KioMedine[vs]one composition

- *Primary component: 20mg/ml animal-free KiOmedine® CM Chitosan*
- *Other ingredients: 35mg/ml sorbitol, phosphate-buffered water for injection*
- *Pack contents: pre-filled 3ml sterile glass syringe in blister pack*
- *Indication: one single-shot intraarticular injection for the symptomatic treatment of knee osteoarthritis (OA)*

Performance and duration of effect

- Clinical data from a randomized controlled trial in patients with OA of the knee have shown that a single intraarticular injection of KioMedine[vs]one provided significant improvement in pain, stiffness and functionality up to 6 months.
- In clinical investigation, the safety profile of a repeated injection of KioMedine[vs]one into the knee was not altered after an interval of 3 months.

Dosage and administration

- Remove synovial fluid before injecting KioMedine[vs]one.
- Strict aseptic injection technique should be employed during the administration of KioMedine[vs]one.
- Do not use disinfectants containing quaternary ammonium salts for skin preparation as KioMedine[vs]one may precipitate in their presence.
- Use a luer needle of appropriate size, i.e. 20G to 23G, and suitable length for injecting KioMedine[vs]one.

Contraindications

For intraarticular use only. Do not inject KioMedine[vs]one in patients who have:
- a known allergy or hypersensitivity to any of the product components especially edible mushrooms.
- infections or skin disease at or around the injection site.
- severe inflammation, synovitis or inflammatory arthritis of the knee joint.
- a history of autoimmune and crystal diseases, evidence of lymphatic or venous stasis or serious blood disorders.

Precaution

- To date no data is available on potential interactions of KioMedine[vs]one injected concomitantly with other intraarticular treatments.
- KioMedine[vs]one should not be used in presence of suspicious inflammatory fluid.

Adverse events

- Potential adverse events may occur after intraarticular injections. Injection of KioMedine[vs]one can cause temporary joint pain, joint effusion, joint swelling, joint stiffness, joint warmth, injection site pain or synovitis of the treated joint. Rare cases of acute synovial inflammation characterized by painful effusion of the knee, and possibly low-grade fever, have been reported following an intraarticular injection of KioMedine[vs]one. Analysis of synovial fluid reveals aseptic fluid with no crystals. These local reactions respond well to rest, cold application, oral painkillers, non-steroidal anti-inflammatory drugs (NSAIDs) and/or arthrocentesis, and may not affect the clinical benefit of the treatment.
- Intraarticular infections did not occur in the clinical trial of KioMedine[vs]one.

Information for patients

Before injecting KioMedine[vs]one, please inform your patient about its composition, performance, contraindications and adverse events:
- As a precautionary measure, the patient should avoid any intense physical or excessive weight-bearing activities for 48 hours after the injection of KioMedine[vs]one. The patient should be advised to progressively use the treated knee and perform regular physical exercise.
- Transient local reactions, such as joint pain, effusion, swelling or stiffness, have been reported following the injection of KioMedine[vs]one. These symptoms are common post-injection complications of intraarticular injections in the target population and can be managed with rest, cold application or/and pressure bandage and may not affect the clinical benefit of the treatment.
- When transient local reactions occur, the patient should be advised to take oral painkillers (paracetamol) or NSAID without delay.

For more information, please refer to the instructions for use provided with the package unit and on our website: www.kiomedine-one.com

About KiOmed Pharma

Capitalizing on a history of innovation and expertise in exclusive natural chitosan chemistry, KiOmed Pharma develops a **unique pipeline of medical devices** that addresses unmet medical needs in high-impact pathologies and major social burdens such as **invalidating osteoarthritis, skin aging and ophthalmology**.

For safety concerns and incident reports please contact our medical device vigilance department immediately (e-mail: vigilance-rheumatology@kiomedpharma.com).

References

1. Worldwide exclusive license to produce chitosan from mushrooms, for applications in medicine/pharmaceuticals: patent family WO03/068824.
2. Patent claiming KiOmedine® chitosan derivatives and products for various clinical indications, filed by KiOmed: WO2019/105719.
3. Douette P, Chausson M, Théatre E, Hermitte L. Biological evaluation of KIO014 for viscosupplementation - E-DND-KIO014-TD017, Sept 2019.
4. Rocasalbas G, Chausson M, Hermitte L. Intended action assessment of KIO014- Verification of non-clinical performance - E-DND-KIO014-TD013, April 2020.
5. ABTS assay: Miller NJ, Rice-Evans C, Davies MJ A new method for measuring antioxidant activity. Biochem Soc Trans 1 May 1993; 21(2):95S. PMID: 8359548.
6. Bentin J, Emans P, Skaliczki G, Haverkamp D, A single injection of animal-free CA-Chitosan provides long-lasting reduction of osteoarthritic symptoms - The APROOVE clinical study. Poster WCO-ESCEO 2020.

