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U.S. Government License No. 308

ALLERGENIC EXTRACTS

Short Ragweed
and
G.S. Ragweed Mix

Suggested Dosage Schedule
and Instructions

WARNING

Allergenic extracts can elicit severe adverse reactions when improperly administered (see below under Warnings). Any person administering allergenic extracts should be experienced in their use, aware of the risk of adverse reactions, and capable of properly handling such reactions.

DESCRIPTION

Each vial contains an extract of Short Ragweed (**Ambrosia elatior**) pollen or of equal parts Short and Giant Ragweed (**A. trifida**) pollen extracts. Extracts are supplied in a buffered saline solution with or without glycerin (50%) added as a stabilizer. Extracts are supplied as a sterile solution intended for subcutaneous or intracutaneous administration.

Each lot of Short Ragweed extract or Mixed Ragweed extract is assayed for Antigen E content using a radial immunodiffusion test¹ employing known Antigen E standards and anti-Antigen E antisera. Extracts containing Short Ragweed at a concentration of 1:20 or stronger are assayed for Antigen E. Extracts more dilute than this are not assayed but the Antigen E content is obtained by calculation based on the Antigen E content of the concentrate.

Antigen E, a protein with a molecular weight of approximately 38,000, has been found to be a major antigenic component of Short Ragweed pollen.^{2,3} Antigen E content has been shown to correlate well with skin test reactivity of ragweed extracts.⁴ For this reason, Antigen E content is being used to standardize Short Ragweed extracts in addition to the protein nitrogen content or weight to volume ratios as have been used.

When transferring patients from non-standardized extracts to a standardized extract, it is advisable to compare the potency of the different lots by comparative skin testing using the same concentrations of each extract. Marked differences in skin reactivity will indicate differences in potency and the need to adjust dosages so as to avoid possible severe reaction.

CLINICAL PHARMACOLOGY

Controlled studies employing Ragweed extracts and Antigen E immunotherapy have demonstrated an increase in Ragweed antigen-specific blocking antibodies. These studies also demonstrated significant symptom amelioration in Ragweed allergic individuals.^{5,6} The total mechanism of immunotherapy is not yet known and is still being investigated.

INDICATIONS

Hyposensitization is indicated when careful testing and patient history can pinpoint allergens responsible for allergic symptoms, and when it is not possible or practical to avoid these allergens. Allergenic extracts are administered to reduce symptoms of allergy of a seasonal or perennial nature.

CONTRAINDICATIONS

Immunotherapy with Ragweed antigens is contraindicated in those individuals who do not exhibit skin test or clinical sensitivity to Ragweed antigens. (See below under Warnings and Precautions)

WARNINGS

Allergenic extracts can elicit adverse local and systemic reactions if initial dosage or rate of dosage increase is too high. These factors must be carefully evaluated by the physician based on history, degree of sensitivity, and skin test results prior to commencement or continuation of therapy. Any person administering a biological product should be aware of the risk of local or systemic reactions if improperly used and be capable of handling such reactions. (See below under Adverse Reactions.) Patients receiving allergenic extracts should be kept under observation a minimum of thirty (30) minutes so that any adverse reaction can be observed and properly handled. See information above in Description category for information on transferring patients from non-standardized to standardized extracts.

PRECAUTIONS

Check lot number and dosage schedule of patient to verify correctness of prescription number or vial number. Only after this verification has been made should an appropriate injection be given. A separate sterile needle and syringe should be used for each patient to prevent transmission of homologous serum hepatitis and other infectious agents.

Pregnancy Category C. Animal reproduction studies have not been conducted with allergenic extracts. It is also not known whether allergenic extracts can cause fetal harm when administered to a pregnant woman or whether it can affect reproduction capacity.

ADVERSE REACTIONS:

Allergic reactions following injections of allergens include generalized erythema, pruritis, rhinitis, asthma, and laryngeal edema. Syncope, shock, and hypotension have also been reported. Adverse reactions should be treated as follows:

- A. A tourniquet should be immediately applied to the extremity above the site of injection. Release tourniquet every few minutes for a few seconds.
- B. Epinephrine 1:1000 should be injected immediately in the opposite arm in amounts of 0.3 to 0.5 mL and 0.2 mL epinephrine should be administered at the site of injection. For children below the age of 6 years, adjust dosage of epinephrine to 0.005 mL per pound of body weight per dose. Repeat epinephrine dosage in 15 minutes if necessary and if symptoms persist.
- C. Adverse reactions not responding to epinephrine therapy may require the use of parenteral bronchodilators, vasopressors, oxygen, or volume replacement therapy.

