HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Greer Standardized Mite Extracts safely and effectively. See full prescribing information for Greer Standardized Mite Extracts.
Standardized Mite Extract (*Dermatophagoides farinae*)
Standardized Mite Extract (*Dermatophagoides pteronyssinus*)
Standardized Mite Extract Mixture (*Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*)
Solution for percutaneous, intradermal, or subcutaneous administration.
Initial U.S. Approval: 1987

WARNING: ANAPHYLAXIS
See full prescribing information for complete boxed warning
- **Do not inject intravenously (2.2)**
- **Allergenic extracts may cause severe life-threatening systemic reactions, including the rare occurrence of anaphylaxis or death (5.1)**
- **Intended for use only by experts experienced in administering allergic extracts and trained to provide emergency treatment (5.1)**
- **Initial dose must be based on skin test (2.1)**
- **Observe patients in the office for at least 30 minutes following treatment. Emergency measures and personnel trained in their use must be available immediately in the event of life threatening reaction (5.1)**
- **Immunotherapy may not be suitable for patients with medical conditions that reduce their ability to survive a systemic reaction (5)**

----------INDICATIONS AND USAGE----------
Greer Standardized Mite Extracts are allergenic extracts indicated for
- Diagnosis of skin test reactivity to dust mite allergen (1)
- Treatment of mite-induced allergic asthma, rhinitis and conjunctivitis in patients that show hypersensitivity to dust mites based on clinical history, allergen exposure history, and skin test reactivity (1)

----------DOSAGE AND ADMINISTRATION----------
The extracts are diluted with sterile diluents for allergenic extracts when used for intradermal testing or subcutaneous immunotherapy. Dosages vary by mode of administration, and by individual response and tolerance.
- Administered percutaneously for diagnostic testing (2.1); stock concentrate 10,000 Allergy Units/mL (2.1)
- Administered intradermally for diagnostic testing (2.1); stock concentrate 5,000, 10,000, or 30,000 Allergy Units/mL (2.3)
- Administered subcutaneously for immunotherapy (2.2); stock concentrate of 5,000, 10,000, or 30,000 Allergy Units/ mL (2.3)

----------DOSAGE FORMS AND STRENGTHS----------
- For percutaneous testing, Greer Standardized Mite Extract stock concentrates containing 10,000 Allergy Units/mL of *Dermatophagoides farinae (D. farinae), Dermatophagoides pteronyssinus (D. pteronyssinus)*, or both *D. farinae* and *D. pteronyssinus* are supplied in 5 mL dropper vials (3)
- For intradermal testing or immunotherapy, Greer Standardized Mite Extracts stock concentrates containing a total of 5,000, 10,000, or

30,000 Allergy Units/mL of *D. farinae, D. pteronyssinus*, or a mixture of *D. farinae* and *D. pteronyssinus* are supplied in 10, 30, and 50 mL multiple-dose vials (3)

----------CONTRAINDICATIONS----------
None

----------WARNINGS AND PRECAUTIONS----------
All concentrates of Greer Standardized Mite Extracts can cause serious systemic reactions of varying degrees of severity, including anaphylactic shock and death, particularly in patients:
- With labile or steroid-dependent asthma (5.1)
- With extreme sensitivity to allergen(s) (5.1)
- Who are currently using beta blockers (5.2)
- Who are on an accelerated immunotherapy build-up schedule (5.1)
- Who are being changed from one allergenic extract to another (5.1)
- Who are receiving high doses of allergen extracts (5.1)

----------ADVERSE REACTIONS----------
- Systemic reactions may be fatal or near fatal (6)
- Systemic reactions (e.g., generalized skin erythema, urticaria, pruritus, angioedema, rhinitis, wheezing, laryngeal edema, and hypotension) occur in 4-7% of patients
- The most common reactions are local reactions at the injection site (e.g., erythema, itching, swelling, tenderness, pain), occurring in 26% to 82% of patients (6)

To report SUSPECTED ADVERSE REACTIONS, contact Greer Laboratories, Inc., at 1-800-438-0088 or the FDA at 1-800-fda-1088 or www.fda.gov/medwatch

