Longidaze®

INTERNATIONAL NON-PROPRIETARY NAME (INN): bovhyarulonidase azoximer.

DOSAGE FORM AND STRUCTURE:
Active ingredient: bovhyaluronidase azoximer (Longidaze®) - 3000 IE;
Excipients: cocoa butter - until a suppository weighing 1.3 g is obtained.

DESCRIPTION: torpedo-shaped suppositories of light yellow colour with a weak specific smell of cocoa butter, mottling of color is allowed.

ATC CODE: V03AX Other therapeutic products.

PHARMACOLOGICAL ACTION: enzyme agent.

PHARMACODYNAMICS:
Longidaze® has hyaluronidase (enzymatic) activity of prolonged action, chelating, antioxidant, immunomodulatory and moderate anti-inflammatory properties. Prolongation of enzyme action is achieved by covalent binding of the enzyme to a physiologically active polymeric carrier (azoximer). Longidaze® exhibits anti-fibrotic properties, reduces the course of the acute phase of inflammation, regulates (increases or decreases, depending on the initial level) the synthesis of inflammatory mediators (interleukin-1 and tumor necrosis factor - alpha), increases the humoral immune response and the body's resistance to infection.
The pronounced anti-fibrotic properties of Longidaze® are provided by the conjugation of hyaluronidase with a carrier, which significantly increases the resistance of the enzyme to denaturing effects and the action of inhibitors: the enzymatic activity of Longidaze® is maintained when heated to 37°C (98.6°F) for 20 days, while the native hyaluronidase loses its activity under the same conditions during the day. In Longidaze® drug, the simultaneous local presence of the hyaluronidase enzyme and a carrier capable of binding the enzyme inhibitors and stimulators of collagen synthesis (iron ions, copper ions, heparin, etc.) released during the hydrolysis of the matrix components is ensured. Due to these properties, Longidaze® has not only the ability to depolymerize the connective tissue matrix in fibrous-granulomatous formations, but also to suppress the reverse regulatory reaction aimed at the synthesis of connective tissue components.
Glycosaminoglycans (hyaluronic acid, chondroitin, chondroitin-4-sulfate, chondroitin-6-sulfate), which form the basis of the connective tissue matrix, are a specific substrate of testicular hyaluronidase. As a result of depolymerization (breaking the bond between C1 acetylglucosamine and C4 glucuronic or induronic acids), glycosaminoglycans change their basic properties: viscosity decreases, the ability to bind water and metal ions decreases, the permeability of tissue barriers temporarily increases, fluid movement in the intercellular space is facilitated, the elasticity of connective tissue increases, which is manifested in a decrease in tissue swelling, flattening of scars, an increase in the range of joint motion, a decrease in contractures and prevention of their formation and a decrease in the adhesion process.
Biochemical, immunological, histological and electron microscopic studies have shown that Longidaze® does not damage normal connective tissue, but causes destruction of the connective tissue that has changed in composition and structure in the area of fibrosis.
Longidaze® has no mutagenic, embryotoxic, teratogenic and carcinogenic effects. The drug is well tolerated by patients; no local and general allergic reactions have been recorded.
The use of Longidaze® in therapeutic doses during or after a surgical treatment does not cause deterioration in the course of the postoperative period or the progression of the infectious process and it does not slow down the restoration of bone tissue.

PHARMACOKINETICS:

An experimental study of pharmacokinetics made it possible to establish that, when administered rectally, Longidaze® is characterized by a high rate of distribution in the body; it is well absorbed into the system blood circulation and reaches a maximum concentration in the blood after 1 hour.

The half-distribution is about 0.5 hours, the half-life is from 42 to 84 hours. The product is excreted mainly by the kidneys.

The drug penetrates into all organs and tissues, including the blood-brain and blood-ophthalmic barriers. The absence of tissue accumulation was established.

The bioavailability of Longidaze® when administered rectally is high: about 90%.

INTENDED USES:

The drug is prescribed to adults and adolescents over 12 years old in the form of monotherapy and as part of complex therapy for diseases accompanied by hyperplasia of the connective tissue, including during the inflammatory process:

- in urology: chronic prostatitis, interstitial cystitis, strictures of the urethra and ureters, Peyronie's disease, the initial stage of benign prostatic hyperplasia, prevention of scarring and strictures after surgery on the urethra, bladder, ureters;
- in gynecology: adhesions (prevention and treatment) in the small pelvis in chronic inflammatory diseases of the internal genital organs, after gynecological manipulations, including artificial abortions, previous surgical interventions on the pelvic organs; intrauterine synechiae, tuboperitoneal infertility, chronic endomyometritis;
- in dermatovenerology: limited scleroderma, prevention of fibrotic complications of sexually transmitted infections;
- in surgery: prevention and treatment of adhesions after surgical interventions on the abdominal organs, long-term non-healing wounds;
- in pulmonology and phthisiology: pulmonary fibrosis, siderosis, tuberculosis (cavernous fibrous, infiltrative, tuberculoma), interstitial pneumonia, fibrosing alveolitis, pleurisy;
- to increase the bioavailability of antibiotic therapy in urology, gynecology, dermatovenerology, surgery, pulmonology, etc.

