HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use the following STANDARDIZED GRASS POLLEN EXTRACTS safely and effectively. See full prescribing information for the following STANDARDIZED GRASS POLLEN EXTRACTS.

STANDARDIZED GRASS POLLEN, BERMUDA GRASS *(Cynodon dactylon)*
STANDARDIZED GRASS POLLEN, KENTUCKY BLUE (JUNE) *(Poa pratensis)*
STANDARDIZED GRASS POLLEN, FESCUE, MEADOW *(Festuca elatior)*
STANDARDIZED GRASS POLLEN, ORCHARD GRASS *(Dactylis glomerata)*
STANDARDIZED GRASS POLLEN, REDTOP (*Agrostis alba)*
STANDARDIZED GRASS POLLEN, PERENNIAL RYEGRASS *(Lolium perenne)*
STANDARDIZED GRASS POLLEN, SWEET VERNAL GRASS *(Anthoxanthum odoratum)*
STANDARDIZED GRASS POLLEN, TIMOTHY *(Phleum pratense)*

Injection for percutaneous, intradermal, or subcutaneous use
Initial U.S. Approval: 1998

WARNING: ANAPHYLAXIS
***See full prescribing information for complete boxed warning*.**

- **Standardized Grass Pollen Extracts can cause anaphylaxis, including anaphylactic shock and death. (5.1)**
- **Do not administer to individuals with severe, unstable or uncontrolled asthma, history of any severe systemic reaction to the allergen extract when administered for diagnosis or treatment, or with medical conditions that reduce the ability to survive anaphylaxis. (4)**
- **Observe individuals for at least 30 minutes following administration. Emergency measures and healthcare providers trained in their use must be available in the event of a life-threatening reaction. (5.1)**
- **Individuals with extreme sensitivity to these products, on an accelerated immunotherapy build-up, switching to another lot, receiving high doses of these products, or exposed to excessive amounts of grass pollen may be at increased risk of anaphylaxis. (5.1)**
- **These products may not be suitable for individuals who may be unresponsive to epinephrine or inhaled bronchodilators, such as those taking beta-blockers. (5.1)**

----------INDICATIONS AND USAGE----------

Standardized Grass Pollen Extracts are indicated for (1):

- Skin test diagnosis of patients with a clinical history of allergy to one or more of the following grass pollen allergens: Bermuda, Kentucky Blue (June), Meadow Fescue, Orchard, Perennial Rye, Redtop, Sweet Vernal, or Timothy.
- Immunotherapy for the reduction of grass pollen-induced allergic symptoms confirmed by positive skin test or by *in vitro* testing for pollen-specific IgE antibodies to one or more of the following grass pollens: Bermuda, Kentucky Blue (June), Meadow Fescue, Orchard, Perennial Rye, Redtop, Sweet Vernal, or Timothy.

----------DOSAGE AND ADMINISTRATION----------

For percutaneous, intradermal, or subcutaneous use only.
Administration:

- Percutaneous for diagnostic testing
- Intradermal for diagnostic testing
- Subcutaneous for immunotherapy

See full prescribing information for details on dosing and dilution preparation. (2)

----------DOSAGE FORMS AND STRENGTHS----------

Injection. Standardized Grass Pollen Extracts are labeled in Bioequivalent Allergy Units per milliliter (BAU/mL). (3, 11) Refer to the vial label for the product concentration. (16)

- Standardized Bermuda grass pollen extract: 10,000 BAU/mL stock concentrate in a multiple-dose vial. (3)
- All other Standardized Grass Pollen Extracts (except Bermuda grass pollen): 100,000 BAU/mL stock concentrate in a multiple-dose dropper vial and in a multiple-dose vial. (3)

----------CONTRAINDICATIONS----------

- Severe, unstable or uncontrolled asthma. (4)
- History of any severe systemic reaction to the allergen extract when administered for diagnosis or treatment. (4)
- Medical conditions that reduce the ability to survive anaphylaxis. (4)

----------WARNINGS AND PRECAUTIONS----------

The risk of anaphylaxis may be increased in the following situations (5.1):

- Extreme sensitivity to Standardized Grass Pollen Extracts.
- Receipt of an accelerated build-up schedule.
- Change from one lot of a particular standardized grass pollen extract to another lot of the same standardized grass pollen extract.
- Receipt of high doses of the Standardized Grass Pollen Extracts.
- Exposure to excessive amounts of grass pollen.

----------ADVERSE REACTIONS----------

Commonly reported adverse reactions for allergenic extracts are:

- Local adverse reactions occurred in 26 to 82 % of all patients who received subcutaneous immunotherapy (e.g., erythema, swelling, pruritus, tenderness and pain at the injection site). (6)
- Systemic adverse reactions occurred in ≤ 7 % of patients who received subcutaneous immunotherapy (e.g., generalized skin erythema, urticaria, pruritus, angioedema, rhinitis, wheezing, laryngeal edema, hypotension, and shock). Systemic adverse reactions may be fatal. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Jubilant HollisterStier at 1-800-495-7437 or Adverse.Reactions@jubl.com; or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

Certain medications may decrease skin test wheal and erythema responses including antihistamine (7.1), topical corticosteroids and topical anesthetics (7.2), tricyclic Antidepressants (7.3).

