STANDARDIZED SHORT RAGWEED POLLEN - standardized short ragweed pollen injection, solution
Antigen Laboratories, Inc.

Allergenic Extract

WARNINGS

Standardized Short Ragweed allergenic extract is intended for use by, or under the guidance of, physicians who are experienced in the administration of allergenic extracts for diagnosis and/or immunotherapy and the emergency care of anaphylaxis. *Patients being switched from other manufacturers' extracts to Antigen Laboratories' allergenic extracts should be started as though they were receiving treatment for the first time.(See "WARNINGS" section below.)* **Severe systemic reactions may occur with all allergenic extracts. In certain individuals, these life-threatening reactions may result in death. Patients should be observed for at least 20 minutes following allergenic extract injections. Treatment and emergency measures, as well as personnel trained in their use, must be available in the event of a life-threatening reaction. Sensitive patients may experience severe anaphylactic reactions resulting in respiratory obstruction, shock, coma and/or death. Patients being switched from one lot of extract to another lot from the same manufacturer should have the dose reduced by 75%.**

Report serious adverse events to MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787, phone 1-800-FDA-1088.

Allergenic extracts should not be injected intravenously. Deep subcutaneous routes have proven to be safe. See the "WARNINGS", "PRECAUTIONS", "ADVERSE REACTIONS" and "OVERDOSAGE" sections.

Patients receiving beta-blockers may not be responsive to epinephrine or inhaled bronchodilators. Patients with respiratory obstruction not responding to parenteral or inhaled bronchodilators may require theophylline, oxygen, intubation and life support systems. Parenteral fluid and/or plasma expanders may be utilized for treatment of shock. Adrenocorticosteroids may be administered parenterally or intravenously. Refer to "ADVERSE REACTIONS" section.

DESCRIPTION

Antigen Laboratories' Standardized Short Ragweed allergenic extracts are sterile and intended for dilution prior to skin testing and/or immunotherapy. The route of administration for immunotherapy is subcutaneous. The routes of administration for diagnostic purposes are intradermal or prick-puncture of the skin.

Standardized Short Ragweed allergenic extract is assigned arbitrary Allergy Units of 100,000 AU/ml based on being equipotent by Enzyme-Linked Immunosorbent Assay (ELISA) to a Center for Biologics Evaluation and Research (CBER) reference.

The following testing is also performed:

1. Microscopic examination to confirm identity and purity of source pollen.
2. Isoelectric focusing (IEF) pattern of source material and final products are compared to respective CBER reference extract.
3. Antigen E (Amb a I) is considered to be the major allergenic protein of short ragweed. The Antigen E content of short ragweed extracts is determined by radial immunodiffusion assay using CBER standards and anti-serum. Standardized Short Ragweed (100,000 AU/ml) extracts contain 200-400 antigen E units per milliliter.
4. Ninhydrin protein analysis.
5. Glycerine analysis.

6. Sterility testing.
7. Safety testing.

Active ingredients: Allergens are described by common and scientific name on container label. Preservative is 50% v/v glycerine. Inactive ingredients are 0.95% sodium chloride, 0.24% sodium bicarbonate and water for injection.

CLINICAL PHARMACOLOGY

The most clinically relevant mechanism of allergenic response begins with cross-linking of plasma membrane receptor-bound IgE molecules by specific antigens causing mast cell mediator release. In vitro, this process is temperature dependent, requires the presence of divalent cations, and activation of a cell membrane-associated serine esterase. Another immunologic mechanism for mast cell degranulation is mediated by complement-derived anaphylatoxins C3a, C4a and C5a. These low molecular weight peptides presumably stimulate degranulation of mast cells by binding to distinct plasma membrane receptor(s) and are active mast cell secretagogues in human skin in vivo. Several naturally occurring and exogenous agents are capable of degranulating and/or stimulating mast cells by nonimmunologic mechanisms.

