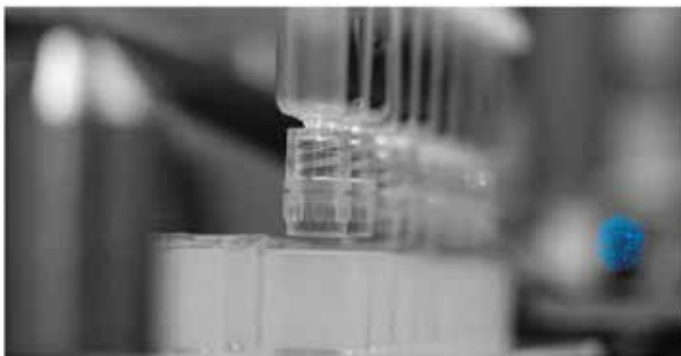


It all started with a desire to help people in need understand that a medical device is not just a product, but rather a chance to return to a normal life.

ORTOBRAND
INTERNATIONAL
MANUFACTURES AND DISTRIBUTES

HYALURONIC ACID BASED PRODUCTS



orto brand ∞
enjoy your life

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ORTHOFLEX

WHY HURT, WHEN YOU CAN PREVENT IT?

Enjoy your life!

ORTOBRAND INTERNATIONAL is a global healthcare company active in the research and development, manufacturing, marketing and sales of innovative orthopedic medical device products for patients suffering from osteoarthritis, based on hyaluronic acid (HA) used for damaged synovial joints.

All production complies with the European Medical Devices Directive and other legal requirements.

The products are accredited to EU standards and regulations by the NSAI (National Standards Authority of Ireland), are CE, ISO, GMP marked and are listed as Class III medical devices.



ORTOBRAND INTERNATIONAL is a Romanian (UE country) multinational company, engaged in R&D, manufacturing, marketing and sales of innovative, hyaluronic acid (HA) based orthopedic medical devices for patients with osteoarthritis.

We are thankful and grateful to Dr. Endre A. Balazs who, back in the 60's, discovered that injections with hyaluronic acid in the arthritic knees of race horses can reduce inflammation and pain.

A hope was born and further research in developing injectable hyaluronic acid for human treatment was encouraged.

Here begins our story, with the desire to engage in the research and development of new products, for a healthier life.

Our team's objective is to reach and help more and more people, by establishing partnerships with specialized companies all over the world.

SODIUM HYALURONATE

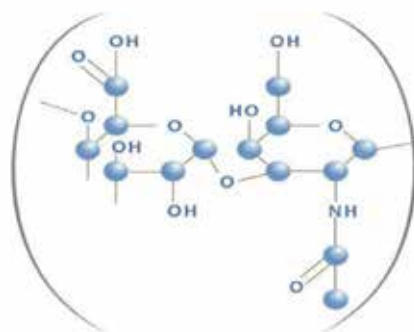
Hyaluronan (also known as sodiumhyaluronate or hyaluronic acid) is a natural and linear glycosaminoglycan. It is ubiquitous in all the tissues and fluids of animals, having the highest concentration in the soft connective tissues.

In 1934, Karl Meyer and his assistant John Palmer first announced the discovery of HA. They purified HA from bovine vitreous and showed that it contained a hexuronic acid and a hexosamine. They proposed "for convenience, the name hyaluronic acid, from hyaloid (vitreous) + uronic acid". Up to the mid-1940s, HA had been isolated successfully from other sources - synovial fluid, skin, umbilical cord, cock's comb etc.

In 1980s, Dr. Endre Balazs and his coworkers developed a procedure to isolate, purify and identify hyaluronic acid from rooster combs and human umbilical cords. Since then, HA has been produced at industrial scale from rooster combs and human umbilical cords.

It is known that the capsules of some bacteria contain HA, therefore, HA can also be isolated from certain strains of bacteria, such as streptococci, which was first reported in 1937 by Kendall. They cultured Group A streptococci and then the mucoid polysaccharide was precipitated with ethanol.

This polysaccharide which was composed of N-acetyl glucosamine and glucuronic acid units was identical with that occurring in bovine vitreous humor and human umbilical cord. The bacterial production of HA involving a *Streptococcus zooepidemicus* strain was first described in 1989, giving rise to the first commercialization of HA produced by fermentation.



