PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

ALLERGENIC EXTRACT – POLLENS, and ALLERGENIC EXTRACT NON-POLLENS

Allergenic Extracts in Bulk Vials for Subcutaneous Injection Immunotherapy

Schedule D-Biologic Drugs

360420-C06

Rev. October 29, 2024

"Allergenic Extracts – Pollens and Allergenic Extracts – Non-Pollens, indicated for:
Use in the diagnosis and immunotherapy of patients presenting symptoms of allergy (hay fever, rhinitis, etc.) to specific environmental allergens have been issued market authorization without conditions."

Manufactured by:	Distributed in Canada by:	Date of Initial Authorization:
Jubilant HollisterStier LLC	Omega Laboratories	Allergenic Extracts-Non-Pollens:
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ALLERGENIC EXTRACT – POLLENS

Submission Control Number: 285785 **Date of Revision:** November 26, 2024

ALLERGENIC EXTRACT NON-POLLENS

Submission Control Number: 285782

RECENT MAJOR LABEL CHANGES

All Sections and Subsections updated to Plain Language Labeling Format	10/2024

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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

ALLERGENIC EXTRACT – POLLENS and ALLERGENIC EXTRACT – NON-POLLENS are indicated for:

- Use in the diagnosis and immunotherapy of patients presenting symptoms of allergy (hay fever, rhinitis, etc.) to specific environmental allergens.

The selection of allergenic extracts to be used for immunotherapy should be based on a thorough and carefully taken history of hypersensitivity and confirmed by skin testing.

The use of mixed or unrelated antigens for skin testing is not recommended since, in the case of a positive reaction, it does not indicate which component of the mix is responsible for the reaction, while, in the case of a negative reaction, it fails to indicate whether the individual antigens at full concentration would give a positive reaction. Utilization of such mixes for compounding a treatment may result, in the former case, in administering unnecessary antigens and, in the latter case, in the omission of a needed allergen.

Avoidance of allergens is to be advocated if possible, but cannot always be attained, e.g., allergy to dog dander in kennel owners and employees, dog breeders, research workers, veterinarians, etc.

Allergens to which a patient is extremely sensitive should not be included in treatment mixes with allergens to which there is much less sensitivity, but should be administered separately. This way, if reactions should occur to the allergens that the patient is highly reactive to, dosage adjustments can be made with these allergens without restraining the dosage increases in the allergens to which the patient is less reactive.

1.1 Pediatrics

Allergenic extracts for immunotherapy have been given safely in infants and young children (see Section 7.1.3 Pediatrics).

1.2 Geriatrics

Geriatrics: Evidence from clinical studies and experience suggests that use in the geriatric population is associated with differences in safety or effectiveness (see Section 7.1.4 Geriatrics).

2 CONTRAINDICATIONS

There are no known absolute contraindications to immunotherapy. Patients with cardiovascular diseases or pulmonary diseases may be at higher risk for severe adverse reactions (see Section 3 SERIOUS WARNINGS AND PRECAUTIONS BOX, Section 7 WARNINGS AND PRECAUTIONS, Section 9.4 Drug-Drug Interactions).**Error! Reference source not found.**

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions
This product is intended for use only by physicians who are experienced in the use of allergenic extracts, or for use under the guidance of an allergist. • Allergenic extracts may potentially elicit a severe life-threatening systemic reaction (anaphylaxis), which can result in death. Therefore, emergency measures and personnel trained in their use must be available

immediately in the event of such a reaction. Patients should be instructed to recognize adverse reaction symptoms and cautioned to contact the physician's office if symptoms occur.

- Standardized glycerinated extracts may be more potent than regular extracts and therefore, are not directly interchangeable with non-standardized extracts, or other manufacturers' products.

  (See **Section 4.1 Dosing Considerations**)
- Patients on 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.
  (See **Section 7 WARNINGS AND PRECAUTIONS**)
- Patients with cardiovascular diseases or pulmonary diseases, such as symptomatic unstable steroid-dependent asthma, and/or those who are receiving cardiovascular drugs such as beta blockers, may be at higher risk for severe adverse reactions. These patients may also be more refractory to the normal allergy treatment regimen. Patients should be treated only if the benefit of treatment outweighs the risk.

  (See **Section 2 CONTRAINDICATIONS**)
- This product should never be injected intravenously.

  (See **Section 4.1 Dosing Considerations**)

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

Allergenic extract should be temporarily withheld from patients or the dose adjusted downward if any of the following conditions exist: (1) severe symptoms of rhinitis and/or asthma; (2) infection or flu accompanied by fever, or (3) exposure to excessive amounts of clinically relevant allergen prior to a scheduled injection. Do not start immunotherapy during a period of symptoms due to exposure. Since the individual components of the extract are those to which the patient is allergic, and to which they will be exposed, typical allergic symptoms may follow shortly after the injection, particularly when the antigen load from exposure plus the injected antigen exceeds the patient's antigen tolerance. Therefore, it is imperative that physicians administering allergenic extracts understand and be prepared for the treatment of severe reactions (see Section 3 SERIOUS WARNINGS AND PRECAUTIONS BOX).

Severe systemic reactions mandate a decrease of at least 50 % in the next dose, followed by cautious increases. Repeated systemic reactions, even of a mild nature, are sufficient reason for the cessation of further attempts to increase the reaction-causing dose.

THE CONCENTRATE SHOULD NOT BE INJECTED AT ANY TIME UNLESS TOLERANCE HAS BEEN ESTABLISHED. DILUTE CONCENTRATED EXTRACTS WITH STERILE ALBUMIN SALINE WITH PHENOL (0.4%) FOR INTRADERMAL TESTING.

INJECTIONS SHOULD NEVER BE GIVEN INTRAVENOUSLY. Subcutaneous injection is recommended. Intracutaneous or intramuscular injections may produce large local reactions or be excessively painful. AFTER INSERTING NEEDLE SUBCUTANEOUSLY, BUT BEFORE INJECTING, ALWAYS WITHDRAW THE PLUNGER SLIGHTLY. IF BLOOD APPEARS IN THE SYRINGE, CHANGE THE NEEDLE AND GIVE THE INJECTION IN ANOTHER SITE.

IF CHANGING TO A DIFFERENT LOT OF EXTRACT: Even though it is the same formula and concentration, the first dose of the new extract should not exceed 50 % of the last administered dose from the previous extract.

IF THE EXTRACT PREVIOUSLY USED WAS FROM ANOTHER MANUFACTURER: Since manufacturing processes and sources of raw materials differ among manufacturers, the interchangeability of extracts from different manufacturers cannot be insured. The starting dose of the extract therefore should be greatly decreased even though the extract is the same formula and dilution. Initiate therapy as though patient had not been receiving immunotherapy, or determine initial dose by skin test using serial dilutions of the extract. In highly sensitive

individuals, the skin test method may be preferable. See Section 4 DOSAGE AND ADMINISTRATION, Section 8 ADVERSE REACTIONS and Section 13 PHARMACEUTICAL INFORMATION.

4.2 Recommended Dose and Dosage Adjustment

IF THE PREVIOUS EXTRACT WAS OUTDATED: The dating period for allergenic extracts indicates the time that they can be expected to remain potent under refrigerated storage conditions (2 ° to 8 °C). During the storage of extracts, even under ideal conditions, some loss of potency occurs. For this reason, extracts should not be used beyond their expiration date. If a patient has been receiving injections of an outdated extract, they may experience excessive local or systemic reactions when changed to a new, and possibly more potent, extract. In general, the longer the material has been outdated, the greater the dose reduction necessary for the fresh extract.

IF CHANGING FROM ALUM-ADSORBED OR ALUM-PRECIPITATED EXTRACT TO AQUEOUS OR GLYCERINATED EXTRACTS: When the patient previously has been receiving alum-adsorbed or alum-precipitated extract, the safest course is to start over as though the patient had not been receiving immunotherapy. See Section 4 DOSAGE AND ADMINISTRATION and Section 8 ADVERSE REACTIONS.

IF ANY OTHER CHANGES HAVE BEEN MADE IN THE EXTRACT CONCENTRATE FORMULA: Changes other than those listed above may include situations such as a difference in extracting fluid (i.e., change from non-glycerin extracts to 50 % glycerin extracts), combining two or more stock concentrates, or any other change.

It should be recognized that any change in formula can affect a patient's tolerance of the treatment. The usual 1/2 of the previous dose for a new extract may produce an adverse reaction; extra dilutions are recommended whenever starting a revised formula. The greater the change, the greater the number of dilutions required.

Immunotherapy

Repeated injections of appropriate allergenic extracts will ameliorate the intensity of allergenic symptoms upon contact with the allergen. Normally immunotherapy can be started with a 1:100,000 dilution of extracts labeled in weight/volume.

Allergenic extracts should be administered using a sterile syringe with 0.01 mL gradations and a 25-27 gauge x 1/2" to 5/8" needle. The injections are given subcutaneously. The most common sites of injection are the lateral aspect of the upper arm or thigh. Intracutaneous or intramuscular injections may produce large local reactions and may be very painful.

The dosage schedule of allergenic extracts is a highly individualized matter and varies according to the degree of sensitivity of the patient, their clinical response, and tolerance to the extract administered during the early phases of an injection regimen. The starting dose should be based on skin tests of the extract to be used for immunotherapy.

To prepare dilutions for intradermal and therapeutic use, make a 1:10 dilution by adding 1.0 mL of the concentrate to 9.0 mL of sterile aqueous diluent. Subsequent serial dilutions are made in a similar manner. To determine the starting dose, begin intradermal testing with the most dilute extract preparation. Inject 0.02 mL and read the reaction after 15 minutes. Intradermal testing is continued with increasing concentrations of the extract until a reaction of 10-20 mm erythema (ΣE 20-40 mm) and/or a 5 mm wheal occurs. This concentration at a dose of 0.03 mL then can serve as a starting dose for immunotherapy. Subsequent doses can be increased by 0.03 mL to as high as 0.12 mL increments each time until 0.3 mL is reached, at which time a dilution 10 times as strong can be used, starting with 0.03 mL. Proceed in this way until a tolerance dose is reached or symptoms are controlled. Suggested maintenance dose for a pollen extract is 0.2 mL of the Concentrate, while for a non-pollen extract the maximum suggested dose is 0.5 mL of the Concentrate. Occasionally, higher doses are necessary to relieve symptoms. Special caution is required in administering doses greater than 0.2 mL. The interval between doses normally is 3 to 7 days during dose building regimen.

This is offered as a suggested schedule for average patients and will be satisfactory in most cases. However, the degree of sensitivity varies in many patients. The size of the dose should be adjusted and should be regulated by the patient's tolerance and reaction. Decrease the size of the dose if the previous injection resulted in marked local or the slightest general reaction. Another dose should never be given until all reactions resulting from the previous dose have disappeared.