Stimulation of mast cells leads to the release and generation of pharmacologically active soluble factors that produce immediate hypersensitivity reactions. Some mediators are rapidly liberated from mast cells granules (e.g., histamine), others remain granule-associated after release from the cell (e.g., heparin). Products of arachidonic acid metabolism are rapidly produced and released from mast cells following stimulation. Select patients demonstrate later reactions (i.e., late-phase reactions) at sites of mast cell degranulation. These reactions begin 2 to 8 hours after mediator release and are characterized by granulocyte-rich infiltrates that are followed by accumulations of mononuclear cells. Clinically these late-phase reactions present as inflammatory, infiltrated plaques or nodules.[15]

Patients who react to a small quantity of antigen by skin testing, or have a high RAST score, are classified as highly sensitive. Those who react only to large quantities of antigen, or have a low RAST score, are classified as less sensitive. It appears there is at least a 50,000-fold range between the most and least sensitive individuals. Certain patients who do not have elevated quantities of allergen specific IgE, and are RAST negative, do have positive skin tests and have symptoms of allergic rhinitis. These patients are considerably less sensitive than patients with detectable levels of specific IgE antibody.[2]

The mode of action of immunotherapy with allergenic extracts is still under investigation. Increasing subcutaneous injection doses of allergenic extract into patients with allergenic disease has shown to result in both humoral and cellular changes. These include production of allergen specific IgG antibodies, suppression of histamine release from target cells, decrease in circulating levels of antigen specific IgE antibody over long periods of time and suppression of peripheral blood T-lymphocyte cell response to antigen.[5, 9, 10]

INDICATIONS AND USAGE

Allergenic extract is indicated for diagnostic testing and treatment (immunotherapy) of patients whose histories indicate allergic symptoms upon natural exposure to short ragweed pollen. Confirmation is determined by skin testing.

CONTRAINDICATIONS

Do not administer in the presence of diseases characterized by bleeding diathesis. Individuals with autoimmune disease may be at risk of exacerbating symptoms of the underlying disease, possibly due to routine immunization. Recent myocardial infarction patients may not tolerate immunotherapy. Children with nephrotic syndrome probably should not receive injections due to a possibility of immunization causing exacerbation of their nephrotic disease.

Standardized Short Ragweed extract is not intended for the treatment of patients who do not experience allergic symptoms upon natural exposure to the allergen.

Allergenic extracts are not intended for diagnosing patients whose skin does not manifest immediate

hypersensitivity reactions (wheal and flare) to the allergenic extract.

WARNINGS

Refer to boxed "WARNINGS", "PRECAUTIONS", "ADVERSE REACTIONS" and "OVERDOSAGE" sections.

Extreme caution is necessary when using diagnostic skin tests or injection treatment in highly sensitive patients who have experienced severe symptoms or anaphylaxis by natural exposure or previous skin testing or treatment. *IN THESE CASES THE POTENCY FOR SKIN TESTS AND THE ESCALATION OF THE TREATMENT DOSE MUST BE ADJUSTED TO THE PATIENT'S SENSITIVITY AND TOLERANCE.*

Benefit versus risk needs to be evaluated in patients with unstable asthma, steroid dependent asthmatics or patients with underlying cardiovascular disease.

Injections should never be given intravenously. A 5/8 inch, 25 gauge needle on a sterile syringe allows deep subcutaneous injection. Withdraw plunger slightly after inserting needle to determine if a blood vessel has been entered.

Proper measurement of dose and caution in making injection will minimize reactions. Adverse reactions to allergenic extracts are usually apparent within 20-30 minutes following injection of immunotherapy.

Extract should be temporarily withheld or dosage reduced in case of any of the following conditions: 1) flu or other infection with fever; 2) exposure to excessive amounts of allergen prior to injection; 3) rhinitis and/or asthma exhibiting severe symptoms; 4) adverse reaction to previous injection until cause of reaction has been evaluated by physician supervising patient's immunotherapy program.

PRECAUTIONS

General:

Immunotherapy must be given under physician's supervision. Sterile solutions, vials, syringes, etc. must be used. Observe aseptic technique when making dilutions from stock concentrates, preparing individual treatment doses or during skin testing and administering immunotherapy. The usual precautions in administering allergenic extracts are necessary, refer to boxed WARNINGS and "WARNINGS" section. Sterile syringe and needle must be used for each individual patient to prevent transmission of serum hepatitis, Human Immunodeficiency Virus (HIV) and other infectious agents.

Epinephrine 1:1000 should be available. Refer to "OVERDOSAGE" section for description of treatment for anaphylactic reactions.

Information for Patients:

Patient should remain under observation of a nurse, physician, or personnel trained in emergency measures for at least 20 minutes following immunotherapy injection. Patient must be instructed to report any adverse reactions that occur within 24 hours after injection. Immediate medical attention must be sought for reactions that occur during or after leaving physician's office.

