STANDARDIZED CAT HAIR - standardized cat hair injection, solution
Nelco Laboratories, Inc.

Allergenic Extract

WARNINGS

Standardized allergenic extract is intended for use by physicians who are experienced in the administration of standardized (BAU/mL) allergenic extracts for immunotherapy and the emergency care of anaphylaxis, or for use under the guidance of an allergy specialist. Standardized allergenic extracts are not directly interchangeable with other allergenic extracts. The initial dose must be based on skin testing as described in the dosage and administration section of this insert. Patients being switched from other types of extract to standardized allergenic extracts should be started as though they were coming under treatment for the first time. **STANDARDIZED CAT HAIR EXTRACT IS NOT INTERCHANGEABLE WITH STANDARDIZED CAT PELT EXTRACTS, STANDARDIZED CAT EXTRACTS LABELED IN AU/mL, OR WITH NON-STANDARDIZED CAT EXTRACTS.**

This product should not be injected intravenously. Deep subcutaneous routes have been safe. Sensitive patients may experience severe anaphylactic reactions resulting in respiratory obstruction, shock, coma and/or death. **(See Adverse Reactions)**

Serious adverse reactions should be reported to Nelco Laboratories immediately and a report filed to: **MedWatch, The FDA Medical Product Problem Reporting Program, at 5600 Fishers Lane, Rockville, Md. 20852-9787, call 1-800-FDA-1088.**

Extreme caution should be taken when using allergenic extracts for patients who are taking beta-blocker medications. In the event of a serious adverse reaction associated with the use of allergenic extracts, patients receiving beta-blockers may not be responsive to epinephrine or inhaled brochodialators. **(See Precautions)**

Allergenic extracts may be used with caution for patients with unstable or steroid-dependent asthma or with underlying cardiovascular disease. **(See Contraindications)**

DESCRIPTION

Standardized cat hair extract is a sterile glycerinated injectable solution containing the extractables of dried, powdered cat hair, wash and dander and 0.5% NaCl, 0.08% Na_2HPO_4, 0.036% KH_2PO_4, water for injection and 0.4%, phenol as preservative in sterile containers. All extracts are aseptically filled. Standardized cat hair extract is to be administered by prick-puncture or intradermal routes when used for diagnostic purposes and administered subcutaneously when used for immunotherapy injections.

The Bioequivalent Allergy Unit (BAU) nomenclature, now used for all Standardized Cat Extracts, replaces the previous Allergy Unit (AU) nomenclature for these products. Bioequivalent Allergy Units are based on quantitative intradermal skin test results and are intended to assure that the labeled unit of different allergenic extracts will correspond to the expected clinical response in sensitive patients. References labeled 10,000 BAU/mL can be diluted to one half million fold to produce an intradermal sum of erythema diameter response of 50 mm in highly puncture reactive subjects.

In vitro assignment of BAU/mL to this product is based on radial immunodiffusion (RID) assay results according to guidelines established by the Center for Biologics Evaluation and Research (CBER) as indicated below.[5, 6]

RID Cat 1 (Fel d I) /mL	BAU/mL	AU/mL

5.0 to 9.9	5,000	50,000
10.0 to 19.9	10,000	100,000

Bioequivalent Allergy Units (BAU) are NOT interchangeable with Allergy Units (AU). Standardized Cat Hair extract labeled in BAU/mL are not interchangeable with standardized cat pelt extracts or with cat hair extracts labeled in AU/mL or with non-standardized cat hair extracts.

It has been recognized through investigation that the allergens responsible for Cat allergy are found in the pelt, hair, dander, saliva, serum and urine.(1) Saliva especially when deposited on and in combination with the hair, root hairs and skin can produce a significant allergic reaction. Repeated surface washing of the animal proved significant enough so that the wash was added to the whole of the raw material producing the cat allergenic extract.(2,3,4) However the amount of Fel d 1 varies widely from animal to animal so it is an advantage to use raw material with a known amount of the antigen. Nelco's raw material, supplied by Biopol Laboratory, is dried, powdered cat hair, wash and dander, labeled with the number of Fel d 1 units in each gram of dried material per container. The raw material is extracted with a 50%(v/v) glycerinated diluent containing glycerin and 0.5% NaCl, 0.08% Na_2HPO_4, 0.036% KH_2PO_4, WFI, and 0.4% phenol as a preservative. Although extracts from whole pelts of cats are similar in content of Fel d 1 to extracts prepared only from wash, hair and dander, pelt extracts may contain other non-Fel d 1 allergenic molecules.