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 3/2026

FULL PRESCRIBING INFORMATION: CONTENTS

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: ANAPHYLAXIS

- **Standardized Grass Pollen Extracts can cause anaphylaxis, including anaphylactic shock and death[1]. (5.1, 11)**
- **Do not administer to individuals with:**
  - **severe, unstable or uncontrolled asthma;**
  - **history of any severe systemic reaction to the allergen extract when administered for diagnosis or treatment;**
  - **medical conditions that reduce the ability to survive anaphylaxis. (4)**
- **Observe individuals for at least 30 minutes following administration. Emergency measures and healthcare providers trained in their use must be available in the event of a life-threatening reaction. (5.1)**
- **Individuals with extreme sensitivity to these products, on an accelerated immunotherapy build-up, switching to another lot, receiving high doses of these products, or exposed to excessive amounts of grass pollen may be at increased risk of anaphylaxis. (5.1)**
- **These products may not be suitable for individuals who may be unresponsive to epinephrine or inhaled bronchodilators, such as those taking beta-blockers. (5.1)**

1 INDICATIONS AND USAGE

Standardized Grass Pollen Extracts *[see Description (11)]* are indicated for:

- Skin testing for diagnosis of patients with a clinical history of allergy to one or more of the following grass pollen allergens: Bermuda, Kentucky Blue (June), Meadow Fescue, Orchard, Perennial Rye, Redtop, Sweet Vernal, or Timothy.[7, 8, 9, 10]

- Immunotherapy for the reduction of grass pollen-induced allergic symptoms confirmed by positive skin test or by *in vitro* testing for pollen-specific IgE antibodies for Bermuda grass pollen, Kentucky Blue (June) grass pollen, Meadow Fescue grass pollen, Orchard grass pollen, Perennial Rye grass pollen, Redtop grass pollen, Sweet Vernal grass pollen, or Timothy grass pollen**.**

2 DOSAGE AND ADMINISTRATION

2.1 Preparation for Administration

Verify that the label on the vial states the intended specific standardized grass pollen extract to be administered.

Standardized Grass Pollen Extracts should appear as clear to slightly opalescent solution with a light yellow to medium brown color. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Discard the solution if either of these conditions exist.

Standardized Grass Pollen Extracts diluted with Albumin Saline with Phenol (0.4 %) (stabilized diluent) may be more potent than Standardized Grass Pollen Extracts diluted with diluents that do not contain albumin. When switching from non-stabilized to stabilized diluent, consider less concentrated initial dilutions for both intradermal testing and immunotherapy.

Different formulations, preparations, or new lots of Standardized Grass Pollen Extracts are not substitutable. Adjust dosage appropriately when formulations, preparations, or lots of Standardized Grass Pollen Extracts are changed *[see Immunotherapy (2.3) and Dosage Forms and Strengths (3)]*.

Standardized Grass Pollen Extracts may be prepared for intradermal (diagnosis) or subcutaneous (immunotherapy) administration by diluting stock concentrates.

- For diluent, use sterile albumin saline with phenol or sterile normal saline with phenol.
- Dilute stock concentrates by a minimum of 100-fold for intradermal testing. Dilutions of 1,000-fold or greater are appropriate starting points for patients with a clinical history of adverse reaction.

To prepare dilutions for intradermal testing and immunotherapy, start with a stock concentrate, and prepare a ten-fold (1:10) dilution by adding 0.5 mL of concentrate to 4.5 mL of sterile aqueous diluent. Prepare subsequent dilutions in a similar manner (see Table 1).

Table 1: 10-fold Dilution Series for Standardized Grass Pollen Extracts Labeled 10,000 BAU/mL* and 100,000 BAU/mL*

Dilution**	Extract	Volume of Diluent	Dilution Strength BAU/mL (Bermuda Grass)	Dilution Strength BAU/mL (All other Individual Grasses, except Bermuda Grass)
0	Stock Concentrate	0 mL	10,000	100,000
1	0.5 mL Concentrate	4.5 mL	1,000	10,000
2	0.5 mL Dilution 1	4.5 mL	100	1,000
3	0.5 mL Dilution 2	4.5 mL	10	100
4	0.5 mL Dilution 3	4.5 mL	1	10
5	0.5 mL Dilution 4	4.5 mL	0.1	1
6	0.5 mL Dilution 5	4.5 mL	0.01	0.1
7	0.5 mL Dilution 6	4.5 mL	0.001	0.01

* BAU/mL = Bioequivalent Allergy Units/mL

** Store extract dilutions at 2 to 8 °C (36 to 46 °F).

2.2 Diagnostic Testing

For percutaneous and intradermal use only.

Use individual standardized grass pollen extracts to identify patients who exhibit an allergic response to specific species of grass pollen. False positive reactions may occur. A positive skin test reaction must be interpreted in the context of the individual's clinical history and known exposure to the allergen.

- Administer percutaneous tests prior to administration of intradermal tests.
- A positive reaction with grass pollen mixtures during diagnostic testing does not permit identification of the specific grass pollen allergen that elicited the reaction. Additionally, a negative reaction fails to indicate whether an individual component allergen would have elicited a positive reaction at full strength.

