WARNING

THIS ALLERGIC PRODUCT IS INTENDED FOR USE BY PHYSICIANS WHO ARE EXPERIENCED IN THE ADMINISTRATION OF ALLERGIC EXTRACTS AND THE EMERGENCY CARE OF ANAPHYLAXIS, OR FOR USE UNDER THE GUIDANCE OF AN ALLERGY SPECIALIST.

THIS PRODUCT SHOULD NOT BE INJECTED INTRAVENOUSLY.

STANDARDIZED GRASS POLLEN EXTRACTS LABELED IN BIOEQUIVALENT ALLERGY UNITS (BAU/mL) ARE NOT INTERCHANGEABLE WITH GRASS POLLEN EXTRACTS LABELED IN ALLERGY UNITS (AU/mL) OR WITH NONSTANDARDIZED GRASS POLLEN EXTRACTS. FOR PREVIOUSLY UNTRATED PATIENTS OR PATIENTS PREVIOUSLY RECEIVING EXTRACTS FROM ANOTHER MANUFACTURER, THE INITIAL DOSE MUST BE BASED ON SKIN TESTING AS DESCRIBED IN THE DOSAGE AND ADMINISTRATION SECTION OF THIS INSERT. PATIENTS BEING SWITCHED FROM OTHER TYPES OF EXTRACTS TO STANDARDIZED EXTRACTS SHOULD BE INSTRUCTED TO RECOGNIZE ADVERSE REACTION SYMPTOMS AND CAUTIONED TO CONTACT THE PHYSICIAN'S OFFICE IF REACTION SYMPTOMS OCCUR. IN CERTAIN INDIVIDUALS THESE SYMPTOMS COULD BE SEVERE AND SHOULD BE MONITORED FOR AT LEAST 20 MINUTES FOLLOWING TREATMENT. PATIENTS WITH LARYNX OR STERNO-DEPENDING ASTHMA ARE "HIGH RISK PATIENTS" WHO REQUIRE SPECIAL CARE IN DOSE ADMINISTRATION AND SHOULD REMAIN IN THE OFFICE FOR AT LEAST 30 MINUTES. AIRWAY OBSTRUCTION IN HIGH RISK PATIENTS CAN BE MONITORED BY PEAK FLOW MEASUREMENTS BEFORE AND AFTER TREATMENT; ENTRAPMENT OF HERD ARRAYS AS WELL AS PERSONNEL TRAINED IN THEIR USE SHOULD BE IMMEDIATELY AVAILABLE IN THE EVENT OF A LIFE THREATENING REACTION. TO REPORT SIDE EFFECTS TO THE MANUFACTURER, THE FOOD AND DRUG ADMINISTRATION MED-WATCH NUMBER IS 1-800-332-1088. PATIENTS BEING SWITCHED FROM ONE LOT OF EXTRACT TO ANOTHER FROM THE SAME MANUFACTURER SHOULD HAVE THEIR DOSE REDUCED BY 75%.

RISK OF ANAPHYLAXIS SHOULD BE WEIGHED AGAINST BENEFITS: IN PATIENTS RECEIVING BETA BLOCKERS AS THEY MAY NOT BE RESPONSIVE TO BETAREACTING DRUGS SHOULD ANAPHYLAXIS OCCUR. PATIENTS WITH UNRESTED OR STERNO-DEPENDING ASTHMA, OR IN PATIENTS WITH CARDIOVASCULAR DISEASE.

REFER ALSO TO THE WARNINGS, PRECAUTIONS, ADVERSE REACTIONS AND OVERDOSAGE SECTIONS BELOW.

Description

Standardized Grass Pollen Extracts are supplied as sterile solutions for intradermal or subcutaneous administration. Standardized Grass Pollen Allergen Extracts include Bermuda (Gynopit custom), Kentucky Blue (June/July period), Meadow Fescue (Festuca elatior), Orchard (Dactylis glomerata), Perennial Rye (Lolium perenne), Radish (Raphanus sativus), Sweet Vernal (Anthoxanthum odoratum), and Timothy (Phleum pratense). Glycine-rich concentrates contain the soluble extractives of the source material with 0.25% sodium bicarbonate, 0.27% sodium bicarbonate and 0.5% glycol. A4 extracts contain 0.4% phenol as the preservative. Source materials for each extract are the specific pollens collected from the respective plants.