CLINICAL PHARMACOLOGY

The mode of action of allergenic extracts is still under investigation. The pharmacological action of allergenic extracts used diagnostically is based on the liberation of histamine and other substances when the allergen reacts with IgE antibodies attached to the mast cells.(11) The pharmacological action of allergenic extracts used for immunotherapy is based on an increase of IgG antibodies and allergen-specific T lymphocyte cells.

a. Prick-puncture tests on Cat allergic subjects: 11 puncture tests (bifurcated needle) on cat allergic subjects yielded the following:

# Persons	Mean sum of wheal (mm)	Range of sum of wheal (mm)	Mean sum of erythema (mm)	Range of sum of erythema (mm)
11	14.272	9-20	60.727	41.92

b. Patients tested only by the intradermal method:

Intradermal tests (using 0.05mL) on 11 puncture positive patients BAU/mL to elicit 50mm sum of dia. of erythema reaction

# Persons	Mean	Range
11	0.019	0.8-0.0032

INDICATIONS AND USAGE

Standardized Cat Hair is intended for use in the diagnosis and therapy of cat allergy patients as established by allergy history and skin test reactivity.

CONTRAINDICATIONS

Standardized Cat Hair extract should not be used if the patient has asthma, cardiovascular disease, emphysema, diabetes, bleeding diathesis or pregnancy, unless a specific diagnosis of Type 1 allergy to

cat is made based on skin testing and the benefits of treatment outweigh the risks of an adverse reaction during testing or treatment. Cat extract is not indicated for use in patients who are not clinically allergic to cat or who are not skin reactive to cat allergenic extract. Limitations on treatment should be considered when treating young, or geriatric patients or patients suffering from auto-immune disorders or severe and unstable allergic disorders.

WARNINGS

Standardized Cat Hair extract is NOT interchangeable with standardized cat pelt extracts or standardized cat extracts labeled in AU/mL or non-standardized cat extracts.

Concentrated extracts must be diluted with sterile diluent prior to first use on a patient for treatment or intradermal testing.

DO NOT INJECT INTRAVENOUSLY This product should not be injected intravenously. Deep subcutaneous routes have proven to be safe. All concentrates of allergenic extracts have the ability to cause serious local and systemic reactions including death in sensitive patients.[(10)] Sensitive patients may experience severe anaphylactic reactions resulting in respiratory obstruction, shock, coma and/or death.

An allergenic extract should be temporarily withheld from patients or the dose of the extract adjusted downward if any of the following conditions exist: (1) Severe symptoms of rhinitis and/or asthma (2) Infections or flu accompanied by fever (3) Exposure to excessive amounts of clinically relevant allergen prior to a scheduled injection.

PRECAUTIONS

General Information:

Epinephrine 1:1000 should be available as well as personnel trained in administering emergency treatment. Allergenic extracts are not intended for intravenous injection. For safe and effective use of allergenic extracts, sterile solutions, vials, syringes, etc. should be used and aseptic precautions observed in making dilutions and administering the allergenic extract injection. A sterile tuberculin syringe graduated in 0.1 mL units to measure each dose for the prescribed dilution should be used.

To reduce the risk of an occurrence of adverse reactions, begin with a careful personal and family history plus a physical exam. Confirm your findings with scratch or intradermal skin testing. Patients should be observed for 30 minutes after any test.

Information for Patients: All concentrates of allergenic extracts have the ability to cause serious local and systemic reactions including death in sensitive patients. To minimize this potential hazard, the relative sensitivity of the patient must be assessed from the allergic history and from clinical observations. In certain individuals, life-threatening reactions may occur. Patients should be informed of this risk prior to skin testing and immunotherapy. Patients should be instructed to recognize adverse reaction symptoms that may occur and to report all adverse reactions to a physician. Patients should be told to wait in the office after injections for at least 30 minutes.

Drug Interactions: Antihistamines and Hydroxyzine can significantly inhibit the immediate skin test reactions as they tend to neutralize or antagonize the action of histamine.[(11)] This effect has been primarily documented when testing was performed within 1 to 2 hours after drug ingestion. Although partial inhibition of the skin test reaction had been observed for longer periods, it was minor. Epinephrine injection inhibits the immediate skin test reactions for several hours. Patients on delayed absorption antihistamine tablets should be free of such medication for 48 hours before testing. Patients using Astemizole (Hismanal) may experience prolonged suppression and should be free from such medication for up to 6 to 8 weeks prior to testing. Refer to package insert from long acting antihistamine manufacturer for more information.

