WARNINGS AND PRECAUTIONS

Severe allergic reactions have occurred following the administration of other allergenic extracts and may occur in individuals following the administration of Cat Hair allergenic extract in the following situations:

- Extreme sensitivity to cat hair, or receiving high doses of Cat Hair extract or concomitant exposure to similar environmental allergens. (5.1)
- Receiving an accelerated immunotherapy build-up schedule (e.g., "rush" immunotherapy), or changing from one allergenic lot to another. (5.1)

ADVERSE REACTIONS

The most common adverse reactions, occurring in over 25% of all patients, are local reactions at the injection site (e.g., erythema, itching, swelling, tenderness, pain). (6) Systemic reactions, occurring in ≤ 7% of patients, include urticaria, angioedema, and hypotension. These can be fatal. (6)

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

DRUG INTERACTIONS

- Beta blockers may cause unresponsiveness to usual doses of epinephrine used to treat serious systemic reactions, including anaphylaxis. (7.1)
- Antihistamines and other medications that suppress histamine, including topical corticosteroids, topical anesthetics and tricyclic antidepressants can interfere with skin test results. (7.2)

USE IN SPECIFIC POPULATIONS

- Pregnancy: No human or animal data. Use only if clearly needed. (8.1)
- Autoimmune Disease: For patients with existing immunologic diseases, administer immunotherapy only if the risk from exposure to the allergens is greater than the risk of exacerbating the underlying disorder. (8.6)

See 17 for PATIENT COUNSELING INFORMATION REVISED: 05/2015

1 INDICATIONS AND USAGE

2 DOSAGE AND ADMINISTRATION

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

1 INDICATIONS AND USAGE

Cat Hair allergenic extract can cause severe life-threatening systemic reactions, including anaphylaxis. (5.1)

Do not administer Cat Hair allergenic extract to patients with severe, unstable, or uncontrolled asthma. (4)

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 a life-threatening reaction. (5.1)

Patients with extreme sensitivity to Cat Hair allergenic extract, those on an accelerated immunotherapy build-up schedule, switching to another allergenic lot, and those receiving high doses of the Cat Hair allergenic extract or are also exposed to similar allergens may be at increased risk of a severe allergic reaction. (5.1)

Cat Hair allergenic extract may not be suitable for patients who are receiving beta blockers as they may be unresponsive to epinephrine. (5.2)

Standardized Cat Hair Allergenic Extract with potency labeling in Bioequivalent Allergy Units/milliliter is not interchangeable with Standardized Cat Pelt Allergenic Extracts labeled in Bioequivalent Allergy Units/milliliter. (5.3)

1 INDICATIONS AND USAGE

GREAT Standardized Cat Hair Allergenic Extract is indicated for:
- Skin test diagnosis of patients with a history of allergy to cats. (1)
- Treatment of cat hair-induced allergic asthma, rhinitis and conjunctivitis when avoidance is not possible. (1)

DOSE FORMS AND STRENGTHS

Stock concentrate vials at 10,000 and 5,000 Bioequivalent Allergy Units/milliliter. (3)

1 INDICATIONS AND USAGE

2 DOSAGE AND ADMINISTRATION

2.1 Preparation for Administration

How SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.
To prepare 5-fold dilutions for percutaneous testing in highly sensitive patients, start with a 10,000 BAU/mliliter or 5,000 BAU/mliliter stock concentrate. Proceed as in Table 2. The 5-fold dilution series uses 1 milliliter of concentrate added to 4 milliliters of sterile 50% glycerin diluent. Subsequent dilutions are made in a similar manner.

### Table 1: 10-fold Dilution Series

<table>
<thead>
<tr>
<th>Dilution</th>
<th>Concentrate</th>
<th>10,000</th>
<th>5,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Concentrate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0.5 milliliters Concentrate</td>
<td>4.5</td>
<td>1,000</td>
</tr>
<tr>
<td>2</td>
<td>0.5 milliliters Dilution 1</td>
<td>4.5</td>
<td>100</td>
</tr>
<tr>
<td>3</td>
<td>0.5 milliliters Dilution 2</td>
<td>4.5</td>
<td>10</td>
</tr>
<tr>
<td>4</td>
<td>0.5 milliliters Dilution 3</td>
<td>4.5</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>0.5 milliliters Dilution 4</td>
<td>4.5</td>
<td>0.1</td>
</tr>
<tr>
<td>6</td>
<td>0.5 milliliters Dilution 5</td>
<td>4.5</td>
<td>0.01</td>
</tr>
</tbody>
</table>

