1. Name of the medicinal product

1.1 Product Name

Brand Name: HYORTH

Product Name: Sodium Hyaluronate Sterile Injection 20mg/ 2ml

1.2 Dosage Strength

20 mg / 2 mL

1.3 Dosage form

Prefilled syringe for Injection,
Description: Clear, colourless viscoelastic liquid

2. Qualitative and quantitative composition

2.1 Qualitative Declaration

2.2 Quantitative Declaration

Formulation: HYORTH (Sodium Hyaluronate Sterile Injection)

Composition:

Each mL contains

Sodium Hyaluronate BP ….. 10 mg

Product Expiry: 36 months.

Packing : 1's x 2 mL Pre-filled syringe

S/N	Ingredients	Specification	Qty./mL	USE
1	Sodium Hyaluronate	BP	10 mg	Active Ingredient
2	Sodium Chloride	USP	8.5 mg	Isotonicity
3	Di-sodium Hydrogen Phosphate di-hydrate	USP	0.28 mg	Buffering Agent
4	Monosodium phosphate monohydrate	USP	0.04 mg	Buffering Agent
5	Water for Injection	USP	q.s.	Solvent

3. Pharmaceutical form

Prefilled syringe for Injection

4. Clinical particulars

4.1 Therapeutic indications

HYORTH is indicated for the treatment of pain in osteoarthritis (OA) of the knee inpatients who have failed to respond adequately to conservative non-pharmacologic therapy, and to simple analgesics.

4.2 Posology and method of administration:

- HYORTH is administered by intra-articular injection. A treatment cycle consists of three to five injections given at weekly intervals. Several joints can be treated simultaneously.

- Strict aseptic administration technique must be followed. Inject subcutaneous lidocaine or similar local anesthetic prior to injection of HYORTH.

- Aspirate joint effusion before injection of HYORTH. Do not use the same syringe for removing joint effusion and for injection of HYORTH.

- Take care to remove the tip cap of the syringe and needle aseptically. Inject HYORTH into the joint through a 19-gauge needle.

- The syringe is intended for single use. The contents of the PFS must be used immediately once the container is opened. Before injection, the air bubble is removed from the injection.

- Inject the full 2 mL in one knee only. If treatment is bilateral, a separate PFS should be used for each knee.

4.3 Contraindications:

- HYORTH is contraindicated in patients with known history of hypersensitivity (allergy) to sodium hyaluronate (hyaluronan) preparations.

- HYORTH is contraindicated in patients with knee joint infections or skin diseases in the area of injection site.

- Do not inject HYORH if there is large intra-articular effusion.

4.4 Special warnings and precautions for use

Warnings

- Do not use concomitantly disinfectants containing quaternary ammonium compounds for skin preparations because sodium hyaluronate is precipitated in their presence.

- Do not inject HYORTH extra-articularly or into the synovial tissues and capsules. This will generally result in local and systemic adverse events.

- Intravascular injections of HYORTH may lead to systemic adverse events.

Precautions

General

- The effectiveness of a single treatment cycle of less than 3-5 injections has not been established.

- The effectiveness and safety of the use of HYORTH in joints other than knee have not been established.

- The safety and effectiveness of the use of HYORTH concomitantly with other intra articular injectables have not been established.

- Strict aseptic administration technique must be followed.

- The safety and effectiveness of the use of HYORTH in severely inflamed Knee joints have not been established.

- The pre-filled syringe is intended for single use. Use the contents of the syringe immediately after its packaging is opened. Discard any unused HYORTH.

- Opened or damaged packages of HYORTH should not be used. Always store in the original packaging (protected from light) at 25º C. DO NOT FREEZE.

- Aspirate synovial effusion if present before each HYORTH injection.

- HYORTH should be used with caution when there is evidence of lymphatic or venous stasis in that leg.

- HYORTH should be used with caution in diabetic patients and patients with chronic disorders.

4.5 Interaction with other medicinal products and other forms of interaction

HYORTH does not interact with analgesics or anti-inflammatory drugs (NSAIDs, Steroids); therefore, these drugs can be applied during HYORTH therapy. There are no reports of abnormal laboratory test results attributed to HYORTH administration, either alone or in conjunction with any other treatments

4.6 Pregnancy and lactation

The safety and effectiveness of sodium hyaluronate injection have not been established in pregnant women.

It is not known if sodium hyaluronate is excreted in human milk. The safety and effectiveness of sodium hyaluronate injection have not been established in lactating women.

The safety and effectiveness of sodium hyaluronate injection have not been established in pediatric patients.

