

Human Normal Immunoglobulin & Histamine Dihydrochloride Injection

हिस्टोग्लोब
Histoglob®

Pre-filled syringe
For Subcutaneous use only

For sale in India only



Description:

Histoglob® is a sterile preparation of Histamine dihydrochloride coupled to active protein fraction extracted from human blood (Gamma-globulin) in strictly defined proportions. This conjugate is capable of eliciting an immunological response in the human body with the production of highly potent antihistaminic antibodies. Gamma-globulin used in Histoglob® is tested negative for HBsAg and Anti-HIV-1,2 and Anti HCV Antibodies by ELISA and HBV, HIV & HCV by Nucleic acid testing. Histoglob® is subjected to rigid stability test and electrophoretic analysis to ensure purity and safety.

1. Generic Name:

Human Normal Immunoglobulin & Histamine Dihydrochloride injection.

2. Qualitative and Quantitative Composition:

Each mL contains:

Human Normal immunoglobulin	I.P.	12 mg
Histamine dihydrochloride	B.P.	0.15 mcg
Excipients		q.s.

3. Dosage form & Strength:

Available in liquid form in pre-filled syringe.

4. Clinical Particulars:

4.1 Therapeutic Indications:

Histoglob® is a basic treatment for allergic conditions. It is therefore recommended for all allergic diseases whatever their symptoms or cause.

Histoglob® is recommended for the following indications:

1. Respiratory system: Allergic rhinitis, hay fever, bronchial asthma, asthmatic bronchitis, chronic bronchitis, spasmodic tracheitis.

2. Cutaneous: Eczema, urticaria, generalized skin allergies.

3. Nervous system: Migraine.

4. Gynecological: Premenstrual syndrome (PMS) of allergic etiology.

Histoglob® may also be used prophylactically with children (where there is a family history of allergy) who are about to undergo an adenoidectomy or tonsillectomy.

4.2 Posology and method of administration:

Dosage in general:

Adults: 3 injections each of 1 mL at intervals of 4 days.

Children: 3 injections each of 1 mL at intervals of 8 days.

The course may be repeated after one month. In chronic allergic cases, booster dose may be given 3 and 6 months after the first injection.

Dosage for seasonal allergies:

Hay fever, asthma, chronic bronchitis & allergic rhinitis etc.: Give the first 6 injections at intervals of 4 days, 3 months before seasonal manifestations are expected.

Dosage for premenstrual syndrome of allergic etiology:

At the time of each menstrual cycle, one injection to be given on each day of the 6th, 13th and 20th day. Then one injection every 20th day of all following cycles until menopause if required.

Dosage for adenoidectomy and tonsillectomy:

A series of 3 injections 6 weeks before the operation, followed by a new series 4 weeks after the operation.

For allergic migraines, chronic urticaria, atopic eczema:

A series of 16 injections, without interruption at 2-days intervals may be given.

Administration:

The content of each PFS is required to be administered by subcutaneous route only.

4.3. Contraindications:

It is advisable to avoid Histoglob® treatment during pregnancy or during menstruation.

DO NOT ADMINISTER Histoglob® FOR AN ACUTE ALLERGIC ATTACK.

4.4. Special warnings and precautions for use:

Histoglob® is thermolabile, hence store the product at recommended temperature of 2°C - 8°C.

Always treat any existing superinfection before beginning Histoglob® treatment. It should not be given for an acute allergic attack, especially an acute asthmatic attack. In such cases the usual specific remedy must be used first. If an acute attack occurs after an injection of Histoglob® treatment, this should be viewed as a positive sign. Discontinue Histoglob® treatment until symptomatic treatment has alleviated the acute attack if required, and then continue the Histoglob® regime. In small doses, corticosteroids therapy is compatible with Histoglob® treatment. In many cases, the doses of corticosteroids can be gradually reduced, or even stopped. Histoglob® is not contraindicated with desensitization treatment. In a good number of cases, a combined treatment appears to reinforce the effects. It is important to remember that results may only be evident 3 to 4 weeks after the end of treatment.

4.5. Drug interactions:

There are no known drug interactions, and no information is available from any published article or report.

4.6. Use in special populations:

Dose in Children is mentioned in Section 4.2.