Percutaneous Skin Testing

Dose

Unless an individual is suspected to be at greater risk for anaphylaxis, the initial starting dose is 1 drop (approximately 0.05 mL) of concentrated standardized grass pollen extract. For individuals suspected to be at greater risk for anaphylaxis such as those with a history of allergen-induced anaphylaxis, initiate percutaneous testing with 1 drop of a diluted standardized grass pollen extract. If negative, retest with the next higher concentration(s). *[see Preparation for Administration (2.1)]* Doses should be administered 15 to 20 minutes apart.

Administration

Place 1 drop (approximately 0.05 mL) of standardized grass pollen extract on the skin and using a skin test device, such as a sterile needle, lancet, or bifurcated needle. Pierce through the drop into the skin with a slight lifting motion.

For self-loading devices refer to the manufacturer's product instructions.

Include a positive histamine skin test control to identify patients whose recent use of drugs with antihistamine activity may result in a false negative skin test *[see Drug Interactions (7.1)]*.

Include a negative control to detect false positive responses, which can occur when the patient has a non-specific reaction to the diluent or due to dermographism. A 50% glycerin solution may be used as the negative control.

Interpreting Results

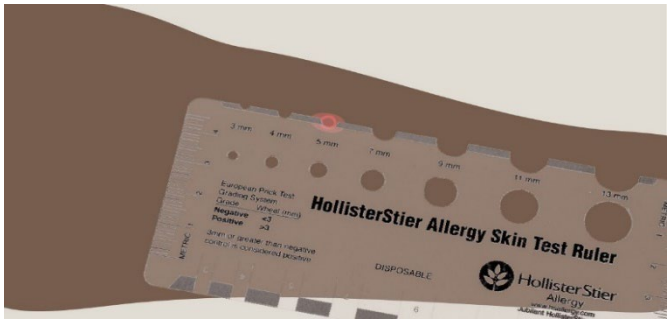
Measure and record skin test responses 15-20 minutes after exposure. Individual patient reactivity can vary with time, allergen potency, and/or immunotherapy, as well as testing technique. The most reliable method of recording a skin test reaction is to measure the largest diameter of both wheal and erythema. While some correlation exists between the size of the skin test reaction and the degree of sensitivity, other factors should be considered in the diagnosis of allergy to specific allergens. Refer to Figure 1 through Figure 5 for the measurement of wheal and flare.

- The negative control (50 % glycerin solution) response should measure < 3 millimeter (mm) wheal and ≤ 10 mm flare.
- Response to the positive control should be at least 3 mm larger than the response to the negative control.
- If either the response to the histamine positive control or to the negative control do not meet the criteria above for acceptable wheal size, the results for the allergenic extracts tested at the same time should be considered invalid and be repeated.

Use a paper or plastic millimeter skin reaction guide as shown below.

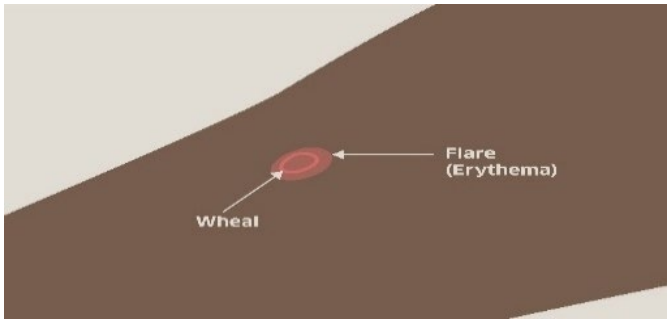
Figure 1: Millimeter Skin Reaction Guide

Figure 2: Millimeter Skin Reaction Guide on Forearm



Fifteen minutes after application of the skin test, measure the length and midpoint orthogonal width of each flare and wheal from the inner edge of the reaction.

Figure 3: Wheal / Flare Diagram



The wheal is a smooth, slightly elevated area which is redder or paler than the surrounding skin. The flare is the red outermost zone of the skin test reaction.

The length of the skin test is defined as the largest diameter and the width of the skin test is defined as the diameter perpendicular to the length at its midpoint. Consider the wheal and flare as separate entities. First, measure the flare (see Figure 4) and then independently measure the wheal (see Figure 5).

Figure 4: Measuring the Flare

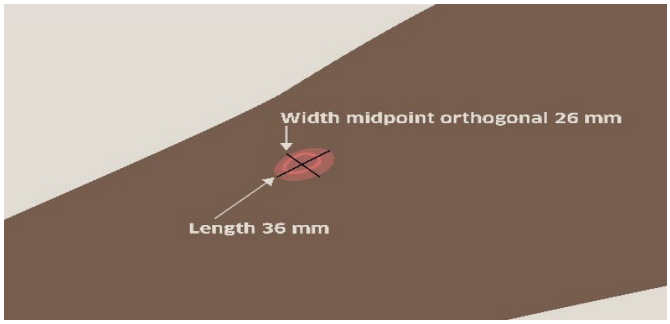
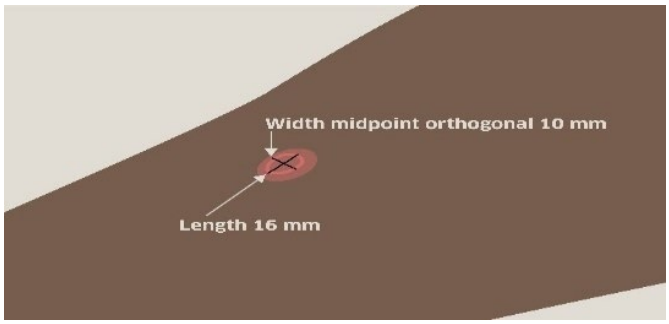


