

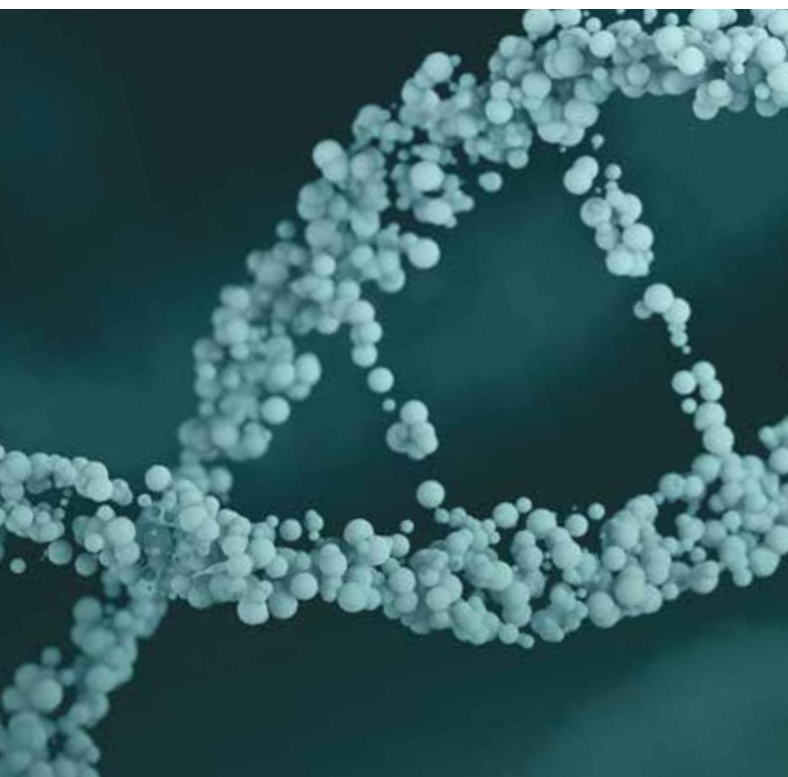
# OSTEOARTICULAR HEALTH LINE

AN INNOVATIVE RANGE OF  
POLYNUCLEOTIDES HPT™ BASED  
PRODUCTS FOR JOINT TREATMENT



**Mastelli**  
At the origin of regeneration

# Mastelli: Polynucleotides Originator since 1952



## MORE THAN 70 YEARS

**Mastelli** is an Italian bio-pharmaceutical company operating in **regenerative medicine** since **1952**

More than 70 Years of **Tradition, Research,** and **Innovation** led Mastelli to be the **Originator** of **Polynucleotides**, organic molecules that boost the ability of human tissues to regenerate

## EVIDENCE-BASED APPROACH

Our **know-how** is backed by more than **100 scientific publications** and is constantly developed in a **cutting-edge R&D department**

## THERAPEUTIC AREAS OF EXPERTISE

**Mastelli** has developed over the years a **wide range of solutions** that integrate different technologies, offering innovative protocols in several therapeutic areas:

- **OSTEOARTICULAR HEALTH**
- **WOUND CARE**
- **AESTHETIC MEDICINE**
- **GYNECOLOGY**
- **DERMATOLOGY**

## FULLY INTEGRATED SUPPLY-CHAIN

**100% in-house handled**, from raw material purification to the finished product, ensuring transparency and safety through our exclusive **High Purification Technology HPT™**

## INTERNATIONAL EXPORT

We are committed in spreading **Polynucleotides HPT™** potential in **over 30 countries** around the world



From Mastelli's R&D

# High Purification Technology HPT™



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

Polynucleotides HPT™ are the first registered PN-based medical device for intra-articular injections

## 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 Devices)

From Polynucleotides to Mastelli's osteoarticular product range:

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



# Polynucleotides HPT™ in Osteoarticular Health

PN HPT™ are polymers of deoxyribonucleotides (DNA fractions) with 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]