4.7. Effects on ability to drive and use machines:

No information is available from any published article or report.

4.8. Undesirable effects:

Histoglob® is normally well tolerated even by children and infants. However, in very rare cases an exacerbation of the clinical symptoms is observed after the 1st and 2nd injection. This is only of a transient nature and is usually a sign that the system is responding favorably to the medication. Histoglob® must always be given subcutaneously.

4.9. Overdose:

No report or information received about administration of accidental overdose.

5. Pharmacological Properties and Actions:

Symptoms of allergy are usually caused by a sudden release of various chemical factors, amongst which histamine is predominant. In allergic conditions, IgE antibodies are produced which bind to mast cells and / or circulating basophils. In the presence of the allergen, an antigen-antigen-antibody reaction occurs leading to degranulation of the mast cells and / or basophils and subsequent capillary permeability and contraction of smooth muscle which in turn give to several distressing symptoms in the individual. The antihistamine antibodies formed by the administration of Histoglob® neutralize the histamine so released and effectively eliminate allergic reactions.

The mechanism of action of histaglobulin is significantly different from other anti-allergic substances. Other anti-allergic substances, usually work and intervene at only one point in the reaction cycle of an allergic event. However, the studies suggest the essential anti-allergic active mechanisms of the complex as below:

- Produces highly potent antihistamine antibodies which neutralize the histamine released during allergic reactions. Increases the serum histamine binding capacity (SHBC), the ability of the histamine to bind in serum, and thus inhibits its clinical effects.
- Inhibits the allergen-induced histamine release from mast cells and basophils.
- Alters cytokine production from T helper cells: a possible inhibition of the IL-4 and the IL-5 production causing the reduction of IgE biosynthesis and inhibiting eosinophil accumulation, respectively.

Histoglob® is a systemic treatment against allergic conditions, but not a remedy for acute allergic attacks. Histoglob® usually leads to the progressive subsidence of allergic conditions within four weeks from the end of treatment. The duration of this protection may vary from patient to patient and may last several months.

6. Nonclinical & Clinical Pharmacology:

Histaglobulin inhibits immune responses in allergic conditions with its immunomodulatory pharmacological property.

Alleviation of histamine release from effector cells: The inhibitory effect the allergen-induced histamine release by histaglobulin is described in a study conducted in rats (1). This in vitro study indicated that the species-specific complex of rats immunoglobulin and histamine dihydrochloride (rat histaglobulin) inhibited degranulation and the associated histamine release from peritoneal rat mast cells. The effect was greater than the rat immunoglobulin or that of Histamine alone. In another study (2), where the mast cells from rats were sensitized with bovine serum albumin and then treated with human histaglobulin or rat histaglobulin. Only in the animal groups, treated with either human histaglobulin or rat histaglobulin, significant suppression of the histamine release can be observed. Two other studies, one in-vitro study (3), and another in vivo (4) study demonstrated that histaglobulin significantly inhibits the degranulation of human basophils.

Increase in histamine binding ability: In another study (5), done on patients with pollen allergies, it was seen that histaglobulin significantly increases the ability of the histamine to bind in serum, thus inhibiting its clinical effect. This mechanism of action is probably also the basis of the results of another two studies: In an in vivo study in rats (6), it was seen that histaglobulin offers protection against symptoms that are normally observed after administration of a histamine-releasing substance and in another study on guinea pigs (7), described that histaglobulin injections significantly extended the inhalation time of histamine and serotonin aerosols.

Inhibition of T Lymphocyte-Dependent Immune Responses: In allergic patients, there is an imbalance at the level of cytokine production by activated CD4 + T cells, which in turn leads to excessive IL-4. IL-4 leads to an increased production of the allergen specifically IgE in B lymphocytes. The study in rats (8) has been to demonstrate that the biosynthesis of IgE under the influence of histaglobulin is significantly inhibited while the IgG level rises. It was assumed that histaglobulin regulates influence on the cytokine production of the T helper cells and possible inhibition of the IL-4 production as the cause of the reduced IgE biosynthesis. (9, 10) described another antiallergic mechanism of histaglobulin, which was thought to be based on an altered cytokine production from T helper cells. Studies done in BALB/c mice found that mouse histaglobulin selectively inhibited eosinophil accumulation possibly by intervening the IL-5 production by TH2 helper cells.