By the end of the 20th century, bacterial fermentation had become the leading production technique for sodium hyaluronate, and it has led to great changes in the sodium hyaluronate industry. The industry is now able to produce a higher quality HA product on an industrial scale, necessary to support the continued expansion of HA applications into new areas of science. The techniques have also lowered the cost of HA production, to a point that has allowed many applications to go mainstream, that might have proved too costly for markets previously.

Commercial HA is commonly presented as the form of sodium salt.

During the manufacture of HA, sodium salts (such as sodium chloride or sodium hydroxide) are often used to increase ionic strength or to adjust pH value, therefore, most of HA products are presented as a form of sodium salt, named sodium hyaluronate.



ORTHO FLEX

WHY HURT, WHEN YOU CAN PREVENT IT?

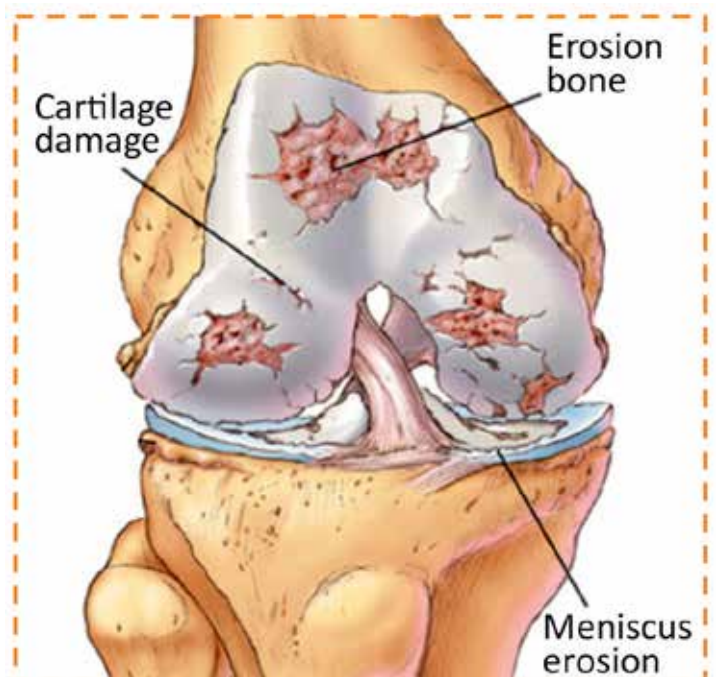
Enjoy your life!

DISEASES AND TREATMENTS

Joint Pain and Arthritis

With overuse or injury, cartilage at the end of the joints can break down, narrowing the joint space and causing the bones to rub together. Painful bony growths or spurs may form. This can lead to swelling, stiffness and possibly osteoarthritis - the most common type of arthritis.

Another type of arthritis is rheumatoid arthritis, an autoimmune disease characterized by extreme inflammation.





What is Osteoarthritis?

Osteoarthritis is a disease that affects the joints in your body.

While it can affect any joint, osteoarthritis most commonly occurs in the hands, hip, knees, neck and lower back.

Osteoarthritis (OA) is the most common joint disease and cause of disabilities, especially in older people (more than 80 % of the population over 55 is affected by osteoarthritis).



Also known as degenerative arthritis, degenerative joint disease or OA, this disease occurs when the cartilage that normally covers and cushions the ends of bones wears down. It is characterized by cartilage erosion, changes in subchondral bone, osteophyte formation and synovial inflammation.

The main symptoms of OA are chronic pain, stiffness and loss of mobility.



Osteoarthritis of the knee

When osteoarthritic joints become swollen and damaged, they can be painful and difficult to move.

If you have OA of the knee, the symptoms may be pain, stiffness, limited range of motion.

In the arthritic joints, the normal concentration and molecular weight of hyaluronate (HA) is decreased by 33% to 50%, limiting its role in maintaining normal joint biomechanics.

