TRB CHEMEDICA (UK) LTD

Flexible treatment scheme with high dose HA 2%

- HA obtained from bacterial fermentation
- HA 2% (40 mg/2 ml)
- Molecular weight: 1-2 million Daltons
- Mannitol 0.5% (10 mg/2 ml)
- 2 ml pre-filled syringe
- Terminal sterilisation for optimal safety: the content and the outer surface of the syringe are sterile.

- **Mannitol-stabilised HA. Mannitol acts as a free radical scavenger which protects HA from rapid depolymerisation.** [1]
- **The formulation offers the possibility of increasing the intervals between injections.** [2]
- **Sustained efficacy with reduced number of injections** [2]
- **One injection of OSTENIL® PLUS reduces pain and improves function in knee OA over 6 months.** [3]

[1] *Mendoza G et al. Carbohydr Res 2007; 342: 96-102*
[2] *Data on file*
[3] *Borràs Verdera A et al. Poster presented at the XXV triennial world congress of the International Society of Orthopedic and Traumatology. September 6-9, 2011.*

OSTENIL® PLUS

Designed for long-term relief in OA

- HA obtained from bacterial fermentation
- HA 1% (20 mg/2 ml)
- Molecular weight: 1-2 million Daltons
- 2 ml pre-filled syringe
- Terminal sterilisation for optimal safety: the content and the outer surface of the syringe are sterile.

- **Treatment cycle of 3-5 injections at weekly intervals into large joints.**
- **OSTENIL® provides long-lasting pain relief and improves function in knee OA patients with excellent tolerability.** [4]
- **12 months effective pain relief for patients suffering from hip OA.** [5]
- **Among patients with advanced OA of the shoulder who either refused or were considered medically unfit for shoulder replacement surgery, OSTENIL® was associated with reduced pain and improved function.** [6]

[4] *Möller I et al. Presented at the 6th World Conference of the Osteoarthritis Research Society International 2001; poster PB22*
[5] *Tsvetkova E et al. Ann Rheum Dis 2010;69(Suppl3):281*
[6] *Funk L et al. Presented at the 9th World Conference of the Osteoarthritis Research Society International 2004; poster P338*

OSTENIL®

Restoring synovial balance in small joints

- HA obtained from bacterial fermentation
- HA 1% (10 mg/1 ml)
- Molecular weight: 1-2 million Daltons
- 1 ml pre-filled syringe
- Terminal sterilisation for optimal safety: the content and the outer surface of the syringe are sterile.

- **Specifically designed & licensed for small joints such as the hand, foot, facet joints and the temporomandibular joint, with 1-3 injections at weekly intervals.**
- **OSTENIL® MINI improves joint mobility and pain-free activity in the treatment of hallux rigidus.** [7]
- **A single injection of OSTENIL® MINI is as effective as an injection of steroid in patients with rhizarthrosis.** [8]
- **In temporomandibular joint disorders, an injection of OSTENIL® MINI reduces pain and improves joint function.** [9]
- **A single injection of OSTENIL® MINI is superior to steroids for patients with ankle OA.** [10]

[7] *Pons M et al. Foot Ankle Int 2007;28(1):38-42*
[8] *Tourret LJ et al. Presented at the 10th World Congress on Osteoarthritis. December 8-11, 2005; poster P157.*
[9] *Oliveras-Moreno JM et al. J Oral Maxillofac Surg 2008;66:2243-46*
[10] *Data on file*

OSTENIL MINI

Restore Tendon Function

- HA obtained from bacterial fermentation
- HA 2% (40 mg/2 ml)
- Molecular weight: 1-2 million Daltons
- Mannitol 0.5% (10 mg/2 ml)
- 2 ml pre-filled syringe
- Terminal sterilisation for optimal safety: The content and the outer surface of the syringe are sterile

- **Viscoelastic solution for peritendinous or intrasheath injection**
- **Reduce pain and improve tendon mobility in painful tendinopathy**
- **Enhance tendon gliding and prevent formation of adhesions**
- **Significantly reduces pain in Achilles, peroneal, and common wrist extensor tendons.** [11]

[11] *N. Lynen, Treatment of chronic tendinopathies with peritendinous hyaluronan injections under sonographic guidance 2012.*

OSTENIL® TENDON

OSTENIL® TENDON

For the treatment of pain and reduced mobility due to tendinopathy.

