HYAJOINT Plus® a safe and efficient solution for knee OA[1,2,3]

one INJECTION

UP TO 6 MONTHS

non ANIMAL

- Long-lasting relief of symptomatic knee OA pain for up to 6 months[2,3]
- Carefully controlled cross-linking[2,3]
- High molecular weight[2]
- Non-animal sourced[1]
- Prolonged degradation time[2,3]

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HYAJOINT Plus®

HYAJOINT Plus® description:

Product code	Active ingredient	Treatment	Package
HYAJOINT Plus®	Sodium hyaluronate 60mg	One-single injection per treatment for adult into the OA joint	3mL x 1 syringe

*This product is a class III medical device. CE marked (Notified body n°2797) in accordance with the rules and regulation in effect.

HYAJOINT Plus® provides pain relief and improves function in patients with knee osteoarthritis for up to 6 months. HYAJOINT Plus® is administered using 1 syringe per treatment directly into the osteoarthritic (OA) joint[1]. The product is injected into the articular cavity of the joint. It must be administered by authorized personnel in accordance with local legislation.
Treatment is contraindicated in cases of past and present infections or skin diseases in the area of the injection site. Do not administer to patients with known hypersensitivity to hyaluronate preparations.
Major side effects are pain, swelling and stiffness localized to the treated joint.
For more information please read the instructions for use[1].

For more information, visit our dedicated HYAJOINT Plus® website:
HP.Macopharma

References
1. Instruction for use HYAJOINT Plus®
2. Tuan S., Liou I., Su H., Tsai Y., Chen G. and Sun S._Improvement of self-reported functional scores and thickening of quadriceps and femoral intercondylar cartilage under ultrasonography after single intra-articular injection of a novel cross-linked hyaluronic acid in the treatment of the knee osteoarthritis. JBMR._2018 ; 31 : 709-718
3. Sun, S.-F., Hsu, C.-W., Lin, H.-S., Liou I.-H., Chen, Y.-H. and Hung C.-L._Comparison of Single Intra-Articular Injection of Novel Hyaluronan (HYA-JOINT Plus) with Synvisc-One for Knee Osteoarthritis. JBJS._2017 ; 99(6) : 462-471

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HYAJOINT Plus® is not available for sale in all countries. Please contact your local sales person/ distributor or Macopharma to enquire about product's availability in your country.

For safety concerns and adverse events reports, please contact our medical device vigilance department, immediately.
E-mail: **cellule.materiovigilance@Macopharma.com**

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HYAJOINT Plus®

Dispel knee pain and improve mobility with a single injection[1,2,3]

SciVision BIOTECH INC.

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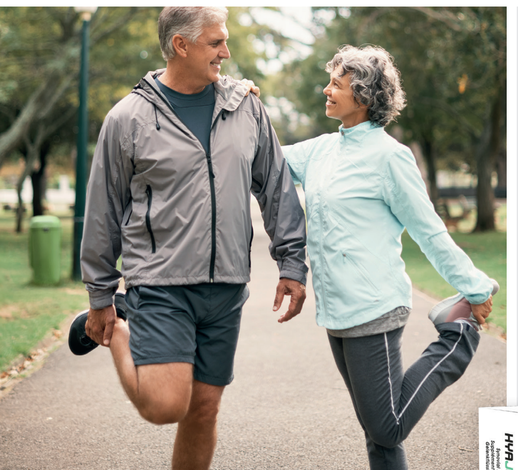
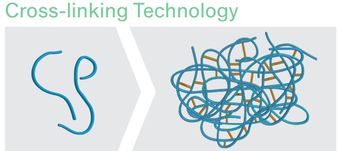
HYAJOINT Plus®: a unique CHAP™ technology*



HYAJOINT Plus® is a safe and efficient viscosupplement that reduces pain and improves mobility in osteoarthritic knee[1,2,3].

