

STANDARDIZED CAT HAIR- felis domesticus hair injection, solution
Allergy Laboratories, Inc.

Standardized Cat Hair

ALLERGY LABORATORIES, INC.
Oklahoma City, OK 73109

INSTRUCTION AND DOSAGE SCHEDULE FOR STANDARDIZED ALLERGENIC EXTRACTS
CAT HAIR

WARNING

This product is intended for use 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.

Extracts standardized using Bioequivalent Allergy Unit (BAU/ml) may be more potent than nonstandardized cat extracts based on the weight to volume, or PNU methods. Allergy Laboratories' standardized cat hair extract is not interchangeable with standardized cat pelt extracts, and also not interchangeable with other standardized cat extracts labelled in Allergy Units (AU/ml). The initial dose must be based on skin testing as described in the dosage and administration section of this insert. Patients being switched from nonstandardized cat extracts to Allergy Laboratories' standardized cat extract should be started as though they were coming under treatment for the first time. Patients should be instructed to recognize adverse reaction symptoms and cautioned to contact the physicians office if reaction symptoms occur. As with all allergenic extracts, severe systemic reactions may occur. In certain individuals these life threatening reactions may be fatal. Patients should be observed for at least 30 minutes following treatment and emergency measures as well as personnel trained in their use should be immediately available in the event of a life threatening reaction.

This product should not be injected intravenously. Subcutaneous injections are recommended.

Patients who are taking non-selective beta blockers may be more reactive to allergens given for testing or treatment and may be unresponsive to the usual doses of epinephrine used to treat allergic reactions.

Refer also to the warnings, precautions, adverse reactions and dosage sections below.

DESCRIPTION

The standardized (BAU/ml) extract in these vials is designed primarily for the physician equipped to prepare dilutions and mixtures as required. The sterile extract is prepared from the extractables of cat hair and cat wash and contains 50% (v/v) glycerine as a preservative. It is intended for subcutaneous injection.

The cat hair extract is assayed for potency using Radial immunodiffusion (1) against a reference extract distributed by the Center for Biologics Evaluation and Research, U.S. Food and Drug Administration. Potency based on Bioequivalent Allergy Units (BAU/ml) is printed on the label. Cat hair extract containing between 10-19.9 Fel d 1 U/ml are labeled 10,000 BAU/ml based on the quantitative skin testing (ID₅₀ EAL Method) (2). Standardized cat hair is compared to an FDA reference cat hair extract by IEF to establish identity.

INACTIVE INGREDIENTS

Glycerinated extracts contain:

| | |
|--------------------|-------------|
| glycerine | 50.0 % v/v |
| sodium chloride | 0.166 % w/v |
| sodium bicarbonate | 0.091 % w/v |

CLINICAL PHARMACOLOGY

The allergic state is initiated by an immune response inducing B cells to produce IgE antibodies to specific allergens. IgE antibodies bind to surface receptors on mast cells and basophils. When antigens gain access to the immune system they react with the bound IgE. The reacting antigen to the surface bound IgE stimulates a number of chemical mediators to be released from the mast cells and basophils. These include histamine, Eosinophil Chemotactic Factor (ECF-A) and leukotrienes. These chemical mediators are pharmacologically active at low concentrations and are partially responsible for the biological manifestation of the allergic response. (3)

The mechanism by which immunotherapy achieves hyposensitization is not completely understood. There is an increase in "blocking antibody" (IgG) titer and in some patients a decrease in specific IgE, a decrease in histamine release to specific allergen and an increase in suppressor cell population to specific allergen. These changes may occur only after prolonged therapy. (4)

INDICATIONS AND USAGE

Standardized Cat Hair Extracts are indicated for the diagnosis of patients with a history of allergy to cats and for treatment of patients with cat allergy. Diagnosis of allergic disease to cat hair is made through a combined medical history sufficiently complete to identify allergic symptoms to cat hair and identification of cat allergy by diagnostic skin testing.

Hyposensitization therapy is a treatment for patients exhibiting allergic reactions to cat. Immunotherapy is intended for patients whose symptoms cannot be satisfactorily controlled by avoidance of the offending allergen or by the use of symptomatic medications. (5)

CONTRAINDICATIONS

There are no known absolute contraindications to hyposensitization therapy. See precautions section for pregnancy risks.