In some patients, the dosage may be increased more rapidly than shown in the schedule. In seasonal allergies, treatment should be started and the interval between doses regulated so that at least the first twenty doses will have been administered by the time symptoms are expected. Thus, the shorter the interval between the start of immunotherapy and the expected onset of symptoms, the shorter the interval between each dose. Some patients may even tolerate daily doses.

A maintenance dose, the largest dose tolerated by the patient that relieves symptoms without producing undesirable local or general reactions, is recommended for most patients. The upper limits of dosage have not been established; however, doses larger than 0.2 mL of the extract may be painful if glycerin is present. The dosage of allergenic extract does not vary significantly with the respiratory allergic disease under treatment. The size of this dose and the interval between doses will vary and can be adjusted as necessary. Should symptoms develop before the next injection is scheduled, the interval between doses should be decreased. Should allergic symptoms or local reactions develop shortly after the dose is administered, the size of the dose should be decreased. In seasonal allergies, it is often advisable to decrease the dose to one-half or a one-quarter of the maximum dose previously attained if the patient has any seasonal symptoms.

The interval between maintenance doses can be increased gradually from one week to 10 days, to two weeks, to three weeks, or even to four weeks if tolerated. Repeat the doses at a given interval three or four times to check for untoward reactions before further increasing the interval. Protection is lost rapidly if the interval between doses is more than four weeks. See Section 7 WARNINGS AND PRECAUTIONS.

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.

4.3 Reconstitution

Parenteral Products:

Sterile aqueous diluent containing albumin (human) [Sterile Albumin Saline with Phenol (0.4 %)] or diluent of 50 % glycerin may be used when preparing dilutions of the concentrate for immunotherapy. If used for intradermal testing, the concentrate must be diluted; Sterile Albumin Saline with Phenol (0.4%) is recommended for dilution.

Dilutions should be made accurately and aseptically, using sterile diluent, vials, syringes, etc. Mix thoroughly and gently by rocking or swirling.

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

Table [1]– Reconstitution

Product	Vial Size	Volume of Diluent to be Added to Vial	Approximate Available Volume	Concentration
AP Dog Hair-Dander	10 mL (Bulk) 50 mL (Bulk)	Calculation Dependent	Calculation Dependent	1:100 w/v
AP Cattle Hair and Dander / AP Horse Hair and Dander	10 mL (Bulk) 30 mL (Bulk)	Calculation Dependent	Calculation Dependent	1:50 w/v

Non-AP Epidermals/Inhalants	10 mL (Bulk) 50 mL (Bulk)	Calculation Dependent	Calculation Dependent	1:10 w/v
UF Dog Hair and Dander	10 mL (Bulk) 50 mL (Bulk)	Calculation Dependent	Calculation Dependent	1:650 w/v
Grass Pollen	10 mL (Bulk) 50 mL (Bulk)	Calculation Dependent	Calculation Dependent	1:20 w/v
Insects	10 mL (Bulk) 50 mL (Bulk)	Calculation Dependent	Calculation Dependent	1:10 w/v
Molds	10 mL (Bulk) 50 mL (Bulk)	Calculation Dependent	Calculation Dependent	1:10 w/v or 1:1,000 w/v
Tree Pollen	10 mL (Bulk) 50 mL (Bulk)	Calculation Dependent	Calculation Dependent	1:20 w/v or 1:50 w/v
Ragweed	10 mL (Bulk) 50 mL (Bulk)	Calculation Dependent	Calculation Dependent	Amb a 1 (UA/mL)
Weed Pollen	10 mL (Bulk) 50 mL (Bulk)	Calculation Dependent	Calculation Dependent	1:20 w/v

4.4 Administration

The presence of asthmatic signs and symptoms appear to be an indicator for severe reactions following allergy injections. An assessment of airway obstruction either by measurement of peak flow or an alternate procedure may provide a useful indicator as to the advisability of administering an allergy injection.

Concentrated extracts must be diluted prior to use: See Section 13 PHARMACEUTICAL INFORMATION for detailed instructions on the dilution of allergenic extracts.

Any evidence of a local or generalized reaction requires a reduction in dosage during the initial stages of immunotherapy, as well as during maintenance therapy.

Allergenic extracts diluted with sterile Albumin Saline with Phenol (0.4 %) diluent may be more potent than extracts diluted with diluents which do not contain stabilizers such as albumin. When switching from non-stabilized to stabilized diluent, consider weaker initial dilutions for both intradermal testing and immunotherapy.

Sterile solutions, vials, syringes, etc., should be used and aseptic precautions observed in making dilutions.

To avoid cross-contamination, do not use the same needle to withdraw materials from vials of more than one extract, or extract followed by diluent.

A sterile tuberculin syringe graduated in 0.01 mL units should be used to measure each dose from the appropriate dilution. Aseptic techniques should always be employed when injections of allergenic extracts are being administered.

A separate sterile syringe should be used for each patient to prevent transmission of hepatitis and other infectious agents from one person to another.

Patient reactions to previous injections should be reviewed before each new injection. A conservative dosage schedule should be followed by the physician until a pattern of local responses is established which can be used to monitor increases in dosage.

Rarely, a patient is encountered who develops systemic reactions to minute doses of allergen and does not demonstrate increasing tolerance to injections after several months of treatment. If systemic reactions or excessive local responses occur persistently at very small doses, efforts at immunotherapy should be stopped.

Proper selection of the dose and careful injection should prevent most systemic reactions. It must be remembered, however, that allergenic extracts are highly potent in sensitive individuals and that systemic reactions of varying degrees of severity may occur, including urticaria, rhinitis, conjunctivitis, wheezing, coughing, angioedema, hypotension, bradycardia, pallor, laryngeal edema, fainting, or even anaphylactic shock and death. Patients should be informed of this, and the precautions should be discussed prior to immunotherapy (See Section 7 WARNINGS AND PRECAUTIONS.). Severe systemic reactions should be treated as indicated in Section 8 ADVERSE REACTIONS.

PATIENTS SHOULD BE OBSERVED IN THE OFFICE FOR 30 MINUTES AFTER EACH TREATMENT INJECTION. Most severe reactions will occur within this time period, and rapid treatment measures should be instituted. See Section 8 ADVERSE REACTIONS for such treatment measures.

In order to avoid darkening and possible precipitation, do not dilute Privet pollen with solutions containing phenol. Injections of this extract discolored by reaction with phenol may produce a lasting tattoo-like discoloration of the skin.

Missed Dose

IF A PROLONGED PERIOD OF TIME HAS ELAPSED SINCE THE LAST INJECTION:

Patients may lose tolerance for allergen injections during prolonged periods between doses. The duration of tolerance is an individual characteristic and varies from patient to patient. In general, the longer the lapse in the injection schedule, the greater the dose reduction required. If the interval since last dose is over four weeks, perform skin tests to determine starting dose.

5 OVERDOSAGE

See Section 4 DOSAGE AND ADMINISTRATION and Section 8 ADVERSE REACTIONS.

For management of a suspected drug overdose, contact your regional poison control center.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table [2] – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form/ Strength/Composition	Non-medicinal Ingredients
Subcutaneous Intracutaneous (intradermal)	Solution/ Refer to Product List Table	50 % Glycerin (v/v) 0.5 % Sodium chloride (w/v) 0.275 % Sodium bicarbonate (w/v)

Table [3] – Product List

ALLERGENIC EXTRACT - POLLENS ANTIGEN		CONC.
TREE	ACACIA, GOLDEN	1:20 w/v
	ALDER, RED	
	ASH, WHITE	
	BEECH, AMERICAN	
	BIRCH MIX (PRW)	
	BOTTLEBRUSH TREE	
	BOXELDER/MAPLE MIX (BHR)	
	CEDAR, MOUNTAIN	
	CEDAR, RED	
	COTTONWOOD, COMMON	
	CYPRESS, ARIZONA	
	ELM, AMERICAN	
	ELM, CHINESE	
	GUM, SWEET	
	HACKBERRY	
	HICKORY, SHAGBARK	
	MAPLE, HARD/SUGAR	
	MELALEUCA	
	MESQUITE TREE	
	MULBERRY MIX (RW)	
	OAK MIX (RVW)	
	OAK, RED	
	OLIVE TREE	
	PALM, QUEEN	
	PECAN TREE	
	PINE MIX (LY)	
	PRIVET, COMMON	
	SYCAMORE, AMERICAN	
	TREE MIX #5	
	TREE MIX #11	
	WALNUT, BLACK	
	WILLOW, BLACK	
	CYPRESS, BALD	1:50 w/v

ALLERGENIC EXTRACT – POLLENS ANTIGEN (CONT.)		CONC.
GRASS	BAHIA GRASS	1:20 w/v
	BROME, SMOOTH	
	CORN, COMMON CULTIVATED	
	JOHNSON GRASS	
	OATS, COMMON CULTIVATED	
WEED	CARELESS WEED	1:20 w/v
	CARELESS/PIGWEED (CR)	
	COCKLEBUR, COMMON	
	DOCK/SORREL MIX (DS)	
	DOG FENNEL, EASTERN	
	GOLDENROD	
	KOCHIA	
	LAMBS QUARTERS	
	MARSHELDER/POVERTY MIX (BPT)	
	NETTLE	
	PIGWEED, ROUGH REDOOT	
	PLANTAIN, ENGLISH	
	RAGWEED, GIANT	
	RAGWEED, WESTERN	
	RUSSIAN THISTLE	
	SAGEBRUSH, MUGWORT	
	SCALE, WING	
	SHEEP SORREL	
	WEED MIX 2630	
	RAGWEED, MIX (GS)	100 Amb a 1 UA/mL
	RAGWEED, SHORT	200 Amb a 1 UA/mL

ALLERGENIC EXTRACT – NON-POLLENS ANTIGEN		CONC.
EPIDERMAL	DOG HAIR & DANDER	1:10 w/v
	FEATHER MIX	
	GUINEA PIG HAIR & DANDER	
	A.P. CATTLE HAIR & DANDER	1:50 w/v
	A.P. HORSE HAIR & DANDER	
	A.P. DOG HAIR & DANDER	1:100 w/v
	U.F. DOG HAIR & DANDER	1:650 w/v
INSECT	COCKROACH, AMERICAN	1:10 w/v
	COCKROACH, GERMAN	
	COCKROACH MIX	
	FIRE ANT, RED	
MOLD	*ALTERNARIA TENUIS*	1:10 w/v
	ASPERGILLUS FUMIGATUS	
	CEPHALOSPORIUM ACREMORIUM	
	EPICACCUM NIGRUM	
	FUSARIUM VASINFECTUM	
	HELMINTHOSPORIUM INTERSEMINATUM	
	MUCOR RACEMOSUS	
	PENICILLIUM NOTATUM	
	PHOMA HERBARUM	
	PULLULARIA PULLULANS	
	CANDIDA ALBICANS	
	CANDIDA ALBICANS	1:1,000 w/v

Most allergenic extracts are assayed for PNU. This unitage can be obtained for patient prescriptions. 10,000 PNU/mL is typically the strength of each allergen used for treatment formulation (if available).