Table II

<table>
<thead>
<tr>
<th>Reference</th>
<th>Pollen</th>
<th>Mean</th>
<th>Range</th>
<th>Activity</th>
<th>Elastin</th>
<th>Activity</th>
<th>Elastin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bermuda</td>
<td>15.7</td>
<td>7</td>
<td>30.0</td>
<td>90.3</td>
<td>43</td>
<td>123</td>
<td>123</td>
</tr>
<tr>
<td>Kentucky (June)</td>
<td>15.9</td>
<td>6</td>
<td>28</td>
<td>73.7</td>
<td>47</td>
<td>107</td>
<td>107</td>
</tr>
<tr>
<td>Meadow Fescue (July)</td>
<td>15.7</td>
<td>7</td>
<td>30</td>
<td>81.1</td>
<td>57</td>
<td>111</td>
<td>111</td>
</tr>
<tr>
<td>Orchard</td>
<td>14.1</td>
<td>9</td>
<td>19</td>
<td>84.3</td>
<td>57</td>
<td>111</td>
<td>111</td>
</tr>
<tr>
<td>Perennial Rye</td>
<td>17.5</td>
<td>6</td>
<td>36</td>
<td>92.3</td>
<td>73</td>
<td>130</td>
<td>130</td>
</tr>
<tr>
<td>Radish</td>
<td>14.1</td>
<td>8</td>
<td>19</td>
<td>77.1</td>
<td>42</td>
<td>98</td>
<td>98</td>
</tr>
<tr>
<td>Sweet Vernal (May)</td>
<td>15.7</td>
<td>8</td>
<td>30</td>
<td>81.2</td>
<td>25</td>
<td>123</td>
<td>123</td>
</tr>
<tr>
<td>Timothy</td>
<td>15.9</td>
<td>40</td>
<td>69</td>
<td>88.3</td>
<td>51</td>
<td>103</td>
<td>103</td>
</tr>
</tbody>
</table>

Intradermal test doses with eight U.S. reference extracts (Table II) in highly reactive subjects (Table I) indicate that a calculated dose of 0.02 BAU/mL should yield an average sum of elasticity reaction of 50 mm, as tested in subjects sensitive to the specific grass pollen extract. However, in the less sensitive subjects, the dose was as low as 0.003 BAU/mL, for one grass to 0.001 BAU/mL, for several others. Conversely, doses of 1.0 to 1.9 BAU/mL were calculated to yield the same reaction in the least-sensitive subjects.
TABLE III
BAUMIL tests: of Previously Marked, Nonstandardized, Grass Pollen Extracts

<table>
<thead>
<tr>
<th>Pollen</th>
<th># of Lots Tested</th>
<th>1:10 w/v Aquous</th>
<th># of Lots Tested</th>
<th>1:20 w/v glycerinated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bermuda</td>
<td>1</td>
<td>10,745</td>
<td>5</td>
<td>4,000 bt14,500</td>
</tr>
<tr>
<td>Meadow Fescue</td>
<td>2</td>
<td>287,300</td>
<td>4</td>
<td>169,200</td>
</tr>
<tr>
<td>Kentucky Bluegrass</td>
<td>3</td>
<td>56,100</td>
<td>4</td>
<td>56,100</td>
</tr>
<tr>
<td>Orchard</td>
<td>2</td>
<td>134,000</td>
<td>5</td>
<td>71,200</td>
</tr>
<tr>
<td>Redtop</td>
<td>3</td>
<td>141,900</td>
<td>4</td>
<td>134,600</td>
</tr>
<tr>
<td>Perennial Rye</td>
<td>4</td>
<td>85,400</td>
<td>4</td>
<td>52,900</td>
</tr>
<tr>
<td>Sweet Vernal</td>
<td>2</td>
<td>171,900</td>
<td>5</td>
<td>63,900</td>
</tr>
<tr>
<td>Timothy</td>
<td>3</td>
<td>186,300</td>
<td>3</td>
<td>63,000</td>
</tr>
</tbody>
</table>

INDICATIONS AND USAGE
Standardized Grass Pollen Extracts are indicated for the skin-test diagnosis of allergy and immunotherapy treatment of patients with a history of allergy to the respective pollen. The diagnosis of IgE-mediated allergy may be established by the allergy history, clinical evaluation, and skin test reactivity.1,2,5,12 Extracts at 10,000 BAUMIL are indicated for use in scratch, prick, or puncture skin test diagnosis. Extracts at 100,000 BAUMIL are indicated for use in scratch, prick, or puncture skin test diagnosis in less sensitive subjects, such as those negative or indifferent upon scratch, prick, or puncture testing at 10,000 BAUMIL. Extracts at 10,000 BAUMIL, or 100,000 BAUMIL are indicated for intradermal skin test diagnosis only when appropriately diluted.