Pregnancy Category C:

Animal reproduction studies have not been conducted with allergenic extracts. It is not known whether allergenic extracts cause fetal harm during pregnancy or affect reproductive capacity. A systemic reaction to allergenic extracts could cause uterine contractions leading to spontaneous abortion or premature labor. Allergenic extracts should be used during pregnancy only if potential benefit justifies potential risk to fetus.[6]

Nursing Mothers:

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

Pediatric Use:

Allergenic extracts have been used routinely in children and no special problems of safety or specific hazard have been found. Children can receive the same dose as adults. Discomfort is minimized by dividing the dose in half and administering injection at two different sites.[13, 14]

Carcinogenesis, Mutagenesis, Impairment of Fertility:

Long term animal studies have not been conducted with Standardized Short Ragweed allergenic extracts to evaluate carcinogenicity, mutagenicity or fertility impairment.

Drug Interactions:

Antihistamines. The H1 antagonists which block the capillary effects of histamine, inhibit the wheal-and-flare reaction. Moreover, H1 antagonists reduce the wheal reaction induced by mast cell secretagogues or allergens in sensitized patients. The most potent H1 antagonist seems to be astemizole, which blocks the wheal and flare induced by histamine for a long period of time, ranging from a few days to 40 days. Although a large interpatient variation exists, hydroxyzine and clemastine seem to be more potent inhibitors than chlorpheniramine, and promethazine. On the other hand, tripelennamine, diphenhydramine, cyproheptadine, and perphenazine induce a variable, but rather low, degree of inhibition. The duration of the inhibitory effect varies from 1 day to up to 10 days, according to the drug and the patient's sensitivity. Hydroxyzine and clemastine usually exhibit a longer blockade. Sustained-release H1 antagonists may produce a longer inhibitory effect. Long-term treatment with antihistamines may reduce the inhibitory effects of these drugs on skin tests. Long et al. noticed that after 3 weeks of treatment with hydroxyzine, its suppressive effect, as well as that induced by other H1 blockers, was significantly reduced. These data indicate that the 24-hour period without antihistamine sometimes recommended prior to skin testing may not be sufficient for reliable testing. If the histamine control is normal, it suggests that accurate testing can be performed, because the reactions to histamine and allergen were found to be equally suppressed by hydroxyzine.[1,11]

Tricylic antidepressents exert a potent and sustained decrease of skin reactions to histamine. This effect may last for a few weeks. Tranquilizers and antiemetic agents of the phenothiazine class have H1 antihistaminic activity and can block skin tests.[1]

Corticosteroids. Short-term (less than 1 week) administration of corticosteroids at the therapeutic doses used in asthmatic patients does not modify the cutaneous reactivity to histamine, compound 48/80, or allergen. Long-term corticosteroid therapy modifies the skin texture and makes the interpretation of immediate skin tests more difficult.[1]

Theophylline. It appears that theophylline need not be stopped prior to skin testing.[1]

Beta-blockers. *PATIENTS RECEIVING BETA-BLOCKERS MAY NOT BE RESPONSIVE TO EPINEPHRINE OR INHALED BRONCHODILATORS.* The following are commonly prescribed *BETA-BLOCKERS:* Levatol, Lopressor, Propanolol Intersol, Propanolol HCL, Blocadren, Propanolol, Inderal-LA, Visken, Corgard, Ipran, Tenormin, Timoptic. Ophthalmic beta-blockers: Betaxolol, Levobunolol, Timolol, Timoptic. Chemicals that are beta-blockers and may be components of other drugs: Acebutolol, Atenolol, Esmolol, Metoprolol, Nadolol, Penbutolol, Pindolol, Propanolol, Timolol, Labetalol, Carteolol.

Beta-adrenergic agents. Inhaled $beta_2$ agonists in the usual doses used for the treatment of asthma do not usually inhibit allergen-induced skin tests. However, oral terbutaline and parenteral ephedrine were shown to decrease the allergen-induced wheal. Such an effect seems to be related to the antianaphylactic properties of $beta_2$ agonists and, to a lesser extent, to a direct action on the dermal vasculature. Conversely, beta-blocking agents such as Propanolol can significantly increase skin reactivity.[1]

Cromolyn. Cromolyn inhaled or injected prior to skin tests with allergens or degranulating agents does not alter the skin whealing response.[1]

Other drugs. Other drugs have been shown to decrease skin test reactivity. Among them, dopamine is the best-documented compound.[1]

ADVERSE REACTIONS

Adverse reactions include, but are not necessarily limited to urticaria; itching; edema of extremities; respiratory wheezing or asthma; dyspnea; cyanosis; tachycardia; lacrimation; marked perspiration; flushing of face, neck or upper chest; mild persistent clearing of throat; hacking cough or persistent sneezing.