----------DRUG INTERACTIONS----------
- Patients who are receiving beta agonists may be unresponsive to the usual doses of epinephrine used to treat serious systemic reactions, including anaphylaxis (7.1)
- Patients should discontinue medications known to suppress the histamine response prior to skin testing including: antihistamine (7.2), tricyclics (7.4), and topical corticosteroids and topical anesthetics (7.3)

----------USE IN SPECIFIC POPULATIONS----------
- Pregnancy: No human or animal data. Use only if clearly needed (8.1)
- Autoimmune Disease: immunotherapy may exacerbate the autoimmune disease. Use only if clearly needed (5.3)

See 17 for PATIENT COUNSELING INFORMATION

Revised 11/2009

FULL PRESCRIBING INFORMATION : CONTENTS*

*Sections or subsections omitted from the Full Prescribing Information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: ANAPHYLAXIS
- Do not inject intravenously. (2.2)
- Allergenic extracts may potentially elicit a severe life-threatening systemic reaction, rarely resulting in death. (5.1)
- This allergenic product is intended for use only by physicians who are experienced in the administration of allergenic extracts and the emergency care of anaphylaxis, or for use under the guidance of an allergy specialist. (5.1)
- The initial dose must be based on skin test. (2.1)
- Observe patients in the office for at least 30 minutes following treatment. Emergency measures and personnel trained in their use must be available immediately in the event of life threatening reaction. (5.1)
- Immunotherapy may not be suitable for patients with medical conditions that reduce their ability to survive a systemic reaction, including significant cardiovascular and/or pulmonary diseases. Patients who are receiving beta blockers may be unresponsive to the usual doses of epinephrine used to treat systemic reactions, including anaphylaxis. (5.2)

1 INDICATIONS AND USAGE

Greer Standardized Mite (*Dermatophagoides farinae* and/or *Dermatophagoides pteronyssinus*) Extracts are allergenic extracts indicated for
- skin test diagnosis of mite allergy
- treatment of patients with mite-induced allergic asthma, rhinitis and conjunctivitis.

For Immunotherapy, patients must show hypersensitivity to *Dermatophagoides farinae (D. farinae)* or *Dermatophagoides pteronyssinus (D. pteronyssinus)* based on their clinical history, allergen exposure history, and skin test reactivity.

2 DOSAGE AND ADMINISTRATION

Do not inject intravenously.

Greer Standardized Mite extracts are diluted with sterile diluent for allergenic extracts when used for intradermal testing or subcutaneous immunotherapy. Dosages vary by mode of administration, and by individual response and tolerance. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Greer Standardized Mite Extracts should be a light brown solution that is free of particulate matter. If particulate matter is observed then the solution should be discarded.

2.1 DIAGNOSTIC TESTING

For diagnosis of a patient with a suspected allergy to either species of dust mite (*D. farinae or D. pteronyssinus*), diagnostic skin testing should include the standardized mite mixture or the single-species mite extracts.
- If a skin test with the standardized mite mixture elicits a positive

reaction, then the single-species mite extracts can be used to determine the degree of sensitivity to each, and to guide in the selection of extracts and their concentration for immunotherapy, if indicated.
- A positive skin test reaction to any allergen must be interpreted in light of the patient's history of symptoms, the time of year, and known exposure to environmental allergens.

2.1.1 Percutaneous Skin Testing

For percutaneous (scratch, prick, or puncture) testing, use 10,000 Allergy Units/mL Greer Standardized Mite Extract stock concentrate in dropper vials. **If patient is suspected of having exquisite sensitivity, such as anaphylaxis, to certain foods and drugs, initiate percutaneous testing with several serial 10-fold dilutions of the usual test concentration.**
- For scratch tests, scarify the skin, and then apply one drop of the extract to the scratch.
- For prick tests, place one drop of extract on the skin and pierce through the drop into the skin with a slight lifting motion.
- For puncture tests, place one drop of extract on the skin and pierce through the drop perpendicular to the skin.