Figure 5: Measuring the Wheal



The average diameter measurement in Figure 4, the example above of the flare is (26 mm + 36 mm)/2 = 31 mm; and the average diameter of the wheal in Figure 5 is (10 mm + 16 mm)/2 = 13 mm.

Intradermal *(Intracutaneous)* Skin Testing

Always perform percutaneous tests prior to intradermal skin tests.[22]

Dose

For patients with negative or equivocal percutaneous testing for whom there is a high index of suspicion of grass pollen allergy, intradermal testing may be performed with:

- 0.02 to 0.05 mL of a 10 BAU/mL for Bermuda Grass extract solution.
- 0.02 to 0.05 mL of a 100 BAU/mL extract solution for all other Standardized Grass Pollen Extracts.

If this test is negative, a second intradermal test may be performed with:

- 0.02 to 0.05 mL of a 100 BAU/mL for Bermuda Grass extract solution.
- 0.02 to 0.05 mL of a 1,000 BAU/mL extract solution for all other Standardized Grass Pollen Extracts.

Extracts are diluted for all intradermal testing. *[see Preparation for Administration (2.1)]*

Administration

Intradermally inject the dose of the diluted allergenic extract using a 1 mL syringe.

Include a positive histamine control at intradermal strength to identify patients whose recent use of drugs with antihistamine activity may result in a false negative skin test. *[see Drug Interactions (7.1)]*

Include an aqueous buffer negative control (Sterile Albumin Saline with Phenol, Sterile Buffered Saline with Phenol) to detect false positive responses, which can occur when the patient has a non-specific reaction to the diluent or due to dermographism.

Interpreting Results

Measure and record skin test responses 15-20 minutes after injection.[22] Refer to Figure 1 through Figure 5 for the measurement of wheal and flare.

- Response to the positive control should be at least 3 mm larger than the response to the negative control.
- The negative control (sterile aqueous diluent) response should measure < 3 mm wheal and ≤ 10 mm flare (erythema).
- If either the response to the histamine positive control or to the negative control do not meet the criteria above for acceptable wheal size, the results for the allergenic extracts tested at the same time should be considered invalid and be repeated.

2.3 Immunotherapy

For subcutaneous use only.

Subcutaneous injections for immunotherapy are prepared by diluting the stock concentrate. See Table 1 for instructions regarding dilution and preparation.

Administration

Administer immunotherapy by subcutaneous injection in the lateral aspect of the arm or thigh. Do not inject directly into any blood vessels.

Observe patients for at least 30 minutes as most adverse reactions occur within 30 minutes after injection.[23]

Dose Build-up

Dosing of Standardized Grass Pollen Extracts for allergen immunotherapy is highly individualized. The initial dose is determined by the patient's percutaneous skin test reactivity and clinical history. The initial dose is typically 0.05 mL of a 0.01 BAU/mL dilution for standardized Bermuda grass pollen extract and 0.05 mL of a 0.1 BAU/mL dilution for all other Standardized Grass Pollen Extracts. In patients who appear to be exquisitely sensitive by skin test and history, consider a lower initial dose. The dose is increased at each injection by no more than 50% of the previous dose, and the next increment is governed by the response to the last injection. Dosing is increased in increments until 0.5 mL is reached, following which 0.05 mL is administered from the next most concentrated allergen extract or allergen mixture vial in the dilution series. Injections are typically given one or two times per week until the maintenance dose is reached.

- Any evidence of a systemic reaction to immunotherapy is an indication for a significant reduction (at least 75%) in the subsequent dose or the cessation of immunotherapy. Proceed cautiously in subsequent dosing if immunotherapy is continued.
- Repeated systemic reactions, even of a mild nature, are sufficient reason for the cessation of further attempts to increase the reaction-causing dose.
- The volume of solution for immunotherapy may produce increased discomfort in pediatric individuals. In order to achieve the total dose required, the volume of the dose may be divided into more than one injection per visit.[23]

Maintenance Dose Selection and Intervals

Select a maintenance dose based on the patient's clinical response and tolerance.

- Typical maintenance dose is 300-1,500 BAU for Standardized Bermuda Grass and 1,000-4,000 BAU for all other Standardized Grass Pollens.[23] Occasionally, higher doses are necessary to relieve symptoms.