Indication
For the treatment of pain and reduced mobility due to tendinopathy.

Content
- 2% fermentative sodium hyaluronate (40mg/2ml); completely free from animal derived protein and therefore particularly well tolerated, practically no allergenic potential.-ph-value of 7.3
- 1.6 M Dalton
- 10mg Mannitol has been added in order to protect the sodium hyaluronate from premature degradation by free radicals, thus stabilising the solution and reducing the rate of deterioration (Mendoza 2007).

Presentation
OSTENIL® TENDON is a pre-filled sterile glass single-use syringe with 2ml content for single application. The syringe is fitted with a Luer-lock™ and back-stop, and sealed in a sterile blister pack.

Production
The fermentative highly purified sodium hyaluronate is filtered sterile into the syringe, followed by terminal sterilisation by moist heat. Batch sizes are kept low to guarantee a fast and secure filling.

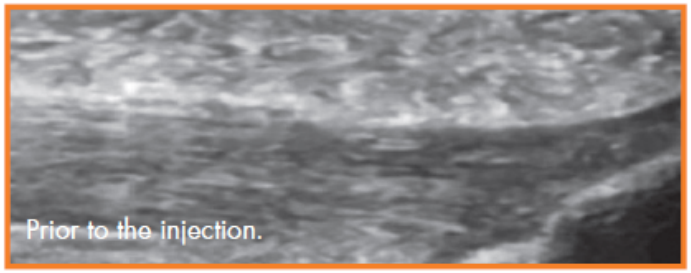
Administration
OSTENIL® TENDON is injected around the affected tendon or into the tendon sheath (e.g. with a needle from G25 to G27 gauge). It is applied twice with an interval of one week, and repeat treatment cycles are possible if needed. Several tendons can be treated at the same time.

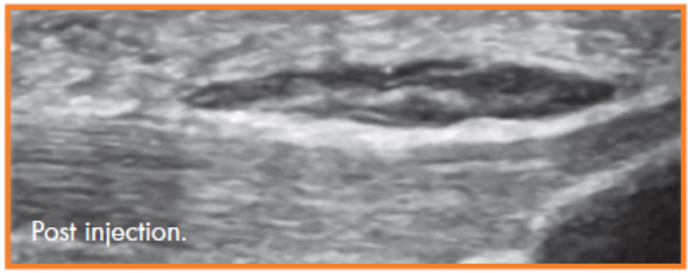
Why 2% Sodium Hyaluronate?
St Onge (1980) and Hagberg (1991) showed early on that the availability of exogenous sodium hyaluronate within the tendon sheath is markedly improved through a higher concentration.

Why 2 Injections?
These same studies prove that after one week the exogenous sodium hyaluronate has already been significantly reduced. The "refresher" after one week serves to further increase availability. A study conducted in Aachen and Munich (Lynen, Reisner 2011, data on file) confirms the high effectiveness of this therapy scheme.

How is OSTENIL® TENDON injected?

Tendons with a sheath: The injection will be administered into the tendon sheath.
Tendons without a sheath: Aim for the point of greatest pain. Place the solution alongside the tendon, not into the tendon. The solution will be distributed along the tendon through movement. This is observable with ultrasound.


Prior to the injection.


Post injection.

How does OSTENIL® TENDON work?

The macro-molecular characteristics of sodium hyaluronate, already proven in their effectiveness in arthritis, increase the gliding effect and reduce agglutinations – the tendon functions again as it is fully lubricated. At the same time sodium hyaluronate blocks the pain receptors and inhibits the movement of inflammatory mediators. This prevents the inflammation from getting any worse. Sodium hyaluronate is a good transport medium for nutrients and enables them in this way to reach the avascular parts of the tendon. Sodium hyaluronate also supports wound healing by creating spaces in-between the cells, in order that the cells can divide and communicate with one another. As a whole, sodium hyaluronate encourages a harmonisation of the tendons and of the structures surrounding them.

