

Choose the **Only** FDA-approved Hyaluronidase Synthesized by a Recombinant Process



OTHER clinically utilized hyaluronidase products contain **cattle** or **sheep** testes-derived hyaluronidase

Hylenex® recombinant (hyaluronidase human injection) is a Safe, Effective and Low Cost Option*

- Hylenex recombinant is:
 - the **ONLY** recombinant human hyaluronidase available and
 - the lowest priced FDA-approved hyaluronidase available.*

	Hylenex® recombinant	Vitrase®	Wydase®	Hydase	Amphadase®	Compounded
Available for Use	YES	YES	Not Since 1999	Not Since 2008	Not Since 2010	YES
FDA-approved	YES	YES	YES	YES	YES	NO
FDA-regulated Manufacturing (cGMP ^{**})	YES	YES	Not Currently Made	Not Currently Made	Not Currently Made	NO
Source of Active Ingredient	Recombinant Human	Sheep Testes	Cattle Testes	Cattle Testes	Cattle Testes	Cattle Testes
Units/mL	150	200	150	150	150	150

*Cost comparison based on published Wholesale Acquisition Cost per single-use vial comparing FDA-approved available products. Red Book March 2012. Price comparison is not indicative of final customer price and is not intended to be a comparison of safety or efficacy of drugs.

**cGMP= Current Good Manufacturing Practices

See Important Safety Information and Brief Summary of Full Prescribing Information.

Hylenex recombinant (hyaluronidase human injection) Conforms to WHO Guidelines on Transmissible Spongiform Encephalopathies¹

WHO Guidelines on
Transmissible Spongiform Encephalopathies
in relation to
Biological and Pharmaceutical Products



World Health Organization
Geneva

3.2 Measures to minimize risks to humans from biological and pharmaceutical products in which **bovine, ovine or caprine** materials are used during manufacture

On the basis of current scientific knowledge about the agents causing BSE and other animal TSEs, **the group stressed that the ideal situation would be to avoid the use of bovine materials in the manufacture of any biological or pharmaceutical product, as well as the use of materials from other animal species in which TSEs naturally occur.** In practice, this is not always feasible, in which case a risk assessment should be performed. The risk assessment should take into account: a) the source of starting materials used as active substances, excipients or reagents and their potential ineffectivity; b) the possibility of cross contamination where starting materials are collected and processed; and c) the production processes for seed and other materials. The TSE risk assessment contributes to the overall risk-benefit analysis of biological and other pharmaceutical products.

bovine = cattle
ovine = sheep
caprine = goat

Note: Emphasis added

- Hylenex recombinant does not contain any animal products.



Henry Schein, Inc. Ordering Information

Order Hylenex recombinant
(NDC 18657-102-04)

Item Code: 248-0470

Phone: 1-800-772-4346



Packaging

- Preservative free
- Ready to use
- 1 mL single-dose vials
- 150 USP units/mL
- 4 vials per box

Shelf Life

- 18 months

Storage

Unopened in a refrigerator at 2° to 8°C (36° to 46°F). DO NOT FREEZE.



For further information, contact
Halozyme toll free at 855-HYLENEX
(855-495-3639) or visit www.hylenex.com


Hylenex[®]
recombinant
(hyaluronidase human injection)

Indication

Hylenex recombinant (hyaluronidase human recombinant) is a tissue modifier indicated as an adjuvant in subcutaneous fluid administration for achieving hydration, to increase the dispersion and absorption of other injected drugs, and in subcutaneous urography for improving resorption of radiopaque agents.

Important Safety Information

- Hypersensitivity to hyaluronidase or any other ingredient in the formulation is a contraindication to the use of this product.
- Discontinue *Hylenex* recombinant if sensitization occurs.
- Hyaluronidase should not be used to enhance the absorption and dispersion of dopamine and/or alpha agonist drugs.
- 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 used for intravenous injections because the enzyme is rapidly inactivated.
- Furosemide, the benzodiazepines and phenytoin have been found to be incompatible with hyaluronidase.
- Anaphylactic-like reactions following retrobulbar block or intravenous injections have occurred, rarely.
- Hyaluronidase should not be applied directly to the cornea. It is not for topical use.

The most frequently reported adverse reactions have been local injection site reactions, such as erythema and pain. Hyaluronidase has been reported to enhance the adverse reactions associated with co-administered drug products.

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.

Edema has been reported most frequently in association with subcutaneous fluid administration. The rate and volume of subcutaneous fluid administration should not exceed those employed for intravenous infusion. As with all parenteral fluid therapy, observe effect closely, with the same precautions for restoring fluid and electrolyte balance as in intravenous injections. Special care must be taken in pediatric patients to avoid over hydration by controlling the rate and total volume of infusion. When solutions devoid of inorganic electrolytes are administered subcutaneously, hypovolemia may occur.

