DESCRIPTION

Standardized grass pollen extract is a sterile solution containing the extractables of grass pollen in 0.2% - 0.125% sodium bicarbonate and 0.4% phenol w/v. Standardized grass pollen extracts include Bermudagrass (Cynodon dactylon), June Grass (Poa pratensis), Meadow Fescue Grass (Festuca elatior), Orchard Grass (Dactylis glomerata), Perennial Rye Grass (Lolium perenne), Redtop Grass (Agrostis alba), sweet Vernal Grass (Anthoxanthum odoratum) and Timothy Grass (Phleum pratense). The extract may be administered by the scratch, prick, puncture, or intradermal methods of skin testing for diagnostic purposes and subcutaneously for therapeutic purposes as directed under Dosage and Administration.

The potency of standardized grass pollen extracts is expressed in Bioequivalent Allergy Units per mL (BAU/mL) and is determined by an in vitro ELISA Competition Assay comparing the extract to a U.S. reference grass pollen extract available from the Center for Biologics Evaluation and Research (CBER), U.S. Food and Drug Administration. Bioequivalent Allergy Units per mL (BAU/mL) have been assigned to the reference extract based on quantitative skin testing (see CLINICAL PHARMACOLOGY). CBER reference extract labeled 100,000 BAU/mL can be diluted 1:5 million and yield a 50 mm sum of erythema diameter response intradermally in highly puncture reactive subjects. CBER reference extract labeled 10,000 BAU/mL can be diluted 1:500,000 for the same response (12).

Grass pollen extract may have as many as 40 components, of which 5 - 10 may be allergenic. The most important allergens are classified into groups I - VI. Allergens in these groups account for 90 - 100% of the IgE binding prevalence in the serum of grass pollen allergic patients (17).

The pharmacologic action of grass pollen extract used diagnostically is based on the liberation of histamine and other substances when allergens in the extract react with specific IgE antibody attached to the basophil. Immunologic changes have been shown to result from mast cell degranulation in the wheal-flare reaction associated with a positive skin test (6,7). The basis for the clinical improvement of allergic symptoms following immunotherapy with grass pollen extract is not clearly understood. Several immunologic changes have been demonstrated that might be responsible for the amelioration of allergic symptoms. These changes include (a) increase in serum IgE antibodies, (b) blunting of the seasonal rise of IgE antibodies, (c) elevation of blocking IgAG antibodies in secretions, (d) reduced basophil reactivity and sensitivity to allergens and (e) reduced in vitro lymphocyte responsiveness to allergens (8). There is evidence that symptoms are effectively altered only by the administration of the relevant allergen (9,10,11).

CONTRAINDICATIONS

Immunotherapy should not be started in patients until a specific diagnosis of Type I allergy to grass pollen has been made from the patient’s allergy history and from a positive skin test to grass pollen extract. Other contraindications include:

- Extremity Sensitivity to Grass Pollen: Patients who experience serious adverse reactions to skin testing with the drug should not be treated with the product.
- Myocardial Infarction: Patients who have experienced a recent myocardial infarction may not be able to tolerate adverse reactions resulting from skin testing or immunotherapy. The benefit-to-risk ratio must be carefully evaluated in these patients.
- Children With Nephrotic Syndrome: Children with nephrotic syndrome require careful medical supervision in the event of severe reactions, including proteinuria, due to a variety of seemingly unrelated events that may cause an exacerbation of nephrotic disease.

WARNINGS

Standardized grass pollen extract must be diluted prior to first use on a patient for immunotherapy or intradermal testing (see DOSAGE AND ADMINISTRATION). Grass pollen extract is manufactured to assure high potency and has the ability to cause serious local and systemic reactions, including fatal anaphylactic reactions. Patients should be informed of this risk and precautions should be discussed prior to initiating skin testing and immunotherapy (see PRECAUTIONS).

Table 1. Puncture data (bifurcated needle) with 10,000 BAU/mL reference grass pollen extracts.

<table>
<thead>
<tr>
<th>REFERENCE POLLEN</th>
<th>BAU/mL</th>
<th>MEAN±</th>
<th>RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bermuda E4-Ber</td>
<td>0.02</td>
<td>0.4</td>
<td>0.003</td>
</tr>
<tr>
<td>June E3-Jjb</td>
<td>0.02</td>
<td>0.1</td>
<td>0.004</td>
</tr>
<tr>
<td>Meadow Fescue E4-MF</td>
<td>0.02</td>
<td>0.2</td>
<td>0.02</td>
</tr>
<tr>
<td>Orchard E4-Or</td>
<td>0.02</td>
<td>1.9</td>
<td>0.002</td>
</tr>
<tr>
<td>Perennial Rye E10-Rye</td>
<td>0.02</td>
<td>0.7</td>
<td>0.002</td>
</tr>
<tr>
<td>Redtop E4-RE</td>
<td>0.02</td>
<td>0.8</td>
<td>0.004</td>
</tr>
<tr>
<td>Sweet Vernal E4-SV</td>
<td>0.02</td>
<td>1.0</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Table 2. Calculated intradermal dose of CBER reference grass pollen extracts to elicit 50 mm sum of erythema.*

<table>
<thead>
<tr>
<th>REFERENCE POLLEN</th>
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<td>Sweet Vernal E4-SV</td>
<td>0.02</td>
<td>1.0</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Table 3. Estimated BAU/mL of non-standardized 1:10 w/v glycerinated grass pollen extracts manufactured and distributed by Allermed.