HYAJOINT Plus® is a synovial fluid supplement made of hyaluronic acid produced by microbial fermentation synthesized by a novel cross-linking process using 1,4-butanediol diglycidyl ether (BDDE) to create an anti-degradation feature. The patented CHAP™ (Crosslinked Hyaluronic Acid Platform) process prolongs the degradation time by carefully transforming linear hyaluronic acid to cross-linked hyaluronic acid and thus increasing the molecular weight. This cross-linking technology enables the creation of a **viscous gel with increased density** (2% HA, 20mg/mL)[2,3].

Cross-linking Technology



Linear hyaluronic acid before cross-linking.

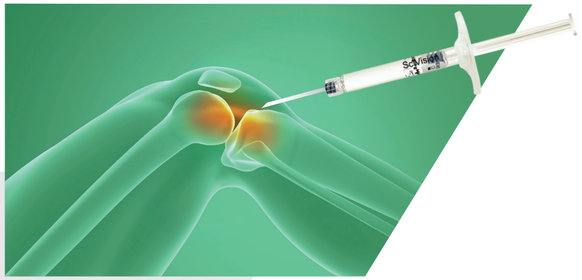
Cross-Linking technology with less BDDE, minimizing the amount of BDDE residue.

Based on the CHAP™ cross-linking technology, no purification of the cross-linked hyaluronic acid is required avoiding washing step that decreases hyaluronic acid lubrication*.

CHAP™ cross-linking technology gives HYAJOINT Plus® a high molecular weight of more than 15MDa. The carefully controlled cross-linked hyaluronic acid increases the viscoelastic properties of the synovial fluid reducing pain and restoring knee joint mobility[2,3].

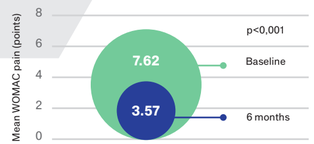
HYAJOINT Plus® is a non-animal sourced hyaluronic acid produced by microbial fermentation, thus eliminating potential risks associated with allergies to avian proteins[2].

*For more information, please consult the available patent

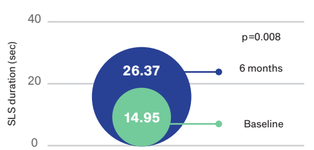


HYAJOINT Plus®, a long term treatment for symptomatic osteoarthritis with a single injection for pain relief and restoring mobility[2].

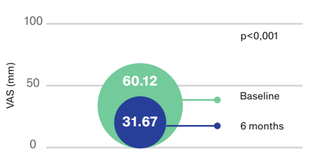
In a prospective study[2], HYAJOINT Plus® relieved pain in patients with symptomatic knee OA for up to 6 months following a single course treatment[2]. HYAJOINT Plus® is both safe and effective for the treatment of knee OA.



The values of WOMAC pain score (points) are given as the mean ± standard deviation (7.62±0.49 and 3.57 ±0.40 at baseline and 6 months respectivley) in 46 patients assessed using a Bonferroni post-hoc test. Adapted from Tuan et al, 2018.



The values of SLS duration (sec) are given as the mean ± standard deviation (14.95±2.97 and 26.37±3.83 at baseline and 6 months respectivley) in 46 patients assessed using a Bonferroni post-hoc test. Adapted from Tuan et al, 2018.



The values of VAS score (mm) are given as the mean ± standard deviation (60.12±2.31 and 31.67±25.02 at baseline and 6 months respectivley) in 46 patients assessed using repeated measures one-way ANOVA and a Bonferroni post-hoc test. Adapted from Tuan et al, 2018.

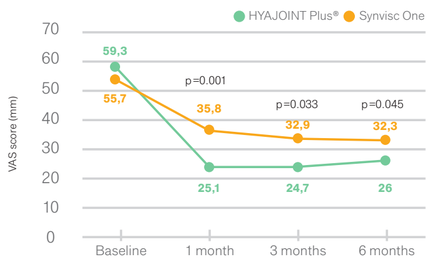
In this prospective study with a 6-month follow-up, 49 patients (both genders, aged 40-85 years) with knee OA (Kellgren-Lawrence grade 2 or 3) received a single intra-articular injection of 3mL of HYAJOINT Plus®, Three patients did non return for follow-up visits[2].