References for OSTENIL® TENDON:

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31 L. Hagberg et al., J Hand Surg 1992c; 17: 935–941
32 M. Özgen et al.; Rheumatol Int. 2010; 31. July (E-publication ahead of print)
33 P. Kasten, Deutsche Zeitschrift für Sportmedizin Jahrgang 61, Nr. 4 (2010), Page 84–90

GB

OSTENIL® PLUS

Viscoelastic solution for injection into the joint cavity

INSTRUCTIONS FOR USE

OSTENIL® PLUS

Sodium hyaluronate from fermentation 2.0 %. Viscoelastic solution for injection into the joint cavity. Sterile by moist heat.

Composition:

1 ml isotonic solution (pH 7.3) contains 20.0 mg sodium hyaluronate from fermentation and sodium chloride, disodium phosphate, sodium dihydrogenphosphate, mannitol and water for injections.

Indications:

Pain and restricted mobility in degenerative and traumatic changes of the knee joint and other synovial joints. Contra-indications: OSTENIL® PLUS should not be used in patients with ascertained hypersensitivity to one of the constituents.

Interactions:

No information on the incompatibility of OSTENIL® PLUS with other solutions for intra-articular use is available to date. The concomitant use of an oral analgesic or anti-inflammatory drug during the first few days of treatment may be helpful for the patient.

Side effects:

Local secondary phenomena such as pain, sensation of heat, redness and swelling may occur in the joint treated with OSTENIL® PLUS. Application of an ice pack for five to ten minutes onto the treated joint will reduce the incidence of these events.

Directions for use:

Inject OSTENIL® PLUS into the affected joint once a week for a total of 1–3 injections. Several joints may be treated at the same time. Repeat treatment cycles may be administered as required. In case of joint effusion it is advisable to reduce the effusion by aspiration, rest, application of an ice pack and/or intra-articular corticosteroid injection. Treatment with OSTENIL® PLUS can be started two to three days later. The content and the outer surface of the OSTENIL® PLUS pre-filled syringe are sterile as long as the sterile pack is intact. Take the pre-filled syringe out of the sterile pack, unscrew the Luer lock cap from the syringe, attach a suitable needle (for example 18 to 25 G) and secure it by turning slightly. Remove any air bubble, if present, before injection.

Precautions:

Caution should be exercised in patients with known hypersensitivity to drugs. The general precautions for intra-articular injections should be observed, including measures to avoid joint infections. OSTENIL® PLUS should be injected accurately into the joint cavity, if necessary under imaging control. Avoid injections into blood vessels or surrounding tissues! As no clinical evidence is available on the use of hyaluronic acid in children, pregnant and lactating women or in inflammatory joint diseases such as rheumatoid arthritis or Bechterew disease, treatment with OSTENIL® PLUS is not recommended in these cases. Do not use if the pre-filled syringe or sterile pack are damaged. Any solution not used immediately after opening must be discarded. Otherwise the sterility is no longer guaranteed. Store between 2 °C and 25 °C! Do not use
after the expiry date indicated on the box. Keep out of the reach of children!

Characteristics and mode of action:

Synovial fluid, which is viscoelastic due to the presence of hyaluronic acid, is found in all synovial joints, particularly the large weight bearing joints, where it ensures normal, painless movement due to its lubricating and shock-absorbing properties. It is also responsible for the nutrition of the cartilage. In degenerative joint disorders such as osteoarthritis, the viscoelasticity of the synovial fluid is markedly reduced thereby decreasing its lubricating and shock-absorbing functions. This increases mechanical loading of the joint and cartilage destruction which ultimately results in pain and restricted mobility of the affected joint. Supplementing this synovial fluid with intra-articular in jections of highly purified hyaluronic acid can ameliorate the viscoelastic properties of synovial fluid. This improves its lubricating and shockabsorbing functions and reduces mechanical overload of the joint. As a rule this results in a decrease in pain and an improvement in joint mobility which may last for several months after a treatment cycle. OSTENIL® PLUS is a transparent solution of natural and highly purified sodium hyaluronate obtained by fermentation and is devoid of animal protein. OSTENIL® PLUS also contains mannitol, a free radical scavenger, which helps to stabilise the chains of sodium hyaluronate. In biocompatibility studies, OSTENIL® PLUS was found to be particularly safe.