## PN HPT™ IN VITRO STUDIES

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

An in vitro study investigated the effect of **PN HPT™** on cartilage degradation, in vitro, and on cartilage extracted cells. A microenvironment capable of inducing cartilage to resume normal physiological function was developed and recreated. Evaluation of the effect of treatment with:

- **Polynucleotides HPT™** (PN HPT™), vs HA, vs Control

### RESULTS [2]:

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

# The alternative to Hyaluronic Acid based treatment

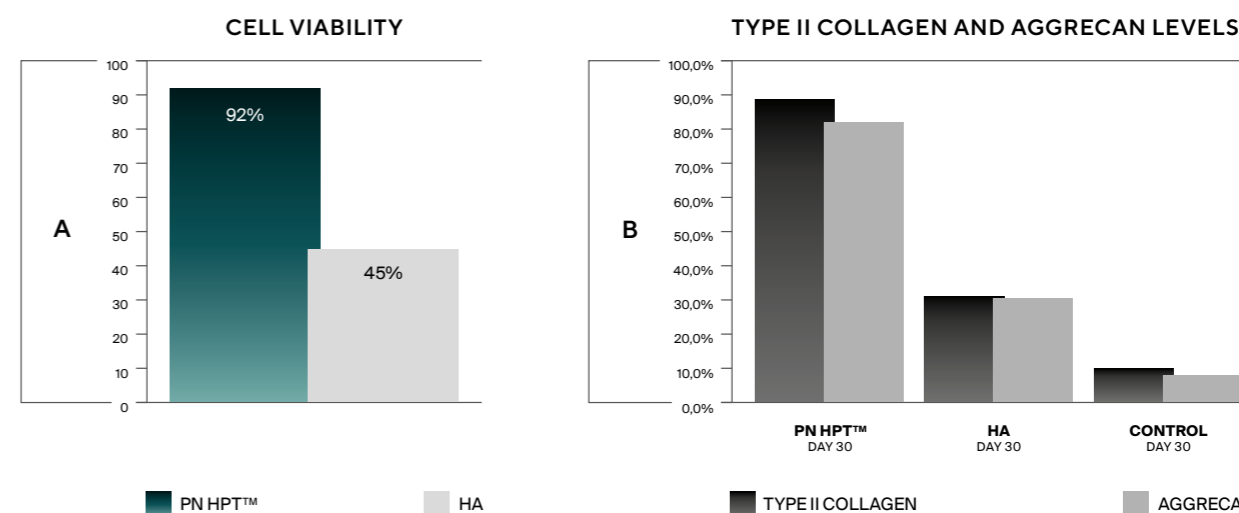


Figure 1. (A) Cell viability assay of biopsy-derived cells 30 days after treatment with PN HPT™ vs. HA  
Figure 1. (B) Percent (%) Type II Collagen and Aggrecan levels 30 days after treatment with PN HPT™, HA, and Control

## PN HPT™ Advantages

- Restoration of the typical physiological microenvironment of the intact cartilage [2]
- Recovery of atrophic tissues [2]
- Direct action on chondrocytes with persistent cell survival and consistent cell apoptosis reduction [2]
- Increased deposition of extracellular matrix, particularly Aggrecan and Type II Collagen [2]
- Reduced degradation of proteoglycans (GAGs) in cartilage explants [2]

# Condrotide


## 2ml

Polynucleotides HPT™ gel for intra-articular injection

### TREATMENT GOAL

**Condrotide** is a viscoelastic solution containing Polynucleotides HPT™ 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 \***
- **Competitive and amateur athletes** 
- **Younger subjects with post-traumatic OA**
- Subjects with **concomitant comorbidities**