Extreme caution should be taken when using allergenic extracts on patients who are taking beta-blockers. Patients receiving beta-blockers may not be responsive to epinephrine or inhaled bronchodialators.

Carcinogenesis, mutagenesis, impairment of fertility:

Long term studies in animals have not been conducted with allergenic extracts, including standardized Cat Hair extracts, to determine their potential carcinogenicity, mutagenicity or impairment of fertility.

Pregnancy: Category C: Animal reproduction studies have not been conducted with standardized Cat Hair extract. It is not known whether this extract can cause fetal harm when administered to pregnant women or can effect reproduction capacity. Standardized Cat Hair extract should be used for pregnant women only if clearly needed.

Nursing Mothers: It is not known whether this drug appears in human milk. Because many drugs are detectable in human milk, caution should be exercised when Allergenic Extract, Standardized Cat Hair, is administered to a nursing woman. There are no current studies on extract components in human milk, or their effect on the nursing infant.

Pediatric Use: Allergenic extracts have been used in children over two years of age. It is recommended that children be treated only when indicated. (7)

ADVERSE REACTIONS

Adverse systemic reactions usually occur within minutes and consist primarily of allergic symptoms such as: generalized skin erythema, urticaria, pruritus, angioedema, rhinitis, induced asthma, itching of nose or throat, wheezing, laryngeal edema, dyspnea, coughing, marked perspiration and hypotension. Less commonly, nausea, emesis, abdominal cramps, diarrhea and uterine contractions may occur. Severe reactions may cause anaphylaxis or shock and loss of consciousness. Fatalities have occurred rarely.(12) To some extent, the reaction rate is related to the type and dose of administered extract and to the degree of sensitivity of the patient.

The treatment of systemic allergic reactions is dependent upon the symptom complex. Antihistamines may offer relief of recurrent urticaria, associated skin reactions and gastrointestinal symptoms. Corticosteroids may provide benefit if symptoms are prolonged or recurrent. (See Overdosage)

Local reactions consisting of erythema, itching, swelling tenderness and sometimes pain may occur at the injection site. These reactions may appear within a few minutes to hours and persist for several days. Local cold applications and oral antihistamines may be effective treatment for local reactions. For marked and prolonged local reactions steroids may be helpful.

Serious adverse reactions should be reported to Nelco Laboratories immediately and a report can be filed to **MedWatch, The FDA Medical Product Problem Reporting Program, at 5600 Fishers Lane, Rockville, MD 20852-9787, call 1-800-FDA-1088.**

OVERDOSAGE

Overdosage can cause both local and systemic reactions. An overdose may be prevented by careful observation and questioning of the patient about the previous injection. If systemic or anaphylactic reaction does occur, apply a tourniquet above the site of injection and inject intramuscularly or subcutaneously 0.3 to 0.5mL of 1:1000 epinephrine hydrochloride into the opposite arm. The dose may be repeated in 5-10 minutes if necessary. Loosen the tourniquet at least every 10 minutes. The epinephrine hydrochloride 1:1000 dose for infants to 2 years is 0.05 to 0.1 mL; for children 2 to 6 years it is 0.15mL; for children 6-12 years it is 0.2mL.

Patients unresponsive to epinephrine may be treated with theophylline. Studies on asthmatic subjects reveal that plasma concentrations of Theophylline of 5 to 20 µg/mL are associated with therapeutic effects. Toxicity is particularly apparent at concentrations greater than 20 µg/mL. A loading dose of

Aminophylline of 5.8 mg/kg intravenously followed by 0.9 mg/kg per hour results in plasma concentrations of approximately 10 µg/mL (for patients not previously receiving theophylline). (Mitenko and Ogilive 1773; Nicholoson and Chick 1973)

Maintenance of a patient airway is critical if upper or lower airway obstruction is present. Other beta-adrenergic drugs such as Isoproterenol, Isoetharine, or Albuterol may be used by inhalation. The usual dose to relieve broncho-constriction in asthma is 0.5 mL of the 0.5% solution for Isoproterenol HCl. The Albuterol inhaler delivers approximately 90 mcg of Albuterol from the mouthpiece. The usual dosage for adults and children would be two inhalations repeated every 4-6 hours. Isoetharine supplied in the Bronkometer unit delivers approximately 340 mcg Isoetharine. The average dose is one to two inhalations. Persistent wheezing may necessitate intravenous aminophylline treatment. For profound shock and hypotension, intravenous fluids, vasopressors and oxygen may also be needed. Respiratory obstruction not responding to parenteral or inhaled bronchodilators may require Theophylline, oxygen, intubation and the use of life support systems.