1) Local Reactions

A mild burning immediately after injection is expected; this usually subsides in 10-20 seconds. Prolonged pain or pain radiating up arm is usually the result of intramuscular injection, making this injection route undesirable. Subcutaneous injection is the recommended route.

Small amounts of erythema and swelling at the site of injection are common. Reactions should not be considered significant unless they persist for at least 24 hours or exceed 50 mm in diameter.

Larger local reactions are not only uncomfortable, but indicate the possibility of a severe systemic reaction if dosage is increased. In such cases dosage should be reduced to the last level not causing reaction and maintained for two or three treatments before cautiously increasing.

Large, persistent local reactions or minor exacerbations of the patient's allergic symptoms may be treated by local cold applications and/or use of oral antihistamines.

2) Systemic Reactions

Systemic reactions range from mild exaggeration of patient's allergic symptoms to anaphylactic reactions.[12] Very sensitive patients may show a rapid response. It cannot be overemphasized that, under certain unpredictable combinations of circumstances, anaphylactic shock is always a possibility. Fatalities are rare but can occur.[16] Other possible adverse reactions include unusual swelling and/or tenderness at injection site, rhinorrhea, sneezing, coughing, wheezing, shortness of breath, nausea, dizziness, fainting, pallor, bradycardia, hypotension, angioedema, conjunctivitis, rhinitis, and urticaria.[8,9]

Careful attention to dosage and administration limits such reactions. Allergenic extracts are highly potent to sensitive individuals and OVERDOSE could result in anaphylactic symptoms. Therefore, it is imperative that physicians administering allergenic extracts understand and prepare for treatment of severe reactions. Refer to "OVERDOSAGE" section.

OVERDOSAGE

Refer to "WARNINGS", "PRECAUTIONS", and "ADVERSE REACTIONS" sections for signs and symptoms of overdose.

If a systemic or anaphylactic reaction does occur, apply tourniquet above the site of allergenic extract injection and inject intramuscularly or subcutaneously 0.3 to 0.5 ml of 1:1000 Epinephrine-hydrochloride into the opposite arm or gluteal area. Loosen tourniquet briefly at 5 minute intervals to prevent circulatory impairment. Repeat dose in 5-10 minutes if necessary.

The epinephrine HCL 1:1000 dose for infants to 2 years is 0.05 to 0.1 ml; for children 2 to 6 years it is 0.15 ml; for children 6 to 12 years it is 0.2 ml.

Symptoms of progressive anaphylaxis include airway obstruction and/or vascular collapse. After administration of epinephrine, profound shock and vasomotor collapse should be treated with intravenous fluids and possibly vasoactive drugs. Monitor airways for obstruction. Oxygen should be given by mask if indicated.

Antihistamines, H2 antagonist, bronchodilators, steroids and theophylline may be used as indicated after giving adequate epinephrine and circulatory support.[12]

Patients who have been taking a beta-blocker may be unresponsive to epinephrine or beta-adrenergic drugs (Alupent). These drugs should be administered even though a beta-blocker may have been taken. The following treatment will be effective whether or not patient is taking a beta-blocker: Aminophylline IV, slow push or drip, Atrovent (Ipratropium bromide) Inhaler, 3 inhalations repeated, Atropine, 0.4 mg/ml, 0.75 to 1.5 ml IM or IV, Solu-Cortef, 100-200 mg IM or IV, Solu-Medrol, 125 mg IM or IV, Glucagon, 0.5-1 mg IM or IV, Benadryl, 50 mg IM or IV, Cimetidine, 300 mg IM or IV, Oxygen via ambu bag.

DOSAGE AND ADMINISTRATION

Refer to "STORAGE" section for proper storage condition for allergenic extract.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Some allergenic extracts naturally precipitate.

