

INFORMATION FOR THE PATIENT Playal FAMILY

MANUFACTURER: INNATE srl, Viale Industria 11/13, 15067 Novi Ligure

(AL)SRN NUMBER: IT-MF-000026730

The information presented below is intended for patients or lay persons.

This document is not intended to give general advice on the treatment of a medical condition. Please contact your healthcare professional in case you have questions about your medical condition or about the use of the device in your situation. Is intended to provide information on the safe use of the device and on the device in accordance with article 18 of MDR EU 745/2017.

SUMMARY

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1. IDENTIFICATION OF THE DEVICE:

BASIC UDI DI: 805104033artsyrniaci77U

Year of first certification under Directive 93/42/EEC: 07/2020

Class of device: Class III, Rule 8

Notified Body: Italcert S.r.l., Viale Sarca, 336 20126 – MILANO, Country: Italy

Phone: +39 02 66104876

ID Number: 0426

2. BRIEF SUMMARY FOR THE PATIENTS

Qualitative Composition of the products: sodium hyaluronate high molecular weight (1800 – 2600 KDa), niacinamide, sodium chloride, sodium phosphate bibasic, sodium phosphate monobasic, water for injections.

Shelf life/Expiration date: 36 months

Re-absorbable long term medical device: duration > 30 days

Stability and storage: Store Playal at 2–25°C (36–77°F) in a dry place in the original box. Protect from light, heat and frost. Keep out of reach of children.

Summary of intended purpose of the product to improve the quality of life of the patients

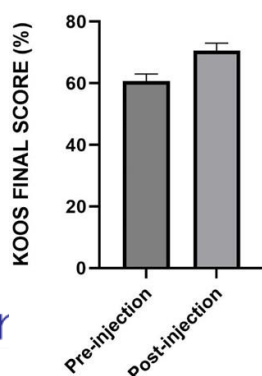
It is a synovial fluid substitute which, thanks to its viscoelastic and lubricant properties, promotes the restoration of rheological conditions of the joints, altered in degenerative or post-traumatic conditions.

The product, improving the characteristics of the synovial fluid, exerts a protective action of the joints and helps to improve joint function and the reduction of pain symptoms. It helps to cushion the joints Playal Family acts only at the joint where it is injected, without exerting any systemic action.

Alleviation and/or remission of pain symptoms and difficulty to perform daily normal actions for those who are prone to joint degenerative diseases or trauma.

Clinical evaluation:

- 1) The outcome of the evaluation collected on the product on the market by the specialist is performed with an evaluation of the index related to different areas related to the patients need (sport, quality of life, normal activity) before and after the injections. This index is named KOOS (Knee Injury and Osteoarthritis Outcome Score). This value is related to the evaluation of different types of normal objective evaluation related to the life of the patient (sport activity, daily activity, pain in movement, general quality of life). To see if a therapy is effective the value must increase after the treatment. From the analysis of every single area (sport activity, daily activity, pain in movement, general quality of life) a medium value is obtained and could be summarized as follow:



Results: The medium final score of all the area evaluated after the injections is increased with a consequential benefit to the patients. The number of patients analyzed and treated were 114 with playal 40 product. 1 side effect (swelling, pain) on 114. Solved in 48 hour.

- 2) Alberto Gobbi; Katarzyna Herman; Leandra Bizzoco; Giulia Avio OASI Bioresearch Foundation Gobbi N.P.O., Milan, Italy.

