ALLERGENIC EXTRACT

Standardized Mite
Dermatophagoides farinae
Dermatophagoides pteronyssinus

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DESCRIPTION

Mite extract is a sterile solution containing the extractables of mite whole bodies in 0.25% sodium chloride, 0.125% sodium bicarbonate, 50% glycerol by volume and 0.4% phenol as a preservative. The mites are ground together with matrix material of yeast and pork and are handled and cleaned in a manner to remove more than 99% of the food medium. The medium contains no material of human origin. The allergy history and skin tests usually are history by the scratch, prick-puncture, or intradermal methods for skin testing for diagnostic purposes and subsequently for therapeutic purposes as directed under Dosage and Administration.

Intradermal skin tests in patients who were puncture test positive (Sum E ≥ 40 mm) to either Der. farinae or D. pteronyssinus extract were performed with duplicate doses of the mite food medium obtained from the same supplier. The results, submitted to the FDA by several manufacturers, were as follows: intradermal skin tests were performed and countere tested to the contact the 44 individuals at an estimated 1% level of medium content (approximately the same as contained in the mite extract). At a ten-fold increase (estimated 10% medium content), 4 positives in 40 individuals were observed. With extracts of the mite food medium obtained from the same supplier. At a ten-fold increase (estimated 1% level of medium content (approximately 44 individuals at an estimated 1% level of medium content (approximately the same as contained in the mite extract). At a ten-fold increase (estimated 10% medium content), 4 positives in 40 individuals were observed. The medium contains no material of human origin. This extract may be administered by a physician based on skin testing with this product. The dosage must be reduced when starting a patient on fresh standardized mite extract or when transferring a patient from non-standardized or modified extract to standardized extract, even though the labeled strength of the old and new vials may be the same. This is necessary due to a loss of extract potency during storage in the physician's office. The mite allergen content of cold chain new extract may be controlled and adjusted by dosage reduction and/or dilution before the new extract is administered. 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 mite allergen. Any evidence of a local or generalized reaction requires a reduction in dosage during the initial intradermal testing as well as during maintenance therapy. Beta-blocking drugs may make patients refractory to the usual dose of epinephrine, in the event epinephrine is required to treat an adverse allergic reaction.

INDICATIONS

Immunotherapy with mite extract has been studied by several investigators. The diagnosis of mite allergy is established by the allergy history and skin test reaction (see DISEASE). Mite extracts are indicated for use in the diagnosis of patients with a history of mite allergy who have established sensitivity to Der. farinae or D. pteronyssinus or to an extract of yeast (Saccharomyces sp.) when tested by the scratch-puncture test. The use of mite extract for the above purposes should be made only by physicians with special familiarity and knowledge of allergy as described in sections below. Other contraindications include:

- FEVER: Patients with nephrotic syndrome or anaphylactic or anaphylactoid urticaria, arteritis, purpura, angioedema, rhinitis, wheezing, laryngeal edema and myocardial infarction. Patients who have experienced a recent myocardial infarction may not be able to tolerate immunotherapy. The benefit-to-risk ratio must be carefully evaluated.

- ADVISORY REACTIONS: Adverse systemic reactions usually occur within minutes and consist primarily of allergic symptoms such as generalized skin erythema, urtica, pruritus, angioedema, rhinitis, wheezing, laryngeal edema and fever; 3) exposure to excessive amounts of clinically relevant allergen because a systemic reaction might conceivably cause uterine muscle contractions leading to abortion. Caution should be exercised in testing or treating pregnant females.

- PREGNANCY CATEGORY C: Animal reproduction studies have not been conducted with mite extract. It is also not known whether mite extract can cause fetal harm when administered to a nursing woman or can affect reproduction capacity. Mite extract should be given to a pregnant woman only if clearly needed.

- 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: Although standardized mite extract has not been studied in children, unstandardized extract of D. farinae has been administered by the prick test to asthma patients, children ages 1 to 16 without any reported adverse reaction (Dr. E. H. Y. Peled, personal communication). The extract of D. farinae has been administered subcutaneously for hypersensitization to children ages 5 to 14 with adverse reactions being limited to local comfort, redness and swelling for one or two days (7).