ORTHO FLEX

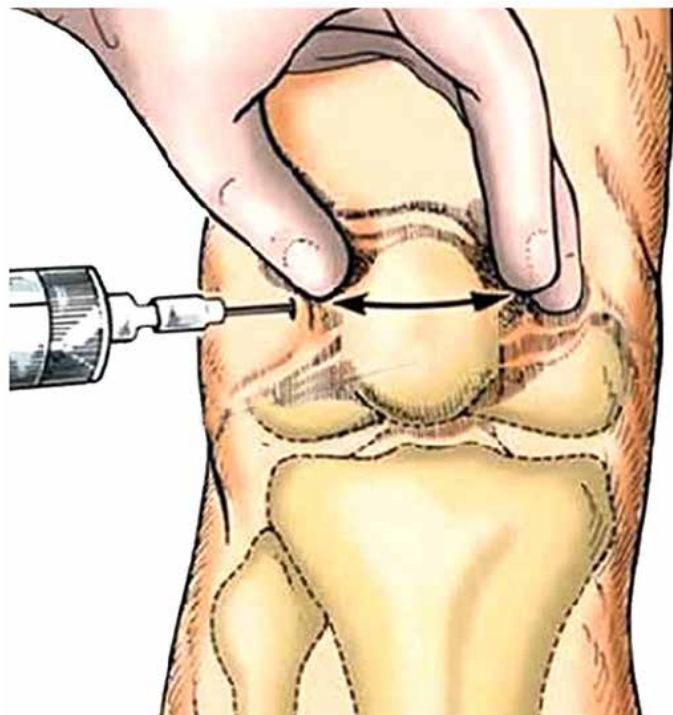
WHY HURT, WHEN YOU CAN PREVENT IT?

Enjoy your life!

VISCOSUPPLEMENTATION

What is Viscosupplementation?

Viscosupplementation refers to a procedure that involves the use of HA solution to supplement or replace synovial fluid in joint with pathological conditions, to alleviate pain and promote the healing of intra-articular wounds. The viscosupplementation should improve the physiological environment of an osteoarthritic joint by restoring the protective viscoelasticity of synovial fluid, reduce friction and improve mobility.





Studies have confirmed the satisfactory effect of HA to treat lameness in race horses and osteoarthritis (OA) in human knees, hips, shoulders, temporo-mandibular joint etc.

The use of HA solution in OA treatment is considered to be the most successful medical use of HA.

The therapeutic goal of viscosupplementation is the restoration of rheological homeostasis in pathological structures, such as osteoarthritic joints. When the normal viscoelasticity of a solid tissue compartment or the elasto-viscosity of a liquid tissue compartment is decreased under pathological conditions, normal function and regenerative processes are impaired.

By introducing viscosupplementary devices, the normal rheological state of such compartments can be restored, or even augmented. These devices stay in the tissue compartment for various periods of time, depending on the nature of the viscosupplement and the pathophysiology of the tissue compartment.



Mechanism of action

Viscosupplementation with HA has various mechanisms of action in the osteoarthritic knee. In addition to its viscous and elastic properties, repletion intra-articular HA also has anti-inflammatory, anabolic and analgesic properties.

HA has been identified as the molecule responsible for imbuing the knee with its rheostatic properties.

HA is a polysaccharide chain composed of repeated disaccharide units of glucuronic acid and N – acetylglucosamine. HA is normally synthesized by type B synoviocytes or fibroblasts and is secreted into the joints.

In the osteoarthritic knee, the concentration of HA is decreased to nearly half of normal, the MW is reduced (as polysaccharide chains are cleaved) and this decreases interaction between HA molecules. These changes of the inherent viscous and elastic properties of HA reduces the joint ability to resist stress and shear forces.

HA is a viscoelastic substance, because it exhibits both viscous and elastic properties. This allows the joint to optimally adapt to different external forces. The knee experiences low shear loads during simple range of motion. Under these conditions, viscous properties predominate and the HA molecules line up and act as a lubricant.

Under high shear loads, HA molecules behave as an elastic substance and absorb the energy that is transmitted across the joint.

Because in the osteoarthritic knee the level of natural HA is low, using viscosupplements in order to restore its lost properties is a reasonable and useful procedure.





What is ORTHOFLEX forte®?

ORTHOFLEX forte® is an injectable viscose elastic solution of 30 mg/2 ml hyaluronic acid, presented in a pre-filled sterile syringe, which is to be administered intra articular in the treatment of osteoarthritis, leading to joint function improvement.

ORTHOFLEX forte® is a product for viscosupplementation, which is a safe, effective and well-established treatment in osteoarthritis (OA), consisting of injecting a hyaluronic acid-based solution into the affected synovial joint.

In the joints, natural hyaluronic acid has several functions, including:

- **Lubrication.** Hyaluronic acid binds well to water, producing a viscous, jelly-like fluid. This viscous fluid provides lubrication and also acts as a cushion in the joint.
- **Growth of cartilage and bone.** Hyaluronic acid helps the growth and development of joint's cartilage and bone by promoting the growth of new cells and tissues.
- **Reducing inflammation.** Hyaluronic acid plays an important role in reducing joint inflammation and pain, caused by injury or tissue degeneration.



What are the indications for treatment with ORTHOFLEX forte®?