When using percutaneous test devices, follow the directions provided with the test devices.

Include a positive control to detect false negative responses to skin testing, which may occur if serum levels of antihistamines remain from prior medication administration [see *Drug Interactions (7.2)*]. A glycerinated histamine phosphate diluted to 10mg/mL (6mg/mL histamine base) may be used as the positive control.

Include a negative control to detect false positive responses, which can occur when the patient has a non-specific reaction to the diluent. A 50% gylcerosaline solution may be used as the negative control.

Read skin tests 15-20 minutes after exposure. Record the induration (wheal) and erythema (flare) response by noting the longest diameter of each, or by the sum of the longest erythema diameter and the mid-point orthogonal diameters of erythema (ΣE).

Percutaneous testing devices often have their own grading systems, as these devices may cause different degrees of trauma to the skin and deliver different volumes of allergenic extract. Follow grading instructions for the device used.

2.1.2 Intradermal Skin Testing

Intradermal tests are commonly used when the reaction to percutaneous testing is negative or equivocal but the patient has a strong clinical history of symptoms triggered by exposure to a specific allergen. Because immediate systemic reactions are more common with intradermal testing, prescreening with percutaneous testing is a practical safety measure.[1]

Dilute the stock concentrate with sterile diluent. Use saline with human serum albumin (HSA), buffered saline, or saline. **If prescreening is not done, or if patients are expected to be high risk, precautions should be observed since some patients have experienced anaphylaxis and death.**
- Patients who do not react to percutaneous skin testing should be tested intradermally at a starting dose of 0.02 to 0.05 mL of a

50 Allergy Units/mL extract dilution.
- Patients suspected of being highly allergic should first receive a test dose of 0.02 to 0.05 mL of a 0.05 Allergy Units/mL extract dilution.
- If the intial dose test is negative, subsequent intradermal tests using increasingly stronger doses may be performed up to the maximum recommended strength of 200 Allergy Units / mL.
- If percutaneous skin testing was not performed, include a positive control to detect false negative responses to skin testing, which may occur if serum levels of antihistamines remain from prior medication administration [see *Drug Interactions (7.2)*]. A glycerinated histamine phosphate diluted to 0.5 mg/mL (0.18 mg/mL histamine base) or aqueous histamine phosphate 0.275 mg/mL (0.1 mg/mL histamine base) may be used as the positive control.
- If percutaneous skin testing was not performed, include a negative control to detect false positive responses, which can occur when the patient has a non-specific reaction to the diluent. A 1% glycerin in 0.9% saline solution may be used as the negative control.
- Measure the wheal-and-flare response after 15-20 minutes, which may be graded using various methods as described in the instructions for the device used.

The mean dose of Greer dust mite allergen required to elicit a positive intradermal test result (ΣE 50 mm) in a total of 83 mite puncture test positive (ΣE 20 mm) persons is shown in Table1.

Table 1. Intradermal Reactivity to Mite Allergens

Allergen	Number of Persons	Dose to Elicit 50 mm Sum of Diameter Erythema Reaction	
		Mean (AU*/mL)	Range (AU/mL)
D. farinae	46	0.00856	0.00004 - 1.75935
D. pteronyssinus	37	0.00570	0.00002 - 1.36341**

* Allergy Units
** Data is available on file with Greer

2.2 IMMUNOTHERAPY

Subcutaneous injection only.

Subcutaneous injections for immunotherapy should be prepared by dilution of stock concentrate based on patient's reactivity. Stock concentrations of Greer Standardized Mite Extract are available in 5,000 Allergy Units/mL, 10,000 Allergy Units/mL, 30,000 Allergy Units/mL for immunotherapy. See Table 2 for dilution preparation. Also see Dosage Modification Guidelines. (2.2.1)
- The initial dose of the extract should be based on the percutaneous test reactivity. In patients who appear to be exquisitely sensitive by history and skin test, the initial dose of the extract should be 0.1 mL of a 0.005 to 0.05

