**DESCRIPTION:** Mite extract is a sterile solution containing the extractables of Dermatophagoides farinae or Dermatophagoides pteronyssinus; 0.5% sodium chloride, 0.275% sodium bicarbonate, and 50% glycerin by volume as a preservative. Source material for the extract is the whole bodies of the mites. The mites are grown on a medium of brine shrimp eggs and wheat germ, and are handled and cleaned in a manner that the maximum level. None of these patients had an E response more than 3mm larger than the negative control by puncture test were tested with an extract of medium components at an estimated 1% carryover level. The histamine release response of circulating basophils to a specific allergen is limited in some patients by immunotherapy, but the mechanism of this change is not yet clear. The relationships among changes in blocking antibody, reaginic antibody, and mediator-releasing cells, and successful immunotherapy need study and clarification.

**WARNINGS**

There is no known absolute contraindication to immunotherapy. See PRECAUTIONS for pregnancy risks.

Patients with cardiovascular diseases or pulmonary diseases such as symptomatic asthma, and/or those who are receiving cardiovascular drugs such as beta blockers, may be at higher risk for severe adverse reactions. These patients may also be more refractory to the normal allergy treatment regimen. Patients should be treated only if the benefit of treatment outweighs the risks.

**INDICATIONS AND USAGE:** Standardized glycerinated allergenic extracts are indicated for use in diagnosis and immunotherapy of patients presenting symptoms of allergy (hay fever, rhinitis, etc.) to specific environmental allergens. The selection of allergenic extracts to be used should be based on a thorough and carefully taken history of hypersensitivity, and confirmed by skin testing.

**CONTRAINDICATIONS:** There are no known absolute contraindications to immunotherapy. See PRECAUTIONS for pregnancy risks.

Patients with cardiovascular diseases or pulmonary diseases such as symptomatic asthma, and/or those who are receiving cardiovascular drugs such as beta blockers, may be at higher risk for severe adverse reactions. These patients may also be more refractory to the normal allergy treatment regimen. Patients should be treated only if the benefit of treatment outweighs the risks.

**REFERENCES:**

1. Allergy Units (AU/mL). The potency of extracts labeled in Allergy Units (AU/mL) is determined by in vitro comparison to a reference standard established by the Center for Biologics Evaluation and Research (CBER) of the Food and Drug Administration.
2. Bioequivalent Allergy Units (BAU/mL). Other standardized allergenic extracts are labeled in Bioequivalent Allergy Units/mL (BAU/mL), based on their comparison (by in vitro assay or major allergen content) to CBER, FDA Reference Preparations. The FDA reference extracts have been assigned Bioequivalent Allergy Units based on the CBER IgE/ELAL method. Briefly, highly sensitive patients are skin tested to the reference preparation using an intradermal technique employing 3-fold extract dilutions. Depending on the dilution which elicits a summation of erythema diameter of 50, Bioequivalent Allergy Units are assigned as follows:
start immunotherapy during a period of symptoms due to exposure. Since the individual components of the extract are those to which the patient is allergic, and to which he or she will be exposed, typical allergic symptoms may follow shortly after the injection, particularly when the antigen load from exposure plus the injected antigen exceeds the patient’s antigen tolerance.

The CONCENTRATE SHOULD NOT BE INJECTED AT ANY TIME UNLESS TOLERANCE HAS BEEN ESTAB-
lished. DILUTE CONCENTRATED EXTRACTS WITH STERILE ALUMINUM SALINE WITH PHENOL (0.4%) FOR
INTRADERMAL TESTING.

INJECTIONS SHOULD NEVER BE GIVEN INTRAVENOUSLY. Subcutaneous injection is recommended. Intrac-
aneous or intramuscular injections may produce large local reactions or be excessively painful.

1. INSERT NEEDLE SUBCUTANEOUSLY, BUT BEFORE INJECTING, ALWAYS WITHDRAW THE PLUNGER
SLIGHTLY. IF BLOOD APPEARS IN THE SYRINGE, CHANGE NEEDLE AND GIVE THE INJECTION IN ANOTHER SITE.