Immunotherapy with Standardized Grass Pollen Extracts is indicated when testing and patient history have identified the offending allergens and when it is not possible or practical to avoid these allergens.6,12 Extracts at 10,000 BAUMIL or 100,000 BAUMIL are indicated for immunotherapy only when appropriately diluted. 10,000 BAUMIL extracts are indicated for immunotherapy on previously untreated patients. 100,000 BAUMIL extracts (if indicated if a higher dose is needed. (See DOSAGE AND ADMINISTRATION)

STANDARDIZED GRASS POLLEN EXTRACTS LABELED IN BAUMIL ARE NOT interchangeable with unpreserved pollen extracts labeled in ALUML or with nonstandardized grass pollen extracts. This is true of Standardized Grass Pollen extracts for the above purposes should be made only by physicians with special familiarity and knowledge of allergy. (See DOSAGE AND ADMINISTRATION)

CONTRADICTIONS
There are no known absolute contraindications to the use of Standardized Grass Pollen Extracts for immunotherapy. Immunotherapy with specific antigens is contraindicated in those individuals who do not exhibit skin test and clinical sensitivity to the particular antigen. (See WARNINGS and PRECAUTIONS)

Allergic extract injections should not be administered in the presence of diseases characterized by a bleeding diathesis.

Children with nephritic syndrome require careful consideration and probably should not receive injection therapy because a variety of seemingly unrelated events, such as immunization, can cause an exacerbation of their nephritic disease.

General contraindications include:

EXTREME SENSITIVITY TO THE SPECIFIC ALLERGEN - Determined from previous histologic or biopsy examination.

AUTOMMUNE DISEASE - Individuals with autoimmune disease may be at risk, due to the possibility of routine immunizations exacerbating symptoms of the underlying disease.

WARNINGS
All concentrations of Standardized Grass Pollen Extracts are manufactured to assure high potency and have the ability during skin testing and immunotherapy to cause local and systemic reactions including death in extremely sensitive patients. Most reactions occur within 20 minutes after injection, but may occur later.19 To minimize the potential for local or systemic reactions, the relative sensitivity of the patient must be assessed from the history, and a test dose of local or systemic reaction. Patients should be informed of these risks prior to skin testing and immunotherapy. (See PRECAUTIONS and ADVERSE REACTIONS)

Concentrated extracts at 10,000 and 100,000 BAUMIL must be diluted with a sterile diluent prior to use in a patient for intradermal testing or for immunotherapy.

Skin testing should be initiated only with 10,000 BAUMIL extracts. If several concentrated extracts at 10,000 BAUMIL are administered concurrently to a sensitive patient, the additive effects of cross-reacting allergens may cause a systemic anaphylactic reaction.

Allergic extracts should be temporarily withheld from patients or the dose adjusted downward if any of the following conditions exist:

1. severe symptoms of rhinitis and/or asthma.
2. infection or flu accompanied by fever.
3. exposure to excessive amounts of clinically relevant allergens prior to a scheduled injection.
4. evidence of a local or systemic reaction to the preceding extract injection during a course of immunotherapy.

The dosage must be reduced: 1) when starting a patient on fresh extract, 2) when transferring a patient from another form of extract to a BAUMIL standardized extract, or 3) when modifying dosages or components in a mixture or an individual prescription, even though the labeled strength of the old and new mix may be the same.

The reduction in dosage may be necessary: 1) due to the previously used extract having lost potency during storage, 2) due to the fact that standardized extracts labeled in BAUMIL differ in potency compared to nonstandardized extracts of the same species (see Table III), or 3) due to different patient sensitivity to different components. The amount of new extract given should not exceed 25% of the last dose given from the old vial, assuming both extracts contain comparable amounts of allergen. Any evidence of a local or generalized reaction requires a reduction in dosage during the initial stages of immunotherapy, as well as during maintenance therapy. The information about nonstandardized extracts shown in Table III may be helpful in confirming the appropriateness of the initial dose. When a patient is first being administered a standard strength labeled in BAUMIL, the new dose can be selected based on a side-by-side comparison with the previously used nonstandardized extract. The availability of 10,000 BAUMIL, and 100,000 BAUMIL doses is intended to facilitate safe bridging by providing the physician access to lower and higher dosages.