DOSAGE AND ADMINISTRATION

It is imperative that the physician determine the initial dose of the product by skin testing. Patients being switched from extracts not labeled in Bioequivalency Allergy Units should be started as if they were coming under treatment for the first time. Patients being switched from one lot of Standardized Cat Hair to another lot of Standardized Cat Hair (from the same or different manufacturers) should have the initial dose from the new lot reduced by 75%. Patients being switched from a Standardized Cat Pelt extract to a Standardized Cat Hair extract (both labeled in BAU/mL) should be skin tested with both extracts to determine the relative potency of the extracts and the dosage adjusted accordingly.

Recommended usual dosage and range: (Scratch or Prick Testing)

The general method of making a scratch test is to first scarify the skin and then apply a drop of extract to the scratch. Make scarifications at least 2.5 cm apart. Hold the scarifier between thumb and index finger, press the sharp edge of the instrument against the skin and twirl instrument rapidly. The scratch should disrupt the outer layers of epidermis but should not produce immediate oozing of blood. One drop (0.05 mL) of extract is rubbed or applied into each scratch. Always apply a control scratch with each test set. Sterile Diluting fluid (for a negative control) is used in exactly the same way as an active test extract. Histamine may be used as a positive control. Scratch or prick test sites should be examined at 15 and 30 minutes. To prevent excessive absorption, wipe off antigens producing large reactions as soon as the wheal appears. Record the size of the reaction.

Recommended usual dosage and range: (Intradermal Testing)

Patients with a negative scratch or prick-puncture test:

Patients who do not react to a valid scratch or prick- puncture test should be tested intradermally with a 0.05 mL of a 50 BAU/mL extract solution. If this test is negative, a second intradermal test may be performed using a 100 BAU/mL extract dilution. The negative puncture control must be diluted appropriately for intradermal use. .

<u>To prepare a 50 BAU/mL dilution from 10,000 BAU/mL vial:</u>

Take 5.0 mL of the 10,000 BAU/mL + 5.0 mL of diluent =Vial A @5,000 BAU/mL.

Take 1.0 of vial A + 9.0 mL diluent = vial B @500 BAU/mL.

Take 1.0 of vial B + 9.0 mL diluent = vial C @50 BAU/mL.

Patients being suspected of being highly allergic should be tested with 0.05 mL of a 0.1 BAU/mL dilution. A negative test should be followed by repeat tests using progressively stronger concentrations until the maximal recommended strength of 100 BAU/mL is reached. The negative puncture test control must be diluted appropriately for intradermal use. To prepare this dilution follow the tenfold dilution series chart for therapeutic allergens.

Allergic response is based on measurement of wheal and erythema with respect to positive and negative control skin tests. Skin tests are graded in terms of the wheal and erythema response noted at 10 to 20 minutes. Wheal and erythema size may be recorded by actual measurement or the extent of both responses.

Recommended dosage and range: (Therapeutic) Dosage of allergenic extracts is a highly individualized matter and varies according to the degree of sensitivity of the patient, and the clinical response and tolerance to the extract administered during the injection regimen. The dosage of allergenic extract does not vary significantly with the respiratory allergic disease under treatment.

In patients who appear to be highly sensitive by history and skin test, the initial dose of the extract should be 0.05mL of 0.01 to 0.1 BAU/mL. Patients with lesser sensitivity may be started using 1.0 BAU/mL. The amount of allergenic extract is increased at each injection by not more than 50%-100% of the previous amount, and the next increment is governed by the response to the last injection.