A patient should not be treated with allergens unless a history of symptoms and a positive skin test reaction have been demonstrated. Allergenic extracts should only be administered to patients that show symptoms of allergy or asthma. The physician must determine if the benefits outweigh the risks in using these products for treating these patients.

Patients who are taking non-selective beta blockers may be more reactive to allergens given for testing or treatment and may be unresponsive to the usual doses of epinephrine used to treat allergic reactions.

WARNINGS

See WARNING at the beginning of the instruction sheet.

Extracts standardized using the Bioequivalent Allergy Unit (BAU/ml) may be more potent than extracts based on weight to volume, or PNU methods. Comparative skin tests can be performed to determine the relative potency before initial use of new extracts. **DO NOT GIVE ALLERGY INJECTIONS INTRAVENOUSLY.** Subcutaneous injections are recommended. Injections may produce large local

reactions that may be painful to the patient. DO NOT GIVE FULL STRENGTH INJECTIONS UNTIL THE COMPARATIVE STRENGTH IS DETERMINED. After inserting the needle, but before injection extract, withdraw the plunger slightly. If blood appears in the syringe, re-insert the needle at another site. Careful selection of dose and injection should prevent most systemic reactions.

PRECAUTIONS

GENERAL

The dosage should be reduced 50-75% from the previous dose when starting a patient on a new lot of standardized cat hair extract from the same manufacturer or from a different manufacturer. When changing from a non-standardized cat hair extract to a standardized cat hair extract, the dose should be based upon comparative skin testing or the patient should be treated as though beginning treatment for the first time.

A separate sterile tuberculin type syringe should be used with each patient to prevent cross contamination of extracts. This will also prevent transmission of disease such as serum hepatitis, AIDS and other infectious diseases. Aseptic technique should always be used when injections of allergic extracts are administered.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY:

Long term studies with extracts have not been conducted in animals to determine their potential for carcinogenesis, mutagenesis, or impairment of fertility.

PREGNANCY:

Pregnancy Category C. 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. Allergenic extracts should be given to a pregnant woman only if clearly needed.

Controlled studies of hyposensitization with moderate to high doses of allergenic extracts in pregnant women have failed to demonstrate any risk to the mother or fetus. (6)

However, with histamines known ability to contract uterine muscles any reaction which would release significant amounts of histamine such as hyposensitization overdose should be avoided. The physician must weigh the benefits of immunotherapy against the risk of anaphylactic reactions that could result in harm to the mother and/or fetus.

Hyposensitization should be used during pregnancy only if clearly necessary and administered cautiously. If a woman is on maintenance dose the occurrence of pregnancy is not an indication to stop injection therapy.

NURSING MOTHERS:

It is not known if allergenic extracts are excreted in human milk therefore caution should be exercised when extracts are administered in nursing women.

PEDIATRIC USE:

Doses of allergenic extracts for children are generally the same as those for adults. The extracts may cause some pain or discomfort when injected. The maximum tolerated dose may be less than the adult dose due to the smaller size of the child. Therefore, the volume of the dose may need to be adjusted from the adult schedules provided.

DRUG INTERACTIONS:

Patients who are taking non-selective beta blockers may be more reactive to allergens given for testing

or treatment and may be unresponsive to the usual doses of epinephrine used to treat allergic reactions. Antihistamines can significantly inhibit the immediate skin test reactions. Patients should be free of such medication for at least 48 hours before testing.

ADVERSE REACTIONS

Local reactions:

Some swelling and redness at the site of injection is not unusual. Mild burning that occurs immediately after the injection is normal; this usually subsides in 10 to 20 seconds. If the swelling and redness persist for a period of 24 hours or longer this should be a sign to proceed with caution in increasing the dosage. With the next injection the dosage should remain the same or be decreased. Large local reactions may indicate that a systemic reaction could occur with the next injection if the dosage was increased. If a patient continues to have reactions at the maintenance dose, the patient is considered to have exceeded the maximum tolerated dosage.