Allergy Units/mL dilution. Patients with lesser sensitivity may be started at a 0.5 to 5 Allergy Units/mL dilution.
- The dose of allergenic extract is increased at each injection by no more than 50% of the previous dose, and the next increment is governed by the response to the last injection.
- Large local reactions which persist for longer than 24 hours are generally considered an indication for repeating the previous dose or reducing the dose at the next administration.
- **Any evidence of a systemic reaction is an indication for a significant reduction (at least 75%) in the subsequent dose. Repeated systemic reactions, even of a mild nature, are sufficient reason for the cessation of further attempts to increase the reaction-causing dose.**
- **Severe reactions require a decrease in the next dose by at least 50%. Proceed cautiously in subsequent dosing.**
- A maximum tolerated maintenance dose should be selected based on the patient's clinical response and tolerance. Doses larger than 0.2 mL of the concentrate are rarely administered because an extract in 50% glycerin may cause discomfort upon injection.
- Since the two mite species tend to cross-react, consider the total Allergy Units content in determining the maximum maintenance dose of the mixture.

2.2.1 Dosage Modifications Guidelines for Immunotherapy

The following conditions may indicate a need to withhold or reduce the dosage of immunotherapy. In situations prompting dose reduction, once the reduced dose is tolerated, a cautious increase in dosage can be attempted.
Immunotherapy should be withheld or reduced in dosage if the following concurrent conditions exist:
- Severe symptoms of rhinitis and/or asthma;
- Infection accompanied by fever; or
- Exposure to excessive amounts of clinically relevant allergen prior to a scheduled injection.

Changing to a different lot of extract: All extracts lose potency over time. A fresh extract may have an effective potency that is substantially greater than that of older extracts. Therefore, the first dose from the fresh vial should not exceed a 25% increase of the previous dose or a 75% reduction of the previous dose, assuming both extracts contain comparable amounts of allergen, defined by Allergy Units.

Unscheduled Gaps between Treatments: Patients may lose tolerance for allergen injections during prolonged periods between doses, thus increasing their risk for an adverse reaction. The duration of tolerance between injections varies from patient to patient.
- During the build-up phase, when patients receive injections 1 to 2 times per week, it is customary to repeat or even reduce the extract dosage if there has been a substantial time interval between injections. This depends on 1) the concentration of allergen immunotherapy extract that is to be administered, 2) a

previous history of systemic reactions, and 3) the degree of variation from the prescribed interval of time, with longer intervals since the last injection leading to greater reductions in the dose to be administered. This suggested approach to dose modification due to unscheduled gaps between treatments during the build-up phase is not based on published evidence. The individual physician should use this or a similar protocol as a standard operating procedure for the specific clinical setting.
- Similarly, if large unscheduled gaps occur during maintenance therapy, it may be necessary to reduce the dosage. The individual physician should devise a protocol as a standard operating procedure for his or her specific clinical setting in determining how to modify doses of allergen immunotherapy due to unscheduled gaps in treatment.

The extract previously used is from another manufacturer: Since manufacturing processes and sources of raw materials differ among manufacturers, the interchangeability of extracts from different manufacturers cannot be assured. The starting dose of the extract from a different manufacturer should be greatly decreased even though the extract is the same formula and dilution. In general, a dose reduction of 50-75% of the previous dose should be adequate, but each situation must be evaluated separately considering the patient's history of sensitivity, tolerance of previous injections, and other factors. Dose intervals should not exceed one week when rebuilding dose.

The previous extract has expired or is near expiry: The dating period for allergenic extracts indicates the time that they can be expected to remain potent under ideal storage conditions (2° - 8°C) [see *How Supplied/Storage and Handling (16)*]. Some loss of potency occurs even when stored under ideal conditions, therefore extracts should not be stored beyond the expiration date. Instead, a new lot should be used (see *"Changing to a different lot of extract"*, above)

Changing from non-stabilized to human serum albumin (HSA) stabilized diluents: Allergenic extracts diluted with HSA and 0.4% phenol are more potent than extracts diluted with diluents that do not contain stabilizers. When switching from a non-stabilized to an HSA stabilized diluent, consider lowering the dose for immunotherapy.