Any evidence of systemic reaction is an indication for a significant reduction (at least 50%) in the subsequent dose. Any evidence of a local or generalized reaction requires a reduction in dosage. After therapeutic injections patients should always be observed for at least 30 minutes. If adverse reactions appear, the next therapeutic injection of extract should be reduced to the dose which does not elicit a reaction and subsequent doses increased more slowly. The upper limits of dosage have not been established. Doses larger than 0.2 mL of 10,000 BAU/mL may be painful due to glycerin content. [(9)]

Preparation Instructions To prepare a dilution for intradermal and therapeutic use, one starts with 10,000 BAU/mL stock concentrate and makes a 1:10 dilution by adding 1.0 mL of the concentrate to 9.0 mL of sterile diluent. Subsequent dilutions are made in similar manner.

TEN-FOLD DILUTION SERIES

Dilution	Extract	Diluent mL	BAU/mL
0	Concentrate	0	10,000
1	1mL concentrate	9	1,000
2	1mL dilution #1	9	100
3	1mL dilution #2	9	10
4	1mL dilution #3	9	1
5	1mL dilution #4	9	0.1
6	1mL dilution #5	9	0.01

Intervals between doses: The optimal interval between doses of allergenic extract has not been definitely established. However, as it is customary practiced, injections are given once or twice per week until the maintenance dose of extract is reached. At this time, the injection interval may be increased to 2 weeks, then 3 weeks and finally to 4 weeks. If the patient does not return for 6-8 weeks after the last injection, the dose should be reduced to 25% of the last dose. If longer than 8 weeks, a dose reduction of 1,2, or 3 dilution's may be made depending on a consideration of the components and the patient's sensitivity. The dosage and the interval between injections may need to be modified according to the clinical response of the patient. When switching patients to a fresh extract the initial dose should be reduced 3/4 so that 25% of previous dose is administered.

Duration of treatment: The usual duration of treatment has not been established. A period of two or three years of injection therapy constitutes an average minimum course of treatment.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

HOW SUPPLIED

Diagnostic Allergens:

Scratch or Prick test:

10,000 BAU/mL in 50% glycerin (v/v) in 5mL dropper vials.

Intradermal test:

100 BAU/mL in 5mL or 10mL sterile multiple dose vials.

Concentrate of Extract for Therapeutic Use Allergens:

10,000 BAU/mL or special dilution according to prescription, are contained in 5mL, 10mL, 50mL multiple dose vials.

Dilutions of concentrate of allergenic extracts can be made with either buffered diluent containing 0.4% phenol or with diluent containing 50% glycerin (v/v) with salts.

STORAGE

The expiration date of Standardized Cat Hair extract containing 10,000 BAU/mL in 50% glycerin (v/v) is listed on the container label. Store extracts at 2° to 8° C and keep them in this range during office use.

WARRANTY: We warrant that this product was prepared and tested according to the standards of the FDA and is true to label. Because of biological differences in individuals and because allergenic extracts are manufactured to be potent and because we have no control over the conditions of use, we cannot and do not warrant either a good effect or against an ill effect following use.

REFERENCES

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7. Murray,A.B., Ferguson,A.C., Morrison,B.J., The frequency and severity of cat allergy vs dog allergy in atopic children. J.Allergy Clin. Immunol:72, 145-9, 1983.

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CONTAINER LABELING

STANDARDIZED CAT HAIR

standardized cat hair injection, solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:36987-1121
Route of Administration	INTRADERMAL, 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**
SODIUM CHLORIDE (UNII: 451W47IQ8X)	
SODIUM PHOSPHATE, DIBASIC (UNII: GR686LBA74)	
POTASSIUM PHOSPHATE, MONOBASIC (UNII: 4J9FJ0HL51)	
PHENOL (UNII: 339NCG44TV)	
WATER (UNII: 059QF0KO0R)	
GLYCERIN (UNII: PDC6A3C0OX)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:36987-1121-1	5 mL in 1 VIAL, MULTI-DOSE		
2	NDC:36987-1121-2	10 mL in 1 VIAL, MULTI-DOSE		
3	NDC:36987-1121-3	30 mL in 1 VIAL, MULTI-DOSE		
4	NDC:36987-1121-4	50 mL in 1 VIAL, MULTI-DOSE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA103384	09/29/1992	

Labeler - Nelco Laboratories, Inc. (054980867)

Registrant - Nelco Laboratories, Inc. (054980867)

Establishment

Name	Address	ID/FEI	Business Operations
Nelco Laboratories, Inc.		054980867	manufacture

Revised: 12/2009 Nelco Laboratories, Inc.