### Table 2: 5-fold Dilution Series (Cont.)

<table>
<thead>
<tr>
<th>Dilution</th>
<th>Extract</th>
<th>Milliliters of Diluent</th>
<th>BAU/ milliliter</th>
<th>BAU/ milliliter</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Concentrate</td>
<td>10,000</td>
<td>5,000</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1 milliliters Concentrate</td>
<td>4</td>
<td>2,000</td>
<td>1,000</td>
</tr>
</tbody>
</table>

### Table 3: Grading Sensitivity (Cont.)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Skin Appearance</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No reaction or reaction no different than negative control</td>
</tr>
</tbody>
</table>

2.3 Immunotherapy

For subcutaneous administration only.

Preparation and Dose

Stock concentrate of GREER Standardized Cat Hair Allergenic Extract is available at 10,000 BAU/mliliter or 5,000 BAU/mliliter in 50% glycerin saline for immunotherapy. Stock concentrates are diluted in normal saline, buffered saline, HSA saline, or 10% glycerin saline, depending on the patient’s reactivity to the diluent. See Table 1 and Table 2 for dilution preparation.

Administration of Immunotherapy

Administer immunotherapy by subcutaneous injection in the lateral aspect of the upper arm or thigh. Avoid injection directly into any blood vessel.

The optimal interval between doses of allergenic extract varies among patients and is usually given 1 to 2 times per week until the maintenance dose is reached, at which time the injection interval is increased to 2, then 3, and finally 4 weeks. Dosages vary by mode of administration, by clinical response and tolerance. The minimum course of treatment may be three to five years, depending on the clinical response.

Guidelines for Immunotherapy

The initial dose of the extract should be based on the skin test reactivity. In patients who appear to be highly sensitive by history and skin test, the initial dose of the extract should be 0.1 milliliter of a 0.5 to 5 BAU/mliliter extract dilution. Patients with lesser sensitivity may be started at a 0.05 milliliter of a 0.005 to 0.05 BAU/mliliter extract dilution. Patients with less sensitivity may be started at a 0.01 milliliter of a 0.001 to 0.005 BAU/mliliter extract dilution.

Dosage Modification Guidelines for Immunotherapy

The following conditions may indicate a need to withhold or reduce the dosage of immunotherapy.

- **Symptoms of rhinitis and/or asthma.**
- **Infection accompanied by fever.**
- **Large local reactions that persist for longer than 24 hours can be 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, are sufficient reason for the cessation of further attempts to increase the reaction-causing dose.**
Local reactions require a decrease in the next dose by at least 50%. Proceed cautiously in subsequent dosing. In situations prompting dose reduction, if the reduced dose is tolerated, a cautious increase in dosage can be attempted.

Changing to a different lot of extract: When switching patients to different lots of the new extract, the dose should not exceed 25% of the previous dose or a 75% reduction of the previous dose, assuming both extracts contain comparable amounts of allergen as measured in BAU/milliliter.

Unscheduled gaps between treatments: Patients can lose tolerance for allergen injections during prolonged periods between doses due to their increasing 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 has been a substantial time interval between injections. This depends on: 1) the concentration of allergen immunotherapy extract that is to be administered; 2) the history of allergic 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 for the specific clinical setting.

Similarly, if large unscheduled gaps occur during maintenance therapy, it may be necessary to reduce the dosage. Devise a protocol in the specific clinical setting in determining how to modify doses of allergen immunotherapy due to unscheduled gaps in treatment.

Extract previously used from different manufacturers: Since manufacturing processes and sources of raw materials differ among manufacturers, the interchangeability of extracts from different manufacturers may not be feasible. Reassure patients that changing the dose of the extract from a different manufacturer even if the extract is the same dilution. In general, a dose reduction of 50 to 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.

Changing from non-stabilized to human serum albumin (HSA) stabilized diluents: Allergenic extracts prepared with diluents containing HSA are milder and are more stable than those prepared with diluents that do not contain stabilizers. When switching from a non-stabilized to an HSA stabilized diluent, consider lowering the starting dose.