Physicians undertaking immunotherapy should be concerned with patient's degree of sensitivity. The initial dilution of allergenic extract, starting dose, and progression of dosage must be carefully determined on the basis of the patient's history and results of skin tests. (See "INDICATIONS AND USAGE" section.) Strongly positive skin tests may be risk factors for systemic reactions. Less aggressive immunotherapy schedules may be indicated for such patients.

PRICK-PUNCTURE TESTING: To identify short ragweed sensitive individuals and as a safety precaution, it is recommended that a prick or puncture test be performed prior to initiating very dilute intradermal testing. Prick (puncture) testing is performed by placing a drop of extract on skin and puncturing skin through the drop with a small needle such as a bifurcated vaccinating needle. The most satisfactory sites on the back for skin testing are from posterior axillary fold to 2.5 cm from the spinal column, and from the top of the scapula to the lower rib margins. The best areas on the arms are the volar surfaces from the axilla to 2.5 or 5 cm above the wrist, skipping the anticubital space. A positive reaction is approximately 10-15 mm erythema with 2.5 mm wheal.

Smaller, less conclusive reactions may be considered positive in conjunction with a definitive history of symptoms on exposure to allergen. Less sensitive individuals can be tested intradermally with appropriately diluted extract. (See Intradermal Testing.)

A positive control using histamine phosphate identifies patients whose skin may not react due to medications, metabolic or other reasons. A negative diluent control would exclude false-positive reactions due to ingredients in diluent or patients who have dermatographism.

SERIAL DILUTIONS
APPROXIMATE AU/ml RESULTING FROM 1:5 DILUTION
OF ALLERGENIC EXTRACT CONCENTRATE

DILUTION #	**DILUTION EXPONENT**	**100,000 AU/ml**
No. 1	5^{-1}	20,000
No. 2	5^{-2}	4,000
No. 3	5^{-3}	800
No. 4	5^{-4}	160
No. 5	5^{-5}	32
No. 6	5^{-6}	6.4
No. 7	5^{-7}	1.28
No. 8	5^{-8}	0.256
No. 9	5^{-9}	0.0512
No. 10	5^{-10}	0.01024
No. 11	5^{-11}	0.002048

SERIAL DILUTIONS
APPROXIMATE AU/ml RESULTING FROM 1:10 DILUTION
OF ALLERGENIC EXTRACT CONCENTRATE

DILUTION #	**DILUTION EXPONENT**	**100,000 AU/ml**
No. 1	10^{-1}	10,000

No. 2	10^{-2}	1,000
No. 3	10^{-3}	100
No. 4	10^{-4}	10
No. 5	10^{-5}	1
No. 6	10^{-6}	0.1
No. 7	10^{-7}	0.01
No. 8	10^{-8}	0.001
No. 9	10^{-9}	0.0001
No. 10	10^{-10}	0.00001

INTRADERMAL TESTING: Upper or lower arm is the usual location for skin testing. A sterile, disposable syringe and needle is used for each extract tested. Intracutaneous test dilutions should be made with aqueous diluent. Three-fold, five-fold or ten-fold dilutions may be prepared from stock concentrates. (1) Start testing with the most dilute allergenic extract concentration. (2) A volume of 0.01-0.02 ml should be injected slowly into the superficial skin layers making a small bleb (superficial wheal). (3) An initial skin test with 0.001 AU/ml (10^{-8} or 5^{-11} dilution) is considered safe for patients with suspected short ragweed sensitivity. Reactions to skin testing are graded 0 to 4+ according to size of wheal and erythema produced (refer to chart below). The reactions should be read after fifteen minutes.

GRADE	**mm ERYTHEMA**	**mm WHEAL**
0	less than 5	less than 5
±	5-10	5-10
1+	11-20	5-10
2+	21-30	5-10
3+	31-40	10-15 or with pseudopods
4+	greater than 40	greater than 15 or with many pseudopods

If after twenty minutes no skin reaction is observed, continue testing using increments of the concentration until a reaction of 5-10 mm wheal and 10-30 mm erythema is obtained, or a concentration of 5^{-2} or 10^{-1} has been tested. A positive control of histamine phosphate and a negative control of 50% v/v glycerine diluted with diluent to 5^{-2} (1:25) or 10^{-1} (1:10) dilution, should be included in interpretation of intradermal testing.[1]

INTRADERMAL TESTING--SKIN ENDPOINT TITRATION: Patient's degree of sensitivity and the initial dose of allergen to be used in immunotherapy can be quantitated using five-fold dilutions of allergenic extract for intracutaneous testing. A concentration of 0.001 AU/ml (5^{-11} dilution) is a safe initial dilution. A sequence of 5-fold dilutions of an allergen are injected intracutaneously (0.01-0.02 ml) to form 4 mm diameter superficial wheals. After 15 minutes the endpoint is determined by noting the dilution that first produces a wheal and erythema 2 mm larger than dilutions that produce a 5 mm or negative wheal. The endpoint dilution is used as a starting dose concentration for immunotherapy.