- Northern prairie grasses (Kentucky Blue [June], Meadow Fescue, Orchard, Perennial Rye, Redtop, Sweet Vernal, and Timothy) are highly cross-reactive. Therefore, consider the total BAU when determining the target maintenance dose for Northern Prairie grasses.
- Maintenance doses larger than 0.2 mL of undiluted allergen extract are rarely administered because an extract in 50% glycerin may cause patient discomfort upon injection.[29]
- After the maintenance dose is achieved, increase the injection interval to 2 weeks, then 3 weeks, and finally 4 weeks as tolerated. The optimal interval between maintenance doses of allergenic extract varies among individuals. Administer the maintenance dose at a given interval three or four times before further increasing the interval to ensure that no reactions occur. Protection may be lost rapidly if the interval between doses is more than 4 weeks.

Dosage Modification for Immunotherapy

Withhold immunotherapy and/or reduce dosage, if any of the following conditions exist:

- Severe symptoms of rhinitis and/or asthma.
- Infection accompanied by fever.

Any evidence of a systemic reaction is an indication for a significant reduction (at least 75%) in the subsequent dose. Repeated systemic adverse reactions are sufficient reason for the cessation of further attempts to increase the dose.

In situations prompting dose reduction, a cautious increase in dose can be attempted once the reduced dose is tolerated. The dose 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.

Prolonged period has elapsed since the last injection: Patients may lose tolerance for allergen injections during prolonged intervals (> 4 weeks) 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 dose reduction required.

Changing to a different lot of standardized extract: All extracts can lose allergenic activity over time and extracts vary in allergenic activity. Two different lots of extract could differ substantially in allergenic activity, even if they are the same formula and concentration. The volume of the first dose from the new vial should not exceed 50% of the previous dose. Do not use extracts beyond their expiry date.

Changing to an extract from a different manufacturer: Since manufacturing processes and sources of raw materials differ among manufacturers, the interchangeability of extracts from different manufacturers cannot be assured. Decrease the starting dose of the new extract when the extract is the same formula and dilution as the one previously used. In general, a volume dose reduction to 50% of the previous product dose is adequate, but each situation must be evaluated separately considering the patient's history of sensitivity, tolerance of previous injections, and other factors. If the patient tolerates the 50% decrease, then raise the next dose to the previous tolerated dose amount. To re-establish the maintenance dose the starting interval between doses should not be greater than one week.

Changes made in the extract concentrate formula: Changes other than those listed above such as a difference in extracting fluid (e.g., change from non-glycerin extracts to 50% glycerin extracts), combining two or more stock concentrates, or any other change can affect a patient's tolerance of the treatment.[23] Extra dilutions are recommended whenever starting a revised formula. The greater the change, the greater the number of dilutions required.

Duration of Treatment

The duration of treatment for immunotherapy has not been established. A period of three to five years of injection therapy constitutes an average minimum course of treatment. Evaluate patients for treatment response at least every 6 to 12 months while they receive immunotherapy. The decision to continue or stop immunotherapy must be individualized.[23]

3 DOSAGE FORMS AND STRENGTHS

Injection. Standardized Grass Pollen Extracts are labeled in Bioequivalent Allergy Units per milliliter (BAU/mL). *[see Description (11)]* Refer to the vial label for the product concentration *[see How Supplied/Storage and Handling (16.1)].*

- For percutaneous testing, standardized Bermuda grass pollen extract stock concentrate containing 10,000 BAU/mL of grass pollen is supplied in 10 mL multiple-dose vials. All other standardized grass pollen extract stock concentrates containing 100,000 BAU/mL of grass pollen are supplied in 5 mL dropper vials *[see Description (11)].*
- For intradermal testing, standardized Bermuda grass pollen extract stock concentrate is available in 10,000 BAU/mL of grass pollen. All other standardized grass pollen extract stock concentrates are available in 100,000 BAU/mL. All standardized grass pollen extract stock concentrates are supplied in 10 mL and 50 mL multiple-dose vials [see *Description (11)*].
- For immunotherapy, standardized Bermuda grass pollen extract stock concentrate is available in 10,000 BAU/mL. All other standardized grass pollen extract stock concentrates are available in 100,000 BAU/mL. All standardized grass pollen extract stock concentrates are supplied in 10 mL and 50 mL multiple-dose vials [see *Description (11)*].

4 CONTRAINDICATIONS

Standardized Grass Pollen Extracts are contraindicated in individuals with:

- Severe, unstable or uncontrolled asthma.
- History of any severe systemic reaction to the allergen extract when administered for diagnosis or treatment.
- Medical conditions that reduce the ability to survive anaphylaxis.

5 WARNINGS AND PRECAUTIONS

5.1 Anaphylaxis

Anaphylaxis, which may lead to death, can occur in individuals following the administration of Standardized Grass Pollen Extracts, particularly in the following situations *[see Adverse Reactions (6)]:* [18, 19, 20, 21]

- Extreme sensitivity to the Standardized Grass Pollen Extracts.
- Receipt of an accelerated build-up schedule.
- Change from one lot of a particular standardized grass pollen extract to another lot of the same standardized grass pollen extract.
- Receipt of high doses of the Standardized Grass Pollen Extracts.
- Exposure to excessive amounts of grass pollen.

Standardized Grass Pollen Extracts may not be suitable for individuals who may be unresponsive to epinephrine or inhaled bronchodilators, such as those taking beta-blockers.

