CONTRAINDICATIONS
- Severe, unstable or uncontrolled asthma. (4)
- History of any severe systemic allergic reaction or any severe local reaction to subcutaneous allergen immunotherapy. (4)

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 generalized skin erythema, urticaria, pruritus, angioedema, rhinitis, wheezing, laryngeal edema, 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

REFERENCES
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action

14 CLINICAL STUDIES
15 REFERENCES
16 HOW SUPPLIED/STORAGE AND HANDLING
16.1 How Supplied
16.2 Storage and Handling

17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.
The extracts are diluted with sterile diluents when used for percutaneous and intradermal testing, or for subcutaneous immunotherapy.

To prepare 10-fold dilutions for percutaneous testing in highly sensitive patients, start with a 10,000 BAU/ml diluer or 5,000 BAU/ml diluter stock concentrate. Proceed as in Table 1. The 10-fold dilution series uses 0.5 milliliters of concentrate added to 4.5 milliliters of sterile 50% glycerin diluent. Subsequent dilutions are made in a similar manner.

To prepare 10-fold dilutions for intradermal testing or immunotherapy, start with a 10,000 BAU/ml diluer or 5,000 BAU/ml diluter stock concentrate. Proceed as in Table 1. The 10-foil dilution series uses 0.5 milliliters of concentrate added to 4.5 milliliters of sterile diluents (glycerin-free diluents for intradermal testing, glycerin-free or 10% glycerin-saline diluents for immunotherapy). Subsequent dilutions are made in a similar manner.

Table 1: 10-fold Dilution Series

<table>
<thead>
<tr>
<th>Dilution</th>
<th>Extract</th>
<th>Milliliters of Diluent</th>
<th>BAU/ml</th>
<th>BAU/ml</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>0.5 mliliter Concentrate</td>
<td>4.5</td>
<td>1,000</td>
<td>500</td>
</tr>
<tr>
<td>2</td>
<td>0.5 mliliter Dilution 1</td>
<td>4.5</td>
<td>1.00</td>
<td>50</td>
</tr>
<tr>
<td>3</td>
<td>0.5 mliliter Dilution 2</td>
<td>4.5</td>
<td>0.50</td>
<td>25</td>
</tr>
<tr>
<td>4</td>
<td>0.5 mliliter Dilution 3</td>
<td>4.5</td>
<td>0.25</td>
<td>12.5</td>
</tr>
<tr>
<td>5</td>
<td>0.5 mliliter Dilution 4</td>
<td>4.5</td>
<td>0.12</td>
<td>6.25</td>
</tr>
<tr>
<td>6</td>
<td>0.5 mliliter Dilution 5</td>
<td>4.5</td>
<td>0.06</td>
<td>3.12</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/ml</th>
<th>BAU/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Concentrate</td>
<td>10,000</td>
<td>5,000</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1 milliliter 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>1</td>
<td>Erythema less than 21 millimeters</td>
</tr>
<tr>
<td>2</td>
<td>Wheat less than 3 millimeters and erythema larger than 21 millimeters</td>
</tr>
<tr>
<td>3</td>
<td>Wheat greater than 3 millimeters with surrounding edema</td>
</tr>
<tr>
<td>4</td>
<td>Wheat with pseudopods and surrounding erythema</td>
</tr>
</tbody>
</table>

Responses to positive controls should be at least 3 millimeters larger than responses to the negative controls.

Negative controls should elicit no reaction or only reactions of small diameters (less than 2 millimeters wheal, less than 5 millimeters erythema). Either the positive or negative control response does not meet the above criteria, results for the allergenic extracts tested at the same time are invalid and should be repeated.

2.2 Diagnostic Testing

Diagnostic testing can be performed via percutaneous or intradermal administration of the Cat Hair Allergenic extract. A positive skin test reaction must be interpreted in relation to the patient’s history and prior exposure to the allergen.

Percutaneous Skin Testing

Determine the patient’s sensitivity to the Standardized Cat Hair Allergenic Extract. Prick or puncture testing: use 10,000 BAU/ml diluer or 5,000 BAU/ml diluter extract stock concentrate. If a lower concentration is desired in highly sensitive patients, 10-fold or 5-fold dilutions of the concentrate can be tested. Prick test: Place one drop of extract or control on the skin and with a skin test device pierce through the drop into the skin with a slight lifting motion. Puncture test: Place one drop of extract or control on the skin and pierce the skin through the drop with a skin test device perpendicular to the skin.

Interpreting Results

When using percutaneous skin test devices, follow the directions provided with the test devices. A glycinated histamine control solution (6 milligrams/ml diluer or 1 milligram/ml histamine base) may be used as the positive control. A 50% glycerin saline solution may be used as the negative control. Read skin test responses 15 to 20 minutes after exposure and measure the average diameter of the induration (wheat) and erythema (flare), or the sum of the longest diameter and the mid-point orthogonal diameters of erythema (ΣE).

