

Condrotide

**POLYNUCLEOTIDES HPT™
FOR OA TREATMENT**



Mastelli
At the origin of regeneration

From Mastelli's R&D

High Purification Technology HPT™



Mastelli has a strong commitment in experiment, expand, and spread polynucleotides' potential through safe and innovative products

PN HPT™ are the only commercially available polynucleotides for intra-articular injections

Mastelli operates in line with the highest **Good Manufacturing Practice** and **Quality Assurance** standards

POLYNUCLEOTIDES HPT™ PRODUCTION

The exclusive Mastelli's PN HPT™ process:

1

ORIGIN

- The whole process, from breeding to processing of Salmon Trouts, is carried out in a Certified European Factory

2

EXTRACTION

From the fish farm to the active ingredients:

- Impurities removal
- Polynucleotides production

3

PURIFICATION

- Polynucleotides purity analysis and release

4

MANUFACTURING (Class III Medical Device)

From Polynucleotides to Condrotide:

- Sterilization
- Quality Assurance analysis
- Packaging
- Warehouse
- Commercialization

Condrotide

WHAT IS CONDROTIDE?

Condrotide is a **Class III Medical Device** for **intra-articular use** consisting of a **viscoelastic solution** containing **Polynucleotides HPT™**

WHAT ARE PN HPT™?

PN HPT™ are DNA fractions formed by the condensation reaction of monomers called deoxyribonucleotides

WHICH ARE THE PROPERTIES OF PN HPT™?

The high degree of hydrophilicity conferred by the chemical structure of PN HPTs makes them capable of:

- binding a large amount of H₂O
- orienting them to form a 3D-gel

How it works?
Condrotide displays a double-edge action for complete joint effectiveness:

1 INITIAL BIOMECHANICAL ACTION ^[1]

- Deep hydration of articular surfaces ^[1]
- Improvement of the synovial fluid rheological properties ^[1]
- Restoring the joint mechanical dynamics ^[1]

2 RECOVERY OF JOINT PHYSIOLOGY

- Replenish the synovial fluid with energy substrates for articular cartilage through physiological degradation of PN HPT™ ^[2]
- Provide a microenvironment similar to the physiological condition of healthy articular cartilage ^[2]
- Improve joint functionality and reduces painful symptoms ^[3]

The **combination** of the **initial biomechanical action** and of the **recovery of joint physiology** makes **Condrotide** a **powerful choice** for patients suffering from the chronic or post-traumatic pain associated with **OA**

Condrotide Scientific Evidences

Protective effects of polynucleotides on cartilage degradation in experimental cultures^[2]

PN HPT™ effect on cartilage degradation in vitro and on cartilage extracted cells was investigated.

A microenvironment capable of inducing cartilage to resume normal physiological function was developed and recreated.

Evaluation of the treatment effect with:

- Polynucleotides HPT™
- Hyaluronic acid (HA)
- Control

RESULTS^[2]:

- A significantly higher cell survival in all biopsies treated with PN HPT™ vs. those treated with HA (Figure 1A)
- Treatment with PN HPT™ increases Type II Collagen and Aggrecan production, compared to the solely administration of Hyaluronic Acid (Figure 1B)
- Human cartilage explants cultered with PN HPT™ displayed eutrophic state of healthy normal cartilage