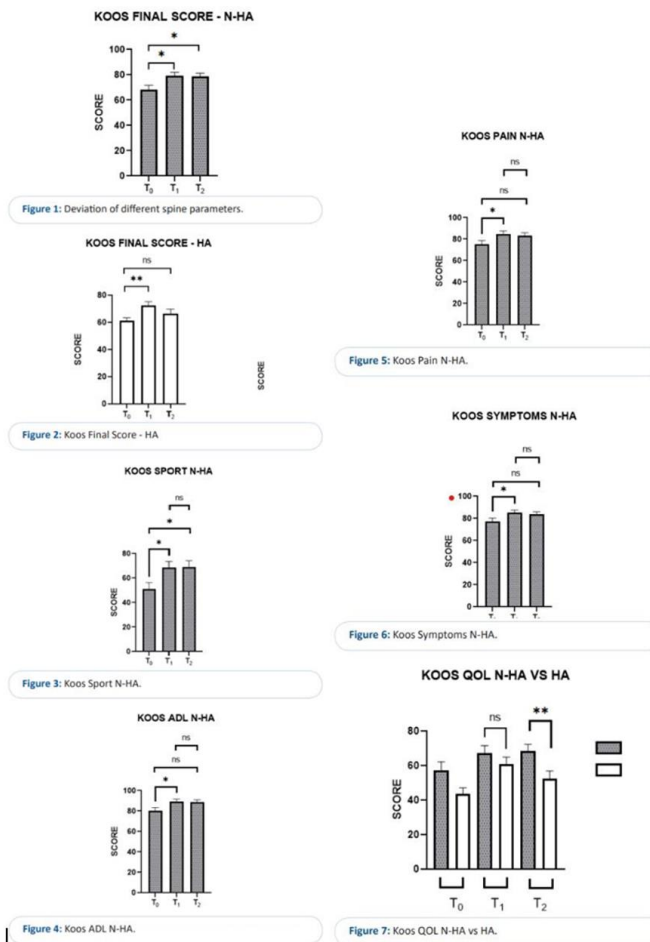
A clinical study aims to evaluate the safety and efficacy of high molecular weight hyaluronic acid with addition of niacinamide (named for simplicity N-HA) versus standard medium molecular weight hyaluronic acid (named for simplicity HA) in patients with joint degenerative and post-traumatic diseases.

60 Patients were enrolled and treated: 30 with HA and 30 with N-HA.

Each patient received 3 doses of the selected product in 15 days intervals, with follow-up at 3 (T1) and 6 (T2) months.

The evaluation was performed with KOOS scale: (Knee Injury and Osteoarthritis Outcome Score). This value is related to the evaluation of different types of normal objective evaluation related to the life of the patient (sport activity, daily activity, pain in movement, general quality of life). To see if a therapy is effective the value must increase after the treatment.

Below the results:



Conclusions: Both HA and N-HA are safe and effective for the treatment of joints degenerative and post-traumatic diseases. N-HA showed superiority in terms of efficacy

and longer-lasting effects when compared to hyaluronic acid alone.

Side effects: There may be some temporary side reactions following injection of Playal Family such as pain, stiffness, warmth, redness or swelling. These secondary manifestations may be relieved by applying ice on the treated articulation. Usually, these effects disappear after a short time (3- 4 days maximum). If symptoms persist, seek medical attention. Any other unwanted side effects associated with the injection must be reported to the doctor. As for any intra-articular treatment, septic arthritis may rarely occur when general precautions for injections are not observed or the site of injection is not aseptic. More rarely, cases of hematoma and arthralgia are reported, as well as skin rash, such as urticaria and pruritus.

1 side effect detected in clinical evaluation. Swelling and pain immediately after the injections (1 detected on 114).

Adverse events:

Contact your healthcare professional if you believe that you are experiencing side-effects related to the device or its use or if you are concerned about risks. This document is not intended to replace a consultation with your healthcare professional if needed.

Unknown, if the correct methods of use and instructions given in the leaflet are observed. Any use outside the normal use described in this leaflet should be avoided. Any adverse event or serious accident must be reported to the Manufacturer in the contacts below and to the Competent Authority of the member state in which the patient / user is established.