Normally, immunotherapy can be started with 0.15 ml of the dilution of allergenic extract causing the endpoint reaction. In any allergenic patient, a safe starting dose can be determined by finding the first dose by intradermal skin testing producing a 1+ reaction or the dilution producing the skin endpoint.

Increasing doses of 5-20% increments can be administered providing initial or preceding dose is tolerated without significant local reactions. The rate of increase in dosage in the early stages of

treatment with highly diluted extracts is usually more rapid than the rate of increase possible with more concentrated extracts. This schedule is intended only as a guide and must be modified to the reactivity of the individual patient. Physicians must proceed cautiously in the treatment of highly sensitive patients who develop large local or systemic reactions.

Some patients may tolerate larger doses of the allergenic extract depending on patient response.[3] Because diluted extract tends to lose activity on storage, the first dose from a more concentrated vial should be the same or less than the previous dose.[4,7]

Dosages progressively increase according to the tolerance of the patient at intervals of one to seven days until, (1) the maintenance dose is reached (the "optimal" tolerated dose for each individual); (2) the patient achieves relief of symptoms; (3) induration at the site of injection is no larger than 50 mm in 36 to 48 hours. Maintenance dose may be continued at regular intervals perennially. It may be necessary to adjust the progression of dosage downward to avoid local and systemic reactions during ragweed pollen season.

The usual duration of treatment has not been established. A period of two or three years on immunotherapy constitutes an average minimum course of treatment.

Clinical studies indicate the "optimal" immunotherapy dose of 2000 AU/ml (range of 1000-4000 AU/ml) consistently provides clinical relief for short ragweed sensitive patients. Physician should be forewarned that peak dose in this range is more commonly associated with severe systemic reactions than doses below 1000 AU/ml. Dose may need adjusting downward for extremely sensitive patients or during periods of increased pollen exposure. Patients unable to tolerate target dose should be treated with lower immunizing dose.[1,17]

HOW SUPPLIED

Standardized Short Ragweed allergenic extract concentration is expressed in AU/ml. Standardized Short Ragweed (100,000 AU/ml) is supplied in 10, 30 and 50 ml containers. Extracts in 5 ml dropper bottles are available for prick-puncture testing. To insure maximum potency for the entire dating period, all stock concentrates contain 50% v/v glycerine.

STORAGE

Store all stock concentrates and dilutions at 2-8 degrees C. Keep at this temperature during office use. The expiration date of allergenic extracts is listed on the container label. Dilutions of allergenic extracts containing less than 50% v/v glycerine are less stable than those containing at least 50% v/v glycerine. If loss of potency is suspected, potency can be checked using side by side skin testing with freshly prepared dilutions of equal concentration on individuals with known sensitivity to the allergen.

REFERENCES

1. Bousquet, Jean: "In vivo methods for study of allergy: Skin tests" Third Edition, Allergy Principles and Practice, C.V. Mosby Co., Vol. I, Chap. 19, pp 419-436, 1988.
2. Matthews, K., et al: Rhinitis, Asthma and the Other Allergic Diseases. NIAID Task Force Report, U.S. Dept. HEW, NIH Publication No. 79-387, Chapter 4, pp. 213-217, May 1979.
3. Ishizaka, K.: Control of IgE Synthesis, Third Edition, Allergy Principles and Practices, C.V. Mosby Co., Vol. I, Chap. 4, p. 52, 1988.
4. Nelson, H.S.: "The Effect of Preservatives and Dilution on the Deterioration of Russian Thistle (Salsola pestifer), a pollen extract." The Journal of Allergy and Clinical Immunology, Vol. 63, No. 6, pp. 417-425, June 1979.
5. Rocklin, R.E., Sheffer, A.L., Grainader, D.K. and Melmon, K.: "Generation of antigen-specific suppressor cells during allergy desensitization", New England Journal of Medicine, Vol. 302, pp. 1213-1219, May 29, 1980.
6. Seebohm, P.M., et al: Panel on Review of Allergenic Extracts, Final Report, Food and Drug Administration, pp. 9-48, March 13, 1981.
7. Stevens, E.: Cutaneous Tests, Regulatory Control and Standardization of Allergenic Extracts, First International Paul Ehrlich Seminar, Frankfurt, Germany, pp. 133-138, May 20-22, 1979.