Product code: UDI-DI : 05404023514004

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V03-2021-06

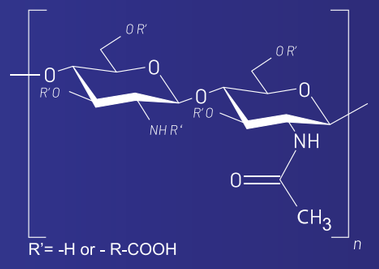
Unique soft implant

FOR SUSTAINABLE OSTEOARTHRITIS PAIN RELIEF AND OUTSTANDING RESPONSE RATE

KioMedine vs one

UNIQUE SOFT IMPLANT FOR OSTEOARTHRITIS TREATMENT

KioMedine[vs]one is the new generation single shot injection intended for the symptomatic treatment of knee osteoarthritis based on world-first exclusive animal-free **KiOmedine® CM Chitosan**.



R'= -H or - R-COOH

KiOmedine® CM Chitosan is a patented technology[1,2] made in Belgium, resulting from years of research and innovation. Thanks to a **unique structure** that differs from hyaluronic acid and natural chitosan, **KioMedine[vs]one** has an exclusive dual mechanism of action to tackle OA pain and other symptoms.

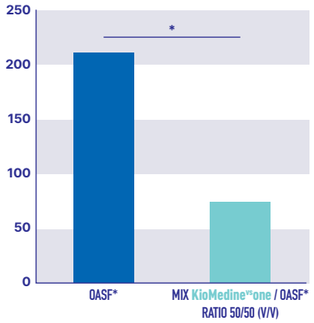
Scientific evidence for improved lubrication and high free radical scavenging

Enhancement of lubrication and mobility[4]

Lubrication capacity demonstrated by a low coefficient of friction (COF) and knee mobility recovery after a lesion assessed using both *in vitro* and *ex vivo* models.

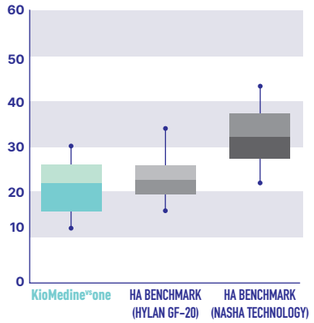
Thanks to its lubrication properties, **KioMedine[vs]one** offers improved joint friction reduction and provides better knee mobility with long-lasting relief[6].

COEFFICIENT OF FRICTION
KioMedine[vs]one VS OASF

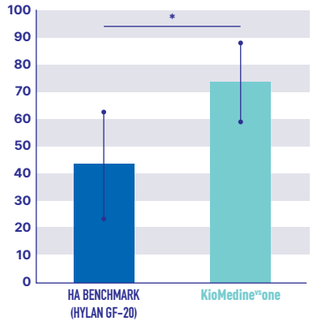


** Synovial Fluid from OsteoArthritis patient*

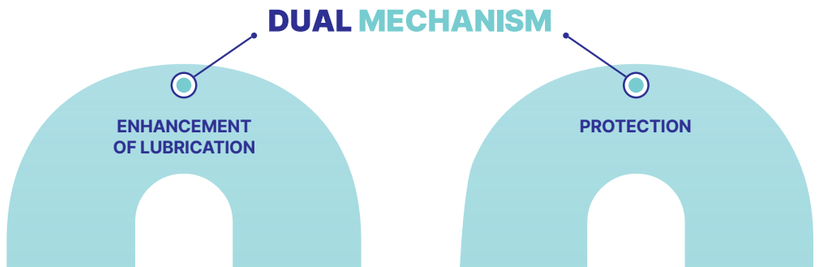
COEFFICIENT OF FRICTION
KioMedine[vs]one VS COMPETITION