ORTHOFLEX forte® is indicated in osteoarthritis, a disease of joints characterized by a progressive degradation of the cartilage and bone deformation, showing symptoms like knee pain, stiffness, articular limited mobility, crack, swelling.

ORTHOFLEX forte® is indicated as a viscose elastic supplement or a replacement for synovial fluid in the human knee joint.

ORTHOFLEX forte® is indicated for symptomatic treatment of knee osteoarthritis. The actions of the product are lubrication and mechanical support.

What areas should I use this product on?

ORTHOFLEX forte® injectable can be administered in any synovial joint of the body. These include the knee joint, hip joint, shoulder joint, and the finger joints.

How long will the treatment take?

ORTHOFLEX forte® is administered in the affected joint once a week, for 3 consecutive weeks. If treatment is bilateral, a separate syringe should be used for each knee.

The effect of the treatment can be maintained for 6 months. In order to prevent complications, the treatment should be repeated.

ORTHOFLEX forte® must be administered only by medical professionals, trained for intra articular administration techniques.

Any joint effusion present should be removed by joint aspiration, before injecting **ORTHOFLEX forte®**.

What are the effects of ORTHOFLEX FORTE® therapy?

ORTHOFLEX forte® have analgesic, anti-inflammatory, antioxidant and chondroprotective effects, stimulates proteoglycan, collagen and hyaluronic acid synthesis, and facilitates the evacuation of cartilaginous debris.

When the articular surfaces rub on each other, the molecules of hyaluronic acid from the synovial fluid act as a lubricant, protecting the articular surfaces from being mechanically damaged.

Under the joint loading pressure the hyaluronic acid acts as a shock dumper, thus protecting the cartilage against compression trauma.

It feeds the cartilage and protects the synovial fluid as the hyaluronic acid represents a protective barrier for the synovial fluid.

It maintains the balance of fluids within the joint and it helps the joint regain its normal function.

Easy to administer, it directly treats the affected joint.

Helps avoiding and preventing surgical interventions and emotional trauma.

ORTHO
FLEX
one

ORTHO FLEX one

INTRA ARTICULAR INJECTION FOR JOINT CARTILAGE REPAIR

Enjoy your life!



UNIQUE COMBINATION OF CROSS-LINKED
HYALURONIC ACID + CHONDROITIN SULFATE



What is ORTHOFLEX one® ?

ORTHOFLEX one® is the first and alone commercial viscose supplement combining HA (hyaluronic acid) and CS (chondroitin sulfate) in the treatment of degenerative joint disease.

ORTHOFLEX ONE® is a sterile, viscoelastic solution, containing two highly purified cross-linked biological polymers: hyaluronic acid in concentration of 60 mg per 3 ml and chondroitin sulfate 90 mg per 3 ml. The solution has high molecular weight - 3,0 MilDa - which guarantees its excellent efficiency and a strong therapeutic effect.

ORTHOFLEX one® presents itself in a prefilled, sterile, single dose syringe, that will be injected as **1 dose per treatment**.

How does it work?

Hyaluronic acid is a major component of the synovial fluid and cartilage and is responsible for the lubrication and cushioning in joints.

It decreases friction between joint surfaces and protects soft tissue from trauma, by acting as a shock absorber.

Hyaluronic acid also has analgesic, anti-inflammatory and antioxidant effects, stimulates proteoglycan synthesis and facilitates the evacuation of cartilaginous remains.

Chondroitin Sulfate is a molecule that occurs naturally in the body. It is an important component of cartilage - the tough connective tissue that cushions the joints.

It delivers nutrients to the joint cartilage. The body needs nourishment to heal and repair itself and Chondroitin Sulfate has been proven to stimulate the growth of new joint cartilage.

It can also block the enzymes that degrade cartilage and provides the building blocks for the body to produce new cartilage.

Chondroitin sulfate also inhibits pro-inflammatory factors secretion.

The elasticity and plasticity, which are the functions of the joint cartilage, can be maintained through the use of Chondroitin Sulfate.

The adjunction of Chondroitin sulfate provides not only pain relief, mobility improvement and cartilage protection, but also cartilage regeneration.

This cartilage repair is particularly useful in severe OA (grade III and IV).

Using Chondroitin Sulfate as a **cross-linking agent** increases bio-compatibility and bio-degradability of the native polymer, creates the premises for delaying cartilage degeneration and supports regeneration.

The outstanding viscoelastic performance of **ORTHOFLEX one®** is due to the unique **cross-linking** process.