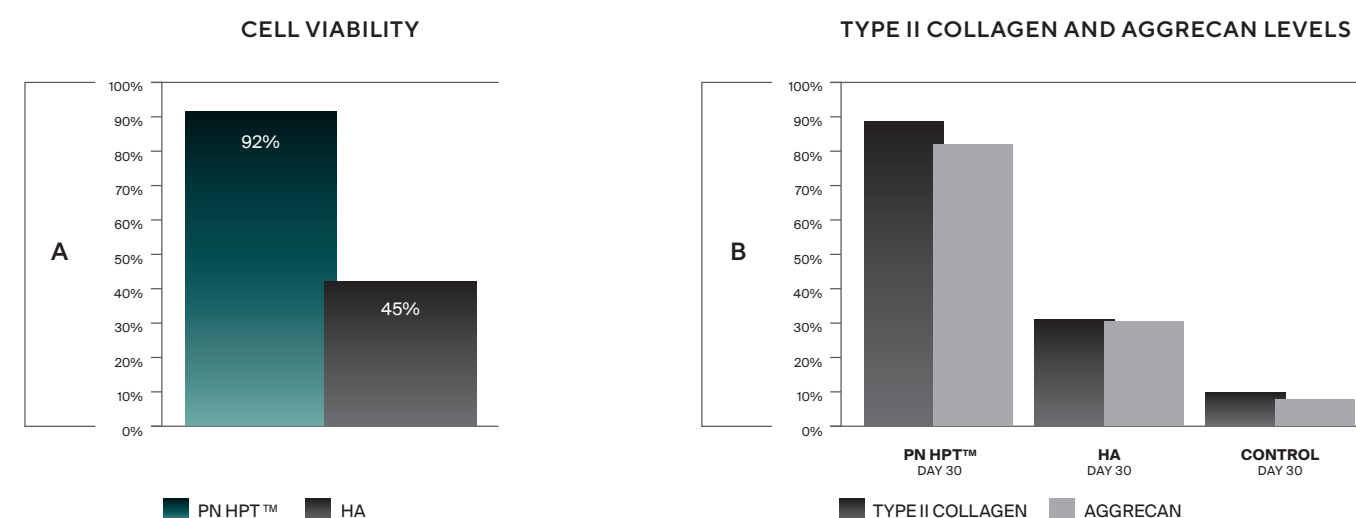


Figure 1. (A) Cell viability assay of biopsy-derived cells 30 days after treatment with PN HPT™ vs. HA (*p<0.001)

Figure 1. (B) Percent (%) Type II Collagen and Aggrecan levels 30 days after treatment with PN HPT™, HA, and Control

Condrotide

SLOW-ACTING PRODUCT for **OA** with a clinically proven effects on:

- Pain Control
- Cut of NSAIDs Consumption
- Joint Mobility and QoL Improvement
- Resumption of Sporting Activity



1 PAIN CONTROL [1, 4, 5, 6, 7]

Patients treated with Condrotide display a rapid and vigorous pain control with an earlier and longer response compared to **Linear HA** administration^[1]

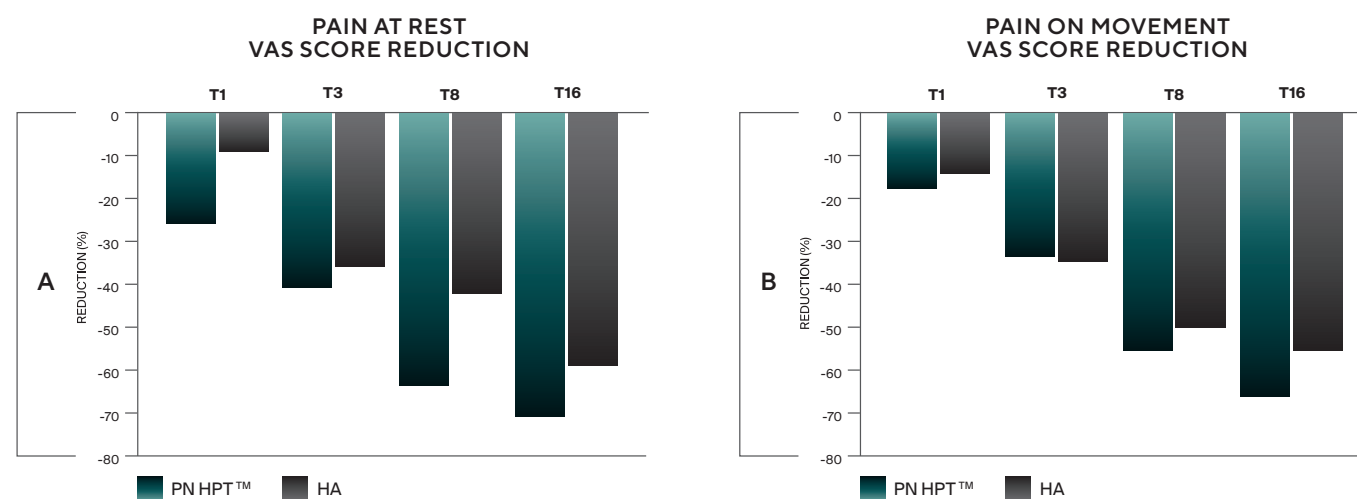


Figure 2. (A) Pain at rest VAS scores reduction for PN HPT™-treated patients and HA-treated patients from T1 to T16 (16 weeks after the first injection) (Adapted from^[1])

Figure 2. (B) Pain on movement VAS scores reduction for PN HPT™ -treated patients and HA-treated patients from T1 to T16 (16 weeks after the first injection) (Adapted from^[1])

2 CUT OF NSAIDs CONSUMPTION [1, 4, 6]

Condrotide-treated patients show a significant reduction in NSAID consumption, with a faster response than HA-treated patients, decreasing gastrointestinal and cardiovascular risks due to NSAID administration