Presentation:

One pre-filled syringe of 40 mg / 2.0 ml OSTENIL® PLUS in a sterile pack.
OSTENIL® PLUS is a medical device. To be used by a clinician only.
Last revision date: December 2010

GB

OSTENIL®

Viscoelastic solution for injection into the joint cavity

INSTRUCTIONS FOR USE

OSTENIL®

Sodium hyaluronate from fermentation 1.0 %. Viscoelastic solution for injection into the joint cavity. Sterile by moist heat.

Composition:

1 ml isotonic solution contains 10.0 mg sodium hyaluronate and sodium chloride, disodium phosphate, sodium dihydrogen phosphate, water for injections.

Indications:

Pain and restricted mobility in degenerative and traumatic changes of the knee joint and other synovial joints.

Contra-indications:

OSTENIL® should not be used in patients with ascertained hypersensitivity to one of the constituents.

Interactions:

No information on the incompatibility of OSTENIL® with other solutions for intra-articular use is available to date. The concomitant use of an oral analgesic or anti-inflammatory drug during the first few days of treatment may be helpful for the patient.

Side effects:

Local secondary phenomena such as pain, feeling of heat, redness and swelling may occur in the joint treated with OSTENIL®. Application of an ice pack for five to ten minutes onto the treated joint will reduce the incidence of these events.

Directions for use:

Inject OSTENIL® into the affected joint once a week for a total of 3–5 injections. Several joints may be treated at the same time. Depending on the severity of the joint disease the beneficial effects of a treatment cycle of five intra-articular injections will last at least six months. Repeat treatment cycles may be administered as required. In case of joint effusion it is advisable to reduce the effusion by aspiration, rest, application of an ice pack and/or intra-articular corticosteroid injection. Treatment with OSTENIL® can be started two to three days later.

The content and the outer surface of the OSTENIL® pre-filled syringe are sterile as long as the sterile pack is intact. Take the pre-filled syringe out of the sterile pack, unscrew the Luer lock cap from the syringe, attach a suitable needle (for example 19 to 21 G) and secure it by turning slightly. Remove any air bubble, if present, before injection.

Precautions:

Caution should be exercised in patients with known hypersensitivity to drugs. The general precautions for intra-articular injections should be observed, including measures to avoid joint infections. OSTENIL® should be injected accurately into the joint cavity, if necessary under imaging control. Avoid injections into blood vessels or surrounding tissues! As no clinical evidence is available on the use of hyaluronic acid in children, pregnant and lactating women or in inflammatory joint diseases such as rheumatoid arthritis or Bechterew di sease, treatment with OSTENIL® is not recommended in these cases. Do not use if the pre-filled syringe or sterile pack are damaged. Any solution not used immediately after opening must be discarded. Otherwise the sterility is no longer guaranteed. Store between 2 °C and 25 °C! Do not use after the expiry date indicated on the box. Keep out of the reach of children.

Characteristics and mode of action:

Synovial fluid, which is viscoelastic due to the presence of hyaluronic acid, is found in all synovial joints, particularly the large weight bearing joints, where it ensures normal, painless movement due to its lubricating and shock-ab sorbing properties. It is also responsible for the nutrition of the cartilage. In degenerative joint disorders such as osteoarthritis, the viscoelasticity of the synovial fluid is markedly reduced thereby decreasing its lubricating and shock-absorbing
functions. This increases mechanical loading of the joint and cartilage destruction which ultimately results in pain and restricted mobility of the affected joint. Supplementing this synovial fluid with intra-articular injections of highly purified hyaluronic acid can ameliorate the viscoelastic properties of synovial fluid. This improves its lubricating and shockabsorbing
functions and reduces mechanical overload of the joint. As a rule this results in a decrease in pain and an improvement in joint mobility which may last for several months after a treatment cycle of five intra-articular injections.