2. AFTER INSERTING NEEDLE SUBCUTANEOUSLY OR DURING INTRADERMAL TESTING, ALWAYS WITHDRAW THE PLUNGER RAPIDLY. IF A PROLONGED PERIOD OF TIME HAS ELAPSED SINCE THE LAST INJECTION: Patients may lose tolerance for allergen injections during prolonged periods between doses. The duration of tolerance is age-related to the individual and varies from patient to patient. In general, the longer the interval between injections, the greater the dose reduction required. If the interval since last dose is over four weeks, perform skin tests to determine starting dose.

3. IF THE PREVIOUS EXTRACT WAS OUTDATED: The dating period for allergic extracts indicates the time that can be expected to remain potent under refrigerated storage conditions (2° - 8° C). During the period of all standard conditions, some loss of potency occurs, even in the most potent extract. The extract should not be used beyond their expiration date. If a patient has been receiving injections of an outdated extract, he may experience excessive local or systemic reactions when changed to a new, and possibly more potent extract. In general, the longer the material has been outdated, the greater the dose reduction necessary for the fresh extract.

4. IF THE PREVIOUS EXTRACT WAS NON-STANDARDIZED: Standardized extracts may be more potent than non-standardized extracts. Initiate therapy as though the patient had not been receiving immunotherapy, or determine initial dose by skin test using serial dilutions of the extract. See PRECAUTIONS and DOSAGE AND ADMINISTRATION Sections.

5. IF ANY OTHER CHANGES HAVE BEEN MADE IN THE EXTRACT CONCENTRATE FORMULA: Changes other than those above may include situations such as a redistribution of component parts or percentages, a difference in extracting fluid (i.e., change from non-glycerin extracts to 50% glycerin extracts), combining two or more stock concentrates, or any other change.

6. It should be recognized that any change in formula can affect a patient’s tolerance of the treatment. The usual 1/2 of the previous dose for a new extract may produce an adverse reaction; extra dilutions are recommended whenever starting a revised formula. The greater the change, the greater the number of dilutions required.

Proper selection of the dose and careful injection should prevent most systemic reactions. It must be remem-
bered that many of these extracts are highly potent in sensitive individuals, and that systemic reactions can occur even in patients with varying degrees of severity may occur, including urticaria, rhinitis, conjunctivitis, wheezing, coughing, angioneurotic edema, bradycardia, pallor, laryngeal edema, fainting, or even anaphylactic shock and death. Patients should be questioned about this, and the precautions should be discussed with the patient before treatment (PRECAU-
TIONS below.) Severe systemic reactions should be treated as indicated in the ADVERSE REACTIONS Section.

PRECAUTIONS:

1. General

The presence of asthmatic signs and symptoms appear to be an indicator for severe reactions following allergy injections2, 3, 4, 5. An assessment of airway obstruction either by measurement of peak flow or an alternate procedure may provide a useful indicator as to the advisability of administering an allergy injection. Concentrated extracts must be diluted prior to use; See DOSAGE AND ADMINISTRATION Section for detailed instructions on the dilution of standardized glycerinated allergenic extracts. Any evidence of local or generalized reaction or disturbance during a reduction in dosage should be discontinued during the initial stages of immunotherapy, as well as during maintenance therapy.

Allergenic extracts diluted with Albumin Saline with Phenol (0.4%) may be more potent than extracts diluted with dextrose which do not contain stabilizers. When switching from non-stabilized to stabilized dextrose, consider weaker initial dilutions for both intradermal testing and immunotherapy. Sterile solutions, vials, syringes, etc., should be used and aseptic precautions observed in making dilutions. To avoid cross-contamination, do not use the same needle to withdraw materials from vials of more than one extract, or extract followed by diluent. A sterile tuberculin syringe graduated in 0.01 mL units should be used to measure each dose from the appropriate dilution. Aseptic techniques should always be employed when injections of allergenic extracts are being administered. A separate 1 mL tuberculin syringe should be used for each patient to prevent transmission of homologous serum hepatitis and other infectious agents from one person to another.