**Condrotide** has a **dual beneficial action** at the level of joints:

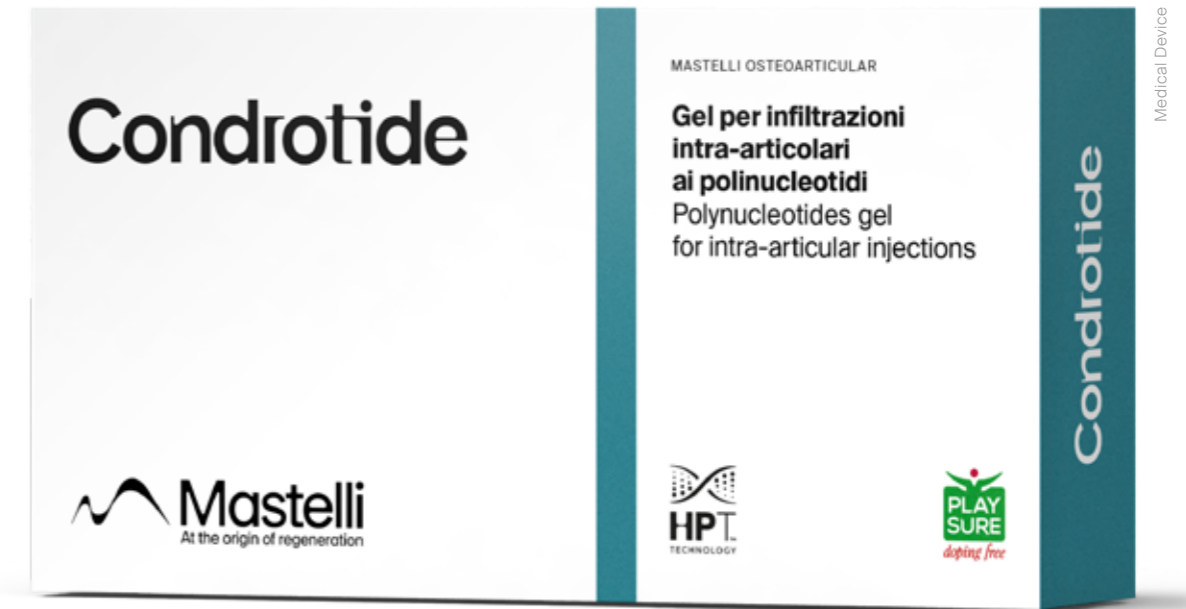
#### 1 INITIAL BIOMECHANICAL ACTION [1]

#### 2 RECOVERY OF JOINT PHYSIOLOGY

**Condrotide** is a “**SLOW-ACTING PRODUCT**” and “**DISEASE MODIFYING-PRODUCT**” for OA with a clinically proven effects on:

- **PAIN CONTROL** [4,5,6]: Display a rapid and vigorous pain control with an earlier and longer response compared with HA [1]
- **CUT OF NSAIDs CONSUMPTION & CARDIOVASCULAR RISK**: Less NSAIDs consumption in PN HPT™ over HA treated patients [1] reducing gastrointestinal and cardiovascular risks related to the consumption of NSAIDs
- **QUALITY OF LIFE IMPROVEMENT** [1, 4]
- **ENHANCEMENT OF JOINT MOBILITY** [1, 5, 7]
- **RESUMPTION OF SPORTING ACTIVITY**: Faster compared with HA [1, 8]

(\*) Kellgren-Lawrence scale



### Technical data [3]

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

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

### Instruction for use [3]

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

### Treatment protocol [3]

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 absorbable



**Mastelli fights doping in all sports**

**Condrotide is a PLAY SURE DOPING FREE certified product**

 Mastelli

Made in Sanremo

Italy



# Condrotide HA

## 2.5ml

Polynucleotides HPT™, Linear Hyaluronic Acid, and Mannitol

### TREATMENT GOAL

Condrotide HA is a fluid gel for intra-articular injections recommended for painful joint diseases caused by degenerative or post-traumatic conditions or by modification of a joint [9]

### PATIENT TYPE

- Patients with **OA grade II-III\***
- **Elder patients with concomitant disorders**
- Conservative approach to **postpone surgical procedures**

Condrotide HA provides a **unique threefold action** in osteoarthritis-affected joints with **persistent pain**:

#### 1 POLYNUCLEOTIDES HPT™

Recovery of physiology and antalgic effect on the joints [2]:

- Replenish energy substrates to synovial fluid, providing similar condition of healthy articular cartilage [2]
- Maximize joint functionality [2]
- Reduce painful symptoms [4,10,11]

Deep moisturization of the articular surface [1]:

- Provide a viscous protective film that improves the rheological characteristics of synovial fluid
- Restores joint mechanical properties

#### 2 LINEAR HYALURONIC ACID

Viscosupplementation:

- Restores the rheological and viscoelastic properties of synovial fluid providing an increased lubrication of the joints [9,11]

Viscoinduction:

- Performs a biological action on articular chondrocytes and synoviocytes, stimulating the endogenous production of hyaluronic acid [11]

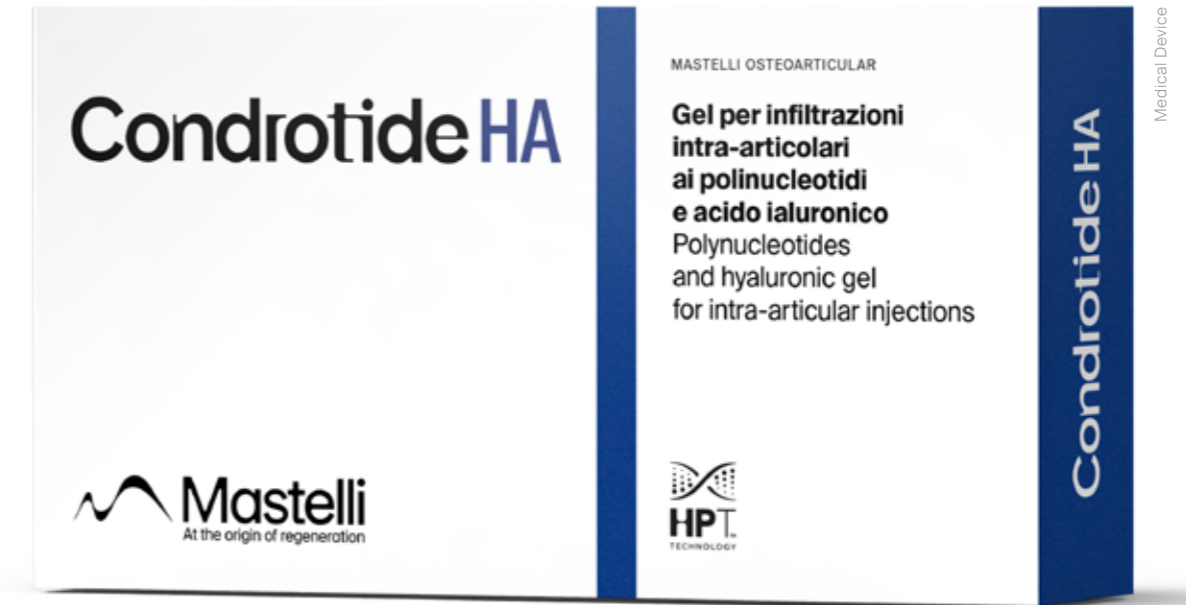
#### 3 MANNITOL

- Maximize the linear HA action over time [12]
- Minimizes HA degradation at the joint level by 34% [13]

Clinically proven effects on: [1, 14]

- **PAIN RELIEF:** display a constant and significant pain reduction with an earlier and longer response over the 2-years follow-up compared with HA
- **JOINT FUNCTIONALITY AND MOBILITY:** enhanced improvement in articular functionality compared with a HA
- **QUALITY OF LIFE IMPROVEMENT**

(\*) Kellgren-Lawrence scale



### Technical data [9]

**Composition:** Polynucleotides HPT™ 25mg/2.5ml  
Linear Hyaluronic Acid 25mg/2.5ml  
Mannitol

**Pack:** Luer-Lock 2.5ml non-pyrogenic pre-filled glass syringe

### Treatment protocol [9]

3 injections of 2.5ml in the joint to be treated.  
The time interval between each injection is 1-3 weeks

### Instruction for use [9]

Condrotide HA must be administered by injecting the solution in the intra-articular space with a sterile needle whose Gauge varies between 18G and 22G, usually being 20G