(1) Weight to volume (w/v). Weight to volume (w/v) describes the weight of allergenic source material added to a given volume of extracting fluid. A 1:10 w/v extract, e.g., indicates that the solution contains the extractable material from one gram of raw material added to each 10 mL glycerinated extracting fluid. The amount and composition of extracted materials will vary with the type of antigen, the extracting fluid, duration of extraction, pH, temperature, and other variables.

Pollens are typically extracted at 1:20 w/v ratio in glycerinated extracts. Epidermal, environmental, molds and insect products are typically extracted at 1:10 w/v with the exception of UF Dog which is extracted at 1:650 w/v.

AP™ (acetone precipitated) Cattle Hair and Dander plus Horse Hair and Dander are prepared at a 1:50 w/v concentration (i.e., 1 gram of dried precipitate in 50 mL of reconstitution fluid) while AP™ Dog Hair-Dander is prepared at 1:100 w/v concentration. (i.e., 1 gram of dried precipitate in 100 mL of reconstitution fluid.)

(2) Amb a 1 (UA/mL). Amb a 1 is considered the most important allergen in Ragweed Pollen and is measured by agar gel immune-diffusion against a reference standard established by the CBER. The concentration of Amb a 1 is expressed as units of Amb a 1 per mL of extract.

If an extract is diluted with a diluent or other allergenic extracts, the Amb a 1 concentration must be determined by calculation.

7 WARNINGS AND PRECAUTIONS

General

Emergency resuscitation measures and personnel trained in their use should be available immediately in the event of a serious systemic or anaphylactic reaction not responsive to the above measures. (see Section 3 SERIOUS WARNINGS AND PRECAUTIONS BOX).

Any injections, including immunotherapy, should be avoided in patients with a bleeding tendency.**Carcinogenesis and Mutagenesis**

Long-term studies in animals have not been conducted with allergenic extracts to determine their potential for carcinogenicity or mutagenicity. See Section 16 NON-CLINICAL TOXICOLOGY.

Cardiovascular

Patients on cardiovascular drugs such as beta blockers, may be at higher risk for severe adverse reactions. These patients may also be more refractory to the normal allergy treatment regimen. Patients should be treated only if the benefit of treatment outweighs the risks (see Section 2 CONTRAINDICATIONS, SECTION 3 SERIOUS WARNINGS AND PRECAUTIONS BOX, Section 9.5 Drug-Drug Interactions).

Reproductive Health: Female and Male Potential

- **Fertility**

  Long-term studies in animals have not been conducted with allergenic extracts to determine their potential for impairment of fertility. See Section 7.1.1 Pregnant Women.

Respiratory

The presence of asthmatic signs and symptoms appear to be an indicator for severe reactions following allergy injections. An assessment of airway obstruction either by measurement of peak flow or an alternate procedure may provide a useful indicator as to the advisability of administering an allergy injection.

Sensitivity/Resistance

Since there are differences of opinion concerning the possibility of routine immunizations exacerbating autoimmune diseases, immunotherapy should be given cautiously to patients with autoimmune diseases and only if the risk from exposure is greater than the risk of exacerbating the underlying disease (see Section 3 SERIOUS WARNINGS AND PRECAUTIONS BOX, Section 4.4 Administration).

Skin

See Section 4.4 Administration and Section 8 ADVERSE REACTIONS.

7.1 Special Populations

7.1.1 Pregnant Women

Use in Pregnancy

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.

Immunotherapy during pregnancy appears to present no added risk to the fetus or to the mother; however, on the basis of histamine's known ability to contract the uterine muscle, allergenic extracts should be used cautiously and hyposensitization overdose avoided if the decision is to treat during pregnancy. For women who have been getting maintenance doses of allergen without side effects, the occurrence of pregnancy is not an indication to stop immunotherapy.

7.1.2 Breast-feeding

There are no current studies on the secretion of the allergenic extract components in human milk or effects on the nursing infant. Because many drugs are excreted in human milk, caution should be exercised when allergenic extracts are administered to a nursing woman.

7.1.3 Pediatrics

The dose for the pediatric population is the same as for adults. Since the dosage is the same, the larger volumes of solution may produce excessive discomfort. Therefore, in order to achieve the total dose required, the volume of the dose may need to be divided into more than one injection per visit.

7.1.4 Geriatrics

The dose for elderly patients is the same as for adult patients under 65. Reactions from immunotherapy can be expected to be the same in elderly patients as in younger adults. Elderly patients may be more likely to be on medication that could block the effect of epinephrine which could be used to treat serious reactions, or they could be more sensitive to the cardiovascular side effect of epinephrine because of pre-existing cardiovascular disease.**Error! Reference source not found.**

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

Information to be Provided to the Patient

PATIENTS SHOULD BE OBSERVED IN THE OFFICE FOR 30 MINUTES AFTER EACH TREATMENT INJECTION. Most severe reactions will occur within this time period, and rapid treatment measures should be instituted. Patients should be instructed in the recognition of adverse reactions to immunotherapy and warned to return to the office promptly if symptoms occur after leaving.

Local Reactions

Some erythema, swelling or pruritus at the site of injection are common, the extent varying with the patient. Such reactions should not be considered significant unless they persist for at least 24 hours. Local reactions (erythema or swelling) which exceed 4-5 cm in diameter are not only uncomfortable, but also indicate the possibility of a systemic reaction if dosage is increased. In such cases, the dosage should be reduced to the last level not causing the reaction and maintained at this level for two or three treatments before cautiously increasing again.

Large persistent local reactions may be treated by local cold, wet dressings and/or the use of oral antihistamines. They should be considered a warning of possible severe systemic reactions and an indication of the need for temporarily reduced dosages.

A mild burning immediately after the injection is to be expected. This usually leaves in 10 to 20 seconds.

Systemic Reactions

See Section 3 SERIOUS WARNINGS AND PRECAUTIONS BOX.

With careful attention to dosage and administration, systemic reactions occur infrequently, but it cannot be overemphasized that in sensitive individuals, any injection could result in anaphylactic shock. Therefore, it is imperative that physicians administering allergenic extracts understand and be prepared for the treatment of severe reactions.

Other possible systemic reactions which may occur in varying degrees of severity are laryngeal edema, fainting, pallor, bradycardia, hypotension, angioedema, cough, wheezing, conjunctivitis, rhinitis, and urticaria. Frequency data for adverse reactions when administering allergenic extracts for testing and treatment show that risk is low.

If a systemic or anaphylactic reaction does occur, apply a tourniquet above the site of injection and inject epinephrine

Emergency resuscitation measures and personnel trained in their use should be available immediately in the event of a serious systemic or anaphylactic reaction not responsive to the above measures.

8.5 Post-Market Adverse Reactions

The most frequently reported serious and expected reaction is anaphylaxis.

9 DRUG INTERACTIONS

9.1 Serious Drug Interactions

Serious Drug Interactions

- Patients on beta blockers. See Section 9.5 Drug-Food Interactions.

9.2 Drug Interactions Overview

Patients on 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.

Certain medications may lessen, for varying time periods, the skin test wheal and erythema responses elicited by allergens and histamine. Conventional antihistamines should be discontinued at least 5 days before skin testing. Long acting antihistamines should be discontinued for at least 3 weeks prior to skin testing. Topical steroids should be discontinued at the skin test site for at least 2-3 weeks before skin testing. Tricyclic antidepressants such as doxepin should be withheld for at least 7 days before skin testing. Topical local anesthetics may suppress the flare responses and should be avoided in skin test sites.

Patients should be instructed in the recognition of adverse reactions to immunotherapy, and in particular, to the symptoms of shock. Patients should be made to understand the importance of a 30-minute observation period, and be warned to return to the office promptly if symptoms occur after leaving.

9.4 Drug-Drug Interactions

The drugs listed in this table are based on either drug interaction case reports or studies, or potential interactions due to the expected magnitude and seriousness of the interaction (i.e., those identified as contraindicated).

Table [4] - Established or Potential Drug-Drug Interactions

[Proper / Common name]	Source of Evidence	Effect	Clinical comment
Beta Blocking Agents (ex. Acebutolol, Atenolol, Bisoprolol, Carvedilol, Labetalol, Metoprolol, Nadolol, Nebivolol, Oxprenolol, Pindolol, Sotalol, Propranolol, Timolol)	C	Increased reactivity on skin test	Beta-blockers may attenuate the response to epinephrine in the treatment of anaphylactic reactions. Noncardioselective beta-blockers, in particular, can antagonize the bronchodilating effects of epinephrine by blocking beta-2 adrenergic receptors in smooth muscles of the bronchial tree. Consider alternative medication or withholding medication for 24 hours prior to skin test or an immunotherapy injection; consult prescribing physician on risks of switching or withholding medication.
	C	Blocks cardio-stimulatory effects of epinephrine	
Beta2 Agonists (ex. Oral terbutaline and parenteral ephedrine)	T	Possible suppression of skin test response to allergen	Do not withhold if prescribed for asthma or other respiratory conditions.
First/Second Generation Antihistamines (ex. Chlorpheniramine, Dexchlorpheniramine, Diphenhydramine, Promethazine, Azelastine nasal, Fexofenadine, Levocabastine)	C	Suppression of wheal & flare response to skin test	First- and second-generation antihistamines should be discontinued 2 to 3 days before skin tests with notable exceptions being cetirizine, hydroxyzine, clemastine, loratadine, and cyproheptadine which may suppress skin test responses for up to 11 days.
Long acting antihistamines (ex. Cetirizine, Fexofenadine, Desloratadine, Hydroxyzine, Astemizole)	C	Suppression of wheal & flare response to skin test	Discontinue for at least 2 weeks prior to skin testing.
Histamine$_2$ Antagonists (ex. Ranitidine)	C	Mild suppression of skin test responses	Discontinue for 24 hours prior to skin testing.
Prostaglandin D_2 Inhibitors (ex. Indomethacin)	C	Increases wheal response on skin test	Withhold on day of skin testing.
Tricyclic antidepressants (ex. Amitriptyline, Amoxapine, Desipramine, Doxepin, Imipramine, Maprotiline, Nortriptyline, Protriptyline, Trimipramine)	C	Suppression of wheal & flare response to skin test	Withhold for at least 7 days before skin testing. Consult with prescribing physician to determine whether the risk of severe depression in patients who discontinue their medication outweighs the benefits that could be obtained from skin testing.
Benzodiazepines (ex. Clonazepam, Diazepam, Lorazepam, Midazolam, Alprazolam)	C, T	Suppression of wheal & flare response to skin test	Withhold for at least 7 days before skin testing. Consult with prescribing physician to determine whether the risk discontinuing medication outweighs the benefits that could be obtained from skin testing.