- 6 months after injection of HYAJOINT Plus®, the WOMAC pain score (Western Ontario and McMaster Universities Osteoarthritis Index) was significantly reduced compared to the baseline (from 7.62 to 3.57; p<0.001).
- The Single Leg Stance (SLS) duration was significantly improved at 6 months after HYAJOINT Plus® injection compared to the baseline (from 14.95 to 26.37 sec; p=0.008).
- The mean VAS decreased by 28.45 mm from baseline at 6-month follow-up (from 60.12 to 31.67mm; p<0.001).
- Safety data: No infections, allergies or other serious adverse effects were reported. Five subjects developed joint pain without inflammatory signs and 1 patient developed mild and painful effusion which spontaneously subsided 9 days later.
- The limitations of this study are the absence of control group, the patients were recruited from a single medical center thus results could not be generalized to all knee OA population and even if all measurements of femoral intercondylar cartilage were done by the same physician there might still be some biases that could not be controlled. Following this study a double-blinded randomized controlled study with larger sample sizes has been designed.

Effectiveness of HYAJOINT Plus® in a prospective, randomized, controlled, double-blind trial of Safety and Efficacy[3].

In a prospective, randomized, controlled, double-blinded study with a 6 month follow-up, 132 patients (both genders, aged 40-85 years) with knee osteoarthritis (Kellgren-Lawrence grade 2 or 3) were randomized to 2 groups. One group (n=66) received one intra-articular knee injection of 3mL of HYAJOINT Plus® (20mg/mL) and the second group (n=66) 6 mL of Synvisc-One® (8mg/mL). Eleven patients did not return for follow-up visits, leaving 121 patients available for the intention to treat analysis at the 6-month follow-up evaluation.

None of these 11 patients reported an adverse event. Both groups (n=66 and n= 66 respectively) had a significant improvement in the VAS, WOMAC and Lesquene index scores. A single injection of either HYA-JOINT Plus® or Synvisc-One® is safe and effective for 6 months in patients with knee osteoarthritis. HYA-JOINT Plus® is superior to Synvisc-One® in terms of reducing the VAS pain score at 1, 3, and 6 months and the WOMAC stiffness score at 6 months, with similar safety. Level of Evidence: Therapeutic **Level I.**[3]



The values of VAS score (mm) are given as the mean ± standard deviation (59.3±15.8; 25.1±18.4; 24.7±19.0; 26.0±15.6 for HYAJOINT Plus® and 55.7 ± 16.4; 35.8±22.1; 32.9±24.0; 32.3±19.6 for Synvisc One® at baseline, 1, 3 and 6 months respectivley) in 66 patients for each group. Between-group difference determined using independant-samples 1-way ANCOVA. Within-group difference using repeated-measures 1-way ANOVA. Adapted from Sun SF et al, 2017.

- Better improvement of pain relief by 33.3 mm on VAS score in patients treated with HYAJOINT Plus® compared to 23.4 mm in the Synvisc-One® group at 6 months (mean difference between groups -6.6; p=0.045)[3].
- Safety data: The frequencies and types of adverse events were comparable between Synvisc-One® and HYA-JOINT Plus® groups. The majority of adverse events were mild or moderate, lasted 1 to 3 days, and resolved spontaneously or responded well to simple analgesics. The adverse events reported in each group were joint pain, joint swelling, joint stiffness, limb weakness, back pain.
  Twelve patients (9 treated with Synvisc-One® and 3 treated with HYAJOINT Plus®) developed joint effusion within 1 week after the injection, all infections resolved except for 2 patients treated with Synvisc-One® who required arthrocentesis for pain relief. No allergies, pseudosepsis or serious adverse events occurred during the study in either group[3].
- The limitations of this study are the absence of placebo group, the patients were recruited from a single medical center thus results could not be generalized to all knee OA population, packaging of the products were different and the injections could not be blinded. Finally the dosage and volume of intra-articular hyaluronan formulations could have an effect on outcomes.