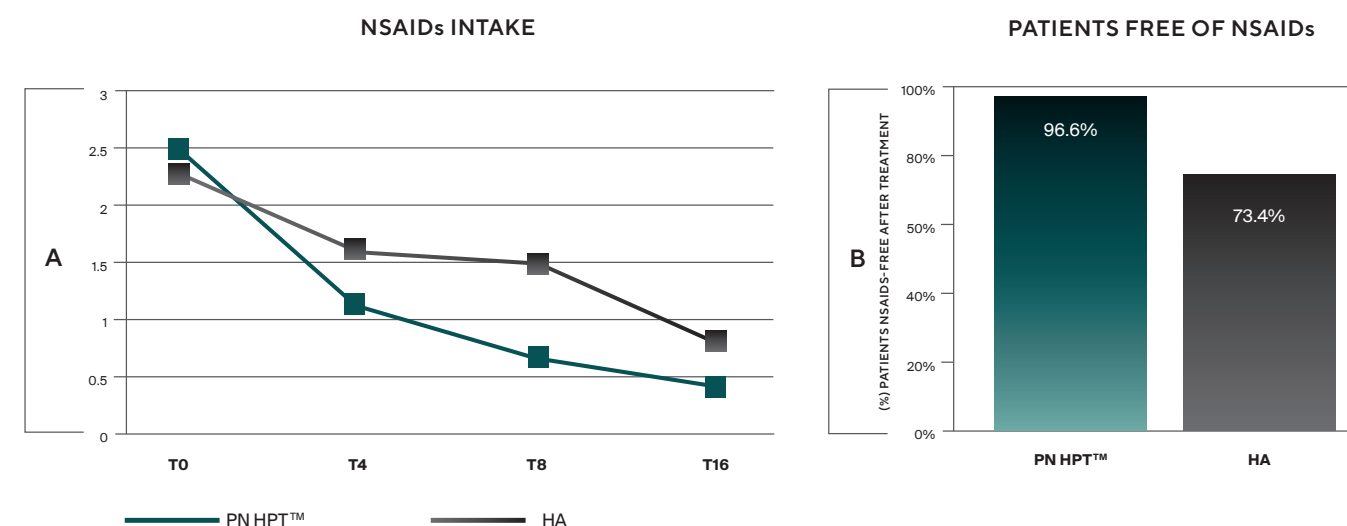


Figure 3. (A) NSAIDs consumption expressed as number of days of the week before the visit in which anti-inflammatory drugs were used. Final results show a minor use of NSAIDs in PN HPT™ group when compared to HA group from T1 to T16, mainly evident at T4 and T8. (Adapted from^[1,6])

Figure 3. (B) Percentage of NSAIDs-free patients after treatment with PN HPT™ vs. HA at T16 (Adapted from^[1])

3 JOINT MOBILITY [1, 8, 9] and QoL [1, 4, 7] IMPROVEMENT

Condrotide enhances daily living activities and quality of life (QoL) with an earlier clinical benefit than linear HA. PN HPT™’s overall efficacy in terms of pain reduction is comparable to High Molecular Weight HA and PRP, and better than Low Molecular Weight HA

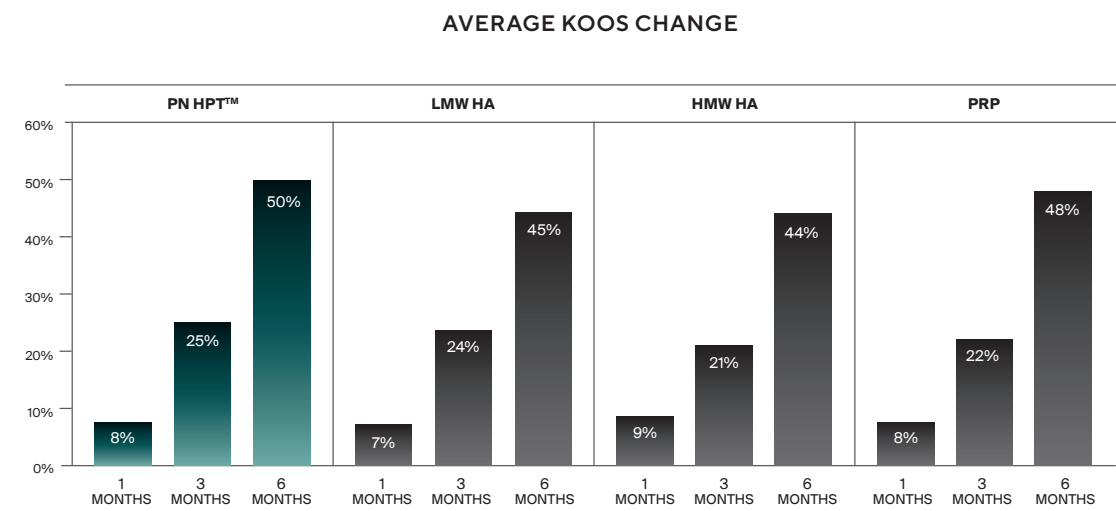


Figure 4. Average Knee Injury and Osteoarthritis Outcome Score (KOOS) showed a comparable efficacy of PN HPT™, PRP, Low (LMW HA), and High Molecular Weight Hyaluronic Acid (HMW HA), whereas with slightly efficiency of PN HPT™ vs other treatments (Adapted from[7])

