/0 for ca. 2 hours/ day (restricted by pain)

# General (Depending on Availability)

- Individual therapy during the first 12 weeks
- Lymphatic drainage when indicated due to excessive swelling
- > Hydrotherapy starting from week 6
- > Carefully dosed medical training, including gait training from week 8

### Active, Weight-Bearing

- > W o-2 sole contact using crutches
- > W 3–4 W partial weight bearing on crutches 10-15 kg
- > W 5-6 partial weight bearing on crutches 10-15 kg
- > W 6-7 transition to full weight bearing

#### (Femoro-patellar) Gentle Treatment with Corresponding Angles for the First 6 Months

- > Extension in open chain: 90°-40°; full flexion in open chain
- > From W 8: squat/3 flex o°-40°
- > From W 12 W: leg press 0°–60°

#### **Passive Mobilization**

- > W o-1 ROM 30°/0/0
- > W 2-3 ROM 60°/0/0
- > W 3-4 ROM 90°/0/0
- > W 5-6 ROM 120°/0/0
- > CPM / Kinetec at home for ca. 3 hrs/d
- > Bicycle ergometer without resistance (max. 90°) from week 6 on: increase progressively from week 8 on (restricted by pain)

#### Muscle Build Up / Proprioception / Coordination

- > Optimize quadriceps innervation immediately
- Increase of load bearing mainly in closed kinetic chain
  Increase progressively from
- W 8 on (below pain threshold)

#### **Active Mobilization**

- > W 0-2 ROM 30°/0/0
- > W 3-4 ROM 60°/0/0
- > W 5-6 ROM 90°/0/0

### Bandage/Orthesis

First 4–6 weeks in order to ensure limitation of movement, thereafter progressive reduction

#### Sport

- > M2 post-op walking on soft surface
- > M2 post-op cycling
- > M6 post-op jogging
- > M6 post-op mountain biking

W=week, ROM= range of motion, M=month, hrs/d= hours per day

Note: This is only an example of a plan that was developed by an orthopedic surgeon (M. Steinwachs, Sport Clinic, Zürich, 2018)<sup>32,33</sup>. It must be noted that there is no agreement on one standardized algorithm in literature or among orthopedic societies.<sup>34</sup>

### **Geistlich Chondro-Gide**<sup>®</sup>



Regulatory approvals for Geistlich Chondro-Gide® vary by country. Please visit www.geistlich-surgery.com or contact the Geistlich distributor in your region to learn more about product availability.

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# Stable Results Over 10+ Years



Image adapted from Volz et al.<sup>11</sup> CC BY 4.0

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