### Safety

- High degree of safety and clinical tolerability [10,14]
- Safety tests performed on Raw Materials and finished product
- Totally absorbable

# Condrotide

## MOVEO


**Nucleotide-enriched** oral chondroprotector for osteoarticular health

### TREATMENT GOAL

**Condrotide Moveo** is suggested to protect and help maintaining articular, tendons, and muscle functionality and proper cartilage physiology in case of:

- Articular pain
- Tendinopathies
- Osteoarthritis in either early or advanced stages
- Post-traumatic degenerative pathology

### IDEAL FOR

- **Competitive** and **amateur athletes** 
- **Younger** and **Elder subjects with OA**

**Condrotide Moveo** is a Mastelli innovative formula developed with keyconstituents essential for maintaining articular function and proper cartilage physiology:

#### 1 NUCLEOTIDES

Keep the **environment hydrated** by aiding the natural biological processes of the **morpho-functionality** of the **locomotor system**

#### 2 GLUCOSAMINE

Of **plant origin**, present in various natural substances as a **precursor** to **glycosaminoglycans**, which are the **main component** of **joint cartilage**

#### 3 CHONDROITIN SULFATE

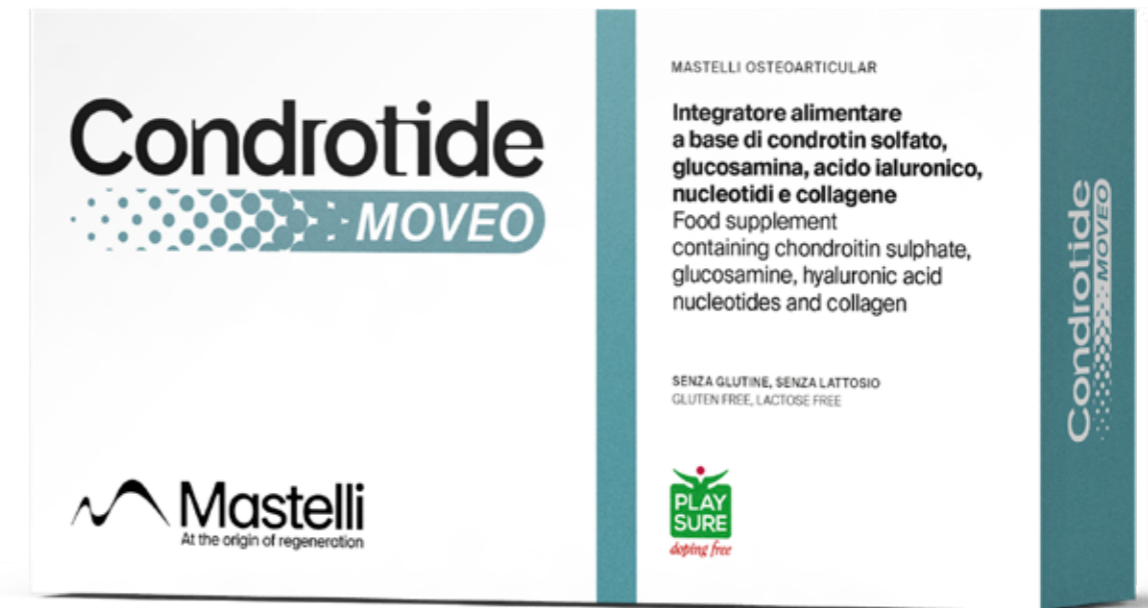
One of the **most important components** of **cartilage** and **primarily responsible** for the **structure** and **maintenance** of **articular cartilage**

#### 4 HYALURONIC ACID

**Distributed** throughout the body, especially in the **synovial fluid** of **joints** and **connective tissues**. It is **able to recall H<sub>2</sub>O**

#### 5 TYPE II NATIVE COLLAGEN

One of the most **important components** of **connective tissue**. Together with Hyaluronic Acid, it **contributes** to the **normal functioning** of **joints** and **cartilage**