Presentation:

One pre-filled syringe of 20 mg/2.0 ml OSTENIL® in a sterile pack.
OSTENIL® is a medical device. To be used by a clinician only.
Last revision date: October 2010

OSTENIL® PLUS

OSTENIL®

GB

OSTENIL® MINI

Viscoelastic solution for injection into small joints

INSTRUCTIONS FOR USE

OSTENIL® MINI

Sodium hyaluronate from fermentation 1.0 %. Viscoelastic solution for injection into small joints. Sterile by moist heat.

Composition:

1 ml isotonic solution contains 10.0 mg sodium hyaluro nate and sodium chloride, disodium phosphate, sodium dihydrogen phosphate, water for injections.

Indications:

Pain and restricted mobility in degenerative and traumatic changes of small synovial joints, for example, the facet joints of the lumbar spine, the saddle joint of the thumb, the interphalangeal joints of the fingers and toes, the proximal joint of the big toe and the temporomandibular joint. In the treatment of larger joints, for example the knee, hip or shoulder, OSTENIL® pre-filled syringes of 20 mg/2.0 ml should be used.

Contra-indications:

OSTENIL® MINI should not be used in patients with ascertained hyper sensitivity to any of its constituents.

Interactions:

No information on the incompatibility of OSTENIL® MINI with other solutions for intraarticular use is available to date. The concomitant use of an oral analgesic or anti-inflammatory drug during the first few days of treatment may be helpful for the patient.

Undesirable effects:

Local secondary phenomena such as pain, feeling of heat, redness and swelling/joint effusion may occur in the joint treated with OSTENIL® MINI. Application of an ice pack onto the treated joint for five to ten minutes will reduce the incidence of these events.

Dosage and administration:

Inject OSTENIL® MINI into the affected joint once a week for a total of 1–3 injections. Several joints may be treated at the same time. Depending on the severity of the joint disease the beneficial effects of a treatment cycle may last at least six months. Repeat treatment cycles may be administered as required. In case of joint effusion it is advisable to reduce the effusion by aspiration, rest, application of an ice pack and/or intraarticular cortico steroid injection. Treatment with OSTENIL® MINI can be started two to three days later. The contents and outer surface of the OSTENIL® MINI pre-filled syringe are sterile as long as the sterile pack is intact.

Take the pre-filled syringe out of the sterile pack, unscrew the Luer lock cap from the syringe, attach a suitable needle (For example 19 to 25 G) and secure it by turning slightly. Remove any air bubble, if present, before injection.

Precautions:

Caution should be exercised in patients with known hypersensitivity to drugs. The general precautions for intraarticular injections should be observed, including measures to avoid joint infections. OSTENIL® MINI should be injected accurately into the joint cavity, if necessary under imaging control. Avoid injec tions into blood vessels or surrounding tissues! As no clinical evidence is available on the use of hyaluronic acid in children, pregnant and lactating women or in inflammatory joint diseases such as rheumatoid arthritis or Bechterew disease, treatment with OSTENIL® MINI is not recommended in these cases. Do not use if the pre-filled syringe or sterile pack are damaged. Any solution not used immediately after opening must be discarded. Otherwise the sterility is no longer guaranteed. Store between 2 °C and 25 °C! Do not use after the expiry date indicated on the box. Keep out of the reach of children.

Characteristics and mode of action:

Synovial fluid, which is viscoelastic due to the presence of hyaluronic acid, is found in all synovial joints where it ensures normal, painless movement due to its lubricating and shock-absorbing properties. It is also responsible for the nutrition of the cartilage. In degenerative joint disorders such as osteoarthritis, the viscoelasticity of the synovial fluid is markedly reduced thereby decreasing its lubricating and shock-absorbing functions. This increases mechanical loading of the joint and cartilage destruction which ultimately results in pain and restricted mobility of the affected joint. Supplementing this synovial fluid with intraarticular injections of highly purified hyaluronic acid can ameliorate the viscoelastic properties of synovial fluid. This improves its lubricating and shock-absorbing functions and reduces mechanical overload of the joint. As a rule this results in a decrease in pain and an improvement in joint mobility which may last for several months after a treatment cycle.