- DRUG INTERACTION: Antihistamines and hydroxyzone can significantly inhibit the immediate skin test reaction (see DRUG INTERACTION). 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.

- Warnings: Concentrated extract must be diluted with saline until prior to first use on a patient for treatment or intradermal testing. All concentrations of allergenic extract are manufactured to assure high potency and therefore have the ability to cause serious systemic reactions, including death in sensitive patients (11). Patients should be informed of this risk and precautions should be discussed prior to initiating immunotherapy (see PRECAUTIONS below). Allergic extract 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 refractory to treatment by, for example: 2) exposure to excessive amounts of clinically relevant allergen prior to a scheduled injection. The dosage must be reduced when starting a patient on fresh standardized mite extract or when transferring a patient from non-standardized or modified extract to standardized extract, even though the labeled strength of the old and new vials may be the same. This is necessary due to a loss of extract potency during storage in the physician's office. The mite allergen content of cold chain new extract may be controlled and adjusted by dosage reduction and/or dilution before the new extract is administered. 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 mite allergen. Any evidence of a local or generalized reaction requires a reduction in dosage during the initial intradermal testing as well as during maintenance therapy. Beta-blocking drugs may make patients refractory to the usual dose of epinephrine, in the event epinephrine is required to treat an adverse allergic reaction.

CONTRAINDICATIONS

- Extensive Sensitivity to Mite: Determined from previous anaphylaxis following skin testing, ingestion or injection of mite, or natural or paternal exposure. Autoimmune Disease: Individuals with autoimmune disease may be at risk, due to the possibility of routine immunizations exacerbating symptoms of the underlying disease.
hypotension. Less commonly, nausea, emesis, abdominal cramps, diarrhea and urticarial reactions occur. Severe reactions may cause shock and loss of consciousness. Fatalities have occurred rarely (1). Systemic reactions occur with a frequency different in clinical trials. To some extent, the reaction rate is related to the type and dose of administration, and is of the order of magnitude of the highest degree of sensitivity of the patient. Despite all precautions, occasional reactions are unavoidable. Reports of reactions in patients in Scandinavian allergists for Biologics Evaluation and Research (CBER) indicated that several deaths have been associated with the use of mite extracts. CBER was subsequently informed that these deaths may have been related to use by physicians of other health professionals unfamiliar with the administration of potent allergens, rather than a product defect. It should be noted that anaphylaxis and deaths following the injection of mite and other extracts also have been reported by the British Committee on Safety in Medicine in the British Medical Journal, 293:943, 1986.

Local reactions consisting of erythema, itching, swelling, tenderness and sometimes pain may occur at the injection site. These reactions may appear immediately after injection and persist for several days. Local cold applications and oral antihistamines may be effective treatment. For many patients and in some situations, steroids may be helpful.

The treatment of systemic allergic reactions is somewhat dependent upon the symptom complex. Epinephrine hydrochloride 1:1,000 aqueous, in an adult dose of 0.3–0.5 mL (or 0.01 mL per kg. for children) administered subcutaneously with the opposite arm is the immediate treatment of choice. A tourniquet should be placed above the site of the extract injection if the injection is given on the extremities. Antihistamines may offer relief of urticaria, associated skin reactions and gastrointestinal symptoms. Persistent wheezing may necessitate intravenous amiphylline treatment. For profound shock and hypotension intravenous fluids, vasopressors and oxygen also may be needed.

Maintenance of an open airway is critical if upper airway obstruction is present. Corticosteroids may provide benefit if symptoms are prolonged or recurrent.

OVERDOSE
A strong local reaction to the injection of extract may be treated with oral antihistamines and the local application of a cold compress. The dosage must be adjusted to the additional reactions and to the adverse effects of the reaction has disappeared. A systemic reaction following the injection of the extract may be treated immediately with Epinephrine hydrochloride 1:1,000 aqueous (see Adverse Reactions, paragraph 4 above).

DOSE AND ADMINISTRATION
Parterenal drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The product should be discarded if discolored or particles are observed.