HYLENEX® recombinant

(hyaluronidase human injection)

150 USP units/mL

Rx Only

BRIEF SUMMARY OF FULL PRESCRIBING INFORMATION

This Brief Summary does not include all the information needed to use HYLENEX recombinant safely and effectively. See full prescribing information for HYLENEX recombinant by visiting www.hylenex.com.

To report SUSPECTED ADVERSE REACTIONS, contact Halozyme Therapeutics, Inc. at 1-877-877-1679 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

INDICATIONS AND USAGE

Subcutaneous Fluid Administration

HYLENEX recombinant is indicated as an adjuvant in subcutaneous fluid administration for achieving hydration.

Dispersion and Absorption of Injected Drugs

HYLENEX recombinant is indicated as an adjuvant to increase the dispersion and absorption of other injected drugs.

Subcutaneous Urography

HYLENEX recombinant is indicated as an adjunct in subcutaneous urography for improving resorption of radiopaque agents.

CONTRAINDICATIONS

HYLENEX recombinant is contraindicated in patients with known hypersensitivity to hyaluronidase or any of the excipients in HYLENEX recombinant. A preliminary skin test for hypersensitivity to HYLENEX recombinant can be performed. The skin test is made by an intradermal injection of approximately 0.02 mL (3 Units) of a 150 Unit/mL solution. A positive reaction consists of a wheal with pseudopods appearing within 5 minutes and persisting for 20 to 30 minutes and accompanied by localized itching. Transient vasodilation at the site of the test, i.e., erythema, is not a positive reaction. Discontinue HYLENEX recombinant if sensitization occurs.

WARNINGS AND PRECAUTIONS

Spread of Localized Infection

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.

Ocular Damage

Hyaluronidase should not be applied directly to the cornea. It is not for topical use.

Enzyme Inactivation with Intravenous Administration

HYLENEX recombinant should not be administered intravenously. Its effects relative to dispersion and absorption of other drugs are not produced when it is administered intravenously because the enzyme is rapidly inactivated.

ADVERSE REACTIONS

The following adverse reactions have been identified during post-approval use of hyaluronidase products. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

The most frequently reported adverse reactions have been mild local injection site reactions such as erythema and pain. Hyaluronidase has been reported to enhance the adverse reactions associated with co-administered drug products. Edema has been reported most frequently in association with subcutaneous fluid administration. Allergic reactions (urticaria or angioedema) have been reported in less than 0.1% of patients receiving hyaluronidase. Anaphylactic-like reactions following retrolubular block or intravenous injections have occurred, rarely.

DRUG INTERACTIONS

It is recommended that appropriate references be consulted regarding physical or chemical incompatibilities before adding HYLENEX recombinant to a solution containing another drug.

Incompatibilities

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

Drug-Specific Precautions

Hyaluronidase should not be used to enhance the dispersion and absorption of dopamine and/or alpha agonist drugs. 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.

Local Anesthetics

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.

Salicylates, Cortisone, ACTH, Estrogens and Antihistamines

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.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Category C. In an embryo-fetal study, mice have been dosed daily by subcutaneous injection with recombinant human hyaluronidase at dose levels up to 2,200,000 U/kg. The study found no evidence of teratogenicity. Reduced fetal weight and increased numbers of fetal resorptions were observed, with no effects found at a daily dose of 360,000 U/kg, which represents several orders of magnitude over

the suggested human dose range of 50-300 U of HYLENEX recombinant (0.8-5 U/kg in a 60 kg subject). In a pre- and postnatal development study, mice have been dosed daily by subcutaneous injection with recombinant human hyaluronidase at dose levels up to 1,100,000 U/kg. The study found no adverse effects on sexual maturation, learning and memory of offspring, or their ability to produce another generation of offspring. It is also not known whether HYLENEX recombinant can cause fetal harm when administered to a pregnant woman. HYLENEX recombinant should be given to a pregnant woman only if clearly needed.

Labor and Delivery

Administration of hyaluronidase during labor was reported to cause no complications: no increase in blood loss or differences in cervical trauma were observed.

Nursing Mothers

It is not known whether hyaluronidase is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when hyaluronidase is administered to a nursing woman.

Pediatric Use

Clinical hydration requirements for children can be achieved through administration of subcutaneous fluids facilitated with HYLENEX recombinant. The dosage of subcutaneous fluids administered is dependent upon the age, weight, and clinical condition of the patient as well as laboratory determinations. The potential for chemical or physical incompatibilities should be kept in mind. The rate and volume of subcutaneous fluid administration should not exceed those employed for intravenous infusion. For premature infants or during the neonatal period, the daily dosage should not exceed 25 mL/kg of body weight, and the rate of administration should not be greater than 2 mL per minute. During subcutaneous fluid administration, special care must be taken in pediatric patients to avoid over hydration by controlling the rate and total volume of the infusion.

Geriatric Use

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

Reference: 1. World Health Organization. WHO Guidelines on Transmissible Spongiform Encephalopathies in Relation to Biological and Pharmaceutical Products. 2003. Available at: http://www.who.int/bloodproducts/publications/en/WHO_TSE_2003.pdf. Accessed July 18, 2011.

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