7. Description:

Histoglob[®] is a sterile preparation of Histamine dihydrochloride coupled to active protein fraction extracted from human blood (Gamma-globulin) in strictly defined proportions.

8. Pharmaceutical particulars:

8.1. Incompatibilities:

Incompatibilities are not assessed or identified.

8.2. Packaging information:

The product is supplied in single use pre-filled syringes containing 1mL of sterile colourless liquid having Histoglob[®].

8.3. Storage and handling instructions:

Store at 2°C - 8°C. Do not freeze. Avoid exposure to sunlight and excessive heat.

9. Patient Counselling Information:

9.1 What does this package leaflet contain?

The physician responsible for treatment of the allergic disorders or other similar patients should be familiar with the contents of this pack insert and the medical literature concerning current concepts of immunological therapy with respect to administration of Histoglob[®] subcutaneous injection.

9.2 What is Histoglob[®]?

Histoglob[®] is a sterile preparation of Histamine dihydrochloride coupled to active protein fraction extracted from human blood (Gamma-globulin) in strictly defined proportions. This conjugate is capable of eliciting an immunological response in the human body with the production of highly potent antihistaminic antibodies. Gammaglobulin used in Histoglob[®] is tested negative for HBsAg and Anti HIV-1,2 and Anti HCV Antibodies by ELISA and HBV, HIV & HCV by Nucleic acid testing. Histoglob[®] is subjected to rigid stability tests and electrophoretic analysis to ensure purity and safety. Your doctor will explain further why this medicine has been given to you.

9.3 Which case this medicine should be used?

Histoglob[®] is a basic treatment for allergic conditions. It is therefore recommended for all allergic complaints whatever their symptoms or cause.

Histoglob[®] is recommended for the following indications:

1. Respiratory system: Allergic rhinitis, hay fever, bronchial asthma, asthmatic bronchitis, chronic bronchitis, spasmodic tracheitis.

2. Cutaneous: Eczema, urticaria, generalized skin allergies.

3. Nervous system: Migraine.

4. Gynecological: Premenstrual syndrome (PMS) of allergic etiology.

Histoglob[®] may also be used prophylactically with children (where there is a family history of allergy) who are about to undergo an adenoidectomy or tonsillectomy.

9.4 Which information you must know before taking Histoglob[®]?

Histoglob[®] should be taken as advised by physician.

9.5 You must not be given / Care should be taken:

It is advisable to avoid Histoglob[®] treatment during pregnancy or during menstruation.

DO NOT ADMINISTER Histoglob[®] FOR AN ACUTE ALLERGIC ATTACK.

9.6 How to take Histoglob[®]? Instruction for good use:

Histoglob[®] is thermolabile, hence store the product at recommended temperature of 2°C - 8°C. Always treat any existing infection before beginning Histoglob[®] treatment.

It should not be given for an acute allergic attack, especially an acute asthmatic attack. In such cases the usual specific remedy must be used first. If an acute attack occurs after an injection of Histoglob[®] treatment, this should be viewed as a positive sign. Discontinue Histoglob[®] treatment until symptomatic treatment has alleviated the acute attack if required, and then continue the Histoglob[®] regime.

In small doses, corticosteroids therapy is compatible with Histoglob[®] treatment. In many cases, the doses of corticosteroids can be gradually reduced, or even stopped. Histoglob[®] is not contraindicated with desensitization treatment. In a good number of cases, a combined treatment appears to reinforce the effects. It is important to remember that results may only be evident 3 to 4 weeks after the end of treatment.

9.7 Warnings and precautions:

Refer to section number 4.4.

9.8 What are the possible side effects?

Refer to section number 4.8.

9.10 How are you given Histoglob®:

Histoglob® must always be given subcutaneously and as advised by physician.

9.11 If you are given more Histoglob® than you should have been given:

In such situation, please contact your physician.

9.12 How to store Histoglob®?

Histoglob® is thermolabile, hence store the product at recommended temperature of 2°C - 8°C. Store in a cool & dark place. Do not freeze. Avoid exposure to excessive heat. Shelf life of Histoglob® PFS is 24 months.