2.2.2. Administration of Immunotherapy

Administer immunotherapy by subcutaneous injection in the lateral aspect of the arm or thigh. Avoid injection directly into any blood vessel.
- The optimal interval between doses of allergenic extract varies among individuals. Injections are usually given 1 or 2 times per week until the maintenance dose is reached, at which time the injection interval is increased to 2,3, and finally 4 weeks.
- Because most adverse reactions occur within 30 minutes after injection, patients should be kept under observation for at least 30 minutes.[2] For high risk patients 30 minutes of observation may not be sufficient.

2.3 DILUTION PREPARATION

To prepare dilutions for intradermal testing and immunotherapy, start with a 5,000, 10,000, or 30,000 Allergy Units/mL stock concentrate, and prepare

a 1:10 dilution by adding 0.5 mL of concentrate to 4.5 mL of sterile aqueous diluent. Subsequent dilutions are made in a similar manner (see Table 2).

Table 2. Ten-fold Dilution Series for intradermal testing and immunotherapy

Dilution	Extract	Diluent	AU*/mL	AU/mL	AU/mL
0	Concentrate		5,000	10,000	30,000
1	0.5 mL Concentrate	4.5 mL	500	1,000	3,000
2	0.5 mL Dilution 1	4.5 mL	50	100	300
3	0.5 mL Dilution 2	4.5 mL	5	10	30
4	0.5 mL Dilution 3	4.5 mL	0.5	1	3
5	0.5 mL Dilution 4	4.5 mL	0.05	0.1	0.3
6	0.5 mL Dilution 5	4.5 mL	0.005	0.01	0.03

*Allergy Units

3 DOSAGE FORMS AND STRENGTHS

For immunotherapy, concentrated extracts are diluted in normal saline, buffered saline, albumin saline or 10% glycerosaline. For intradermal testing extracts may be diluted in normal saline, buffered saline, or albumin saline.

Greer Standardized Mite Extract *D. farinae* and Greer Standardized Mite Extract *D. pteronyssinus* are supplied as stock concentrates containing 10,000 Allergy Unit/mL and Greer Standardized Mite Extract mixture (*D. farinae* and *D. pteronyssinus*) is supplied as a stock mixture concentrate containing 5,000 Allergy Units/mL of each species for use in percutaneous skin testing.

Greer Standardized Mite Extract *D. farinae* and Greer Standardized Mite Extract *D. pteronyssinus* are supplied as stock concentrates containing 5,000, 10,000, or 30,000 Allergy Unit/mL. Greer Standardized Mite Extract mixture (*D. farinae* and *D. pteronyssinus*) is supplied as a stock mixture concentrate containing 5,000 and 15,000 Allergy Units/mL of each species for use in intradermal testing and immunotherapy.

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Serious Systemic Reactions

All concentrates of Greer Standardized Mite Extracts have the ability during skin testing and immunotherapy to elicit serious systemic reactions including anaphylactic shock and death [see *Adverse Reactions (6)*].

A review of the literature indicates that the incidence of near-fatal reactions to immunotherapy, defined as severe respiratory compromise, hypotension, or both, and requiring emergency treatment with epinephrine, has been estimated at 5.4 events per million injections in a 10-year retrospective survey of allergists.[3] Fatalities from immunotherapy injections have been estimated to occur at a rate of approximately one death per 2.0 to 2.8 million injections in 4-, 10- and 12-year retrospective surveys of allergists.[4-6]

Because of the danger of serious reactions, caution is required in testing and treating high risk patients and those with medical conditions that reduce their ability to survive a serious systemic adverse event.
High-risk patients are defined as those patients:

- with labile or steroid-dependent asthma, particularly in those suffering an exacerbation of their symptoms at the time of extract administration;
- with extreme sensitivity to a particular allergen(s);
- who are currently using beta blockers;
- who are receiving an accelerated immunotherapy build-up schedule (e.g., rush immunotherapy);
- who are being changed from one allergenic extract to another;
- who are receiving high doses of allergenic extracts.