Patient reactions to previous injections should be reviewed before each new injection. A conservative dosage schedule should be followed by the physician until a pattern of local responses is established which can be used to monitor increases in dosage. Rarely, a patient is encountered who develops systemic reactions to minute doses of allergen and does not demonstrate increasing tolerance to injections after several months of treatment. If systemic reactions or excessive local responses occur persistently at very small doses, efforts at immunotherapy should be stopped.

POTENTIAL INFECTIONS AND ADVERSE REACTIONS. Most severe reactions will occur within this time period, and rapid treatment measures should be instituted. See ADVERSE REACTIONS Section for such treatment measures.

2. Information for Patients

Patients should be instructed in the recognition of adverse reactions to immunotherapy, and in particular, to the symptoms of shock. Patients should be made to understand the importance of a 30 minute observation period, and be warned to return to the office promptly if symptoms occur after leaving.


Long-term studies in animals have not been conducted with allergenic extracts to determine their potential for carcinogenicity, mutagenicity or impairment of fertility.

4. Pregnancy

Allergenic Extracts. 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 can affect reproduction capacity. Allergic extracts should be given to a pregnant woman only if clearly needed. For women who have been getting maintenance doses of allergen without side effect, the occurrence of pregnancy is not an indication to stop immunotherapy.

5. Nursing Mothers

There are no current studies on secretion of the allergenic extract components in human milk, or of their effect on the nursing infant. Because many drugs are excreted in human milk, caution should be exercised when allergenic extracts are administered to a nursing woman.

6. Pediatric Use

Since dosage for the pediatric population is the same as for adults20-27, the larger volumes of solution may produce excessive discomfort. Therefore, in order to achieve the total dose required, the volume of the dose may need to be divided into more than one injection per visit.

7. Geriatric Use

The reactions from immunotherapy can be expected to be the same in elderly patients as in younger ones. Elderly patients may be more likely to be on medication that could block the effect of epinephrine which could be used to treat serious reactions, or they could be more sensitive to the cardiovascular side effect of epinephrine because of pre-existing cardiovascular disease28.

8. Drug Interactions

Patients on non-selective beta blockers may be more reactive to allergens given for diagnosis or treatment, and may be unresponsive to the usual doses of epinephrine used to treat allergic reactions18. Certain medications may lessen the skin test wheal and erythema responses elicited by allergens and should be discontinued for varying time periods. Conventional antihistamines should be discontinued at least 5 days before skin testing. Long acting antihistamines should be discontinued for at least 3 weeks prior to skin testing2. Topical steroids should be discontinued at the skin test site for at least 2-3 weeks before skin testing2. Topical antihistamine lotions such as Dowegan should be withheld for at least 7 days before skin testing2. Topical local anesthetics may suppress the flare responses and should be avoided in skin test sites2.

ADVERSE REACTIONS:

1. Local Reactions

Some erythema, swelling or pruritus at the site of injection are common, the extent varying with the patient. Such reactions should not be considered significant unless they persist for at least 24 hours. Local reactions (erythema or swelling) which exceed 4-5 cm in diameter are not only uncomfortable, but
DOSAGE AND ADMINISTRATION:

OVERDOSAGE:

Diagnosis

General

Adverse Event Reporting

20852-9787 or Fax to: 1 (800) FDA-0178. The FDA MEDWATCH program. Preprinted forms (FDA Form 3500) are available from the FDA by calling 1 (800) 992-1120. A voluntary adverse event reporting system for health professionals is available through the immunotherapy section below.

To administer the intradermal strength dilutions, a 1 mL tuberculin syringe with a short 27-gauge needle should be used. The needle is inserted intradermally at a 90° angle, bevel down, and 0.05 mL of the extract is injected. Fifteen minutes following injection, the diameter of wheal and erythema reactions are measured, and the patient’s sensitivity class is determined by the table on the following page.