An example of a commonly used scale is provided in Table 3 below.1,2

Table 3: Grading Sensitivity

<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

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 0.005 to 0.05 BAU/ml diluer extract dilution. Patients with lesser sensitivity may be started at a 0.1 milliliter of a 0.5 to 5 BAU/ml diluer extract dilution.

The dose of allergenic extract is increased at each injection by no more than 20% of the previous dose, and the next increment is governed by the response to the last injection. Select the maximumtolerated maintenance dose based on the patient's clinical response and tolerance. Doses larger than 0.2 milliliter of the stock concentrate are rarely administered because an extract in 50% glycerin can cause discomfort upon injection.

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.
- Exposure to excessive amounts of clinically relevant environmental allergens prior to a scheduled injection. 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 a 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 lot of extract, the first dose from the new vial 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 tolerate for adverse reactions during prolong periods between doses is 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, 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) the 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 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 for the specific clinical setting in determining how to modify doses of allergen immunotherapy due to unscheduled gaps in treatment.

Extract previously used from different manufacturer: Since manufacturing processes and sources of raw materials differ among manufacturers, the interchangeability of extracts from different manufacturers may not be assured. When changing the vial 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 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 dosage of the allergenic extract.

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.

3.1 Standardized Cat Hair Allergenic Extract is contraindicated in patients with:
- Severe, unstable or uncontrolled 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 simultaneous 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 Standardized Cat Pelt Extracts or with cat extracts labeled in Allergy Units. Determine the initial dilution of allergenic extract, starting dose, and progression of dosage based on the patient’s history and results of skin tests. [see Dosage and Administration (2.2)] Strongly positive skin tests can be an indicator for potential systemic reactions.

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 indicate anaphylaxis, can occur and may include generalized skin erythema, urticaria, pruritus, angioedema, rhiitis, wheezing, chest tightness, laryngeal edema and vascular collapse. [see Warnings and Precautions (5.2)]

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 allergic extracts within 10 days to 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 allergic extract exposure. These products suppress histamine skin test reactions and could mask a positive response.3

7.3 Topical Corticosteroids and Topical Anesthetics

Topical corticosteroids can suppress skin reactivity; therefore, discontinue use the skin test 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.1

7.4 Tricyclic Antidepressants

Tricyclic antidepressants can have potent antihistamine effects that can mask a positive response. If tricyclic medication can be stopped, this can occur between 7 and 14 days before initiating skin testing.

7.5 INACTIVE INGREDIENTS

Inactive ingredients include 0.5% sodium chloride for isotonicity

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 allergic extract exposure. These products suppress histamine skin test reactions and could mask a positive response.3

7.6 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)]

7.7 Antihistamines

Do not perform skin testing with allergic extracts within 10 days to 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 allergic extract exposure. These products suppress histamine skin test reactions and could mask a positive response.3

7.8 Topical Corticosteroids and Topical Anesthetics

Topical corticosteroids can suppress skin reactivity; therefore, discontinue use the skin test 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.1

7.9 Tricyclic Antidepressants

Tricyclic antidepressants can have potent antihistamine effects that can mask a positive response. If tricyclic medication can be stopped, this can occur between 7 and 14 days before initiating skin testing.

8 CLINICAL PHARMACOLOGY

8.1 MECHANISM OF ACTION

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 cat allergens has been proved effective by studies demonstrating a reduction in signs and symptoms of allergic rhinitis and asthma in patients treated with immunotherapy. [see Clinical Studies (14)]

8.2 LABORATORY AND DELIVERY

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

8.3 NURSING MOTHERS

It is not known whether allergic extracts or their antigens are excreted in human milk. Because many drugs are excreted in human milk, exercise caution when administering Standardized Cat Hair Allergenic Extract to a nursing woman.

8.4 PEDICIAN USE

Safety and effectiveness in pediatric patients have not been established.

8.5 ADULT USE

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

8.6 AUTOIMMUNE 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 pelt 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 is not contaminated with thimerosal, benzyl alcohol or chlorohydroxy isonitric acid 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 allergenic extracts labeled in Allergy Units. The extract is standardized by comparing potency of cat allergens (Fel d 1) units by radial immunodiffusion against a reference standard from the Center for Biologics Evaluation and Research (CBER) of the U.S. Food and Drug Administration (FDA).1,3 An extract with 10.0 to 19.9 Fel d 1 units per milliliter is designated as 10,000 BAU/milliliter by the FDA based on quantitative skin testing.

REFERENCES


4. Keutelbach PA, Rastogi SC. Quantitative Intradermal Procedure for Evaluation of Subjective Sensitivity to
Standardized Allergenic Extracts and for Assignment of Bioequivalent Allergy Units to Reference Preparations Using the ID$_{50}$EAL 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.