High risk patients have had fatal reactions. In addition, patients not high-risk but on beta blockers have had fatal reactions because beta blockers interfere with beta adrenergics such as epinephrine used in treatment of anaphylaxis.

Patients should be kept under observation for a minimum of 30 minutes after receiving allergenic extracts so that any adverse reaction can be observed and properly handled.[2]

Medications to treat systemic reactions, as well as emergency equipment should be available for immediate use. Extracts must only be administered by persons who are aware of the risk of systemic reactions, including anaphylaxis; are capable of handling such reactions; and have the necessary drugs and equipment on hand to do so.

5.2 Patients on Beta Blockers

Patients receiving beta blockers may be unresponsive to the usual doses of epinephrine used to treat serious systemic reactions, including anaphylaxis. Inhalant allergy immunotherapy should be approached with caution in patients taking beta blockers. The risks of anaphylaxis in these patients should be carefully weighed against the benefits of immunotherapy [see *Drug Interactions (7.1)*].

5.3 Autoimmune Disease

Immunotherapy should be given cautiously to patients with other immunologic diseases and only if the risk from exposure to the allergen is greater than the risk of exacerbating the underlying disorder[2].

6 ADVERSE REACTIONS

Systemic reactions consist primarily of allergic symptoms, such as generalized skin erythema, urticaria, pruritus, angioedema, rhinitis, wheezing, laryngeal edema, and hypotension. Additional symptoms that are not usually associated with allergy also may occur, such as nausea, emesis, abdominal cramps, and diarrhea. Serious reactions may cause shock, loss of consciousness, and even death. Based on published studies,[7,8] systemic reactions occur in less than 1% of patients receiving conventional immunotherapy to greater than 36% in some studies of patients receiving rush immunotherapy.

Local reactions at the injection site are the most commonly occurring reactions (e.g., erythema, itching, swelling, tenderness, pain). Although most adverse systemic reactions occur within 30 minutes of injection (some within minutes of extract exposure), such reactions also can occur up to six hours after skin tests of immunotherapy [see *Dosage and Administration (2.2)*][9].

7 DRUG INTERACTIONS

7.1 Beta Adrenergic Drugs

Patients receiving beta blocker drugs may not be responsive to beta adrenergic drugs used to treat anaphylaxis[10], and may wish to temporarily postpone treatment day of skin testing. All such decisions should be made in consultation with the physician. [see *Warnings* and *Precautions (5.2)*].

7.2 Antihistamines[1]

Skin testing with allergenic extracts should not be performed within 2-3 days of first-generation H1-histamine receptor blockers (e.g., clemastine, diphenhydramine) and within 3 to 10 days of second-generation antihistamines (e.g., loratadine, terfenadine), except for astemizole, which requires an interval of 30-60 days between allergenic extract exposure and use. These products suppress histamine skin test reactions and could mask a positive response.

7.3 Topical Corticosteroids and Topical Anesthetics[1]

Topical corticosteroids may suppress skin reactivity and should be discontinued at the skin test site for at least 2-3 weeks before skin testing. Topical local anesthetics may suppress flare responses and should be avoided at skin test sites.

7.4 Tricyclic Antidepressants[1]

Tricyclic antidepressants can have potent antihistamine effects and will affect skin testing. Since use of tricyclics may alter skin test results, dosing for both skin testing and immunotherapy should be done with caution. If tricyclic medication has been recently discontinued, allow 7-14 days prior to skin testing to obviate the antihistamine effect. The risk of anaphylaxis in these patients should be carefully weighed against the risks and benefits of stopping tricyclics.

7.5 Other drugs

The suppressive action of other drugs should be considered and emphasizes the need for a histamine positive-control test.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

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

Studies have not been performed in animals to determine whether extracts affect fertility in males or females, have teratogenic potential, or have other adverse affects on the fetus. Exercise caution in testing or treating pregnant females because a systemic reaction may cause maternal cardiovascular compromise leading to fetal distress with sequelae.

8.3 Nursing Mothers

It is not known whether allergenic extracts or their antigens are excreted in human milk. Because many drugs are excreted in human milk, exercise caution when extracts are administered to a nursing woman.