Systemic Reactions:

Systemic reactions occur infrequently but must be looked for in all patients, especially highly sensitive patients. Anaphylactic shock and death are always possible, therefore, physicians must be prepared for the treatment of these reactions. Systemic reactions can also be characterized by one or more of the following symptoms: angioedema, tachycardia, conjunctivitis, cough, fainting, hypotension, pallor, rhinitis, urticaria, and wheezing.

Systemic reaction can be treated by the immediate application of a tourniquet above the site of injection and the administration of 0.3 to 0.5ml of 1:1000 Epinephrine - Hydrochloride subcutaneously or intramuscularly at the site of allergen injection. The dosage may be repeated two times at 15 minute intervals. Loosen the tourniquet at least every 10 minutes.

The pediatric dosage for 1:1000 Epinephrine-Hydrochloride is 0.05 to 0.1ml for infants to 2 years of age; 0.15ml, for children 2 to 6 years; and 0.2ml, for children 6 to 12 years.

Patients should always be observed for at least 30 minutes after any injection. Hypotension can be reversed by using vasopressor agents and volume expanders. Parenteral aminophylline and inhalation bronchodilators may be required for bronchospasm. Oxygen may also be needed. Maintenance of an open airway is critical if upper airway obstruction is present. Adrenal corticosteroids and intravenous antihistamine can be given after adequate epinephrine and circulatory support has been administered. Physicians must be familiar with these systemic reactions and have all the equipment and drugs necessary for proper treatment. (7)

DOSAGE AND ADMINISTRATION

DIAGNOSTIC SKIN TESTING:

Puncture tests performed on 10 highly sensitive patients with 10,000 BAU/ml Cat Hair Extract showed a mean sum of diameter wheal of $17.00\text{mm} \pm 4.59$ and a mean sum of diameter Erythema of $71.60 + 14.01$.

Intradermal skin test results in highly sensitive patients is shown below, using the same extract as used in the puncture test above.

| <u>Number of Patients</u> | <u>BAU/ml to elicit 50mm sum of Diameter of Erythema reaction</u> | |
|---------------------------|---|---------------|
| | <u>Mean</u> | <u>Range</u> |
| 10 | 0.0128 | 0.0021-0.1957 |

These products are used to determine a patient's sensitivity to specific antigens and aid in the diagnosis and treatment of atopic diseases. After a thorough history a decision can be made as to which allergens will be appropriate to use for testing. The recommended procedure is to initially perform puncture tests, then follow with intradermal tests. See recommended dosage below.

SCRATCH OR PUNCTURE TEST:

| <u>Concentration BAU/ml</u> | <u>Dosage ml</u> |
|-----------------------------|------------------|
| 10,000 | 0.05 (1 drop) |

INTRADERMAL TEST:

A. Patients with a negative scratch or puncture test.

| <u>Concentration BAU/ml</u> | <u>Dosage ml</u> |
|---|------------------|
| 1) 50 BAU/ml | 0.02 |
| 2) 100 BAU/ml* if 50 BAU/ml is negative | |

B. Patients tested by intradermal only.

| <u>Concentration BAU/ml</u> | <u>Dosage ml</u> |
|-----------------------------|------------------|
| 0.5 BAU/ml | 0.02 |

If negative repeat tests with stronger concentrations until a maximum of 100 BAU/ml* is reached.

* The negative intradermal control used for the 100 BAU/ml concentration should contain 0.5% (v/v) glycerine.

FREQUENCY OF ADMINISTRATION:

The number of skin tests applied at one time will depend on the particular patient and their allergic history. These tests should be performed and observed in 15 to 20 minutes. Additional tests may be applied in sequence. Perform tests on the anterolateral aspect of the upper arm on an area that permits the effective application of a tourniquet proximal to the site of the test. The skin at the site of injection should be disinfected with rubbing alcohol before testing.

Puncture testing: Apply one drop (0.05ml) of extract to the skin. Pierce the drop of extract and skin using a sterile hypodermic needle or vaccinating needle. Maintain the needle perpendicular to the skin surface and rock the needle back and forth to produce a small hole without bleeding. Do not rotate or gouge the needle. Remove needle from skin and wipe excess extract from skin surface.