DIAGNOSTIC USE:
Percutaneous Tests: The skin test concentration of 10,000 AU/mL in dropper vials is used for scratch or prick-puncture testing. Puncture tests performed with 1% D. farinae extract on 5 persons sensitive to mite showed a mean diameter wheal of 10 mm ± 1.6 mm and mean diameter erythema of 29.2 mm ± 5.3 mm. Puncture tests with a D. pteronyssinus extract on 10 persons sensitive to mite showed a mean diameter wheal of 7.8 mm ± 4.1 mm and mean erythema of 33.7 mm ± 12.0 mm.

Intradermal Tests: Extract for intradermal testing should be prepared by diluting the 10,000 AU/mL stock concentrate in bulk vials with sterile saline with or without human serum albumin. Intradermal skin tests (0.05 mL) in persons highly sensitive to mite showed the following results:

Table 1

<table>
<thead>
<tr>
<th>AU/mL to inject</th>
<th>mm diameter of wheal</th>
<th>mm diameter of erythema</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:10,000</td>
<td>10</td>
<td>50</td>
</tr>
<tr>
<td>1:1,000</td>
<td>5.0</td>
<td>50</td>
</tr>
<tr>
<td>1:100</td>
<td>5.0</td>
<td>100</td>
</tr>
<tr>
<td>1:10</td>
<td>5.0</td>
<td>100</td>
</tr>
<tr>
<td>No Dilution</td>
<td>5.0</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 2: Volume per unit dilutions of 5,000 AU/mL and 10,000 AU/mL concentrations to prepare a 1:10 dilution series.

Vial No. | Concentrate | Concentrate | Concentrate |
---------|-------------|-------------|-------------|
| 1       | 1:10,000    | 1:10,000    | 1:10,000    |
| 2       | 1:1,000     | 1:1,000     | 1:1,000     |
| 3       | 1:100       | 1:100       | 1:100       |
| 4       | 1:10        | 1:10        | 1:10        |
| 5       | No Dilution | No Dilution | No Dilution |

PREPARING DILUTIONS
To prepare dilutions for intradermal skin tests and therapeutic use as shown in the table below, make a series of ten-fold dilutions starting with the 5,000 AU/mL or 10,000 AU/mL as follows: add 1.0 mL of the 10,000 AU/mL concentration to 9.0 mL of sterile diluent to make the 1:10 dilution; add 1.0 mL of the 1:10 dilution to 9.0 mL of sterile diluent to make the 1:100 dilution. Continue making dilutions as shown in the table below until the highest desired dilution is reached. The number of allergy units per mL in each dilution is shown in the table below.

Table 2. Volume per unit dilutions of 5,000 AU/mL and 10,000 AU/mL concentrates to prepare a 1:10 dilution series.

Vial No. | Concentrate | Concentrate | Concentrate |
---------|-------------|-------------|-------------|
| 1       | 1:10,000    | 1:10,000    | 1:10,000    |
| 2       | 1:1,000     | 1:1,000     | 1:1,000     |
| 3       | 1:100       | 1:100       | 1:100       |
| 4       | 1:10        | 1:10        | 1:10        |
| 5       | No Dilution | No Dilution | No Dilution |

How Supplied
Extract of D. farinae and D. pteronyssinus containing 5,000 and 10,000 Allergy Units per mL is supplied in 50% glycerol in 10 mL, 30 mL and 50 mL vials. Extract containing 10,000 Allergy Units per mL is supplied in 50% glycerol in 5 mL dropper vials for scratch or prick-puncture testing. An equal v/v mixture of the two mites is offered in 10, 30 and 50 mL vials at a concentration of 2,500 AU/mL or 5,000 AU/mL for each mite. See DESCRIPTION above for the complete list of the active and inactive ingredients of this product.

Extract of D. farinae and D. pteronyssinus may be diluted in sterile buffered saline containing 0.4% phenol or in sterile buffered saline containing human serum albumin and 0.4% phenol.

STORAGE AND HANDLING
Extract should be stored at 2–8°C since higher temperatures may adversely affect stability. Do not freeze.

REFERENCES

Date of Revision: February 2013