[Proper / Common name]	Source of Evidence	Effect	Clinical comment
Dopamine (ex. Pramipexole, Ropinirole, Rotigorine, Apomorphine, Bromocriptine, Amantadine, Fenoldopam, Piribedil, Aripiprazole, Brexpiprazole, Cabergoline, Cariprazine) (ex. Pramipexole, Ropinirole, Rotigorine, Apomorphine, Bromocriptine, Amantadine, Fenoldopam, Piribedil, Aripiprazold, Brexpiprazole, Cabergoline, Cariprazine)	C	Suppression of skin test response	Withhold on day of skin testing.
Topical local anesthetics (ex. Lidocaine, Mepivacaine, Ropivacaine, Bupivacaine, Chloroprocaine, Etidocaine, Tetracaine, Benzocaine, Prilocaine, Procaine, Proparacaine, Cocaine, Dibucaine, Lidoderm, Tetracaine)	C	May suppress the flare (i.e. erythema) response to skin test	Avoid skin testing at sites of topical administration; or withhold on day of test.
Oral corticosteroids (ex. Dexamethasone, Prednisolone, Betamethasone, Decadron, Beclomethasone Methylprednisolone, Medrol, Kenalog)	C	Suppression of skin test response	Avoid skin testing at sites where medication was applied for greater than 3 weeks.
	T	Reduced efficacy of allergy immunotherapy	There is a theoretical risk of reduced immune response to allergy immunotherapy in patients requiring systemic corticosteroid treatment
Topical steroids (ex. Hydrocortisone, Betamethasone, Mometasone, Clobetasol, Fluocinonide, Diflorasone)	C	Suppression of skin test response	Avoid skin testing at sites where medication was applied for greater than 3 weeks.
Omalizumab (Xolair)	C, T	Suppression of wheal & flare response to skin test	Discontinue for 5 half-lives (~100 days) prior to skin testing
In Vitro Immunoglobulin (IVIG)	T	Possible suppression of skin test response	Discontinue for 5 half-lives (4-6 months) prior to skin testing
Immunomodulating Biologics (ex. Tecfidera, Abetacept, Enbrel, Humira)	T	Reduced efficacy of allergy immunotherapy	There is a theoretical risk of reduced immune response to allergy immunotherapy in patients treated with biologics for other immune disorders.
* Legend: C = Case Study; CT = Clinical Trial; T = Theoretical			

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

The mechanisms by which hyposensitization is achieved are not completely understood. It has been shown that repeated injections of appropriate allergenic extracts will ameliorate the intensity of allergic symptoms upon contact with the allergenClinical studies which address the efficacy of immunotherapy are available. The allergens which have been studied are cat, mite, and some pollen extracts.

IgE antibodies bound to receptors on mast cell membranes are required for the allergic reaction and their level is probably related to serum IgE concentrations.

Immunotherapy has been associated with decreased levels of IgE, and also with increases in allergen specific IgG "blocking" antibody.

The histamine release response of circulating basophils to a specific allergen is reduced in some patients by immunotherapy, but the mechanism of this change is not yet clear.

The relationships among changes in blocking antibody, reaginic antibody, and mediator- releasing cells, and successful immunotherapy need study and clarification.

11 STORAGE, STABILITY AND DISPOSAL

The expiration date of the therapeutic extracts is listed on the container label. The extract should be stored at 2° - 8 °C and kept in this temperature range during office use. Dilutions are less stable than concentrates. If loss of potency is suspected, dilutions should be checked by skin testing with equal v/v dilutions of a freshly prepared dilution on individuals known to be allergic to the specific allergen.

12 SPECIAL HANDLING INSTRUCTIONS

A number of factors beyond our control could reduce the efficacy of this product or even result in an ill effect following its use. These include storage and handling of the product after it leaves our hands, diagnosis, dosage, method of administration and biological differences in individual patients. Because of these factors, it is important that this product be stored properly and that the directions be followed carefully during use.

For disposal of allergenic extracts, consider the use of a licensed disposal company or dispose of product in accordance with local, provincial, and federal regulations.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: Allergenic Extract-Pollens and Allergenic Extract-Non-Pollens

Pharmaceutical standard: The allergenic extract in each vial is referred to as a "bulk" extract or stock concentrate since it is designed primarily for the physician equipped to prepare dilutions and mixtures as required. The extract is sterile and intended for subcutaneous injection for immunotherapy. Unless specified otherwise, the concentration of extract supplied will in most cases be expressed in weight to volume (e.g., 1:10, 1:20 w/v, etc.) and will be the strongest available.

Active ingredients are the allergen(s) noted on the vial label. Preservative is 50 % glycerin (v/v), 0.4 % phenol, as indicated on the vial label. Additional ingredients are 0.5 % sodium chloride and 0.275 % sodium bicarbonate.

Source materials utilized in allergenic extract products include pollen, mold, animal epidermals, and insects.

Pollens are collected using techniques such as waterset or vacuuming, cleaned and purified to greater than 99 % single specie pollen (less than 1 % foreign particle presence).

Molds are typically grown on synthetic nutrient medias. Molds are derived from the surface growth (mycelia).

Animal source materials are collected from animals deemed to be healthy at the time of collection by a veterinarian or individual trained and certified by a veterinarian. Epidermals include feathers, hair and dander, or the whole epidermis (pelt), as described on product labelling.

Regular process epidermals are extractions of the source material without additional processing except that certain materials are defatted. AP™ (acetone precipitated) Epidermal source materials are derived from the precipitate formed when acetone is added to an aqueous extract. The resulting precipitate is dried, and becomes the source material for the AP™ product.

Insects are collected in whole body form. Extractions take place as whole body or ground insects.

Various other environmental materials are available as allergenic extracts, and information on these materials can be obtained by contacting Omega Laboratories' Customer Service Department.

Product Characteristics: Appearance is clear to slightly opalescent. Parenteral Drug Products should be inspected visually for particulate matter and discoloration, prior to administration, whenever solution and container permit.

14 CLINICAL TRIALS

No clinical trials were sponsored by Jubilant HollisterStier LLC for the Allergenic Extract – Pollens or the Allergenic Extract Non-Pollens when the products were approved in 1997.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology: No long-term animal studies have been performed to evaluate carcinogenic or mutagenic potential or whether ALLERGENIC EXTRACT – POLLENS and ALLERGENIC EXTRACT – NON-POLLENS affects fertility in males or females.

Carcinogenicity: No long-term animal studies have been performed to evaluate carcinogenic or mutagenic potential or whether ALLERGENIC EXTRACT – POLLENS and ALLERGENIC EXTRACT – NON-POLLENS affects fertility in males or females.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

ALLERGENIC EXTRACT – POLLENS and
ALLERGENIC EXTRACT – NON-POLLENS
Allergenic Extracts in Bulk Vials for Subcutaneous Injection Immunotherapy

Read this carefully before you are provided ALLERGENIC EXTRACT – POLLENS or ALLERGENIC EXTRACT – NON-POLLENS. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare

professional about your medical condition and treatment and ask if there is any new information about ALLERGENIC EXTRACT – POLLENS or ALLERGENIC EXTRACT – NON-POLLENS prior to each doctor visit where an injection is provided.

Serious Warnings and Precautions
• The product should only be provided by physicians who are experienced in the use of allergenic extracts, or for use under the guidance of an allergist. • Allergenic extracts may potentially cause a severe life-threatening systemic reaction (anaphylaxis), which can result in death. Therefore, emergency measures and personnel trained in their use must be available immediately in the event of such a reaction. You should also be instructed to recognize serious symptoms and contact the physician's office if symptoms occur. • If you are on beta blockers, you 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. • The treatment process with this product should not cause bleeding.

What are ALLERGENIC EXTRACT – POLLENS or ALLERGENIC EXTRACT – NON-POLLENS used for?

"ALLERGENIC EXTRACT – POLLENS and ALLERGENIC EXTRACT – NON-POLLENS have been approved for the following indication(s) by Health Canada. This means they have passed Health Canada's review and can be purchased and administered in Canada. For more information, talk to your healthcare professional."

- These products are used for the treatment of patients with specific allergic conditions.

How do ALLERGENIC EXTRACT – POLLENS or ALLERGENIC EXTRACT – NON-POLLENS work?

You will receive injections of specific extracts based upon skin testing results. The injections are initially diluted. The concentration is increased over time until maintenance concentration doses can be achieved. The injections are taken to alleviate and/or eliminate your allergenic response to environmental allergens.

What are the ingredients in ALLERGENIC EXTRACT – POLLENS and ALLERGENIC EXTRACT – NON-POLLENS?

- **ALLERGENIC EXTRACT – POLLENS:**
  Medicinal ingredients: Various Pollen Extracts
  Non-medicinal ingredients: Glycerin, Sodium chloride and Sodium bicarbonate
- **ALLERGENIC EXTRACT – NON-POLLENS:**
  Medicinal ingredients: Various Epidermal, Insect and Mold Extracts
  Non-medicinal ingredients: Glycerin, Sodium chloride and Sodium bicarbonate

ALLERGENIC EXTRACT – POLLENS and ALLERGENIC EXTRACT – NON-POLLENS come in the flowing dosage forms:

- **ALLERGENIC EXTRACT – POLLENS:**
  Dosage Form: Solution
  Strength *(Product Dependent)*: 1:20 w/v, 1:50 w/v, 100 Amb a 1 UA/mL and 200 Amb a 1 UA/mL)
- **ALLERGENIC EXTRACT – NON-POLLENS:**
  Dosage Form – Solution
  Strength *(Product Dependent)*: 1:10 w/v, 1:50 w/v, 1:100 w/v, 1:650 w/v and 1:1,000 w/v)

Do not use ALLERGENIC EXTRACT – POLLENS or ALLERGENIC EXTRACT – NON-POLLENS if:
Your healthcare professional has not prescribed it and administered it within their medical office.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take ALLERGENIC EXTRACT – POLLENS or ALLERGENIC EXTRACT – NON-POLLENS. Talk about any health conditions/circumstances you may have, including:

- Cancer
- Heart Disease
- Female/Male Fertility concerns
- Respiratory Issues
- Allergen Sensitivity/Resistance
- Skin irritations
- Pregnancy
- Nursing Mother

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines. The following may interact with ALLERGENIC EXTRACT – POLLENS or ALLERGENIC EXTRACT – NON-POLLENS:

When discussing with your healthcare professional, make specific reference to the following type of medications:

Medication Type	Treatment of:
Beta Blockers	High blood pressure
Dopamine	Low blood pressure, Parkinson's disease, Cardiac or Kidney function
Beta2 Agonists Omalizumab/Xolair Oral corticosteroids/Inhalers	Asthma/COPD
Prostaglandin D2 Inhibitors	Asthma, allergic rhinitis, and atopic dermatitis
Antihistamines	Motion Sickness, nausea or insomnia
Histamine2 Antagonists	Gastric ulcers, acid reflux or heart burn
Antidepressants	Depression, chronic pain, addiction or mental health conditions
Benzodiazepines	Anxiety, insomnia and seizures
Topical local anesthetics	Creams or lotions that numb the skin to reduce pain or itching
Topical steroids	Inflammatory skin conditions
In Vitro Immunoglobulin	In vitro fertilization (IVF) and recurrent pregnancy loss
Immunomodulating Biologics	Autoimmune diseases, rheumatoid arthritis, psoriasis, Crohn's disease; oncologic, allergic, rheumatologic, and neurologic conditions

How to take ALLERGENIC EXTRACT – POLLENS or ALLERGENIC EXTRACT – NON-POLLENS:

- Immunotherapy treatment is performed by a healthcare professional by injecting specific extract(s) at specific dilutions to build tolerance until maintenance dosing is achieved and completed. The healthcare provider will inject the extract subcutaneously with a sterile needle.
- This process should not make you bleed.