Scratch testing: Using a scarifier or needle, make a scratch 1/16 inch long on the epidermis penetrating the outer cornified area but being careful not to draw blood. Apply one drop (0.05ml) of allergen to the scratch.

Intradermal testing: use a separate sterile syringe (tuberculin type equipped with a 27 gauge by 3/8 inch needle with intradermal bevel) for each antigen. The tests are made by injecting 0.02ml of allergen into the epidermis. If the test has been performed properly, the solution should raise a bleb 2 to 3mm in diameter. If the bleb does not appear, the injection was made too deeply.

A negative control consisting of the same solution that the extract was prepared in should be applied to one of the sites in the same manner as the tests being performed. For example, the negative intradermal control should contain 0.5% (v/v) glycerine, if a 100 BAU/ml concentration cat hair is used for intradermal testing. Histamine phosphate should be used as a positive control for evaluation of skin testing. Histamine phosphate is available from other manufacturers. See their directions for use, for recommended dosage and interpretation of results.

A positive reaction usually develops in 15-20 minutes. The positive response is a wheal and flare reaction that is larger than the negative control and judged on the size of the reaction. Scratch or puncture tests may not elicit as large and well defined reaction as the intradermal. (5)

The following system is recommended (8):

| Reaction | Erythema | Wheal |
|----------|----------|-------------------------------|
| 0 | <5mm | <5mm |
| ± | 5-10mm | 5-10mm |
| 1+ | 11-20mm | 5-10mm |
| 2+ | 21-30mm | 5-10mm |
| 3+ | 31-40mm | 10-15mm or with pseudopods |
| 4+ | >40mm | >15mm or with many pseudopods |

IMMUNOTHERAPY:

The following are two methods of injection therapy:

1. Pre-seasonal in which treatment is begun three months before seasonal difficulty begins and brought to maintenance dose by injections four to seven days apart and discontinued after that season ends.
2. Perennial treatment is the recommended mode of therapy in which the patient is, by injection therapy, brought up to tolerated maintenance dose and remains at that dose until amelioration of allergic symptoms occurs. Injections may be given at intervals of 4 to 7 days.

Allergenic extracts must be diluted before use. Normally immunotherapy can be started with a 1 BAU/ml dilution. If a patient appears to be extremely sensitive, dilutions of the antigen can further be made before injections are started. The following are suggested procedures for making a proper dilution series. Recommended diluents contain 0.9% sodium chloride and 0.4% phenol as a preservative.

| TEN FOLD DILUTION SERIES: | | | | |
|---------------------------|------------------------------|----------------|-------------------------------|--|
| EXTRACT VOLUME | EXTRACT CONCENTRATION BAU/ml | DILUENT VOLUME | DILUTION CONCENTRATION BAU/ml | |
| 1 part | 10,000 + | 9 parts | = 1,000 | |
| 1 part | 1,000 + | 9 parts | = 100 | |
| 1 part | 100 + | 9 parts | = 10 | |
| 1 part | 10 + | 9 parts | = 1 | |
| 1 part | 1 + | 9 parts | = 0.1 | |
| 1 part | 0.1 + | 9 parts | = 0.01 | |

Perennial treatment may be started using the following dosage and dilution schedule. **THIS SCHEDULE IS ONLY ILLUSTRATIVE AND HAS NOT BEEN SUBJECTED TO ADEQUATE OR WELL-CONTROLLED TRIALS TO DETERMINE EITHER ITS SAFETY OR EFFICACY.**

| DOSE # | DOSE VOLUME | CONCENTRATION |
|--------|-------------|---------------|
| 1 | 0.05 | 1 BAU/ml |
| 2 | 0.10 | |
| 3 | 0.20 | |
| 4 | 0.30 | |
| 5 | 0.40 | |
| 6 | 0.50 | |

| | | |
|---|------|-----------|
| 7 | 0.05 | 10 BAU/ml |
|---|------|-----------|