Presentation:

One pre-filled syringe of 10 mg/1.0 ml OSTENIL® MINI in a sterile pack.
OSTENIL® MINI is a medical device. To be used by a clinician only.
Last revision date: March 2011

GB

OSTENIL® TENDON

Visco-elastic solution for peritendinous or intrasheath injection

INSTRUCTIONS FOR USE

OSTENIL® TENDON

Sodium hyaluronate from fermentation 2.0%. Visco-elastic solution for peritendinous or intrasheath injection. Sterile by moist heat.

Composition:

1ml isotonic solution contains 20.0mg sodium hyaluronate from fermentation, sodium chloride, disodium phosphate, sodium dihydrogen phosphate, mannitol and water for injections.

Indications:

For the treatment of pain and reduced mobility in tendon disorders.s.

Contra-indications:

OSTENIL® TENDON should not be used in patients with ascertained hypersensitivity to any of the constituents.

Interactions:

No information on the incompatibility of OSTENIL® TENDON with other medications administered to tendons is available to date.

Side Effects:

Local secondary phenomena such as pain, feeling of heat, bruising, redness or swelling may occur following treatment with OSTENIL® TENDON.

Dosage and Administration:

Inject OSTENIL® TENDON around the affected tendon or into the affected tendon sheath once a week for a total of 2 injections. Several tendons may be treated at the same time. Repeat treatments may be administered as required.

The content and outer surface of the OSTENIL® TENDON pre-filled syringe are sterile as long as the sterile pack remains unbroken. Take the pre-filled syringe out of the sterile pack, unscrew the Luer-Lok™ cap, attach a suitable needle (e.g. 25 to 27 G) and secure it by turning slightly. If present remove any air bubble from the syringe prior to injection.

Precautions:

Caution should be exercised in patients with known hypersensitivity to drugs. The general precautions for peritendinous and intrasheath injections should be observed. OSTENIL® TENDON should be injected accurately into the tendon sheath or around the affected tendon, if necessary under imaging control. Avoid nerve lesions or injections into blood vessels! As no clinical evidence is available on the use of sodium hyaluronate in children or in pregnant and lactating women, treatment with OSTENIL® TENDON is not recommended in these cases. Do not use if the pre-filled syringe or sterile pack are damaged. Any solution not used immediately after opening must be discarded. Otherwise the sterility is no longer guaranteed. Store between 2 °C and 25°C! Do not use after the expiry date indicated on the box! Keep out of the reach of children!

Characteristics and Mode of Action:

A tendon is a robust structure consisting of fibrous tissue designed to transmit power from muscle to bone and to resist load during muscle contraction. Tendons may be surrounded by different structures: e.g. fibrous ligaments, synovial sheaths, tendon sheaths, or bursae. Overuse or inappropriate straining can cause inflammation and/or degenerative changes of the tendon, leading to pain and loss of function. Lubricating the tendon could reduce pain, improve tendon function and reduce the potential for adhesions. The lubricating and visco-elastic properties of OSTENIL® TENDON promote tendon gliding and the physiological repair process. In addition, due to its macro-molecular structure OSTENIL®TENDON reduces the free passage of inflammatory cells and molecules through the tendon sheath.

OSTENIL® TENDON is a transparent solution of natural, highly purified sodium hyaluronate obtained by fermentation and is devoid of animal protein. OSTENIL® TENDON also contains mannitol, a free radical scavenger, which helps to stabiles the chains of sodium hyaluronate. In biocompatibility studies OSTENIL®TENDON was found to be particularly safe.

Presentation and Package size:

One pre-filled syringe of 40mg/2.0ml OSTENIL® TENDON in a sterile pack.
OSTENIL® TENDON is a medical device. To be used by a clinician only.
Last revision date: November 2011

TRB CHEMEDICA AG
Richard-Reitzner-Allee 1
85540 Haar/München, Germany

OSTENIL® MINI

OSTENIL® TENDON

OSTENIL® Range,

Designed for long-term relief in OA and tendinopathy

TRB CHEMEDICA (UK) LTD
9 Evolution, Lymedale Business Park, Hooters Hall Road, Newcastle-under-Lyme, Staffordshire, ST5 9QF
Tel: 0845 330 7556 Fax: 0845 330 7557 Email info@trbchemedica.co.uk www.trbchemedica.co.uk