% KNEE MOBILITY RECOVERY OF INJURED KNEE IN THE SHEEP MODEL



DUAL MECHANISM



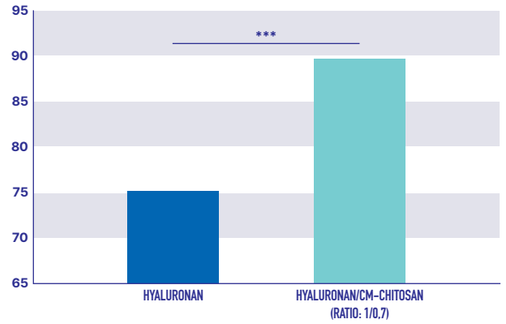
Scavenging property[5]

As a natural free radical scavenger, **KioMedine[vs]one** shows an unprecedented free radical scavenging capacity, which protects the endogenous hyaluronic acid in synovial fluid. This protection can slow down the irreversible degradation caused by oxidative stress, which occurs naturally during the development of OA.

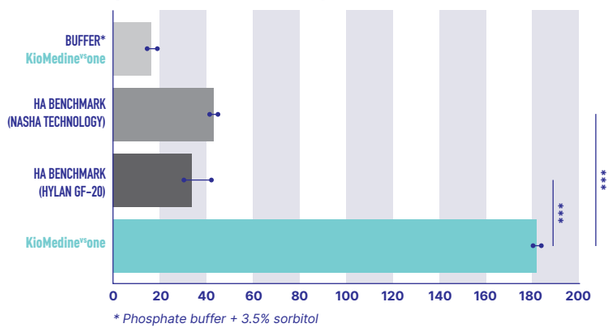
KioMedine[vs]one contributes significantly to the protection of endogenous synovial components and has a **scavenging capacity** that is roughly **five times higher** (*in vitro*) than that of existing HA technologies. This is potentially linked to specific interactions and the attraction between CM-chitosan molecules and Reactive Oxygen Species (ROS).

Furthermore, **KiOmedine® CM Chitosan** has enabled the development of a resorbable implant with unique **degradation resistance and up to 1-month** joint residence time with **no need for crosslinking[3,5]**.

% REMAINING MOLECULAR WEIGHT OF HYALURONAN PLACED 24H IN AN OXIDATIVE ENVIRONMENT



FREE RADICAL SCAVENGING CAPACITY (IN EQUIVALENT OF TROLOX)



** Phosphate buffer + 3.5% sorbitol*

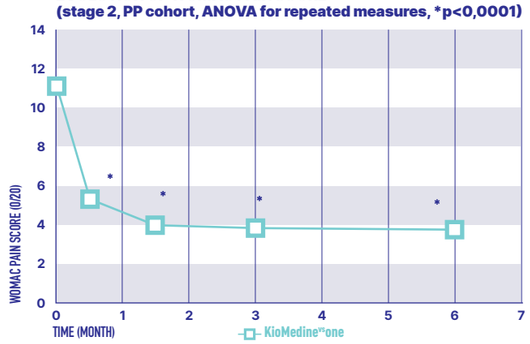
Proven safety and effectiveness in OA knee pain reduction after a single injection of **KioMedine[vs]one**

In a randomized single-blind APROOVE clinical trial, the safety and efficacy of a single shot of **KioMedine[vs]one** have been proven after injection in 70 patients[6].

No serious or unexpected adverse events or patient withdrawals related to the safety of the treatment were reported. Treatment Related Adverse Events (TRAEs) were transient post-injection local effects that are commonly observed after IA injection of single shot products and were consistent in nature (e.g. pain, swelling), intensity and incidence with effects reported after injection of crosslinked HA-based products[o].

Reference	APROOVE - stage 2 (63 patients)
Arthralgia	**25.4%(16)**
Joint effusion	**6.3% (4)**
Joint swelling	**6.3% (4)**
Musculoskeletal stiffness	**/**
Synovitis/Arthritis	**4.8% (3)**

EVOLUTION OF WOMAC PAIN SCORE
(stage 2, PP cohort, ANOVA for repeated measures, *p<0,0001)



Effective up to **6 months**

Sustainable **OA pain relief**

Outstanding **response rate**

Treatment response up to **76%**

66% reduction in WOMAC PAIN

86% of patient satisfied

90% of physicians satisfied

[o]For more information about adverse events and contraindications, please refer to the instructions for use provided with the package unit and available on our website