Medications to treat systemic reactions, as well as emergency equipment should be available for immediate use. Administer Standardized Grass Pollen Extracts in a healthcare setting under the supervision of a healthcare provider prepared to manage anaphylaxis. Individuals should remain in the provider's office for a minimum of 30 minutes after receiving an injection of Standardized Grass Pollen Extracts, so that any adverse reaction can be observed and appropriately managed.

6 ADVERSE REACTIONS

Common adverse reactions reported for allergenic extracts are:

- Local adverse reactions occurred in 26 to 82 % of all patients who received subcutaneous immunotherapy, at the injection site (e.g., erythema, swelling, pruritus, tenderness and pain).[23]
- Systemic adverse reactions occurred in ≤ 7 % of patients who received subcutaneous immunotherapy (e.g., generalized skin erythema, urticaria, pruritus, angioedema, rhinitis, wheezing, laryngeal edema, hypotension, and shock).[24] Systemic reactions may be fatal.[1, 12, 23]

Published studies of allergenic extracts report systemic reactions occurring in fewer than 1% in patients receiving conventional immunotherapy and greater than 36% in patients receiving rush immunotherapy.[1, 12, 26, 27] Most systemic

reactions occurred within 30 minutes of injection. However, systemic reactions have been reported to occur up to 2 hours after the final injection with rush schedules. Some reactions have occurred up to 6 hours after skin tests or immunotherapy.[23, 24, 28]

7 DRUG INTERACTIONS

7.1 Antihistamines

Do not perform skin testing with Standardized Grass Pollen Extracts within 3 to 10 days of first-generation H1-histamine receptor blockers (e.g., clemastine, diphenhydramine) and second-generation antihistamines (e.g., loratadine, fexofenadine) being used. These products suppress histamine skin test reactions and could mask a positive response.[13, 22, 23]

7.2 Topical Corticosteroids and Topical Anesthetics

Topical corticosteroids may suppress skin reactivity; therefore, discontinue use at the skin test site for at least 2 to 3 weeks before skin testing.[13, 14] Avoid use of topical local anesthetics at skin test sites because they can suppress flare responses.[16, 22, 23]

7.3 Tricyclic Antidepressants

Tricyclic antidepressants, such as doxepin, can have potent antihistamine effects and may alter skin test results. Allow 7 to 14 days after discontinuation of tricyclic medication prior to skin testing.[15, 22, 23]

8 USES IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4 % and 15 to 20 %, respectively. There are no human or animal data to establish the presence or absence of Standardized Grass Pollen Extracts associated risks during pregnancy.[17]

8.2 Lactation

Risk Summary

It is not known whether Standardized Grass Pollen Extracts are present in human milk. Data are not available to assess the effects of these extracts on the breastfed child or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Standardized Grass Pollen Extracts and any potential adverse effects on the breastfed child from the extracts or from the underlying maternal condition.

8.4 Pediatric Use

For use of these products in children younger than 5 years of age, consideration should be given to the patient's ability to comply and cooperate with receipt of the product and the potential for difficulty in communicating with the child regarding systemic reactions.[11, 23]

The volume of a dose for immunotherapy may need to be divided for pediatric patients *[see Immunotherapy (2.3)].*

8.5 Geriatric Use

Data are not available to determine if patients 65 years of age and older respond differently to allergen immunotherapy than younger patients.[3]

11 DESCRIPTION

This prescribing information covers eight Standardized Grass Pollen Extracts. The term 'Standardized Grass Pollen Extracts' as used throughout labeling specifically refers to all eight products listed in the Product Title in Highlights of Prescribing Information.

Standardized Grass Pollen Extracts include Standardized Bermuda Grass Pollen *(Cynodon dactylon)* at 10,000 BAU/mL, 0.5 % sodium chloride, 0.275 % sodium bicarbonate and 50 % glycerin by volume as a preservative and Standardized Kentucky Blue (June) Grass Pollen *(Poa pratensis)*, Standardized Meadow Fescue Grass Pollen *(Festuca elatior)*, Standardized Orchard Grass Pollen *(Dactylis glomerata)*, Standardized Perennial Rye Grass Pollen *(Lolium perenne)*, Standardized Redtop Grass Pollen *(Agrostis alba)*, Standardized Sweet Vernal Grass Pollen *(Anthoxanthum odoratum)*, and Standardized Timothy Grass Pollen *(Phleum pratense)* at 100,000 BAU/mL, 0.5 % sodium chloride, 0.275 % sodium bicarbonate, and 50 % glycerin by volume as a preservative. Inactive ingredients include 0.25% sodium chloride for isotonicity and 0.25% sodium bicarbonate as a buffer. Standardized Grass Pollen Extracts are administered percutaneously, intradermally and subcutaneously.

Standardized Grass Pollen Extracts are clear light yellow to brownish solutions that are free of particulate matter.