| | | |
|-------|------|---------------|
| 8 | 0.10 | |
| 9 | 0.20 | |
| 10 | 0.30 | |
| 11 | 0.40 | |
| 12 | 0.50 | |
| <hr/> | | |
| 13 | 0.05 | 100 BAU/ml |
| 14 | 0.10 | |
| 15 | 0.20 | |
| 16 | 0.30 | |
| 17 | 0.40 | |
| 18 | 0.50 | |
| <hr/> | | |
| 19 | 0.05 | 1,000 BAU/ml |
| 20 | 0.10 | |
| 21 | 0.20 | |
| 22 | 0.30 | |
| 23 | 0.40 | |
| 24 | 0.50 | |
| <hr/> | | |
| 25 | 0.05 | 10,000 BAU/ml |
| 26 | 0.10 | |
| 27 | 0.20 | |
| 28 | 0.30 | |
| 29 | 0.40 | |
| 30 | 0.50 | |
| <hr/> | | |

Gradually increase the dose as outlined in the schedule. If you give a dose that causes a mild local reaction manifested by warmth or redness, repeat the same dose. If the reaction is severe or systemic (manifested as hives, asthma, or hay fever), drop back a dose in schedule and build again. If a severe local reaction or a systemic reaction is again encountered, this should be considered more than the maximum tolerance for this patient. The maintenance dose is the largest dose that relieves symptoms without producing local reactions. The size and interval of doses will vary and can be adjusted as necessary. The normal interval between doses is 4 to 7 days.

HOW SUPPLIED

Bulk extract (stock concentrate) in 50% (v/v) glycerine containing 10,000 BAU/ml is supplied in 10ml, 30ml, and 50ml vials. Scratch testing in 50% (v/v) glycerine containing 10,000 BAU/ml is supplied in 2ml dropper vials. Intradermal testing (aqueous) containing 100 BAU/ml is supplied in 5ml vials.

STORAGE

These extracts should be stored at 2 to 8 degrees Celsius. Excessive heating (above room temperature) and repeated freeze-thawing should be avoided. The dating period (expiration date) is shown on the vial label. Once extracts are diluted the shelf life decreases. Extracts should be re-ordered when out of date. Please allow a minimum of three (3) weeks for delivery due to the holding period for sterility testing.

REFERENCES

1. Anderson, M.C., Baer, H.: Methodology for Assay of Cat Allergen 1 May 1986, In Methods of the Laboratory of Allergenic Products, Division of Bacterial Products, Food and Drug Administration.
2. Turkeltaub, P.C., Rastogi, S.C., Baer, H.: Assignment of Allergy Units to Reference Preparations using the ID₅₀ EAL Method, May 1986, In Methods of the Laboratory of Allergenic Products, Division of Bacterial Products, Food and Drug Administration.
3. Wasserman, S.I.: Biochemical mediators of allergic reactions. In Patterson, R. (ed): Allergic diseases: diagnosis and management, p. 86. Philadelphia, J.B. Lippincott Co. 1985.
4. Grammer, L.C.: Principle of immunologic management of allergic diseases due to extrinsic antigens. In Patterson, R. (ed): Allergic diseases: diagnosis and management, p. 358. Philadelphia, J.B. Lippincott Co. 1985.
5. Booth, B.H.: Diagnosis of Immediate Hypersensitivity. In Patterson, R. (ed): Allergic diseases: diagnosis and management, p. 102. Philadelphia, J.B. Lippincott Co. 1985.
6. Metzger, W.J., et al.: The safety of immunotherapy during pregnancy. *J. Allergy Clin. Immunol.*, 64 (4): 268-272, 1978.
7. Patterson, R. et al.: Immunotherapy. In Middleton, E. Jr., Reed, C.E. and Ellis, E.F. (ed): Allergy; Principles and Practice, (Vol. 2) p. 1119. St. Louis, The C.V. Mosby Co. 1983.
8. Norman, P.S.: In vivo methods of study of allergy: Skin and Mucosal tests, techniques and interpretation. In Middleton, E. Jr., Reed, C.E. and Ellis, E.F. (ed): Allergy Principles and Practice, (Vol 1), p. 258. St. Louis, The C.V. Mosby Co. 1978.

ALLERGY LABORATORIES, INC.

