

Hyaluronidase should not be injected into or around an infected or acutely inflamed area because of the danger of spreading a localized infection. Hyaluronidase should not be used to reduce the swelling of bites or stings. Hyaluronidase should not be applied directly to the cornea. Hyaluronidase should not be used for intravenous injections because the enzyme is rapidly inactivated.

**PRECAUTIONS**

**General**

Furosemide, the benzodiazepines and phenytoin have been found to be incompatible with hyaluronidase.

When considering the administration of any other drug with hyaluronidase, it is recommended that appropriate references first be consulted to determine the usual precautions for the use of the other drug; e.g., when epinephrine is injected along with hyaluronidase, the precautions for the use of epinephrine in cardiovascular disease, thyroid disease, diabetes, digital nerve block, ischemia of the fingers and toes, etc., should be observed.

**Drug interactions**

When hyaluronidase is added to a local anesthetic agent, it hastens the onset of analgesia and tends to reduce the swelling caused by local infiltration, but the wider spread of the local anesthetic solution increases its absorption; this shortens its duration of action and tends to increase the incidence of systemic reaction.

Patients receiving large doses of salicylates, cortisone, ACTH, estrogens, or antihistamines may require larger amounts of hyaluronidase for equivalent dispersing effect, since these drugs apparently render tissues partly resistant to the action of hyaluronidase.

**Geriatric use**

No overall differences in safety or effectiveness have been observed between elderly and younger adult patients.

**ADVERSE REACTIONS**

The most frequently reported adverse experiences have been local injection site reactions. Hyaluronidase has been reported to enhance the adverse events associated with co-administered drug products. Edema has been reported most frequently in association with hypodermoclysis. Allergic reactions (urticaria, angioedema) have been reported in less than 0.1% of patients receiving hyaluronidase. Anaphylactic-like reactions following retrobulbar block or intravenous injections have occurred, rarely.

**OVERDOSAGE**

Symptoms of toxicity consist of local edema or urticaria, erythema, chills, nausea, vomiting, dizziness, tachycardia, and hypotension. The enzyme should be discontinued and supportive measures initiated immediately.

**DOSAGE AND ADMINISTRATION**

As directed by the physician. Injection should be used immediately after preparation. Preparation is not intended for Intravenous Injection.



→ **Vial preparation**  
Clean the exposed portion of the rubber stopper of the vial with IPA (70%) prior to insertion of the needle.



→ **Water for injection addition**  
After vertical insertion of the needle through the rubber stopper, the vacuum will draw the water into the vial. Gently inject any remaining water for injection in to the vial to avoid foam formation.



→ **Mixing**  
Remove the syringe from the vial and mix Hyaluronidase Injection with the water for injection by carefully swirling and inverting/flipping the vial — **“Do not shake”**

**Note:** Reconstituted **Hyaluronidase Injection** is a clear, colourless solution free of particulate matter. Because this is a protein solution, slight flocculation (thin translucent fibres) may occur. The occurrence of translucent fibres has not impact on the quality of the product.

**STORAGE**

Store protected from moisture at a temperature not exceeding 15°C.

**PRESENTATION**

10 vials in a box.

**Manufactured by:**



**UNIT II:** Plot No.2, Industrial Area, Lodhimajra, Baddi, H.P. -173 205 , India.

**H.O.:** Ram Mandir Road, Goregaon (W), Mumbai - 400 104, India.

<sup>TM</sup> Trade Mark of Samarth

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R<sub>x</sub>

# Hyaluronidase Injection IP 1500 IU

**HINEX<sup>TM</sup>**

For IM/SC use only  
(Not for I.V. Use)  
(Lyophilized)

**COMPOSITION**

Each vial contains:  
Hyaluronidase IP 1500 IU  
Excipients q.s.

**DESCRIPTION**

Hyaluronidase Injection is a preparation of purified ovine testicular hyaluronidase, a protein enzyme. The exact chemical structure of this enzyme is unknown. However, the amino acid sequence for the primary structure of the enzyme has been deduced from the sequence of purified peptides.

Hyaluronidase Injection dehydrated in the solid state under high vaccum is supplied as a sterile white, odorless, amorphous solid. The product is to be reconstituted with suitable diluent before use.

The reconstituted solution is clear and colorless, with an approximate pH of 6.4 to 7.2 after reconstitution with water for Injection.

**CLINICAL PHARMACOLOGY**

Hyaluronidase is a spreading or diffusing substance, which modifies the permeability of connective tissue through the hydrolysis of hyaluronic acid, a polysaccharide found in the intercellular ground substance of connective tissue, and of certain specialized tissues, such as the umbilical cord and vitreous humor. Hyaluronic acid is also present in the capsules of type A and C hemolytic streptococci. Hyaluronidase hydrolyzes hyaluronic acid by splitting the glucosaminidic bond between C1 of the glucosamine moiety and C4 of glucuronic acid. This temporarily decreases the viscosity of the cellular cement and promotes diffusion of injected fluids or of localized transudates or exudates, thus facilitating their absorption.

Hyaluronidase cleaves glycosidic bonds of hyaluronic acid and, to a variable degree, some other acid mucopolysaccharides of the connective tissue. The activity is measured in vitro by monitoring the decrease in the amount of an insoluble serum albumen-hyaluronic acid complex as the enzyme cleaves the hyaluronic acid component.

When no spreading factor is present, material injected subcutaneously spreads very slowly, but hyaluronidase causes rapid spreading, provided local interstitial pressure is adequate to furnish the necessary mechanical impulse. Such an impulse is normally initiated by injected solutions. The rate of diffusion is proportionate to the amount of enzyme, and the extent is proportionate to the volume of solution.

Knowledge of the mechanisms involved in the disappearance of injected hyaluronidase is limited. It is known, however, that the blood of a number of mammalian species brings about the inactivation of hyaluronidase. Studies have demonstrated that hyaluronidase is antigenic; repeated injections of relatively large amounts of this enzyme may result in the formation of neutralizing antibodies.

The reconstitution of the dermal barrier removed by intradermal injection of hyaluronidase (20, 2, 0.2, 0.02, and 0.002 Units/mL) to adult humans indicated that at 24 hours the restoration of the barrier is incomplete and inversely related to the dosage of enzyme; at 48 hours the barrier is completely restored in all treated areas.

Results from an experimental study, in humans, on the influence of hyaluronidase in bone repair support the conclusion that this enzyme alone, in the usual clinical dosage, does not deter bone healing.

**INDICATIONS AND USAGE**

Hyaluronidase Injection is indicated as an adjuvant to increase the absorption and dispersion of other injected drugs; for hypodermoclysis; and as an adjunct in subcutaneous urography for improving resorption of radiopaque agents.

**CONTRAINDICATIONS**

Hypersensitivity to hyaluronidase or any other ingredient in the formulation is a contraindication to the use of this product.

**WARNINGS**

Discontinue Hyaluronidase Injection if sensitization occurs. Hyaluronidase should not be used to enhance the absorption and dispersion of dopamine and/or alpha agonist drug