4 RESUMPTION OF SPORTING ACTIVITY [1, 10]

Condrotide-treated patients display a faster return to sporting activity and physical exercise when compared to HA-treated patients [1,4,8]

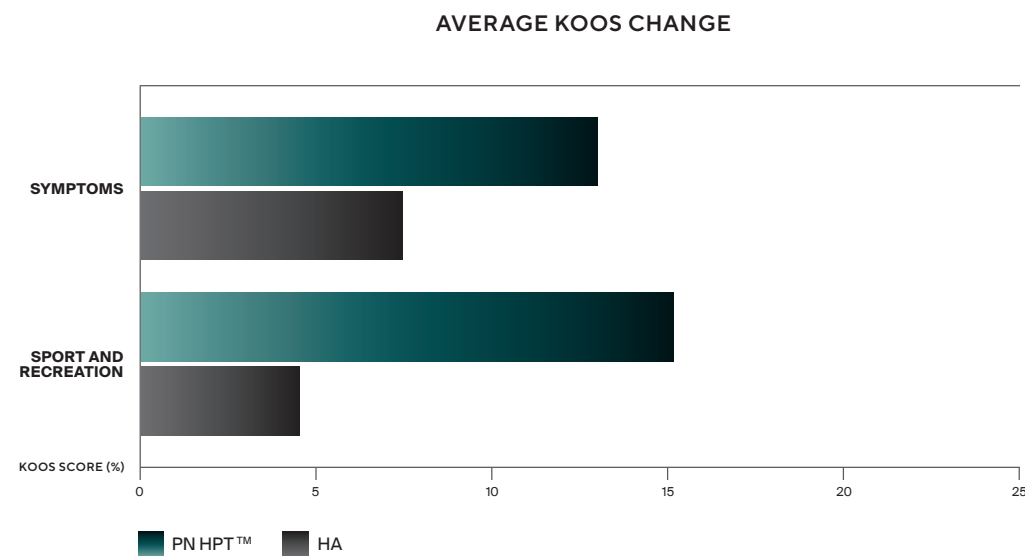


Figure 5. Mean KOOS scores subscales (Symptoms, Sport/Recreation) show a higher improvement in patients treated with PN HPT™ vs. HA after 16 weeks as compared to baseline



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WHAT IS CONDROTIDE?

Condrotide is a Class III Medical Device for intra-articular use consisting of a viscoelastic solution containing **Polynucleotides HPT™**

TREATMENT GOAL:

Condrotide is recommended for painful joint diseases caused by degenerative or post- traumatic conditions and by modification of a joint^[3]

PATIENT TYPE

- Patients with **OA grade I-II** Kellgren-Lawrence Scale
- **Competitive** and **amateur athletes**
- **Subjects with post-traumatic OA**
- Subjects with **concomitant comorbidities**

Technical data

Composition: **Polynucleotides HPT™**
40mg/2ml

Pack: Luer Lock 2ml non-pyrogenic pre-filled glass syringe

Instruction for use

Condrotide must be administered by intra-articular injection into the articular cavity using a sterile needle (18-22 G), usually 20G

Treatment protocol

3 injections of 2ml in the joint to be treated. The time interval between each injection is 1-3 weeks

Safety

- High degree of safety and clinical tolerability^[4,5,6,7]
- Safety tests performed on Raw Materials and finished product
- Totally resorbable



Mastelli fights doping in all sports
Condrotide is a PLAY SURE DOPING FREE certified product



Made in Sanremo

Italy

Condrotide

● **EXCLUSIVE MASTELLI'S HPT™ PROCESS**

● **HIGH DEGREE OF SAFETY
& TOLERABILITY** [4,5,6,7]

● **DOUBLE-EDGE ACTION:**
Biomechanical Action & Recovery
of Joint Physiology [1,2]

● **PAIN CONTROL
& REDUCTION** [1,4,5,6,7]

● **MAXIMIZE SPORTS RECOVERY** [1,10]

● **QoL IMPROVEMENT** [1,4,7]

● **REGAIN MOBILITY** [1,8,9]

● **CUT OF NSAIDs
CONSUMPTION** [1,4,6]



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