Patients receiving beta blocker drugs may not be responsive to beta adrenergic drugs used to treat anaphylaxis. The risks of anaphylaxis in these patients should be carefully weighed against the benefits of immunotherapy. (See PRECAUTIONS)

INFOMATION FOR PATIENTS
Most serious reactions following the administration of allergic extracts occur within 30 minutes. The patient should remain under observation for this period of time or longer if instructed by the physician. The size of any local reaction should be measured. Large local reactions may be indicative of subsequent systemic reactions as doses increase. The patient should be instructed to seek medical attention for any unusual reactions. This includes unusual swelling and/or tenderness at the injection site or reactions such as hives, itching, wheezing, shortness of breath, nausea, dizziness, or faintness. Reactions may occur some time after leaving the physician's office, in which case medical attention should be sought immediately.

DRUG INTERACTIONS
Skin test diagnosis with Allergic Extracts may result in false negative responses when used with 5-10 days of beta-blockers or beta-adrenergic agents such as atenolol or betaxolol. In addition, patients on beta blockers may not respond to beta adrenergic drugs used to treat anaphylaxis. The risks of anaphylaxis in these patients should be carefully weighed against the benefits of immunotherapy. (See ADVERSE REACTIONS)

Other products suppress histamine skin test reactions and could mask a positive reaction. The suppressive action of other drugs should be considered and the emphasis is needed for a histamine positive control test.

Patients receiving beta blocker drugs may not be responsive to beta adrenergic drugs used to treat anaphylaxis. The risks of anaphylaxis in these patients should be carefully weighed against the benefits of immunotherapy.
PREGNANCY

Teratogenic Effects

Pregnancy Category C - Animal reproductive studies have not been conducted with Standardized Grass Pollen Extracts. It is also not known whether Standardized Grass Pollen Extracts can cause fetal harm when administered to a pregnant woman or whether they can affect reproduction capacity. Standardized Grass Pollen Extracts should be given to a pregnant woman only if clearly needed.

There is no evidence of adverse effects of allergenic extracts on the fetus. (25) Studies have not been performed in animals to determine whether extracts affect fertility in males or females, have teratogenic potential, or have other adverse effects on the fetus. Caution should be exercised in testing or treating pregnant females because a systemic reaction may cause an abortion as a result of uterine muscle contractions.

Labor and Delivery

There is no known adverse effect of labor and delivery. It is not known whether allergenic extracts or their antigens are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when extracts are administered to a nursing woman.

Pediatric and Geriatric Use:

Allergic extracts have been studied systematically in several age groups, older children and geriatric patients appear to tolerate injections of allergenic extracts well. Children less than five years of age on extract therapy may have a higher risk of wheal and flare reactions and may need to be monitored more closely.

OBSERVATIONS

Systemic reactions are uncommon after injection, but if the patient receives extract therapy for the first time, be sure the patient is observed for six minutes in case of anaphylaxis. The patient is then observed for one hour or until the patient is discharged.

If anaphylaxis develops, it is important to treat the patient immediately with diphenhydramine and epinephrine.

ADVERSE REACTIONS

Adverse systemic reactions may occur within minutes upon use of an allergenic extract to which a patient has specific sensitivity. These reactions consist primarily of allergic symptoms such as generalized skin erythema, urticaria, pruritus, angioedema, rhinitis, wheezing, laryngeal edema, and hypotension. Less commonly, nausea, emesis, abdominal cramps, diarrhea, and uterine contractions may occur. Systemic reactions occur with varying frequency in different clinics and are usually less than 1%. To date, no deaths have been reported in the U.S. and the event of a systemic reaction occurring, the dosing schedule should be carefully reviewed and if necessary adjusted as above under WARNING.

DOSE AND ADMINISTRATION

1. DIAGNOSTIC TESTING

For the patient with a suspected diagnosis of allergy to more than one antigen, initial screening skin tests should include the individual extracts. If a screening skin test with a mixture is used, a positive response should be followed by testing with the individual extracts to determine the degree of sensitivity to each and to guide in the selection of extracts and their concentration for immunotherapy if indicated. However, because a negative skin test with a mixture may not be indicative of the absence of allergy to one or more of the components due to their dilution, testing with individual extracts is more precise.

False negative results may occur if serum levels of antihistamines remain from prior medication administration. (See PRECAUTIONS) The use of a histamine positive control is especially recommended on patients who have been given prior medications which may decrease the histamine skin test response.