Usual dose:

- The usual dose is dependent on where you are in the treatment process, if a new lot of product is being used, if you miss an injection time-line or if an adverse reaction occurs. If you are not aware, be sure to ask your health care provider where you are in the process and what dose you are receiving.

Overdose:

- An overdose could occur based on your sensitivity to the extract(s) and in rare instances could result in anaphylactic symptoms. It is imperative that the physician administering your allergenic extracts understand and be prepared for the treatment of severe reactions.

What are possible side effects from using ALLERGENIC EXTRACT – POLLENS or ALLERGENIC EXTRACT – NON-POLLENS?

These are not all the possible side effects you may have when taking ALLERGENIC EXTRACT – POLLENS or ALLERGENIC EXTRACT – NON-POLLENS. If you experience any side effects not listed here, tell your healthcare professional.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
VERY COMMON			
N/A			
COMMON			
N/A			
RARE			
Anaphylaxis		X	Seek emergency medical help immediately.

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

This leaflet was prepared by Jubilant HollisterStier LLC.

Last Revised: November 26, 2024

HollisterStier Allergy

PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

ALLERGENIC EXTRACT – POLLENS, ALLERGENIC EXTRACT NON-POLLENS and
NEGATIVE SKIN TEST CONTROL - GLYCERIN

Allergenic Extracts for Scratch, Prick, Puncture (Percutaneous) Testing Diagnostic Agent

Schedule D-Biologic Drugs

360400-C09

Rev. October 18, 2024

Allergenic Extract – Pollens and Allergenic Extract – Non-Pollens, indicated for: The diagnosis of allergic conditions have been issued market authorization without conditions.

Manufactured by:	Distributed in Canada by:	Date of Initial Authorization:
Jubilant HollisterStier LLC 3525 North Regal Street Spokane, Washington 99207 USA	Omega Laboratories 11 177 Hamon Montréal, Québec H3M 3E4 Canada	ALLERGENIC EXTRACT-NON-POLLENS: December 01, 1997 ALLERGENIC EXTRACT-POLLENS: December 05, 1997 NEGATIVE SKIN TEST CONTROL – GLYCERIN: June 06, 2014

ALLERGENIC EXTRACT – POLLENS

Submission Control Number: 285785

Date of Revision: November 26, 2024

ALLERGENIC EXTRACT NON-POLLENS

Submission Control Number: 285782

RECENT MAJOR LABEL CHANGES

All Sections and Subsections updated to Plain Language Labeling Format	10/2024

TABLE OF CONTENTS

Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1. INDICATIONS

ALLERGENIC EXTRACT – POLLENS and ALLERGENIC EXTRACT – NON-POLLENS Scratch, Prick, Puncture (Percutaneous) Diagnostic Testing labeled in 50 % Glycerin are indicated for:

- Diagnosis of allergic conditions.

In addition to a carefully taken history, the use of glycerin-containing extracts in scratch, prick or puncture testing is an accepted method in the diagnosis of allergic conditions. Extracts of all allergens do not produce equivalent results in scratch, prick or puncture tests. The intensity of the skin reactions produced will be determined by two factors: the degree of sensitivity of the patient, and the nature of the allergenic extract applied.

Scratch, prick or puncture tests are not as sensitive as the intradermal test, but are safer and cause less discomfort. They may, therefore, be the method of choice when a large number of tests are needed, or when testing the pediatric patient. In some cases, where the relatively insensitive scratch, prick or puncture tests are negative or do not confirm the allergic history, follow-up intradermal tests may be positive. However, ANTIGENS PRODUCING LARGE 3 to 4+ SCRATCH, PRICK OR PUNCTURE TESTS SHOULD NOT BE TESTED INTRADERMALLY.

Certain diagnostics carry labelling which states Allergenic Extract for Diagnostic Use Only. Data to support the therapeutic use of products labelled with this statement have not been established.

1.1. Pediatrics

Allergenic extracts for diagnostic use have been given safely in infants and young children (see Section 7.1.3 Pediatrics).

1.2. Geriatrics

Geriatrics: Evidence from clinical studies and experience suggests that use in the geriatric population is associated with differences in safety or effectiveness (see Section 7.1.4 Geriatrics).

2. CONTRAINDICATIONS

- There are no known absolute contraindications to allergy skin testing. Patients with cardiovascular diseases or pulmonary may be at higher risk for severe adverse reactions (see Section 3 SERIOUS WARNINGS AND PRECAUTIONS BOX, Section 7 WARNINGS AND PRECAUTIONS, Section 9 DRUG INTERACTIONS).

3. SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions
• The product is intended for use only by physicians who are experienced in the use of allergenic extracts, or for use under the guidance of an allergist. • Allergenic extracts may potentially elicit a severe life-threatening systemic reaction (anaphylaxis), which can result in death. Therefore, emergency measures and personnel trained in their use must be available immediately in the event of such a reaction. Patients should be instructed to recognize adverse reaction symptoms and cautioned to contact the physician's office if symptoms occur. • Patients on 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 (see Section 9 DRUG INTERACTIONS). • This product should never be injected intravenously. Refer also to the Section 2 CONTRAINDICATIONS, Section 4 DOSAGE AND ADMINISTRATION, Section 5 OVERDOSAGE, Section 7 WARNINGS AND PRECAUTIONS, and Section 8 ADVERSE REACTIONS for further

discussion.

4. DOSAGE AND ADMINISTRATION

4.1. Dosing Considerations

For individuals suspected to be at greater risk for anaphylaxis (for example, as indicated by a history of allergen-induced anaphylaxis), initiate percutaneous testing with a sequence of serial 10-fold dilutions of undiluted allergenic extract spaced 15-20 minutes apart (see Section 4.2 RECOMMENDED DOSE AND DOSAGE ADMINISTRATION).

There is a potential for systemic reactions to occur, but it must be remembered that allergenic extracts are highly potent in sensitive individuals and OVERDOSE could result in anaphylactic symptoms. Therefore, it is imperative that physicians administering allergenic extracts understand and be prepared for the treatment of severe reactions.

4.2. Recommended Dose and Dosage Adjustment

The dose is the same in patients of all age groups. Unless an individual is suspected to be at greater risk for anaphylaxis (see Section 4.1 DOSING CONSIDERATIONS), the initial starting dose is 1 drop (approximately 0.05 mL) of undiluted allergenic extract. The dose amount may be less when using self-loading skin test devices.

4.3. Reconstitution

See Section 4.2 RECOMMENDED DOSE AND DOSAGE ADJUSTMENT and Section 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.

Table – Reconstitution

Product	Vial Size	Volume of Diluent to be Added to Vial	Approximate Available Volume	Concentration
AP Dog Hair-Dander	5 mL (Diagnostic)	N/A – Concentrate Used	5 mL	1:100 w/v
AP Cattle Hair and Dander / AP Horse Hair and Dander	5 mL (Diagnostic)	N/A – Concentrate Used	5 mL	1:50 w/v
Non-AP Epidermals/Inhalants	5 mL (Diagnostic)	N/A – Concentrate Used	5 mL	1:10 w/v
UF Dog Hair and Dander	5 mL (Diagnostic)	N/A – Concentrate Used	5 mL	1:650 w/v
Grass Pollen	5 mL (Diagnostic)	N/A – Concentrate Used	5 mL	1:20 w/v
Insects	5 mL (Diagnostic)	N/A – Concentrate Used	5 mL	1:10 w/v
Molds	5 mL (Diagnostic)	N/A – Concentrate Used	5 mL	1:10 w/v or 1:1,000 w/v
Tree Pollen	5 mL (Diagnostic)	N/A – Concentrate Used	5 mL	1:20 w/v or 1:50 w/v
Ragweed	5 mL (Diagnostic)	N/A – Concentrate Used	5 mL	100 Amb a 1 UA/mL or 200 Amb a 1 UA/mL
Weed Pollen	5 mL (Diagnostic)	N/A – Concentrate Used	5 mL	1:20 w/v

4.4. Administration

All skin tests should be validated by appropriate positive control tests (e.g., histamine) and negative control tests [e.g., Glycerin, Sterile Albumin Saline with Phenol (0.4%), or Buffered Saline with Phenol (0.4%)]. The negative control test should be the same material used as a diluting fluid in the tested extracts. Diluting fluid is used in the same way as an active test extract.

Test sites should be examined at 15 and 20 minutes immediate reactions to allergens typically peak at 15 minutes. To prevent excessive absorption, wipe off antigens producing large reactions as soon as the wheal appears. Record the size of the reaction. Delayed reactions rarely occur from tests, so it may be helpful to examine the test sites in 24 hours.

Use of Self-Loading Devices. The criteria for interpretation of positive and negative results of percutaneous allergen tests (wheal diameter) are specific to the device used.

Use of Scarifiers and Spacing. Make scarifications at least 2.5 cm apart. Use more space between pollen tests to prevent smearing into adjacent sites. Hold the scarifier between the thumb and index finger, press the sharp edge of the instrument against the skin and twirl instrument rapidly. The scratch should disrupt only the outer layers of epidermis, but should not produce immediate oozing of blood. The amount of pressure needed to produce a satisfactory scratch will vary between patients according to the thickness or fragility of their skin. Experience will indicate the proper amount of pressure to exert in making the scratch. If the scarifier is kept sharp and the scratch made quickly, discomfort to the patient is minimized.