Standardized Grass Pollen Extracts are labeled in BAU/milliliter. Bioequivalent Allergy Units are assigned based on comparison by enzyme-linked immunosorbent assay (ELISA) to references from the U.S. Food and Drug Administration, Center for Biologics Evaluation and Research (CBER). CBER references are assigned unitage based on quantitative skin testing. [2, 4, 5, 6] CBER references which can be diluted 1:5,000,000 to intradermally elicit a 50 millimeter sum of erythema diameter response in highly puncture reactive subjects are assigned 100,000 BAU/milliliter; whereas references diluted 1:500,000 which elicit the same 50 millimeter sum of erythema diameter response are assigned 10,000 BAU/milliliter.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The mechanisms of action of allergen immunotherapy have not been fully established.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No studies in animals have been performed to evaluate carcinogenicity, mutagenicity or impairment of fertility.

14 CLINICAL STUDIES

Specific immunotherapy with allergenic extracts is helpful in reducing symptoms associated with exposure to the offending allergens. A summary of effectiveness by the Panel on Review of Allergenic Extracts, an advisory committee to the U.S. Food and Drug Administration, has been published.[25]

15 REFERENCES

1. Lockey, Richard F., Linda M. Benedict, Paul C. Turkeltaub, Samuel C. Bukantz. Fatalities from immunotherapy (IT) and skin testing (ST). J. Allergy Clin. Immunol., 79 (4): 660-677, 1987.
2. U.S. Food & Drug Administration (FDA), Center for Biologics Evaluation and Research (CBER). ELISA competition assay (Enzyme-linked Immunosorbent Assay). Methods of Allergenic Products Testing Laboratory. October 1993. CBER Docket No. 94N.0012.
3. Peebles, Ray Stokes, Jr., B. Bochner, Howard J. Zeitz, ed. Anaphylaxis in the elderly. Immunology and Allergy Clinics of North America. 13 (3): 627-646, August 1993.
4. Turkeltaub, PC, S. Rastogi. Quantitative intradermal test procedure for evaluation of subject sensitivity to standardized allergenic extracts and for assignment of bioequivalent allergy units to reference preparations using the ID50EAL method, Allergenic Products Testing Laboratory, Center for Biologics Evaluation and Research (CBER), FDA. Revised November 1994.

5. Turkeltaub PC, Rastogi SC, Baer H, et al. A standardized quantitative skin-test assay of allergen potency and stability: studies on the allergen dose-response curve and effect of wheal, erythema, and patient selection on assay results. *J Allergy Clin Immunol*. 1982; 70:343-352.
6. Turkeltaub PC. Assignment of bioequivalent allergy units based on biological standardization methods. *Arb Paul Ehrlich Inst Bundesamt Sera Impfstoffe Frankf A M*. 1988;(82):19-40.
7. Sheldon, J. M., R. G. Lovell, K. P. Matthews. A Manual of Clinical Allergy. Second Edition. W.B. Saunders, Philadelphia, 1967, pp. 107-112.
8. Sherman, W. B. Hypersensitivity mechanism and management. W. B. Sanders, Philadelphia, 1968, pp. 169-172.
9. Swineford, O. Asthma and Hay Fever. Charles C. Thomas, Springfield, IL, 1971, pp. 148-155.
10. Patterson, Roy, et al. Allergy Principles and Practice, 2nd ed. E. Middleton, Jr., C.E. Reed, E.F. Ellis, Ed., C.V. Mosby Co., 1983, St. Louis, MO, 1983, Chapter 52.
11. Levy, D.A., L.M. Lichtenstein, E.O. Goldstein, and K. Ishizaka. Immunologic and cellular changes accompanying the therapy of pollen allergy. J. Clinical Investigation, 50:360, 1971.
12. Turkeltaub, Paul C., MD, and Peter J. Gergen, MD. The risk of adverse reactions from percutaneous prick-puncture allergen skin testing, venipuncture, and body measurements: data from the Second National Health and Nutrition Examination Survey, 1976-80 (NHANES II). J. Allergy Clin. Immunol. 84(6): 886-890, Dec. 1989.
13. Pipkorn, Ulf. Pharmacological influence of anti-allergic medication on In Vivo allergen testing. Allergy. 43: 81-86, 1988.
14. Andersson, M. and U. Pipkorn. Inhibition of the dermal immediate allergic reaction through prolonged treatment with topical glucocorticosteroids. J. Allergy Clin. Immunol. 79 (2): 345-349, February 1987.
15. Rao, Kamineni S., et al. Duration of suppressive effect of tricyclic anti-depressants on histamine induced wheal and flare reactions on human skin. J. Allergy Clin. Immunol. 82: 752-757, November 1988.
16. Pipkorn, Ulf, and M. Andersson. Topical dermal anesthesia inhibits the flare but not the wheal response to allergen and histamine in the skin prick test. Clinical Allergy. 17: 307-311, 1987.
17. Metzger, W.J., E. Turner and R. Patterson. The safety of immunotherapy during pregnancy. J. Allergy Clin. Immunol. 61 (4): 268-272, 1978.
18. Reid, M.J., R.F. Lockey, P.C. Turkletaub, T.A.E. Platts-Mills. Survey of fatalities from skin testing and immunotherapy. J. Allergy Clin. Immunol. 92 (1): 6-15, July 1993.
19. Reid, M.J., G. Gurka. Deaths associated with skin testing and immunotherapy. J. Allergy Clin. Immunol. 97(1) Part 3:231, Abstract 195, January 1996.
20. Thompson, R.A. et al, report of a WHO/IUIS working group. The current status of allergen immunotherapy (hyposensitization). Allergy. 44: 369-379, 1989.
21. Malling, H.-J., B. Weeke, et al, The European Academy of Allergology and Clinical Immunology. Position Papers. Allergy. 48 (Supplement 14): 9-82, 1993.
22. Bernstein IL, Li JT, Bernstein Dl, et al. Allergy diagnostic testing: an updated practice parameter. Ann Allergy Asthma Immunol. 2008 Mar;100:S1-148.
23. Cox L, Nelson H, Lockey R, Calabria C, Chacko T, Finegold I, et al. Allergen immunotherapy: A practice parameter third update. J Allergy Clin Immunol. 2011 Jan;127:S1-55.
24. Greineder DK. Risk management in allergen immunotherapy. J Allergy Clin Immunol. 1996 Dec;98(6 Pt 3):S3304
25. Federal Register Proposed Rule: Biological Products: Implementation of Efficacy Review, Allergenic Extracts, Federal Register 1985;50:3082-3288.
26. Lockey RF, Nicoara-Kasti GL, Theodoropoulos DS, Bukantz SC. Systemic reactions and fatalities associated with allergen immunotherapy. Ann Allergy Asthma Immunol 2001;87(suppl 1):47-55.
27. Malling HJ. Minimizing the risks of allergen-specific injection immunotherapy. Drug Saf 2000;23:323-332.
28. Greenberg MA, Kaufman CR, Gonzalez GE, et. al. Late and immediate systemic-allergic reactions to inhalant allergen immunotherapy. J Allergy Clin Immunol 1986; 77:865-870.