8.4 Pediatric Use

No studies have systematically examined differences in response to immunotherapy among child and adult patients. Children appear to tolerate injections of allergenic extracts very well.[2] Very young children

(under age 5) can have difficulty cooperating with an immunotherapy program and for this reason, the physician should consider the benefits and risks of immunotherapy and individualize treatment in patients under the age of 5 years. [See *Warnings and Precautions (5)*].

8.5 Geriatric Use

Clinical studies of Greer Standardized Mite Extract did not include sufficient numbers of subjects aged 65 and older to determine whether they respond differently from younger subjects. Other reported clinical experiences has not identified differences in responses between the elderly and younger patients. In general, dose selections for an elderly patient should be cautious, usually starting at the low end of the dosing range. reflecting the greater frequency of concomitant disease or other drug therapy including beta blockers.[2]

10 OVERDOSAGE

For all allergenic extracts the therapeutic dose varies per individual. If a dose exceeds the window for a particular patient this may be considered an overdose and the patient may experience anaphylaxis. Systemic reactions are uncommon after injection, but if the patient receives more extract than can be tolerated at that particular time, and begins to experience immediate hypersensitivity anaphylaxis, institute emergency treatment by trained personnel.

Overdosage may occur because of an error in the volume of extract or incorrect diluents injected. An overdose may also occur when, in addition to immunotherapy, the patient is exposed concomitantly to similar environmental allergens. In the event of a systemic reaction, the preparation of allergen and dosage schedule should be carefully reviewed.

11 DESCRIPTION

Greer Standardized Mite (*Dermatophagoides farinae and/or Dermatophagoides pteronyssinus*) extracts are sterile solutions used for intradermal testing or subcutaneous immunotherapy. Each vial contains 5,000, 10,000, or 30,000 Allergy units/mL of sterile mite extract (*D. farinae* and/or *D. pteronyssinus*), 50% glycerin v/v, and 0.4% phenol (preservative). Inert ingredients include 0.50% sodium chloride for isotonicity and 0.25% sodium bicarbonate as a buffer.

For immunotherapy, concentrated extracts are diluted in normal saline, buffered saline, albumin saline or 10% glycerosaline based on patient's reactivity. For intradermal testing, extracts may be diluted in normal saline, buffered saline, or albumin saline.

Source materials for the extract are whole mite bodies. The mites are cultured, handled, and cleaned to remove at least 99% of the food medium. The medium contains no material of human origin.

The mite extract is standardized by comparison to a reference preparation supplied by the Center for Biologics Evaluation and Research of the FDA, labeled 10,000 Allergy Unit/mL. The relative potency of the extract is determined by ELISA inhibition compared to the FDA mite reference, and is labeled in Allergy Unit/mL.

12 CLINICAL PHARMACOLOGY

Dust mites belonging to the genus *Dermatophagoides* are indoor allergens found in humid geographic locations worldwide. *D. farinae* and *D. pteronyssinus* occur widely with most homes in the United States coinhabited by both species.[11]

12.1 Mechanism of Action

The complete mechanisms of allergen immunotherapy are not clear and remain the subject of investigation. The allergic reaction is dependent on the presence of allergen-specific immunoglobulin E (IgE) antibodies that are bound to specific receptors on mast cells and basophils. The presence of IgE antibodies sensitizes these cells, and upon interaction with the appropriate allergens, histamine and other mediators are released which produce local or systemic responses in sensitive individuals, and characteristic symptoms of atopic diseases, such as allergic rhinitis and allergic asthma. Changes in serum antibody and T-lymphocyte responses resulting from immunotherapy have been demonstrated, and these changes often correlate closely with clinical (symptom) improvements. Specific mechanisms may vary depending on the nature of the allergic disease, the allergenic specificities of patients and populations, extract formulations, route of administration, dose and duration of treatment.[2]

Subcutaneous administration of allergenic extracts is known to elicit numerous immunological changes that are both time and dose-dependent. Many of these changes appear to be related to (or a precursor to) improvements in symptoms and other clinical parameters, as noted above. Specific changes found after immunotherapy with dust mite extracts include significant increases in mite-specific IgG4 antibodies[12], interleukin-10-positive T cells, and several T-cell receptors, and significant decreases in serum nitric oxide, eosinophil cationic protein, interleukin-4-positive T cells and IgE-mediated basophil histamine release.[13]

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenicity, Mutagenesis or Impairment of Fertility

No studies in animals have been performed to evaluate carcinogenicity, mutagenicity or impairment of fertility.