Use of Prick Test Needles. The skin is cleaned and single drops of each extract applied to the properly identified test sites. A small, sterile disposable needle, such as a 1/2-inch 26-gauge needle (with the bevel up), a bifurcated vaccinating needle, or a Prick Lancetter™ is inserted through the drop superficially into the skin, the skin lifted slightly and the needle withdrawn. No bleeding should be produced. After about 1 minute the extract may be wiped away.

Most Satisfactory Sites for Testing

Prior to testing, clean the skin area to be tested with ether or alcohol and allow to dry. Use a sterile instrument for each patient. The back or the volar surface of the arms are the most satisfactory sites for testing. Skin of the posterior thighs or abdomen may be used if necessary. Avoid very hairy areas where possible, since the reactions will be smaller and more difficult to interpret. The most satisfactory areas of the back are from the posterior axillary fold to 2.5 cm from the spinal column, and from the top of the scapula to the lower rib margins. The best areas of the arms are the volar surfaces from the axilla to 2.5 or 5 cm above the wrist skipping the antecubital space.

Use of Antigen Mixes

The use of mixed or unrelated antigens for skin testing is not recommended since in the case of a positive reaction it does not indicate which antigens are responsible, and in the case of a negative reaction it fails to indicate whether the individual antigens at full concentration would give a positive reaction.

The extracts for scratch, prick or puncture testing are supplied in dropper vials and should be kept in a rack or box in rows of 10 vials corresponding to the rows of tests to be applied to the skin.

Reading Skin Test Reactions

Testing is performed to identify patients that exhibit an allergic response at the site of administration. False positive/negative reactions may occur. A positive reaction consists of an urticarial wheal with surrounding erythema (resembling somewhat a mosquito bite reaction) larger than the control site. The smallest reaction considered positive is erythema with a central papule at least 3-5 mm in diameter. In some instances when there

is no reaction at the control site, erythema may be considered an indication of sensitivity. In general, the size of wheal and erythema response correlates directly with the patient's sensitivity to that allergen. If using self-loading devices, refer to the manufacturer's directions for use.

Interpretation of test results is variable depending on the test method and device employed. Manufacturers of commercially available skin test devices often recommend a specific grading system. When available, follow the manufacturer's recommended grading system.

The sum of a skin response is the sum of the longest diameter and the mid-point orthogonal diameter.

Ragweed Pollen: (Short Ragweed or Giant and Short Ragweed Mixture) Amb a 1: Short Ragweed extract in 50 % glycerin containing 200 Units of Amb a 1/mL or Giant and Short Ragweed Mix in 50 % glycerin containing 100 Units of Amb a 1/mL, are usually used for scratch, prick or puncture testing.

Refer to the following table to determine the skin test sensitivity grade. The corresponding ΣE (sum of the longest diameter and the mid-point orthogonal diameters of erythema) is also presented.

Grade	Erythema mm	Papule or Wheal mm	Corresponding mm Σ
0	<5	<5	<10
±	5-10	5-10	10-20
1+	11-20	5-10	20-40
2+	21-30	5-10	40-60
3+	31-40	10-15[a]	60-80
4+	>40	>15[b]	>80
a. or with pseudopods.			
b. or with many pseudopods.			

A positive skin reaction to any allergen must be interpreted in light of the patient's history of symptoms, time of the year, known exposures, and eating habits.

THE SKIN TESTS ARE IN NO WAY A SUBSTITUTE FOR A CAREFUL ALLERGIC HISTORY. RATHER THEY SERVE AS ADDITIONAL INFORMATION TO AID IN IDENTIFYING CAUSATIVE ALLERGENS IN PATIENTS WITH ALLERGIC DISORDERS.

5. OVERDOSAGE

See Section 4 DOSAGE AND ADMINISTRATION and Section 8 ADVERSE REACTIONS.

For management of a suspected drug overdose, contact your regional poison control center.

6. DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

In 5 mL dropper bottles of extract at 1:10 w/v, except pollens at 1:20 w/v; Short Ragweed at 200 Amb a 1 Units/mL, Giant and Short Ragweed Mixture at 100 Amb a 1 Units/mL; and AP™ Cattle Hair and Dander plus Horse Hair and Dander extracts at 1:50 w/v, AP™ Dog Hair and Dander at 1:100 w/v; and UF Dog 1:650 w/v.

Weight per volume (w/v). For regular extracts this describes the extraction ratio, i.e., the amount of crude allergen added to the extracting fluid. A 1:10 extract, therefore indicates that the solution contains the extracted material from one gram of raw material added to each 10 mL of extracting fluid. The amount and composition of extracted materials will vary with the type of antigen, the extracting fluid, duration of extraction, pH, temperature, and other variables.

AP™ (acetone precipitated) extracts, if present, are prepared by reconstituting dry, allergenically active concentrates produced by precipitation process from extracts of raw materials. For those AP™ extracts labelled on

a weight per volume (w/v) basis, the strength designation indicates the dry weight of finished (acetone) precipitate per volume of reconstituting fluid. For example, 1:50 (w/v) means that each gram of dry precipitate obtained from the original extract is reconstituted in 50 mL of solution.

Amb a 1 (UA/mL). Amb a 1 is considered the most important allergen in Ragweed Pollen and is measured by agar gel immune-diffusion against a reference standard established by the CBER. The concentration of Amb a 1 is expressed as units of Amb a 1 per mL of extract.

Table #1 – ALLERGENIC EXTRACT – NON-POLLENS Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength / Composition	Non-medicinal Ingredients
Percutaneous (scratch, prick/puncture)	Solution/ Refer to Product List Table	50 % Glycerin (v/v) 0.5 % Sodium chloride (w/v) 0.275 % Sodium bicarbonate (w/v)

Table #2 – ALLERGENIC EXTRACT – POLLENS Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength / Composition	Non-medicinal Ingredients
Percutaneous (scratch, prick/puncture)	Solution/ Refer to Product List Table	Variable % Glycerin or Phenol 0.5 % Sodium chloride (w/v) 0.275 % Sodium bicarbonate (w/v)

Table – Product List

ALLERGENIC EXTRACT - POLLENS ANTIGEN		CONC.
TREE	ACACIA, GOLDEN	1:20 w/v
	ALDER, RED	
	ASH, WHITE	
	BEECH, AMERICAN	
	BIRCH MIX (PRW)	
	BOTTLEBRUSH TREE	
	BOXELDER/MAPLE MIX (BHR)	
	CEDAR, MOUNTAIN	
	CEDAR, RED	
	COTTONWOOD, COMMON	
	CYPRESS, ARIZONA	
	ELM, AMERICAN	
	ELM, CHINESE	
	GUM, SWEET	
	HACKBERRY	
	HICKORY, SHAGBARK	
	MAPLE, HARD/SUGAR	
	MELALEUCA	
	MESQUITE TREE	
	MULBERRY MIX (RW)	
	OAK MIX (RVW)	
	OAK, RED	
	OLIVE TREE	
	PALM, QUEEN	
	PECAN TREE	
	PINE MIX (LY)	
	PRIVET, COMMON	
	SYCAMORE, AMERICAN	
	TREE MIX #5	
	TREE MIX #11	
	WALNUT, BLACK	
	WILLOW, BLACK	
	CYPRESS, BALD	1:50 w/v

ALLERGENIC EXTRACT – POLLENS ANTIGEN (CONT.)		CONC.
GRASS	BAHIA GRASS	1:20 w/v
	BROME, SMOOTH	
	CORN, COMMON CULTIVATED	
	JOHNSON GRASS	
	OATS, COMMON CULTIVATED	
WEED	CARELESS WEED	1:20 w/v
	CARELESS/PIGWEED (CR)	
	COCKLEBUR, COMMON	
	DOCK/SORREL MIX (DS)	
	DOG FENNEL, EASTERN	
	GOLDENROD	
	KOCHIA	
	LAMBS QUARTERS	
	MARSHELDER/POVERTY MIX (BPT)	
	NETTLE	
	PIGWEED, ROUGH REDOOT	
	PLANTAIN, ENGLISH	
	RAGWEED, GIANT	
	RAGWEED, WESTERN	
	RUSSIAN THISTLE	
	SAGEBRUSH, MUGWORT	
	SCALE, WING	
	SHEEP SORREL	
	WEED MIX 2630	
	RAGWEED, MIX (GS)	100 Amb a 1 UA/mL
	RAGWEED, SHORT	200 Amb a 1 UA/mL

ALLERGENIC EXTRACT – NON-POLLENS ANTIGEN		CONC.
EPIDERMAL	DOG HAIR & DANDER	1:10 w/v
	FEATHER MIX	
	GUINEA PIG HAIR & DANDER	
	A.P. CATTLE HAIR & DANDER	1:50 w/v
	A.P. HORSE HAIR & DANDER	
	A.P. DOG HAIR & DANDER	1:100 w/v
	U.F. DOG HAIR & DANDER	1:650 w/v
INSECT	COCKROACH, AMERICAN	1:10 w/v
	COCKROACH, GERMAN	
	COCKROACH MIX	
	FIRE ANT, RED	
MOLD	*ALTERNARIA TENUIS*	1:10 w/v
	ASPERGILLUS FUMIGATUS	
	CEPHALOSPORIUM ACREMORIUM	
	EPICACCUM NIGRUM	
	FUSARIUM VASINFECTUM	
	HELMINTHOSPORIUM INTERSEMINATUM	
	MUCOR RACEMOSUS	
	PENICILLIUM NOTATUM	
	PHOMA HERBARUM	
	PULLULARIA PULLULANS	
	CANDIDA ALBICANS	
	CANDIDA ALBICANS	1:1,000 w/v

7. WARNINGS AND PRECAUTIONS

General

Please see Section 3 SERIOUS WARNINGS AND PRECAUTIONS BOX.

Always have injectable epinephrine and a tourniquet available when tests are being made. Emergency resuscitation measures and personnel trained in their use should be available immediately in the event of a serious systemic or anaphylactic reaction not responsive to the above measures. See Section 8 ADVERSE REACTIONS.

Generally, 50-60 scratch, prick or puncture tests can be applied safely at one sitting. Patients whose history suggests severe sensitivity should have only 5-10 tests applied at a time and these tests applied to the volar surface of one arm. These tests should not all be of the same type of antigen; that is, all grass pollens, all weed pollens, all danders, etc. One or two tests from several classes of antigens should be applied at a time.

As soon as a large wheal begins to develop, wipe the antigen from it with a damp cotton sponge. After 30 minutes wipe off all the antigens with a damp cotton sponge, followed by a dry cotton sponge. Be careful not to wipe antigen from a positive reaction into an adjacent scratch site.

Carcinogenesis and Mutagenesis

Long-term studies in animals have not been conducted with allergenic extracts to determine their potential for carcinogenicity or mutagenicity. See Section 16 NON-CLINICAL TOXICOLOGY.