29. Ref. Van Metre Jr, Thomas E., et al. "Pain and dermal reaction caused by injected glycerin in immunotherapy solutions." Journal of allergy and clinical immunology 97.5 (1996): 1033-1039.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

Standardized Grass Pollen Extracts are supplied as 50 % glycerin stock concentrates labeled in Bioequivalent Allergenic Units per Milliliter (BAU/mL) and provided in 10 mL and 50 mL multiple-dose vials for percutaneous and intradermal skin testing and subcutaneous immunotherapy. These extracts may also be supplied in 5 mL multiple-dose dropper vials for percutaneous testing only. These products are supplied as listed in Table 2.

Table 2: Available Standardized Grass Pollen Extracts

Extracts	Strength	NDC	Vial Size
Standardized Grass Pollen, Bermuda Grass *(Cynodon dactylon)*	10,000 BAU/mL	65044-0537-2	10 mL
		65044-0537-4	50 mL
Standardized Grass Pollen, Kentucky Blue (June) *(Poa pratensis)*	100,000 BAU/mL	65044-0546-1	5 mL
		65044-0546-2	10 mL
		65044-0546-4	50 mL
Standardized Grass Pollen, Fescue, Meadow (*Festuca elatior*)	100,000 BAU/mL	65044-0612-1	5 mL
		65044-0612-2	10 mL
		65044-0612-4	50 mL
Standardized Grass Pollen, Orchard Grass *(Dactylis glomerata)*	100,000 BAU/mL	65044-0719-1	5 mL
		65044-0719-2	10 mL
		65044-0719-4	50 mL
Standardized Grass Pollen, Redtop *(Agrostis alba)*	100,000 BAU/mL	65044-0778-1	5 mL
		65044-0778-2	10 mL
		65044-0778-4	50 mL
Standardized Grass Pollen, Perennial Ryegrass *(Lolium perenne)*	100,000 BAU/mL	65044-0788-1	5 mL
		65044-0788-2	10 mL
		65044-0788-4	50 mL
Standardized Grass Pollen, Sweet Vernal Grass *(Anthoxanthum odoratum)*	100,000 BAU/mL	65044-0826-1	5 mL
		65044-0826-2	10 mL
		65044-0826-4	50 mL
Standardized Grass Pollen, Timothy *(Phleum pratense)*	100,000 BAU/mL	65044-0832-1	5 mL
		65044-0832-2	10 mL
		65044-0832-4	50 mL
Standardized Grass Mix #4 (25 % each of *Poa pratensis*, *Dactylis glomerata*, *Agrostis alba*, *Phleum pratense*)	100,000 BAU/mL	65044-0842-1	5 mL
		65044-0842-2	10 mL
		65044-0842-4	50 mL

16.2 Storage and Handling

Store extracts at 2 to 8 °C (36 to 46 °F). Dilutions with under 50% glycerin are less stable. If potency loss is suspected, verify the potency by skin testing with equal units of a freshly prepared dilution on individuals with known pollen allergies.

17 PATIENT COUNSELING INFORMATION

Instruct patients to remain in the office under observation for a minimum of 30 minutes after an injection or longer, if deemed necessary for the individual.

Inform patients that reactions may occur more than 30 minutes after skin testing or an injection.

Instruct patients to recognize the following symptoms as systemic adverse reactions and seek emergency medical care right away if any of these occur:

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

Manufacturer:
Jubilant HollisterStier LLC
Spokane, WA 99207 U.S.A.
U.S. Lic. No. 1272
385407-H09