3 DOSAGE FORMS AND STRENGTHS

Standardized Cat Hair Allergenic Extract is supplied as stock concentrate vials at 10,000 BAU/milliliter and 5,000 BAU/milliliter.

4 CONTRAINDICATIONS

Standardized Cat Hair Allergenic Extract is contraindicated in patients with:

- Severe, unstable or uncontrollable asthma.
- History of any severe systemic allergic reaction or any severe local reaction to subcutaneous allergen immunotherapy.

5 WARNINGS AND PRECAUTIONS

5.1 Serious Systemic Reactions

Severe allergic reactions have occurred following the administration of other allergenic extracts and may occur in individuals following the administration of Standardized Cat Hair Allergenic Extract in the following situations:

- Extreme sensitivities to Cat Hair allergenic extract.
- Receiving an accelerated immunotherapy build-up schedule (e.g., “rush” immunotherapy).
- Receiving high doses of Cat Hair allergenic extract or concomitant exposure to similar environmental allergens.
- Changing from one allergenic lot to another allergenic lot.

High-risk patients have had fatal reactions. In addition, patients who are not high-risk, but are on beta blockers, have had fatal reactions because beta blockers interfere with beta adrenergic, such as epinephrine, used in the treatment of anaphylaxis. Administer Cat Hair Allergenic Extract in a healthcare setting under the supervision of a physician prepared to manage a severe systemic or a severe local allergic reaction. Observe patients in the office for at least 30 minutes following administration.

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. [see Drug Interactions (7.1)]

5.3 Cross-Reactions and Dose Sensitivity

GREER Standardized Cat Hair Allergenic Extract is labeled in BAU/milliliter. This allergenic extract is not interchangeable with Standard Cat Petl Extracts or with extracts labeled in Allergy Units. Determine the initial dilution of allergenic extract, starting dose, and CPT code. The allergenic extract concentration and strengths are: 10,000 BAU/milliliter and 5,000 BAU/milliliter.

6 ADVERSE REACTIONS

Allergenic extracts including Standardized Cat Hair can cause local reactions at the injection site, which may include erythema, itching, swelling, tenderness and pain. Additionally, systemic reactions which may include anaphylaxis may occur and may include generalized skin erythema, urticaria, pruritus, angioedema, rhinits, wheezing, chest tightness, laryngeal edema and hypotension.

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. [see Warnings and Precautions (5.2)]

7.2 Antihistamines

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

7.3 Topical Corticosteroids and Topical Anesthetics

Topical corticosteroids can suppress skin reactivity; therefore, discontinue use at the site for 2 to 3 weeks before skin testing. Avoid use of topical local anesthetics at skin test sites as they can suppress flare responses.

7.4 Tricyclic Antidepressants

Tricyclic antidepressants can have potent antihistaminic effects that can mask a positive response. If tricyclic medication has been recently discontinued allow 7 to 14 days before initiating skin testing.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C: Animal reproduction studies have not been conducted with GREER Standardized Cat Hair Allergenic Extract. It is not known whether allergenic extracts can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Standardized Cat Hair Allergenic Extract should be given to a pregnant woman only if needed. Immunotherapy is typically not initiated during pregnancy due to the risks associated with systemic reactions and their treatment.

8.2 Labor and Delivery

Safety and effectiveness of allergenic extracts in labor and delivery have not been established.

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, caution the patient when administering Standardized Cat Hair Allergenic Extract to a nursing woman.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

Safety and effectiveness of GREER Standardized Cat Hair Allergenic Extract have not been established in patients >65 years of age.

8.6 Asthma and Airway Disease

For patients with existing immunologic diseases, give immunotherapy only if the risk from exposure to the allergens is greater than the risk of exacerbating the underlying disorder.

9 DESCRIPTION

GREER Standardized Cat Hair Allergenic Extract is a sterile solution of extracted cat pel and cat dander. Each vial contains sterile Standardized Cat Hair Allergenic Extract at 10,000 BAU/milliliter or 5,000 BAU/milliliter, 50% glycerin volume/volume, and 0.4% phenol volume/volume (preservative). It also contains 0.1 mg of sodium thiosulfate for isotonicity and 0.25% sodium bicarbonate as a buffer.