Cardiovascular

Patients with cardiovascular diseases or pulmonary diseases such as symptomatic asthma, and/or who are receiving cardiovascular drugs such as beta blockers, may be at higher risk for severe adverse reactions (see Section 3 SERIOUS WARNINGS AND PRECAUTIONS BOX, Section 9 DRUG INTERACTIONS). These patients may also be more refractory to the normal anaphylaxis treatment regimen.

Reproductive Health: Female and Male Potential

- **Fertility**

  Long-term studies in animals have not been conducted with allergenic extracts to determine their potential for impairment of fertility. See Section 7.1.1 Pregnant Women.

Respiratory

The presence of asthmatic signs and symptoms appear to be an indicator for severe reactions following allergy testing or injections. An assessment of airway obstruction either by measurement of peak flow or an alternate procedure may provide a useful indicator as to the advisability of administering diagnostic testing or an allergy injection.

Sensitivity/Resistance

Excessively large local reactions or systemic reactions are more likely to occur if the patient is skin tested shortly after exposure to large amounts of antigen to which they are sensitive. Use caution when skin testing patients during a season when pollen is present or after exposure to inhalant allergens that produce symptoms. See Section 8 ADVERSE REACTIONS.

Skin

Allergenic extracts for percutaneous testing, used according to Section 4 DOSAGE AND ADMINISTRATION, produce erythema or erythema and wheal reactions in patients with significant IgE-mediated sensitivity to the relevant allergen. This allergic inflammatory response, although not completely understood, is thought to begin with reaction of antigen with IgE on the surface of basophils or mast cells, which initiates a series of biochemical events resulting in the production of histamine and other mediators. These, in turn, produce the immediate-type "wheal and flare" skin reaction. See Section 8.1 Adverse Reaction Overview.

If a severe local reaction occurs during scratch, prick or puncture testing, WIPE OFF test antigen. Large, persistent local reactions or minor exacerbations of the patient's allergic symptoms may be treated by local cold applications and/or the use of oral antihistamines, but they should be considered a warning of possible severe systemic reactions.

7.1. Special Populations

7.1.1. Pregnant Women

Use in Pregnancy

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.

On the basis of histamine's known ability to contract the uterine muscle, allergenic extracts should be used cautiously in pregnant women.

7.1.2. Breast Feeding

There are no current studies on the secretion of the allergenic extract components in human milk, or effect on the nursing infant. Because many drugs are excreted in human milk, caution should be exercised when allergenic extracts are administered to a nursing woman.

7.1.3. Pediatrics

The dose is the same in patients of all age groups.

Wheal sizes in response to allergen skin testing can be smaller in infants than in adults. The skin response to histamine parallels that for allergens; therefore, appropriate positive control skin tests should always be performed.

7.1.4. Geriatrics

The dose is the same in patients of all age groups. Skin test wheal size decreases with age, therefore, appropriate positive skin test controls should always be performed.

8. ADVERSE REACTIONS

8.1. Adverse Reaction Overview

Information to be Provided to the Patient

Patients should be instructed in the recognition of adverse reactions to diagnostic testing. Patients should be made to understand the importance of a 30-minute observation period, and be warned to return to the office promptly if symptoms occur after leaving.

Systemic Reactions

See Section 3 SERIOUS WARNINGS AND PRECAUTIONS BOX.

Frequency data for adverse reactions resulting from allergenic extract administration for testing and treatment show that risk is low

It cannot be overemphasized that, under certain unpredictable combinations of circumstances, anaphylactic shock is a possibility. Other possible systemic reaction symptoms include fainting, pallor, bradycardia, hypotension, angioedema, cough, wheezing, conjunctivitis, rhinitis and urticaria.

If a systemic or anaphylactic reaction does occur, WIPE OFF test antigen, and apply epinephrine.

Emergency resuscitation measures and personnel trained in their use should be available immediately in the event of a serious systemic or anaphylactic reaction not responsive to the above measures. Patients should have an emergency anaphylaxis kit containing epinephrine available and be instructed in its use for emergency treatment of possible systemic reactions occurring at times after the patient has departed from treatment premises.

8.5. Post-Market Adverse Reactions

The most frequently reported serious and expected reactions is anaphylaxis.

9. DRUG INTERACTIONS

9.1. Serious Drug Interactions

Serious Drug Interactions

- Patients on beta blockers. See Section 9.4 Drug-Drug Interactions.

9.2. Drug Interactions Overview

Patients on 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.

Certain medications may lessen the skin test wheal and erythema responses elicited by allergens and histamine for varying time periods. Conventional antihistamines should be discontinued at least 5 days before skin testing. Long acting antihistamines should be discontinued for at least 3 weeks prior to skin testing. Topical steroids should be discontinued at the skin test site for at least 2-3 weeks before skin testing.

Tricyclic antidepressants such as doxepin should be withheld for at least 7 days before skin testing. Topical local anesthetics may suppress the flare responses and should be avoided in skin test sites.

9.4. Drug-Drug Interactions

The drugs listed in this table are based on either drug interaction case reports or studies, or potential interactions due to the expected magnitude and seriousness of the interaction (i.e., those identified as contraindicated).

Table #3 - Established or Potential Drug-Drug Interactions

[Proper/Common name]	*Source of Evidence	Effect	Clinical comment
Beta Blocking Agents (ex. Acebutolol, Atenolol, Bisoprolol, Carvedilol, Labetalol, Metoprolol, Nadolol, Nebivolol, Oxprenolol, Pindolol, Sotalol, Propranolol, Timolol)	C	Increased reactivity on skin test	Beta-blockers may attenuate the response to epinephrine in the treatment of anaphylactic reactions. Noncardioselective beta-blockers, in particular, can antagonize the bronchodilating effects of epinephrine by blocking beta-2 adrenergic receptors in smooth muscles of the bronchial tree. Consider alternative medication or withholding medication for 24 hours prior to skin test or an immunotherapy injection; consult prescribing physician on risks of switching or withholding medication.
	C	Blocks cardio-stimulatory effects of epinephrine	
Beta2 Agonists (ex. Oral terbutaline and parenteral ephedrine)	T	Possible suppression of skin test response to allergen	Do not withhold if prescribed for asthma or other respiratory conditions.
First/Second Generation Antihistamines (ex. Chlorpheniramine, Dexchlorpheniramine, Diphenhydramine, Promethazine, Azelastine nasal, Fexofenadine, Levocabastine)	C	Suppression of wheal & flare response to skin test	First- and second-generation antihistamines should be discontinued 2 to 3 days before skin tests with notable exceptions being cetirizine, hydroxyzine, clemastine, loratadine, and cyproheptadine which may suppress skin test responses for up to 11 days.
Long acting antihistamines (ex. Cetirizine, Fexofenadine, Desloratadine, Hydroxyzine, Astemizole)	C	Suppression of wheal & flare response to skin test	Discontinue for at least 2 weeks prior to skin testing.
Histamine$_2$ Antagonists (ex. Ranitidine)	C	Mild suppression of skin test responses	Discontinue for 24 hours prior to skin testing.
Prostaglandin D$_2$ Inhibitors (ex. Indomethacin)	C	Increases wheal response on skin test	Withhold on day of skin testing.

[Proper/Common name]	*Source of Evidence	Effect	Clinical comment
Tricyclic antidepressants (ex. Amitriptyline, Amoxapine, Desipramine, Doxepin, Imipramine, Maprotiline, Nortriptyline, Protriptyline, Trimipramine)	C	Suppression of wheal & flare response to skin test	Withhold for at least 7 days before skin testing. Consult with prescribing physician to determine whether the risk of severe depression in patients who discontinue their medication outweighs the benefits that could be obtained from skin testing.
Benzodiazepines (ex. Clonazepam, Diazepam, Lorazepam, Midazolam, Alprazolam)	C, T	Suppression of wheal & flare response to skin test	Withhold for at least 7 days before skin testing. Consult with prescribing physician to determine whether the risk discontinuing medication outweighs the benefits that could be obtained from skin testing.
Dopamine (ex. Pramipexole, Ropinirole, Rotigorine, Apomorphine, Bromocriptine, Amantadine, Fenoldopam, Piribedil, Aripiprazole, Brexpiprazole, Cabergoline, Cariprazine) (ex. Pramipexole, Ropinirole, Rotigorine, Apomorphine, Bromocriptine, Amantadine, Fenoldopam, Piribedil, Aripiprazold, Brexpiprazole, Cabergoline, Cariprazine)	C	Suppression of skin test response	Withhold on day of skin testing.
Topical local anesthetics (ex. Lidocaine, Mepivacaine, Ropivacaine, Bupivacaine, Chloroprocaine, Etidocaine, Tetracaine, Benzocaine, Prilocaine, Procaine, Proparacaine, Cocaine, Dibucaine, Lidoderm, Tetracaine)	C	May suppress the flare (i.e. erythema) response to skin test	Avoid skin testing at sites of topical administration; or withhold on day of test.
Oral corticosteroids (ex. Dexamethasone, Prednisolone, Betamethasone, Decadron, Beclomethasone Methylprednisolone, Medrol, Kenalog)	C	Suppression of skin test response	Avoid skin testing at sites where medication was applied for greater than 3 weeks.
	T	Reduced efficacy of allergy immunotherapy	There is a theoretical risk of reduced immune response to allergy immunotherapy in patients requiring systemic corticosteroid treatment
Topical steroids (ex. Hydrocortisone, Betamethasone, Mometasone, Clobetasol, Fluocinonide, Diflorasone)	C	Suppression of skin test response	Avoid skin testing at sites where medication was applied for greater than 3 weeks.
Omalizumab (Xolair)	C, T	Suppression of wheal & flare response to skin test	Discontinue for 5 half-lives (~100 days) prior to skin testing
In Vitro Immunoglobulin (IVIG)	T	Possible suppression of skin test response	Discontinue for 5 half-lives (4-6 months) prior to skin testing
Immunomodulating Biologics (ex. Tecfidera, Abetacept, Enbrel, Humira)	T	Reduced efficacy of allergy immunotherapy	There is a theoretical risk of reduced immune response to allergy immunotherapy in patients treated with biologics for other immune disorders.

* Legend: C = Case Study; CT = Clinical Trial; T = Theoretical

9.5. Drug-Food Interactions

Interactions with food have not been established.

9.6. Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7. Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10. CLINICAL PHARMACOLOGY

10.1. Mechanism of Action

Allergenic extracts for scratch, prick or puncture testing, used according to the DOSAGE AND ADMINISTRATION section, produce erythema or erythema and wheal reactions in patients with significant IgE-mediated sensitivity to the relevant allergen. This allergic inflammatory response, although not completely understood, is thought to begin with reaction of antigen with IgE on the surface of basophils or mast cells, which initiates a series of biochemical events resulting in the production of histamine and other mediators. These, in turn, produce the immediate-type “wheal and flare” skin reaction.10.2 Pharmacodynamics

11. STORAGE, STABILITY AND DISPOSAL

The expiration date of the diagnostic extracts is listed on the container label. The extract should be stored at 2-8 °C and kept at this temperature range during office use.