4.7 Effects on ability to drive and use machines

HYORTH does not provide a general systemic effect and will not cause drowsiness or impair the ability to drive or use machinery.

4.8 Undesirable effects

Intra-articular injection may lead to local side effects like pain, heat sensation, reddening and swelling at the treated joint.

Placing an ice pack on the treated joint for 5 to 10 minutes would reduce the occurrence of such side effects.

Potential Adverse Events

The following adverse events are among those that may occur in association with intraarticular injections:

- Arthralgia
- Joint stiffness
- Joint effusion
- Joint swelling
- Joint warmth
- Injection site pain
- Arthritis

• Arthropathy
• Gait disturbance

Reported Adverse Events

The most commonly reported adverse events associated with sodium hyaluronate are:
• Arthralgia
• Arthritis
• Arthropathy
• Injection site pain
• Joint effusion

4.9 Overdose

NA

5. Pharmacological properties

5.1 Pharmacokinetic properties

The half-life of sodium hyaluronate depends on molecular weight, and varies from 15-30days. It is cleared from the joint through lymphatic system. Once it passes into the blood, liver endothelial cells via a receptor-mediated endocytic pathway rapidly take it up. After degradation it is excreted through kidneys.

5.2 Mechanism of action

It is well established that the molecular weight and concentration of HA are reduced in synovial fluid of patients with osteoarthritis (OA). HA is responsible for the viscoelastic quality of synovial fluid that acts both as a lubricant and shock absorber. In a joint, HA coats the surface of the articular cartilage, and shares space deeper in the cartilage among collagen fibers and sulfated prostaglandins (PGs). In this respect, HA probably protects the cartilage and also blocks the breakdown of the PGs from the cartilage matrix into the synovial space, thus maintaining the normal cartilage matrix. It may also prevent invasion of inflammatory cells into the joint space. Exogenous HA may promote the production of HA. In the synovial fluid, HA binds to chondrocytes via the CD44 receptor, supporting the role for HA in healthy cartilage.

The effects of HA on nerve impulses and nerve sensitivity may be responsible for observed relief of pain in OA with HA in clinical studies. Knee joint inflammation influences excitability of no ciceptors of articular nerves. In experimental OA models, it has been shown that these nerves become hyper algesic, spontaneously discharge, and are sensitive to non-noxious joint movements. Administration of HA to isolated medial articular nerves from an experimental model of OA significantly decreased ongoing nerve activity. HA also has antioxidant effects in various systems. Its significant antioxidant effect has been demonstrated i*n vitro*, and it is suggested that through this mechanism HA also protects from destruction of chondrocytes in the cartilage.

1 Pharmaceutical particulars

1.1 List of excipients

INGREDIENTS	SPECIFICATION
Sodium Chloride	USP
Di-sodium Hydrogen Phosphate di-hydrate	USP
Sodium dihydrogen phosphate monohydrate	USP
Water for Injection	USP

1.2 Incompatibilities

Not Known.

1.3 Shelf life

3 years (36 months)

1.4 Special precautions for storage

Store below 30°C. Protect from light. Do not freeze.

1.5 Nature and contents of container

HYORTH is a sterile, non-pyrogenic viscoelastic preparation supplied in a 2.25 mL USP type I glass PFS containing 2 mL HYORTH, with bromo butyl rubber stopper, finger grip and plunger rod.

HYORTH syringe is terminally sterilized, aseptically packaged and is supplied with 19 gauge sterile needle.

1.6 Special precautions for disposal and other handling

- Do not use HYORTH if package is opened or damaged.
- HYORTH can be stored in the original package at room temperature below 25°C.
- Protect from freezing.
- The HYORTH syringe is intended for single use.
- Discard partially used HYORTH syringes.
- Do not resterilize HYORTH.

7. Marketing Authorization Holders

Name	**:**	VIRCHOW HEALTHCARE PRIVATE LIMITED
Address	:	901, DLH Park, S.V. Road, Goregaon (West), Mumbai – 400062. INDIA
Tel.	:	91 22 28795600
Fax	:	91 22 28795699
Email	:	regulatorymgr@virchowhealthcare.com

8 Marketing Authorization Number

NA

9 Manufacturer Name

Name :	Virchow Biotech Private Limited
Address:	Survey No.172 Part, Gagillapur (V), Dundigal Gandimaisamma (M), Medchal- Malkajgiri (D), Telangana-500043, India
Phone :	91-40-65194227/25/26
Fax :	91-8418255131
E-mail :	virchowbiotech@rediffmail.com

10 Date of first authorization/renewal of the authorization

Not applicable

11 Date of revision of the text

Not applicable