14 CLINICAL STUDIES

The dust mites *D. farinae* and *D. pteronyssinus* are the major source of allergens in house dust[14]. The efficacy of immunotherapy for Type I hypersensitivity (i.e., allergy) to airborne allergens[2,15,16] including dust mite has been well established. Specifically, immunotherapy for allergic hypersensitivity to house dust mite allergens has been addressed in a 1995 Cochrane meta-alalysis of 20 randomized, controlled trials of immunotherapy[17], and two subsequent updated Cochrane meta-analysis published in 1999 [18] and 2003 [19]. In addition, efficacy for immunotherapy in rush or cluster protocols, in which the dose escalation is compressed over days or weeks, has also been demonstrated[20, 21].

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16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 Storage and Handling

Store dust mite extract at 2°-8°C (36° to 46°F).

Keep dust mite extract at 2°- 8°C (36° to 46°F) during office use.

Dilutions of concentrated extract result in a glycerin content of less than 50% which results in reduced stability of the extracts. 1:100 dilutions should be kept no longer than a month, and more dilute solutions no more than a week. The potency of a dilution can be checked by skin test comparison to a fresh dilution of the extract on a known mite allergic individual.

16.2 How Supplied

Mite extracts in 50% Glycero-Coca solution are supplied as follows:

D. farinae: NDC 22840-0033	5,000 Allergy Unit/mL, 10, 30, and 50 mL vials
D. farinae: NDC 22840-0034	10,000 Allergy Unit/mL, 10, 30, and 50 mL vials
D. farinae: NDC 22840-0038	30,000 Allergy Unit/mL, 10, 30, and 50 mL vials
D. pteronyssinus NDC 22840-0035	5,000 Allergy Unit/mL, 10, 30, and 50 mL vials
D. pteronyssinus: NDC 22840-0036	10,000 Allergy Unit/mL, 10, 30, and 50 mL vials
D. pteronyssinus: NDC 22840-0039	30,000 Allergy Unit/mL, 10, 30, and 50 mL vials
D. farinae/D. pteronyssinus mixture: NDC 22840-0037	5,000 Allergy Unit/mL each species, 10, 30, and 50 mL vials
D. farinae/D. pteronyssinus mixture: NDC 22840-0040	15,000 Allergy Unit/mL each species, 10, 30, and 50 mL vials
D. farinae: NDC 22840-0034	10,000 Allergy Unit/mL, 5 mL percutaneous test vial
D. pteronyssinus: NDC 22840-0036	10,000 Allergy Unit/mL, 5 mL percutaneous test vial
D. farinae/D. pteronyssinus mixture: NDC 22840-0037	5,000 Allergy Unit/mL each species, 5 mL percutaneous test vial

17 PATIENT COUNSELING INFORMATION

Instruct the patient to remain in the office for observation for a minimum of 30 minutes after an injection; longer, if deemed necessary for the individual.

Caution patients that reactions may occur more than 30 minutes after skin testing or an injection.

Instruct patient to recognize the following symptoms as adverse reactions and to immediately return to the office or immediately seek other medical attention if any of these symptoms occur following an injection.

- Unusual swelling and/or tenderness at the injection site
- Swelling of face and/or mouth
- Sneezing, coughing or wheezing
- Shortness of breath
- Nausea
- Dizziness or faintness

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ALLERGENIC EXTRACT STANDARDIZED MITE *Dermatophagoides farinae and/or Dermatophagoides pteronyssinus*

SUGGESTED DOSAGE SCHEDULE AND INSTRUCTIONS