Skin tests read after 15 to 20 minutes are graded in terms of the induration (wheal) and erythema (flare) response compared to the appropriate controls. Wheal and flare sizes may be recorded by actual measurements. The largest diameter of the wheal and flare may be recorded, or the sum of the largest diameter and the orthogonal (right angle) diameter of wheal flare may be used as in the studies in Tables I and II.

Scratch or Prick-Puncture Skin Testing:

For punctuation, prick, or scratch skin testing, the 10,000 BAU/mL strength is recommended and will detect the more sensitive patients. Inconclusive results at 10,000 BAU/mL may be followed by a puncture, prick, or scratch test skin at 100,000. At the higher concentration, some nonspecific positives may occur.

Controls for Scratch, Prick-Puncture Testing:

As a positive control, glycinehistamine phosphate 5 mg/mL (1.8 mg/mL histamine base) or aqueous histamine phosphate 0.27 mg/mL (1.2 mg/mL histamine base) may be used as a positive control. A 50% glycerol solution can be used as the negative control.

Intrastratal Skin Testing:

Extracts for intrastratal testing must be diluted by the concentrated extract with sterile diluent (such as normal or buffered saline, or normal saline with human serum albumin).

Intrastratal skin tests with eight U.S. reference extracts (Table II) indicate that a calculated dose of 0.02 BAU/mL should yield an average size of erythema reaction of 50 mm, as tested in subjects with similar puncture reactances described in Table I to that specific grass pollen extract. However, in the more sensitive subjects, the dose was as low as 0.0005 BAU for one grass to 0.002 BAU for several others. Conversely, doses of 0.1 to 1.9 BAU/mL were calculated to yield the same reaction in the least sensitive subjects.

Controls for Intradermal Testing:

As a positive control, use glycinehistamine phosphate diluted to 0.5 mg/mL (0.18 mg/mL histamine base) or aqueous histamine phosphate 0.27 mg/mL (0.1 mg/mL histamine base).

As a negative control, use 0.5% to 1% glycerol solution.

a. Patients with a negative scratch or prick-puncture test:

Patients with a negative scratch or prick-puncture test should be tested intradermally, using a 36 or 27 gauge 1/4 inch needle, with 0.02 to 0.05 mL of a 50 BAU/mL extract dilution. A negative test should be followed by repeat tests using progressively stronger concentrations until significant wheal and flare reaction sizes are attained or until the maximum recommended strength of 10,000 BAU/mL is reached. As a positive control, use glycinehistamine phosphate dilute to 0.5 mg/mL (0.15 mg/mL histamine base) or aqueous histamine phosphate 0.27 mg/mL (0.1 mg/mL histamine base).

b. Patients tested only by the intradermal method:

Since highly reactive patients may react intrastratally at doses even smaller than indicated above, it is recommended that intradermal testing be preceded by a puncture test and the dose adjusted accordingly. Other patients suspected of being moderately allergic may be tested with an intradermal dose of 0.01 to 0.05 BAU/mL (0.001 to 0.005 mg/mL histamine) and the negative test should be followed by repeat tests using progressively stronger concentrations until the maximum recommended strength of 200 BAU/mL is reached. As a negative control use 0.5% to 1% glycerol solution. As a positive control, use glycinehistamine phosphate dilute to 0.5 mg/mL (0.18 mg/mL histamine base) or aqueous histamine phosphate 0.27 mg/mL (0.1 mg/mL histamine base).

2. THERAPY:

Standardized versus Nonstandardized Extracts: Dosage with extracts standardized in BAU must be derived from a knowledge of the patient's sensitivity to the specific pollen. Switching from an extract not standardized in BAU cannot be made by a calculated ratio. There are no equivalent dosages of bioequivalent allergen units applicable to all the grass species that can be related to previously marketed nonstandardized extracts labeled in weight-to-volume (w/v), Protein Nitrogen Units (PNU), or Allergy Units (AU). The information about nonstandardized extracts shown in Table III may be helpful in selecting the initial dose for the side-by-side skin test comparison. Patients being switched from nonstandardized extracts to extracts standardized in BAU can be evaluated by diagnostic skin test judging to the dose for starting immunotherapy or building up to new maintained dosages. When a patient is first being administered a standardized extract labeled in BAU, the new dose can be selected based on a side-by-side comparison.

Immunotherapy is administered by subcutaneous injection. Dosage is individualized according to the patient's sensitivity, the clinical response, and tolerance to the extract administered during the early phases of an injection regimen. (Extracts for immunotherapy must be prepared by diluting the concentrate with sterile diluent (such as normal or buffered saline, or normal saline with human serum albumin).