What are the indications of ORTHOFLEX one®?

ORTHOFLEX one® is a product for viscose supplementation, which is a safe, efficient and well established treatment in osteoarthritis, consisting of injecting a hyaluronic acid and chondroitin sulfate based solution into the affected synovial joint.

ORTHOFLEX one® acts as a temporary replacement and supplement for synovial fluid. It is also recommended for :

- post-arthroscopy pain relief,
- following meniscus repair procedure,
- following previous crossed ligament reconstruction as auxiliary treatment for patients with osteochondral defects.

What is the treatment with ORTHOFLEX one®?

Just one injection per treatment can treat the symptoms of osteoarthritis.

ORTHOFLEX one® is administered in the affected joint as a single dose per treatment.

If the treatment is bilateral, a separate syringe should be used for each knee.

Approved for all synovial joints (particularly the knee and hip, but also the ankle, shoulder, elbow, wrist, fingers, toes, the temporo mandibular and facet joints).

This effect can be maintained for up 1 year. In order to prevent complications, the treatment should be repeated.

Any joint effusion present should be removed by joint aspiration, before injecting **ORTHOFLEX one®**.

After the injection, an articular rest of approximately 24 hours is recommended (no strenuous exercise), in order to increase the duration of effect. General rest and applying ice to the injected joint are helpful.

ORTHO
FLEX
gel

ORTHO FLEX gel

INTRA ARTICULAR INJECTION FOR THE TREATMENT OF OSTEOARTHRITIS
SINGLE INJECTION PER TREATMENT

Enjoy your life!



DISCOVER

THE NEW PRODUCT CONTAINING
ESSENTIAL ELEMENTS OF THE
NATURAL ARTICULAR CARTILAGE

CROSS-LINKED
HYALURONIC ACID
CHONDROITIN SULFATE
GLUCOSAMINE



What is ORTHOFLEX gel?

ORTHOFLEX gel® is a bio-matrix in the form of a sterile, viscoelastic solution, consisting of a combination of highly purified cross-linked biopolymers: hyaluronic acid, chondroitin sulfate and n-acetylglucosamine.

ORTHOFLEX gel® is an intra-articular injectable viscoelastic gel, used for treating osteoarthritis and it comes in a prefilled, single dose syringe.

ORTHOFLEX gel® is very similar to the synovial fluid, a substance that occurs naturally in the joints, where it acts as a lubricant and shock absorber.

ORTHOFLEX gel® contains:

- **hyaluronic acid: 36 mg / 2,25 ml,**
- **chondroitin sulfate: 67,5 mg / 2,25 ml**
- **glucosamine 67,5 mg / 2,25 ml.**

The high molecular weight of the gel (3,0 milDA) guarantees its excellent efficiency and a strong therapeutic effect.

**HYALURONIC ACID +
CHONDROITIN SULFATE +
GLUCOSAMINE**

Much more effective when used together!

How does it work?

Hyaluronic acid is a major component of the synovial fluid and cartilage and is responsible for the lubrication and cushioning in joints, providing mechanical support.

Chondroitin Sulfate is a molecule that occurs naturally in the body. It is an important component of cartilage - the tough connective tissue that cushions the joints.

Chondroitin sulfate delivers nutrients to the joint cartilage. The body needs nourishment to heal and repair itself and Chondroitin Sulfate has been proven to provide the body with the building blocks for producing new cartilage, therefore stimulating the growth of new joint cartilage.

It can also block the enzymes that degrade cartilage and inhibits pro inflammatory factors secretion.

The elasticity and plasticity, which are the functions of the joint cartilage, can be maintained through the use of Chondroitin Sulfate.

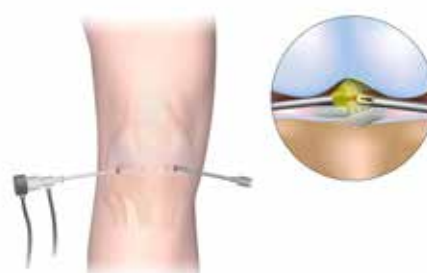
Glucosamine plays a vital role in building and repairing cartilage.

One of the primary physiological roles of Glucosamine is in the joints, where it stimulates the manufacture of glycosaminoglycans (GAGs) and other

key structural components of cartilage. Glucosamine is now considered an essential substance for maintaining healthy joints.

Studies have shown that Glucosamine and Chondroitin complement each other in inhibiting the production of inflammatory cells.