Warnings dedicated to the patients: As no clinical experience is available for the use of Hyaluronan in children, treatment with Playal Family is not recommended in these cases. The device must not be used for pregnant or breastfeeding women, as it has not been tested in such cases. The device must not be used in patients with ascertained individual hypersensitivity to any of the ingredients of the product. Playal Family must be administered with caution to patients with a history of hypersensitivity to other drugs and patients with liver failure or impairment. After the intra-articular injection, it is advisable to recommend to avoid physical activities demanding stress for the articulation and resume normal activities after a few days. After the intra-articular injection, it is advisable to recommend to avoid driving for at least 48 hours. Playal Family is a disposable product, the quality and sterility are guaranteed only if the syringe is sealed. Any residue must be discarded and not reused even after new sterilization. Do not use the product if the package is already opened or damaged.

Implant card: An implant card is given with the product. The doctor will give to the patients implant card filled in the area related to the doctor. The variable data related to the product (batch number, expiration date and UDI data, medical type) are being already put in implant card by the manufacturer under a form of label.

The patient will have to carry the implant card to allow the traceability of the implanted device to have complete traceability in case of any issue (for example: information about recall of a batch, information for the healthcare worker in case of any problem).

Alternative treatment options: must be prescribed by a specialist, after visited the patient. The alternative treatments identified are the following:

- Paracetamol: Paracetamol is widely recommended as a first-line step for rescue analgesia, despite the fact that the effect of paracetamol on symptoms is minimal and has no significant effect on stiffness and physical function in patients with knee Osteoarthritis (OA) and it represents the first pharmacological option for glenohumeral OA (Colen 2014). In primary care, paracetamol may still be used to treat pain in mild-moderate OA at daily doses up to 3g/day. However, if paracetamol proves is ineffective or insufficient effective, the physician should consider discontinuing and switching treatment regimen, or augmenting it with additional therapies (Bruyère 2016). Do not exceed 3g /day due to the liver toxicity of the substance. In case of exceeding of the safe dose, goes immediately to the hospital to ask for the antidote n-acetylcysteine;
- Glucosamine Sulfate (GS): Glucosamine is an important sugar for the synthesis of various natural substances, such as sugars, lipids (fats) and proteins. There are different forms: glucosamine sulphate, glucosamine hydrochloride and N-acetylglucosamine. Being an important precursor of essential components of articular cartilage (proteoglycans and glycosaminoglycans, GAGs), glucosamine contributes to maintaining the integrity of the cartilage, a tissue that acts as a shock-absorbing cushion protecting the joint ends of the bones from friction. Glucosamine sulphate, alone or in combination with chondroitin and/or other components, such as methylsulfonylmethane (MSM), is also available as a food supplement, a form that does not require a medical prescription and generally has lower dosages than those present in preparations prescribable. In the form of a supplement it is widely used for the treatment of arthrosis and, more generally, to alleviate joint pain and stiffness. taken in recommended quantities, glucosamine sulfate is well tolerated. Reported unwanted effects (side effects) are very rare, however, oral use of glucosamine sulfate may cause nausea, heartburn, constipation, drowsiness, skin reactions, headache. Additionally, since glucosamine products often come from shellfish, the supplement could cause an allergic reaction.
- Chondroitin Sulfate (CS): Studies using prescription-grade CS have shown that CS may offer similar benefits on joint structure changes in patients with mild to moderate Osteoarthritis (OA). The effect size of CS on pain is reportedly variable. CS has an effect on joint structural changes that could be clinically relevant, with efficacy on symptoms of the disease that could be of similar magnitude to that of GS. Glucosamine and CS are often used in combination as dietary supplements, which raises the question of whether there is any additional benefit derived from the combination (Bruyère 2016);
- Topical and oral NSAIDs (non steroidal anti-inflammatory drugs): Topical NSAIDs may be incorporated into the treatment regimen if the patients remain symptomatic after establishing appropriate background pharmacological therapy with slow-acting drugs for OA, and if rescue analgesia with paracetamol provides insufficient symptom relief. If the previous step treatments show inadequate efficacy and the patient is still symptomatic, or in patients presenting with moderate-severe pain, benefit may be obtained with advanced pharmacological treatments. Oral NSAIDs have traditionally played a central role in the pharmacological management of OA. Oral NSAIDs have a moderate effect on pain relief, and with demonstrated greater efficacy in patients with more severe OA accompanied by a higher degree of patient preference;