Intradermal skin test results in selected highly sensitive subjects are presented for reference purposes:

<table>
<thead>
<tr>
<th>Allergen</th>
<th>Number of Persons</th>
<th>Mean</th>
<th>± 5 mm</th>
<th>± 10 mm</th>
<th>± 15 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>D. farinae</td>
<td>12</td>
<td>0.950</td>
<td>0.0015 - 2.5016</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D. pteronyssinus</td>
<td>12</td>
<td>0.033</td>
<td>0.0003 - 0.007</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Intradermal extract should be used as follows:

a. Patients with a negative scratch, prick or puncture test:
   - Who do not react to a valid scratch, prick or puncture test should be tested intradermally with 0.02 to 0.05 mL of a 30 AU/mL extract solution. If this test is negative, a second intradermal test may be performed using a 300 AU/mL extract solution. The negative control used with this latter dilution should contain 0.5% glycerin.

b. Patients tested only by the intradermal method:
   - Allergen extracts should be administered using a sterile syringe with 0.01 mL gradations and a 25-27 gauge needle, and gently by rocking or swirling. The negative control used with this latter dilution should contain 0.5% glycerin.

Skin tests are graded in terms of the wheel and erythema response noted at 10 to 20 minutes. Wheel and erythema size may be recorded by actual measurement or by the extent of the erythema reaction. Refer to the following table to determine the skin test sensitivity class. The corresponding 2E (sum of the longest diameter and the mid-point orthogonal diameters of erythema) is also presented.

<table>
<thead>
<tr>
<th>Allergen</th>
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</tr>
</thead>
<tbody>
<tr>
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<td>12</td>
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<td>12</td>
<td>0.033</td>
</tr>
</tbody>
</table>

Class | Diameter | Diameter | Corresponding 2E |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>&lt;5 mm</td>
<td>&lt;5 mm</td>
<td>&lt;10 mm</td>
</tr>
<tr>
<td>1</td>
<td>5-10 mm</td>
<td>10-20 mm</td>
<td>10-30 mm</td>
</tr>
<tr>
<td>2</td>
<td>10-15 mm</td>
<td>20-40 mm</td>
<td>20-40 mm</td>
</tr>
<tr>
<td>3</td>
<td>15-20 mm</td>
<td>40-50 mm</td>
<td>40-50 mm</td>
</tr>
<tr>
<td>4</td>
<td>&gt; 15 mm²</td>
<td>&gt;40 mm</td>
<td>&gt;80 mm</td>
</tr>
</tbody>
</table>

3. IMMUNOTHERAPY

Allergen extracts should be administered using a sterile syringe with 0.01 mL gradations and a 25-27 gauge 1/2” to 5/8” needle. The injections are given subcutaneously. The most common sites of injection are the lateral aspect of the upper arm or thigh. Intracutaneous or intramuscular injections may produce large local reactions which may be very painful.

Dosage of allergen extracts is a highly individualized matter and varies according to the degree of sensitivity of the patient, his clinical response, and tolerance to the extract administered during the early phases of an injection regimen. The starting dose should be based on skin tests of the extract to be used for immunotherapy. To prepare dilutions for intradermal and therapeutic use, make a 1:10 dilution by adding 0.005 mL of the concentrate to 9.0 mL of Sterile Albumin Saline with Phenol (0.4%). Subsequent serial dilutions
A mixture of the two mite species, in equal parts, resulting in D. pteronyssinus at 15,000 AU/mL and D. farinae at 15,000 AU/mL, is available for therapeutic use in 10 mL and 30 mL vials. A mixture of the two species is also available in 5,000 AU/mL, each species in 10 mL, 30 mL and 50 mL.

Storage:

The expiration date of the mite extract in 50% glycerin is listed on the container label. The extract should be stored at 2° - 8°C and kept in this temperature range during office use. Dilutions containing more than 50% glycerin are less stable, and if loss of potency is suspected, should be checked by skin testing with equal units of a freshly prepared dilution on known mite allergic individuals.

The expiration date of the intradermal tests is listed on container labels. Store at 2° - 8°C.

LIMITED WARRANTY: A number of factors beyond our control could reduce the efficacy of this product or even result in an ill effect following its use. These include storage and handling of the product after it leaves our hands, diagnosis, dosage, method of administration and biological differences in individual patients. Because of these factors, it is important that this product be stored properly and that the directions be followed carefully.

No warranty, express or implied, including any warranty of merchantability or fitness, is made. Representatives of the Company are not authorized to vary the terms or the contents of any printed labeling, including the package insert, for this product except by printed notice from the Company's headquarters. The prescriber and user of this product must accept the terms hereof.

REFERENCES