Knee Arthroscopy



What are the indications?

ORTHOFLEX gel® is a product for viscose supplementation, which is a safe, efficient and well established treatment in osteoarthritis. The treatment consists of injecting a hyaluronic acid and chondroitin sulfate based solution into the affected synovial joint.

ORTHOFLEX gel® acts as a supplement and a temporary replacement for synovial fluid. It protects the cartilage and it treats the pain and the restricted mobility and elasticity that follow traumatic pathology in the knee joint and other synovial joints.

ORTHOFLEX gel® is a solution for joint recovery after arthroscopy. By replacing the synovial fluid post-arthroscopy it will prevent post-operative complications.

It is also indicated for:

- reducing pain after arthroscopy,
- meniscus repair,
- previous crossed ligament reconstruction
- as an auxiliary treatment for patients with osteochondral defects.

What is the treatment?

ORTHOFLEX gel® must be administered strictly intra-articular, twice a year, every 6 months, according to the doctor's recommendations.

Any joint effusion present should be removed by joint aspiration, before injecting **ORTHOFLEX gel®**.

After the injection, an articular rest of approximately 24 hours is recommended (no strenuous exercise), in order to augment the duration of the effect. General rest and applying ice to the injected joint are helpful.

ORTHO
FLEX
TENDON

ORTHO FLEX tendon

INJECTION FOR THE TREATMENT OF TENDON DISORDERS
TREATS PAIN AND RESTORES MOBILITY IN DAMAGED TENDON

Enjoy your life!



DISCOVER
THE NEW INNOVATIVE
TREATMENT FOR TENDINOPATHY

**INJECTABLE
HYALURONIC ACID + MANNITOL**



What is ORTHOFLEX tendon®?

ORTHOFLEX tendon® is used for the treatment of pain and reduced mobility due to tendon disorders.

ORTHOFLEX tendon® will be injected around the affected tendon or into the tendon sheath.

Due to its lubricating and visco-elastic properties, a single injection with **ORTHOFLEX tendon®** provides rapid pain relief, helping restore the regenerative and restorative functions.

ORTHOFLEX tendon® is an injectable solution, presented in a prefilled syringe.

ORTHOFLEX tendon® consists of:

- 40mg/2ml hyaluronic acid, obtained by bio fermentation,
- 10 mg mannitol - a free radical scavenger that helps stabilize the chains of sodium hyaluronate.



What is tendinopathy?

Tendinopathy is a disease of the tendon caused by wear and tear, overuse, or incorrect use of the joints in the body.

Most tendon injuries occur near joints. The most well-known tendons are the Achilles tendon (the largest tendon in the human body, located at the heel), the biceps tendon, the hand tendons, and the elbow tendon.

How does ORTHOFLEX tendon® work?

A tendon is a strong structure of fibrous connective tissue designed to transmit forces from muscle to bone and resist load during muscle contraction.

Overuse and biomechanical stress may cause inflammation and /or degenerative changes of the tendon, leading to pain and loss of function.

Because of its lubricating and viscoelastic properties, **ORTHOFLEX tendon®** promotes tendon gliding and the physiologic repair process. It also reduces pain.

Due to its macromolecular meshwork **ORTHOFLEX tendon®** reduces the free passage of inflammatory cells and molecules and is a good transport medium for nutrients.



What are the indications?

ORTHOFLEX tendon® is used for treating pain and restricted mobility in tendon disorders:

Ankle and foot tendinopathy

- Achilles tendinopathy
- posterior tibial tendinopathy
- peroneal tendinopathy

Shoulder - rotator cuff tendinopathy

Elbow - lateral and medial epicondylalgia

Knee – patellar tendinopathy

How is ORTHOFLEX tendon® administered?

ORTHOFLEX tendon® will be injected around the affected tendon or into the tendon sheath, once a week, 2 injections in total.

Intrasheath injection - in tendon with a sheath - **ORTHOFLEX tendon®** will be injected into the tendon sheath, in the affected area.

Peritendinous injection - in tendon without a sheath - **ORTHOFLEX tendon®** will be injected along the affected tendon, but not in the tendon.

In both cases, **ORTHOFLEX tendon®** will spread throughout the tendon.

Several tendons may be treated at the same time. If symptoms return, the treatment can be repeated.

Ultrasound guidance is recommended during injection, to avoid nerve and blood vessels damage.

Thank you for using **ORTHOFLEX®** to prevent complications, which might lead to surgical interventions and psycho-emotional trauma.