- Tramadol: Tramadol is a weak opioid that has small but significant efficacy for the relief of pain and improvement of function in knee OA. Treatment of knee OA with short-term tramadol has been found to reduce pain, reduce stiffness, and improve function and overall well-being, with significant results for patients' overall assessment of therapy compared with placebo. The short-term use of tramadol may be considered for severely symptomatic OA patients and there is good evidence that tramadol works if prescribed properly (Bruyère 2016).

The use of tramadol - especially for long periods - can lead to the onset of physical and mental dependence. Should this occur, you should immediately contact your doctor who will take all necessary measures to counteract this side effect.

Tramadol should not be used in patients who have been addicted to drugs, as it can cause relapse. Do not use tramadol without medical advice, due to the high number of interaction with different substances.

- Corticosteroids: the mechanism of action of corticosteroids for the symptomatic relief of arthritis-related pain is thought to involve a local decrease in inflammation of the synovial tissues and inflammatory cell load, stimulation of fibroblast, and blood vessel formation, as well as stimulation of collagen repair. Although multiple studies have demonstrated glucocorticoid injections to have a clear benefit over placebo controls with respect to reducing pain and swelling, there has been little research on the short- and long-term toxicity and safety of these injections (Bernardoni 2016). Triamcinolone preparations are used most frequently and are approved by the US FDA and in Europe as crystalloid suspensions. However, major limitations of IA corticosteroids include a short duration of effect and safety concerns that limit the frequency of use (Wehling 2017). Corticosteroids used for short periods of time should be well tolerated by most people; however, excessive or prolonged use can give rise to various side effects. Among these, some examples (non-exhaustive list):

- Sodium retention;

- Edema;

- Water retention resulting in swelling, such as swelling of the face or swelling of the hands;

- Increased body weight;

- Facial redness;

- Skin changes;

- Hyperglycemia;

- Hypertension;

- Muscle weakness;

- Bone weakness;

- Bone demineralization, osteoporosis;

Do not use without medical advice, due to the high number of interaction with different substances.

- Hyaluronic acid (HA) in combination with PRP: Viscosupplementation is classically implemented in OA, on condition that the OA is symptomatic, that medical treatment (non-pharmacologic, analgesics, NSAIDs) has failed or induced intolerance, and that there

is no acute inflammation (i.e., no severe effusion) (Legré-Boyer 2015). Intra-articular HA is currently indicated only as a symptom-modifying treatment for OA of the knee. The immediate benefit of viscosupplementation is the relief of pain. Longer-term benefits are believed to include the return of joint mobility by the restoration of trans-synovial flow and, ultimately, the metabolic and rheological homeostasis of the joint (Necas 2008)

The most commonly used injectable is hyaluronic acid (HA), but studies have shown that PRP is more efficient both in short or long-term pain and functional recovery. PRP contains a large number of growth factors and proteins stored in the alpha granules of platelets which were found to have regenerative and analgesic effects. Additionally, studies have shown that platelet-rich plasma (PRP) has an anti-inflammatory effect and counteracts catabolic processes within the joint. PRP is obtained from patients' peripheral blood, which is centrifuged in a special processing kit. The PRP is injected into the joint after careful disinfection of the needle entry point. The peak of the beneficial effect is observed at 6 months after the cycle of injections, but it may last up to 2 years.

3. HISTORY OF REVISION

Revision number	Date	Description
00	08/11/2024	First Issue.

Date: 08/11/2024

Responsible Person for Regulatory Compliance: Giulia Avio