Oklahoma City, OK 73109

U.S. License #103

(405) 235-1451 • 800 654-3971

PRINCIPAL DISPLAY PANEL

ALLERGENIC EXTRACT

STANDARDIZED CAT HAIR

Felis domesticus

10,000 BAU/mL

50 mL

RX ONLY

ALLERGENIC EXTRACT

STANDARDIZED CAT HAIR

RX ONLY

Felis domesticus

10,000 VAU/mL

50 mL

Lot:

Not interchangeable with Cat Pelt or
Cat extracts labeled in AU/mL

Preservative: 50% Glycerin (v/v).

Dose/Route: See Enclosure.

Store at 2-8°C. NON-RETURNABLE.

EXP.:



Allergy
Laboratories, Inc.
Oklahoma City, OK 73109
U.S. Govt. Lic. No. 103

PRINCIPAL DISPLAY PANEL

ALLERGENIC EXTRACT
SCRATCH TESTING
STANDARDIZED CAT HAIR
Felis domesticus
10,000 BAU/mL
Dose: 1 Drop
2 mL
RX ONLY

ALLERGENIC EXTRACT

SCRATCH TESTING STANDARDIZED CAT HAIR

RX ONLY

Felis domesticus

10,000 BAU/mL

Dose: 1 Drop

2 mL

Lot:

Not interchangeable with Cat Pelt
or Cat extracts labeled in AU/mL

Preservative: 50% Glycerin (v/v).

Dose/Route: See Enclosure.

Store at 2-8°C. NON-RETURNABLE.



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U.S. Govt. Lic. No. 103

EXP:

STANDARDIZED CAT HAIR

felis domesticus hair injection, solution

Product Information

| | | | |
|-------------------------|----------------------------|--------------------|---------------|
| Product Type | STANDARDIZED ALLERGENIC | Item Code (Source) | NDC:54575-288 |
| Route of Administration | PERCUTANEOUS, SUBCUTANEOUS | | |

Active Ingredient/Active Moiety

| Ingredient Name | Basis of Strength | Strength |
|--|-------------------|---------------------|
| FELIS CATUS HAIR (UNII: 1564HD0N96) (FELIS CATUS HAIR - UNII:1564HD0N96) | FELIS CATUS HAIR | 10000 [BAU] in 1 mL |

Inactive Ingredients

| Ingredient Name | Strength |
|---------------------------------------|-------------------|
| GLYCERIN (UNII: PDC6A3C0OX) | 0.5 mL in 1 mL |
| SODIUM CHLORIDE (UNII: 451W47IQ8X) | 0.00166 g in 1 mL |
| SODIUM BICARBONATE (UNII: 8MDF5V39QO) | 0.00091 g in 1 mL |
| WATER (UNII: 059QF0KO0R) | |

Packaging

| # | Item Code | Package Description | Marketing Start Date | Marketing End Date |
|---|------------------|--|----------------------|--------------------|
| 1 | NDC:54575-288-02 | 2 mL in 1 VIAL, MULTI-DOSE; Type 0: Not a Combination Product | | |
| 2 | NDC:54575-288-10 | 10 mL in 1 VIAL, MULTI-DOSE; Type 0: Not a Combination Product | | |
| 3 | NDC:54575-288-30 | 30 mL in 1 VIAL, MULTI-DOSE; Type 0: Not a Combination Product | | |
| 4 | NDC:54575-288-50 | 50 mL in 1 VIAL, MULTI-DOSE; Type 0: Not a Combination Product | | |

Marketing Information

| Marketing Category | Application Number or Monograph Citation | Marketing Start Date | Marketing End Date |
|--------------------|--|----------------------|--------------------|
| BLA | BLA103324 | 10/30/1992 | |

Labeler - Allergy Laboratories, Inc. (007191810)

Establishment

| Name | Address | ID/FEI | Business Operations |
|----------------------------|---------|-----------|---|
| Allergy Laboratories, Inc. | | 007191810 | ANALYSIS(54575-288) , LABEL(54575-288) , MANUFACTURE(54575-288) , PACK(54575-288) |

Revised: 12/2017

Allergy Laboratories, Inc.