<table>
<thead>
<tr>
<th>EXTRACT</th>
<th>BAU/mL</th>
<th>RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bermuda</td>
<td>21,400 - 22,300</td>
<td>Perennial Rye 183,000 - 205,000</td>
</tr>
<tr>
<td>Meadow Fescue</td>
<td>136,000 - 150,000</td>
<td>Orchard Grass 128,000 - 160,000</td>
</tr>
<tr>
<td>Orchard</td>
<td>153,000 - 244,000</td>
<td>Sweet Vernal 77,000 - 80,000</td>
</tr>
</tbody>
</table>

Note: Relative potency compared to the U.S. Reference with a potency of 10.0. The U.S. Reference extract is standardized at 10,000 BAU/mL (range: 9,000 - 14,310 BAU/mL). The U.S. References for other allergens are 100,000 BAU/mL (range: 99,000 - 143,000 BAU/mL).
When switching from alum precipitated grass pollen extract to standardized grass pollen extract, the patient should be managed as a new patient coming under treatment for the first time.

**PRECAUTIONS**

**GENERAL:** The risk of a severe allergic reaction usually can be reduced by eliciting the patient’s allergy history and by percutaneous testing by the scratch, prick or puncture method. If a scratch, prick or puncture test is negative for allergens, it is advisable to do a saline test with a one-thousand-fold dilution of the extract used for the percutaneous test. If there is a history of unusual sensitivity, it is advisable to use a weaker dilution of the extract for skin testing. Systemic allergic reactions may occur as a result of immunotherapy. The risk can be reduced by adherence to a careful injection schedule, which starts with a low concentration of extract and is increased slowly. The physician must be prepared to treat anaphylaxis should it occur and further dosing be withheld until a diagnosis is established. Experiments should not be administered by the patient or by other individuals who are not prepared to treat anaphylaxis, should it occur. 

**PREGNANCY CATEGORY C:** Animal reproduction studies have not been conducted with standardized grass pollen extract. It is also not known whether standardized grass pollen extract can cause fetal harm when administered to a pregnant woman or can affect labor. There are no adequate and well-controlled studies in pregnant women. 

**ABORTION:** Standardized grass pollen extract should be given to a pregnant woman only if clearly needed (15). 

**NURSING MOTHERS:** It is not known whether standardized grass pollen extract is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when allergenic extract is administered to a nursing woman.

**DRUG INTERACTION:** Antihistamines and hydroxyzine can inhibit the immediate skin test reaction, while corticosteroids and diphenhydramine hydrochloride may antagonize the effects of these drugs. 

**DATA FOR THE PUNCTURE TEST USING 10,000 BAU/mL EXTRACT ARE SUMMARIZED IN TABLE 1 UNDER CLINICAL PHARMACOLOGY.** 

**PREDIATRIC USE:** The dose of allergenic extract recommended for children is the same as for adults. Allowable doses of extract for treatment. In this case, it may be advisable to modify the dose and frequency of injections, so that the discomfort is minimized. 

**NURSING MOTHERS:** It is not known whether standardized grass pollen extract is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when allergenic extract is administered to a nursing woman. 

**INFORMATION FOR PATIENTS:** Because the most serious reactions occur within 20 minutes after the injection of allergenic extract, the physician should remain available for the patient and should educate the patient about the symptoms of immediate hypersensitivity reactions for this length of time. The physician also should be instructed to report any unusual reactions to the physician, such as swelling and/or tenderness at the injection site or rhinorrhea, sneezing, coughing, wheezing, shortness of breath, nausea, dizziness or faintness following the injection.

**PREPARING DILUTIONS**

To prepare dilutions for intradermal skin tests and therapeutic use, the stock concentrate may be diluted as shown in Table 4. 

**Directions for diluting standardized grass pollen extract containing 10,000 BAU/mL**

*If 100,000 BAU/mL extract is used to prepare dilutions, the 100,000 BAU/mL extract should be diluted 1:10 v/v before the directions shown in the table are followed.**

**REFERENCES**


Date of Revision: April 2010  C-SG

**INTRADERMAL TEST:**

An intradermal test should only be performed after a puncture test has been properly administered with a negative result. It is usually safe to initiate intradermal testing with a 1:1,000 v/v dilution of the extract to which a negative puncture test was observed. For example, if a puncture test is done with 10,000 BAU/mL extract and is negative, the intradermal test may be performed with a 0.05 mL of 10 BAU/mL extract. The dose may be increased to 0.05 mL of 100 BAU/mL extract if the intradermal test with 10 BAU/mL extract is negative.

**THREATENIC USE:**

The dosage of grass pollen extract administered by subcutaneous injection during immunotherapy is highly individualized and varies according to the patient. In patients who appear to be highly sensitive by history and skin test, the initial dose of the extract should probably be 0.01 mL of a 0.01 BAU/mL dilution. The amount is increased at each injection, but not more than 50%-100% of the previous amount, and the next increment is governed by the response to the last injection. Local reactions that persist longer than 24 hours are undesirable and any systemic reaction is an indication that the dose should be reduced. The upper limit of dosage has not been established, but doses larger than 0.2 mL of concentrate containing 50% glycerol may be painful due to the glycerol in the extract. The potency of each standardized grass pollen in a final mixture should not exceed 10,000 BAU/mL obtained from a 0.1 mL of a 0.1 BAU/mL dilution added to the mix. Concentrate containing 100,000 BAU/mL should be diluted to 10,000 BAU/mL before being used to prepare final mixtures, or alternatively, the volume of 100,000 BAU/mL extract added to the mixture should be reduced (at least 50%).

A period of three to five years of injection therapy constitutes an average course of treatment.

Children and geriatric patients appear to tolerate injections of allergenic extract well, and no special recommendations need to be made for these groups (see PRECAUTIONS - PEDIATRIC USE).