GREER Standardized Cat Hair Allergenic Extract is labeled in BAU/milliliter. This allergenic extract is not interchangeable with other standardized cat hair allergen extracts labeled in Allergy Units. The extract is standardized by comparing potency of cat allergens (Fel d I) units by radial immunodiffusion against standard adapted to the Center for Biologics Evaluation and Research (CBER) of the U.S. Food and Drug Administration (FDA). An extract with 10.0 to 19.9 Fel d I units per milliliter is designated as 10,000 BAU/milliliter by the FDA based on quantitative skin testing.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The precise mechanisms of action of allergy immunotherapy are not known.

The allergic reaction is dependent upon the presence of antigen-specific IgE antibodies that are bound to specific receptors on mast cells and basophils and has been demonstrated for cat-allergic individuals. The presence of IgE antibodies on mast cells and basophils sensitizes these cells and upon interaction with the appropriate allergen-histamine and other mediators are released. In the skin these mediators are responsible for the characteristic wheal and flare reaction. An increase in cat antigen-specific IgE antibodies has been demonstrated as a result of immunotherapy.

14 CLINICAL STUDIES

The efficacy of immunotherapy for Type I hypersensitivity (i.e., allergy) to airborne allergens including cat hair/dander has been well established. Specifically, immunotherapy for allergy to airborne allergens was addressed in a 2003 Cochrane meta-analysis which included 10 randomized controlled trials of immunotherapy,11 which expanded on prior meta-analyses of the effectiveness of allergen immunotherapy in asthma.12,13 In addition, efficacy for immunotherapy for rush or cluster protocols, in which dose escalation is compressed over days or weeks, has also been demonstrated.14

REFERENCES


Standardized Allergenic Extracts and for Assignment of Bioequivalent Allergy Units to Reference Preparations Using the ID50EAL Method (Intradermal Dilution for 50 mm Sum of Erythema Determines Bioequivalent Allergy Units). In Methods of the Allergenic Products Testing Lab, LIB, DAPP, CBER, FDA, 1994.


16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

GREER Standardized Cat Hair Allergenic Extract containing 10,000 BAU/milliliter and 5,000 BAU/milliliter in 50% Glycerin solution is supplied as follows:

<table>
<thead>
<tr>
<th>NDC Number</th>
<th>Strength/Container</th>
</tr>
</thead>
<tbody>
<tr>
<td>NDC 22840-0101-5</td>
<td>10,000 BAU/ml 5 mL dropper vial for prick testing</td>
</tr>
<tr>
<td>NDC 22840-0101-2</td>
<td>10,000 BAU/ml 10 mL multiple-dose vial</td>
</tr>
<tr>
<td>NDC 22840-0101-3</td>
<td>10,000 BAU/ml 30 mL multiple-dose vial</td>
</tr>
<tr>
<td>NDC 22840-0101-4</td>
<td>10,000 BAU/ml 50 mL multiple-dose vial</td>
</tr>
<tr>
<td>NDC 22840-0100-2</td>
<td>5,000 BAU/ml 10 mL multiple-dose vial</td>
</tr>
<tr>
<td>NDC 22840-0100-3</td>
<td>5,000 BAU/ml 30 mL multiple-dose vial</td>
</tr>
<tr>
<td>NDC 22840-0100-4</td>
<td>5,000 BAU/ml 50 mL multiple-dose vial</td>
</tr>
</tbody>
</table>

16.2 Storage and Handling

Maintain at 2 to 8 °C (36 to 46 °F) during storage and use. Dilutions of concentrated extract result in a glycerin content of less than 50%, which can result in reduced stability. Extract dilutions at 1:100 v/v dilution of 10,000 BAU/milliliter Standardized Cat Hair Allergenic Extract stock concentrates 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 cat hair allergic patient.

17 PATIENT COUNSELING INFORMATION

Instruct patient to remain under observation in the office for 30 minutes or longer after an injection. Caution patient that reactions can 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 skin testing or an injection:

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

Manufacturer: GREER Laboratories, Inc. Lenoir, NC 28645 U.S.A

Suggested Dosage Schedule and Instructions