The initial dose of an extract in BAU should be calculated based on the puncture test reactivity. Note in Tables I and II the puncture and intradermal skin test reactivity of sensitive subjects evaluated with the US reference extracts.

The initial dose of the extract may be as low as 0.1 mL of a 0.005 to 0.025 BAU/mL dilution (0.0005 to 0.005 BAU) dilution or 5 mL of 50% glycerin or even less for the exquisitely sensitive patient. Patients with lesser sensitivity may be started at 0.01 mL of a 0.05 to 0.2 BAU/mL dilution (0.005 to 0.05 BAU).

The amount of allergic extract is increased at each injection by no more than 50% of the previous amount, and the next increment is governed by the response to each dose. Large local reactions which persist for longer than 24 hours are generally considered an indication for repeating the previous dose and fractionating for the next dose. The amount of systemic reaction is an indication for a reduction of 75% in the subsequent dose. The upper limits of dosage in BAU have not been established. Dosages larger than 2 mL of 50% glycerin may cause discomfort upon injection. The dosages of allergenic extracts do not vary significantly with the allergic reaction under treatment.

To prepare dilutions starting from a 100,000 BAU/mL concentrate, proceed as in Table IV. The 100,000 BAU/mL concentrate can be made by using equal parts of 0.9% NaCl and 50% glycerin. When a single 0.9% NaCl and 50% glycerin fold dilution series uses 0.5 mL of concentrate to 4.5 mL of sterile diluent with additional dilutions made in the same manner.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY

There is no evidence of carcinogenicity, mutagenesis or impairment of fertility in animals treated with standard extracts. There are no long-term studies in animals have been performed to evaluate carcinogenic potential.
### TABLE IV

<table>
<thead>
<tr>
<th>Dilution</th>
<th>Extract</th>
<th>BAU/mL</th>
<th>BAU/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 Concentrate</td>
<td>5,000,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0.5 mL, concentrate</td>
<td>4.5 mL</td>
<td>10,000</td>
</tr>
<tr>
<td>2</td>
<td>0.5 mL, dilution 1</td>
<td>4.5 mL</td>
<td>1,000</td>
</tr>
<tr>
<td>3</td>
<td>0.5 mL, dilution 2</td>
<td>4.5 mL</td>
<td>100</td>
</tr>
<tr>
<td>4</td>
<td>0.5 mL, dilution 3</td>
<td>4.5 mL</td>
<td>10</td>
</tr>
<tr>
<td>5</td>
<td>0.5 mL, dilution 4</td>
<td>4.5 mL</td>
<td>1</td>
</tr>
<tr>
<td>6</td>
<td>0.5 mL, dilution 5</td>
<td>4.5 mL</td>
<td>0.1</td>
</tr>
</tbody>
</table>

*Due to differences such as source material, preservative, potency dilutions, storage conditions, and length of storage, there is no common potency correlation ratio between extracts standardized in Bioequivalent Allergy Units (BAU) and:

1) standardized extracts previously labeled in Allergy Units (AU);
2) nonstandardized extracts labeled weight-to-volume (w/v);
3) nonstandardized extracts labeled in Protein Nitrogen Units (PNU); or 4) aluin-precipitated extracts.

The optimal interval between doses of allergic extracts has not been established. Injections usually are given 1 to 2 times per week until the maintenance dose is reached. The injection interval is then increased to 2 weeks, then to 3 weeks and finally to 4 weeks. If the patient does not return for 6 to 8 weeks, the dose should be reduced to 25% of the last dose. If longer than 8 weeks, a dose reduction of one, two or three dilutions may be made considering the components and the patient's sensitivity. The dosage and the interval between injections may need to be modified according to the clinical response of the patient. When switching patients to fresh extract, the initial dose should be reduced to 25% of the previous dose.

The usual duration of treatment has not been established. A period of two or three years of injection therapy constitutes an average minimum course of treatment. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Some concentrated extracts naturally develop a cloudy appearance over time under refrigeration, the material settling to the bottom on standing.

### REFERENCES

2. EUA's competition assay. Methods of the Allergic Products Testing Laboratory, Laboratory of Immunobiology, Division of Allergic Products and Parasitology, Center for Biologics Evaluation and Research, Food and Drug Administration, 401 Food Rockville Pike, Rockville, MD 20852-1449, 1994.
30. Data on File - Center for Biologics Evaluation and Research, Food and Drug Administration, Rockville, MD.
34. Manufacturer: Greer Laboratories, Inc., Lenox, NC 28645, USA

L-516 Rev. 3/06