8. Van Metre, T., Adkinson, N., Amodio, F., Lichtenstein, L., Mardinay, M., Norman, P., Rosenberg, G., Sobotka, A., Valentine, M.: “A Comparative Study of the Effectiveness of the Rinkel Method and the Current Standard Method of Immunology for Ragweed Pollen Hay Fever,” The Journal of Clinical Allergy and Immunology, Vol. 66, No. 6, p. 511, December 1980.
9. Wasserman, S.: The Mast Cell and the Inflammatory Response. The Mast Cell--its role in health and disease. Proceedings of an International Symposium, Davos, Switzerland, Pitman Medical Publishing Co., pp. 9-20, 1979.
10. Perelmutter, L.: IgE Regulation During Immunotherapy of Allergic Diseases. Annals of Allergy, Vol. 57, August 1986.
11. Long, W.F., Taylor, R.J., Wagner, C.J., et al: Skin test suppression by antihistamines and the development of subsensitivity, J. Allergy Clin. Immunol., pp. 76-113, 1985.
12. Wasserman, S., Marquart, D.: Anaphylaxis, Third Edition, Allergy Principles and Practice, C.V. Mosby Co., Vol. 1, Chap. 58, pg. 1365-1376, 1988.
13. Bullock, J., Frick, O.: Mite Sensitivity in House Dust Allergic Children, Am. J. Dis. Child., pp. 123-222, 1972.
14. Willoughby, J.W.: Inhalant Allergy Immunotherapy with Standardized and Nonstandardized Allergenic Extracts, American Academy of Otolaryngology-Head and Neck Surgery: Instructional Courses, C.V. Mosby Co., Vol. 1, Chapter 15, September 1988.
15. Holgate, S.T., Robinson, C., Church, Mike: Mediators of Immediate Hypersensitivity, Third Edition, Allergy Principles and Practice, C.V. Mosby Co., Vol. I and II, pp 135-163, 1988.
16. Reid, Michael J., Lockey, Richard F., Turkeltaub, Paul C., M.D., Platts-Mills, Thomas:”Survey of Fatalities from Skin Testing and Immunotherapy 1985-1989”, Journal of Allergy and Clinical Immunology, Vol. 92, No. 1, pp. 6-15, 1993.
17. Turkeltaub, Paul C., M.D.:”Standardized Extracts in Practice”, Immunotherapy, A Practical Guide to Current Procedures, Sponsored by American Academy of Allergy and Immunology, 1994.

STANDARDIZED SHORT RAGWEED POLLEN

standardized short ragweed pollen injection, solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:49288-0448
Route of Administration	SUBCUTANEOUS, INTRADERMAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
AMBROSIA ARTEMISIIFOLIA POLLEN (UNII: K20Y81ACO3) (AMBROSIA ARTEMISIIFOLIA POLLEN - UNII:K20Y81ACO3)	AMBROSIA ARTEMISIIFOLIA POLLEN	100000 [AU] in 1 mL

Inactive Ingredients	
Ingredient Name	**Strength**
GLYCERIN (UNII: PDC6A3C0OX)	0.525 mL in 1 mL
SODIUM CHLORIDE (UNII: 451W47IQ8X)	0.0095 g in 1 mL
SODIUM BICARBONATE (UNII: 8MDF5V39QO)	0.0024 g in 1 mL
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:49288-0448-2	5 mL in 1 VIAL, MULTI-DOSE		
2	NDC:49288-0448-3	10 mL in 1 VIAL, MULTI-DOSE		
3	NDC:49288-0448-4	30 mL in 1 VIAL, MULTI-DOSE		
4	NDC:49288-0448-5	50 mL in 1 VIAL, MULTI-DOSE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA102232	01/15/1983	

Labeler - Antigen Laboratories, Inc. (030705628)

Establishment

Name	Address	ID/FEI	Business Operations
Antigen Laboratories, Inc.		030705628	manufacture

Revised: 8/2009 Antigen Laboratories, Inc.