12. SPECIAL HANDLING INSTRUCTIONS

A number of factors beyond our control could reduce the efficacy of this product or even result in an ill effect following its use. These include storage and handling of the product after it leaves our hands, diagnosis, dosage, method of administration, and biological differences in individual patients. Because of these factors, it is important that this product be stored properly, and that the directions be followed carefully during use.

For disposal of allergenic extracts, consider the use of a licensed disposal company or dispose of product in accordance with local, provincial, and federal regulations.

PART II: SCIENTIFIC INFORMATION

13. PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: ALLERGENIC EXTRACT- POLLENS and ALLERGENIC EXTRACT- NON-POLLENS.

Various Proteins extracted from biological source materials:

- Chicken, Duck and Goose: Feathers
- Variable Bovine Type: Hair/Dander
- Mixed Breed Canine Type: Hair/Dander
- Variable Equine: Hair/Dander
- Guinea Pig: Hair/Dander
- Whole Body Insects: Fire Ant and Cockroach
- Various Grasses
- Various Molds
- Various Trees
- Various Weeds

Pharmaceutical standard: Sterile extracts for scratch, prick or puncture (percutaneous) testing are supplied in dropper vials containing, in addition to the extract allergens and antigens, 50 % (v/v) glycerin as preservative, 0.5 % sodium chloride and 0.275 % sodium bicarbonate. The extracts may be labelled in terms of:

1. Weight to Volume (w/v)
2. Amb a 1 Units/mL

Product Characteristics: Appearance is clear to slightly opalescent. Parenteral Drug Products should be inspected visually for particulate matter and discoloration, prior to administration, whenever solution and container permit.

14. CLINICAL TRIALS

No clinical trials were sponsored by Jubilant HollisterStier LLC for the ALLERGENIC EXTRACT – POLLENS or ALLERGENIC EXTRACT – NON-POLLENS when the products were approved in 1997.

15. MICROBIOLOGY

No microbiological information is required for this drug product.

16. NON-CLINICAL TOXICOLOGY

General Toxicology: No long-term animal studies have been performed to evaluate carcinogenic or mutagenic potential or whether ALLERGENIC EXTRACT – POLLENS and ALLERGENIC EXTRACT – NON-POLLENS affects fertility in males or females.

Carcinogenicity: No long-term animal studies have been performed to evaluate carcinogenic potential on ALLERGENIC EXTRACT – POLLENS and ALLERGENIC EXTRACT – NON-POLLENS.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

ALLERGENIC EXTRACT – POLLENS,
ALLERGENIC EXTRACT – NON-POLLENS and
NEGATIVE SKIN TEST CONTROL – GLYCERIN
Allergenic Extracts for Scratch, Prick, Puncture (Percutaneous) Testing Diagnostic Agent

Read this carefully before you are provided ALLERGENIC EXTRACT – POLLENS, ALLERGENIC EXTRACT – NON-POLLENS or NEGATIVE SKIN TEST CONTROL – GLYCERIN. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there ia any new information about ALLERGENIC EXTRACT – POLLENS, ALLERGENIC EXTRACT – NON-POLLENS or NEGATIVE SKIN TEST CONTROL – GLYCERIN prior to each doctor visit where an injection is provided.

Serious Warnings and Precautions
• The product should only be provided by physicians who are experienced in the use of allergenic extracts, or for use under the guidance of an allergist. • Allergenic extracts may potentially cause a severe life-threatening systemic reaction (anaphylaxis), which can result in death. Therefore, emergency measures and personnel trained in their use must be available immediately in the event of such a reaction. You should also be instructed to recognize serious symptoms and contact the physician's office if symptoms occur. • If you are on beta blockers, you 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. • The diagnosis process with this product should not cause bleeding.

What are ALLERGENIC EXTRACT – POLLENS, ALLERGENIC EXTRACT – NON-POLLENS or NEGATIVE SKIN TEST CONTROL – GLYCERIN used for?

"ALLERGENIC EXTRACT – POLLENS, ALLERGENIC EXTRACT – NON-POLLENS and NEGATIVE SKIN TEST CONTROL – GLYCERIN have been approved for the following indication(s) by Health Canada. This means they have passed Health Canada's review and can be purchased and administered in Canada. For more information, talk to your healthcare professional."

- These products are used for the diagnosis of patients with specific allergic conditions.

How do ALLERGENIC EXTRACT – POLLENS, ALLERGENIC EXTRACT – NON-POLLENS and NEGATIVE SKIN TEST CONTROL – GLYCERIN work?
You will have allergenic extracts placed on your skin. A prick will be made through the extract into your skin. If you are allergic to a specific extract, a bump in the skin will form. Your physician will measure the bump. Based on the size of the bump, the physician will determine if treatment (immunotherapy) is an option to relieve or lessen your responses to that allergen.

What are the ingredients in ALLERGENIC EXTRACT – POLLENS, ALLERGENIC EXTRACT – NON-POLLENS and NEGATIVE SKIN TEST CONTROL – GLYCERIN?

- **ALLERGENIC EXTRACT – POLLENS:**
  Medicinal ingredients: Various Pollen Extracts

Non-medicinal ingredients: Glycerin, Sodium chloride and Sodium bicarbonate

- **ALLERGENIC EXTRACT – NON-POLLENS:**
  Medicinal ingredients: Various Epidermal, Insect and Mold Extracts
  Non-medicinal ingredients: Glycerin, Sodium chloride and Sodium bicarbonate
- **NEGATIVE SKIN TEST CONTROL – GLYCERIN:**
  Non-medicinal ingredients: Glycerin, Sodium chloride and Sodium bicarbonate

ALLERGENIC EXTRACT – POLLENS, ALLERGENIC EXTRACT – NON-POLLENS and NEGATIVE SKIN TEST CONTROL – GLYCERIN come in the flowing dosage forms:

- **ALLERGENIC EXTRACT – POLLENS:**
  Dosage Form: Solution
  Strength *(Product Dependent)*: 1:20 w/v, 1:50 w/v, 100 Amb a 1 UA/mL and 200 Amb a 1 UA/mL)
- **ALLERGENIC EXTRACT – NON-POLLENS:**
  Dosage Form – Solution
  Strength *(Product Dependent)*: 1:10 w/v, 1:50 w/v, 1:100 w/v, 1:650 w/v and 1:1,000 w/v)
- **NEGATIVE SKIN TEST CONTROL – GLYCERIN:**
  Dosage Form – Solution
  Strength: 52.5 % v/v

Do not use ALLERGENIC EXTRACT – POLLENS, ALLERGENIC EXTRACT – NON-POLLENS or NEGATIVE SKIN TEST CONTROL – GLYCERIN if:
Your healthcare professional has not prescribed it and administered it within their medical office.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take ALLERGENIC EXTRACTS – POLLENS, ALLERGENIC EXTRACTS – NON-POLLENS or NEGATIVE SKIN TEST CONTROL – GLYCERIN. Talk about any health conditions/circumstances you may have, including:

- Cancer
- Heart Disease
- Female/Male Fertility concerns
- Respiratory Issues
- Allergen Sensitivity/Resistance
- Skin irritations
- Pregnancy
- Nursing Mother

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines. The following may interact with ALLERGENIC EXTRACT – POLLENS, ALLERGENIC EXTRACT – NON-POLLENS or NEGATIVE SKIN TEST CONTROL – GLYCERIN:

When discussing with your healthcare professional, make specific reference to the following type of medications:

Medication Type	Treatment of:
Beta Blockers	High blood pressure
Dopamine	Low blood pressure, Parkinson's disease, Cardiac or Kidney function
Beta2 Agonists Omalizumab/Xolair Oral corticosteroids/Inhalers	Asthma/COPD
Prostaglandin D2 Inhibitors	Asthma, allergic rhinitis, and atopic dermatitis
Antihistamines	Motion Sickness, nausea or insomnia
Histamine2 Antagonists	Gastric ulcers, acid reflux or heart burn

Antidepressants	Depression, chronic pain, addiction or mental health conditions
Benzodiazepines	Anxiety, insomnia and seizures
Topical local anesthetics	Creams or lotions that numb the skin to reduce pain or itching
Topical steroids	Inflammatory skin conditions
In Vitro Immunoglobulin	In vitro fertilization (IVF) and recurrent pregnancy loss
Immunomodulating Biologics	Autoimmune diseases, rheumatoid arthritis, psoriasis, Crohn's disease; oncologic, allergic, rheumatologic, and neurologic conditions

How to take ALLERGENIC EXTRACT – POLLENS, ALLERGENIC EXTRACT – NON-POLLENS or NEGATIVE SKIN TEST CONTROL – GLYCERIN:

- Skin testing is performed by a healthcare professional by placing a drop of specific extract(s), positive skin test control and a negative skin test control on your skin. The healthcare provider will then superficially prick your skin with a sterile needle.
- This process should not make you bleed.

Usual dose:

- A single drop of a specific extract. The amount of extracts tested are based on the history you provide your healthcare professional and their expert recommendation.

Overdose:

- An overdose could occur based on your sensitivity to the extract(s) and in rare instances could result in anaphylactic symptoms. It is imperative that the physician administering your allergenic extracts understand and be prepared for the treatment of severe reactions.

What are possible side effects from using ALLERGENIC EXTRACT – POLLENS, ALLERGENIC EXTRACT – NON-POLLENS or NEGATIVE SKIN TEST CONTROL – GLYCERIN?

These are not all the possible side effects you may have when taking ALLERGENIC EXTRACT – POLLENS, ALLERGENIC EXTRACT – NON-POLLENS or NEGATIVE SKIN TEST CONTROL – GLYCERIN. If you experience any side effects not listed here, tell your healthcare professional.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
VERY COMMON			
N/A			
COMMON			
N/A			
RARE			
Anaphylaxis		X	Seek emergency medical help immediately.

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

This product will be stored at 2-8 °C by your healthcare professional.

Keep out of reach and sight of children.

If you want more information about ALLERGENIC EXTRACT – POLLENS, ALLERGENIC EXTRACT – NON-POLLENS and NEGATIVE SKIN TEST CONTROL – GLYCERIN:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the:
  - Health Canada website https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drugproduct-database.html;
  - Manufacturer's website https://www.hsallergy.com/,
  - Manufacturer's phone 1-800-992-1120

This leaflet was prepared by Jubilant HollisterStier LLC.

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HollisterStier Allergy