DOSAGE AND ADMINISTRATION

A. Testing:

1. Scratch and Prick testing normally employ 1:20 glycerinated extracts, which contain 125-250 units Antigen E per mL (Short Ragweed) or 75-150 units Antigen E per mL (Ragweed Mix).
2. Intradermal testing with Short Ragweed and G.S. Ragweed Mix is routinely performed using 1:1000 w/v and 1,000 PNU/mL or more dilute material. It has been reported that as little as 10^{-6} unit (0.000001 μg) is sufficient to cause a positive skin test. In another study of 25 Antigen E sensitive individuals, the dose required for a 2+ reaction (8-10 mm wheal) ranged from 10^{-6} to 10^{-1} μg Antigen per mL using a 0.5 mL dose.³

Individual sensitivity to Ragweed extracts will vary greatly and it is recommended that intradermal testing be started at low concentrations (i.e. 0.05 mL at 0.1 $\mu\text{g}/\text{mL}$ - dose equals 0.005 μg Antigen E). If no reaction occurs, testing may be repeated with a stonger dilution.

B. Treatment:

Initial and subsequent treatment dosage must be based on careful testing procedures and evaluation of patient history. Studies have shown a definite correlation between symptom amelioration and maximum or cumulative dosage achieved. One study⁵ has shown significant clinical improvement with an average cumulative preseasonal dosage equivalent to 252 μg of Antigen E, but no significant improvement with an average cumulative dosage of 32 μg Antigen E. In another study⁸ a mean cumulative dosage of 84.9 μg Antigen E (as whole ragweed extract) was significantly effective in reducing allergenic symptoms compared to placebo.

The dosage schedule shown below, based on Antigen E content, will deliver approximately 85 μg Antigen E in 18 injections. Initial and subsequent treatment dosage must be based on careful testing procedures and patient history. Highly sensitive individuals will require lower initial dosage, more moderate dosage increase, and may not tolerate as high a maintenance dosage as the moderately sensitive individual. The suggested schedule shown below is for a moderately sensitive individual and must be modified by the physician to suit each patient if necessary.

**SUGGESTED DOSAGE SCHEDULE
OF SHORT RAGWEED AND G.S. RAGWEED MIX
ANTIGEN E STANDARD**

Injection Number	Vial Number	Antigen E per mL	Volume (mL)	Dose AgE
1	1	0.3	0.05	0.015
2	1	0.3	0.10	0.03
3	1	0.3	0.20	0.06
4	1	0.3	0.40	0.12
5	1	0.3	0.70	0.21
6	2	3.0	0.10	0.30
7	2	3.0	0.20	0.60
8	2	3.0	0.30	0.90
9	2	3.0	0.50	1.50
10	2	3.0	0.70	2.10
11	3	30.0	0.10	3.00
12	3	30.0	0.15	4.50
13	3	30.0	0.20	6.00
14	3	30.0	0.30	9.00
15	3	30.0	0.40	12.00
16	3	30.0	0.50	15.00*
17	3	30.0	0.50	15.00*
18	3	30.0	0.50	15.00*

*Maintenance dosage

It is recommended that patients receive injections at five to seven day intervals until maintenance dosage is achieved. Maintenance dosage can be given at 2 to 4 week intervals. All doses of allergenic extract are administered subcutaneously in the lateral aspect of the upper arm or thigh. Avoid injecting directly into any blood vessel and use a 26 or 27 gauge needle ³/₈" in length.

OVERDOSAGE

Systemic reactions are uncommon after injection, but if the patient receives more extract than can be tolerated at that particular time, the procedures listed under Adverse Reactions should be instituted.

Overdosage may occur because of an error in the volume of extract injected, an incorrect dilution injected, or because the patient may be exposed to airborne antigens simultaneously with injection of the same antigens. In the event of a systemic reaction occurring, the dosage schedule should be carefully reviewed and if necessary adjusted as outlined above.

STORAGE

Short Ragweed containing extracts should be stored at 2°-8°C at all times, even during use, to prolong the potency of the extracts. Our studies indicate that Antigen E in aqueous extracts decays approximately ten times more rapidly at room temperature (20°-25°C) than at refrigerator temperature (2°-8°C).

HOW SUPPLIED

Short Ragweed and G.S. Ragweed Mix extracts are supplied as sterile solutions 5, 10, 30 and 50 mL multiple dose vials and in 5 mL dropper vials for scratch testing. Various concentrations are available to suit the varying needs of the physician.

REFERENCES

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- ⁷Norman, Phillip S., "A rational approach to desensitization," **The Journal of Allergy**, 44:3, pp. 129-145, 1969.
- ⁸Van Metre, Thomas E., et al., "A comparative study of the effectiveness of the Rinkel method and the current standard method of immunotherapy for ragweed pollen hay fever," **The Journal of Allergy and Clinical Immunology**, 66:6, pp. 500-513, 1980.