CONTRAINDICATIONS:

- Hypersensitivity to medicinal products on the basis of hyaluronidase;
- Pulmonary hemorrhage and hemoptysis;
- Recent vitreous hemorrhage;
- Malignant neoplasms;
- Acute renal failure;
- Age under 12 years old (no clinical study data available);
- Pregnancy and lactation.

WITH CAUTION

Chronic liver failure and pulmonary hemorrhage with history (if administered more than once per week).

DOSAGE AND ADMINISTRATION:

Longidaze® suppositories 3000 IU are recommended for rectal or vaginal administration once a day at night in a course of 10 to 20 intakes.

- For adolescents from 12 to 18 years old suppositories are administered only rectally.
- Rectally for adults and adolescents over 12 years old: 1 suppository 1 time per day after cleansing the intestines.
- Vaginally for adults: 1 suppository 1 time per day (at night), the suppository is inserted into the vagina in a prone position.

- The scheme of administration is adjusted depending on the severity, stage and duration of the disease: Longidaze® is prescribed every other day or at intervals of 2-3 days.

Recommended regimens and doses:

- ✓ In urology: 1 suppository every other day 10 intakes, then another 10 intakes after 2-3 days, the general course is 20 suppositories.
- ✓ In dermatovenerology: 1 suppository every 1-2 days, 10-15 intakes.
- ✓ In pulmonology and phthisiology: 1 suppository every 2-4 days, 10-20 intakes.
- ✓ In surgery: 1 suppository every 2-3 days, 10 intakes.
- ✓ In gynecology: rectally or vaginally, 1 suppository after 2 days, 10 intakes, then, if necessary, supportive therapy is prescribed.

If necessary, a repeated course of Longidaze® is recommended no earlier than after three months or a long-term maintenance therapy of 1 suppository 1 time in 5-7 days for 3-4 months can be prescribed.

SIDE EFFECTS:

The frequency of adverse reactions is presented according to the following classification: very common ≥ 10%; common ≥ 1% and <10%; uncommon ≥ 0.1% and <1%; rare ≥ 0.01% and <0.1%; very rare <0.001%.

Very rare: local reactions in the form of redness, edema, itching of the perianal zone, vaginal itching due to individual sensitivity to the components of the drug.

OVERDOSE:

Overdose symptoms can be expressed in chill, temperature increase, dizziness, hypotension. The medicinal product is discontinued and symptomatic therapy is prescribed.

INTERACTION WITH OTHER DRUGS:

Bovhyaluronidase azoximer can be combined with antibiotics, antiviral, antifungal drugs, bronchial spasmolytics. When administered in combination with other medicinal product (antibiotics, local anesthetics, diuretics) bovhyaluronidase azoximer increases their bioavailability and enhances their effect. In case of co-administration with high doses of salicylates, cortisone, adrenocorticotrophic hormone (ACTH), estrogens or antihistaminic drugs bovhyaluronidase azoximer enzymatic activity can decrease.

Do not co-administer bovhyaluronidase azoximer with medicinal products containing furosemide, benzodiazepines, phenytoin.

PRECAUTION:

When taking the drug, strictly follow the instructions given in the description.

If you have any questions, please consult your doctor or a pharmacist.

- If an allergic reaction develops discontinue the medicinal product and consult your doctor.
- When used against the background of exacerbation of an infection, it is necessary to prescribe the drug alongside with antimicrobial agents to prevent the spread of the infection.
- In the event of adverse reactions, as well as in the event of an adverse reaction not mentioned in the instructions for medical use, you should consult your doctor.
- Do not use the product in case of visual signs of its invalidity (package defect, change of color).
- If a medicinal product dose is missed continue its further administration as usual, according to the present instruction on use or the doctor's recommendations. A patient should not administer double dose to compensate for the missed one.
- When required Longidaze® can be discontinued at once, without gradual dose decrease.

PREGNANCY AND LACTATION:
Longidaze® is contraindicated to pregnant and breast-feeding women (no clinical data are available).

INFLUENCE ON THE ABILITY TO DRIVE VEHICLES AND OPERATE MECHANISMS:
Longidaze® administration does not influence the ability to perform hazardous activities requiring increased concentration of attention and quick psychomotor reactions (including driving, using moving mechanisms).

STORAGE CONDITIONS:
Store in a dry, dark place at a temperature of 2 to 15°C (35.6 to 59°F). Keep out of the reach of children.

SHELF LIFE:
2 years. Do not use after the expiry date.

MANUFACTURER: NPO Petrovax Pharm, LLC,
http://petrovax.com/medication/catalog/longidaze/