9.13 Contents of the pack and other information:

Each mL contains:

Human Normal immunoglobulin	I.P.	12 mg
Histamine dihydrochloride	B.P.	0.15 mcg
Excipients		q.s.

9.14 What Histoglob® PFS looks like and contents of the pack:

The product is supplied in single use pre-filled syringes containing 1mL of sterile colourless liquid having Histoglob®.

10. Marketed by:

BHARAT SERUMS AND VACCINES LIMITED

Ghar No. 372, Lower Ground Floor, Survey No. 14/4(P), 17/2A(P), Thane-Nashik Highway, Nimbavali, Yewai, Bhiwandi - 421302, Dist. Thane, India.

Manufactured by: VIRCHOW BIOTECH PVT. LTD.

Sy No. 172 Part, Gagilapur (V), Dundigal-Gandimaisamma (M), Medchal-Malkajigiri (D), Telangana State-500043, India.

11. Details of manufacturing license number:

Mfg. Lic. No.: 01/RR/AP/2013/BP/R.

12. Date of revision:

29/08/2024.

References:

- (1) Ishikawa, T., Shimada, T., Kessoku N., Kiyoi, M.; Inhibition of rat mast cell degranulation and histamine release by histamine-rat gamma globuline conjugate.; Int. Arch. Allergy appl. Immunol. 1979; 59: 403-407.
- (2) Lallouette, P. et al.; Histamine release from sensitized rat mast cell. Effect of in vivo treatment with gammaglobulin-histamine. Poster communic. 1981; 8. Int. Congr. Pharmacol., Tokyo
- (3) Tanizaki, Y., Komagoe, H., Sudo, M., Kitani, H., Tada, S., Takahashi, K., Kimura, I.; Inhibitory effect of histamine-gamma globulin conjugate on IgE-mediated reactivity of human basophils. Jpn. J. Allergol. 1984; 33, 12: 1025-1029.
- (4) Tanizaki, Y., Tani, M., Tada, S., Komagoe, H., Nakagawa, S., Takahashi, K., Shuto, M., Otani, A., Kimura, I.; The in vivo suppression effect of histamine and y-globulin against allergy reactions of the immediate type. Monthly Clinic and Research 1989; 64, 6: reprint.
- (5) Ward, J. P.; Double-blind study with histaglobulin triplex in the treatment of grass pollinosis. Switzerland, Rundschau f. Med. (Practice) 1989; 78, 4: 62-65.
- (6) Varonos, D.; Effect and biological neutralization of histamine released in vivo. Pharmaceutical research 1961; 11: 591-592.
- (7) Scheiffarth, F., Zicha, L., Schott, G., Schmid, E., Alms, U.; Studies on the mechanism of action of a histamine-globulin complex in guinea pigs. Pharmaceutical Research 1961; 11: 595-598.
- (8) Hanashiro, K., Sunagawa, M., Saitoh, S., Nakamura, M., Kosugi, T.; The administration of histaglobulin conjugate suppress the production of IgE on rats. Personal communication 1994.
- (9) Yoshii, H., Fukada, Y., Yamamoto, K., Yayiri, H., Suehiro, S., Yanagibara, Y., Okudaira, H.; A new antiallergic mechanism for histaglobulin (1): inhibitory action against T cell-dependent eosinophils. 1993; 21 st. general meeting of Japan association for clinical immunology, Sapporo, 8-10 Sept.
- (10) Yoshii, H., Fukada, Y., Yamamoto, K., Nakai, M., Yago, S., Suehiro, S., Yanagibara, Y., Okudaira, H.; Selective inhibition of eosinophil accumulation with histaglobulin. Experimental research: Basic mechanisms eosinophils 1994; IV. Int. Congr. Allergology and Clinical Immunology, Ann. meet. Europ. Academy of Allergology and Clinical Immunology, Stockholm, 26.06 -01.07.

To Report Suspected Adverse Reaction, Contact Bharat Serums and Vaccines Ltd. at pv@bsvgroup.com or visit the website <https://www.bsvgroup.com/adverse/>