### Technical Data <sup>[20]</sup>

<b>Average Contents:</b>	<b>Nucleotides 100mg</b> Glucosamine 415mg Chondroitin Sulfate 360mg Sodium Hyaluronate 30mg Total Type II Collagen 10mg of which Native 4mg
<b>Pack:</b>	20 uncoated and divisible tablets, net weight 29g

### Method of use and dosage <sup>[20]</sup>

Take one tablet a day of Condrotide Moveo swallowed with a bit of water. It is recommended to follow the dosage indicated and not to exceed it



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



# An all-around conservative approach for knee, shoulder, hip, and ankle treatment

Mastelli's osteoarticular portfolio includes a full range of treatment options to fit patients' lifestyle and needs

## OA I

Small narrowing of the articular space and osteophyte genesis



### Conventional treatment

- Physiotherapy
- Body weight reduction
- Physical exercise
- Orthotics
- Nutraceuticals

## OA II

Minimal alterations of marginal joint profile and narrowing of the articular space



### Conventional treatment

- Low-dosage NSAIDs
- Analgesics
- Linear Hyaluronic Acid

## OA III

Moderate osteophyte genesis, visible narrowing of the articular space, initial bone sclerosis



### Conventional treatment

- High-dosage NSAIDs
- Steroids
- Platelet Rich Plasma (PRP)
- Hyaluronic Acid: Linear or Cross-linked HA

QUALITY OF LIFE (PAIN INCREASE & MOBILITY REDUCTION)



### Condrotide: PN HPT™

**Condrotide** is a viscoelastic solution containing Polynucleotides HPT™ suggested for painful joint diseases caused by degenerative or post-traumatic conditions and by modification of a joint

Patient type:

- Patients with **OA grade I-II\***
- **Competitive** and **amateur athletes**
- **Younger subjects with post-traumatic OA**
- Subjects with **concomitant comorbidities**



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### Condrotide HA: PN HPT™, Linear HA, Mannitol

**Condrotide HA** is a fluid gel for intra-articular injections indicated for painful joint diseases caused by degenerative or post-traumatic conditions or by modification of a joint

Patient type:

- Patients with **OA grade II-III\***
- **Elder patients with concomitant disorders**
- Conservative approach to **postpone surgical procedures**



### Condrotide Moveo: Nucleotides, Glucosamine, Chondroitin Sulphate, Sodium Hyaluronate, and Type II Collagen

**Condrotide Moveo** is suggested to protect and help maintaining articular, tendons, and muscle functionality and proper cartilage physiology in case of articular pain, tendinopathies, osteoarthritis in either early or advanced stages, post-traumatic degenerative pathology

Ideal for:

- **Competitive** and **amateur athletes**
- **Younger** and **Elder subjects**



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# MASTELLI'S OSTEOARTICULAR HEALTH LINE



Product

**Condrotide**

**Condrotide HA**

**Condrotide**  
MOVEO

Composition

**Polynucleotides HPT™**

**Polynucleotides HPT™**  
Linear Hyaluronic Acid  
Mannitol

**Nucleotides**  
Glucosamine  
Chondroitin sulphate  
Sodium Hyaluronate  
Type II collagen

Concentration

**PN HPT™ 40mg/2ml**

**PN HPT™ 25mg/2.5ml**  
Linear HA 25mg/2.5ml  
Mannitol 200mM/L

**Nucleotides 100mg**  
Glucosamine 415mg  
Chondroitin Sulfate 360mg  
Sodium Hyaluronate 30mg  
Total Type II Collagen 10mg  
of which Native 4mg

Pack

1 sterile, non-pyrogenic, pre-filled glass syringe x 2ml

1 sterile, non-pyrogenic, pre-filled glass syringe x 2.5ml

20 uncoated and divisible tablets (net weight 29g)

Treatment Protocol

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

3 injections of 2.5ml in the joint to be treated.  
The time interval between each injection is 1-3 weeks

1 Tablet/day

Regulatory Status

Medical Device

Medical Device

Food Supplement

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