Intradermal Testing

**Instructions**

**Allergenic Extracts**

For Intradermal Testing

Holister-Stier

Jubilant Holister-Stier LLC
Spokane, WA 99207
www.holisterstier.com
U.S. License No. 1272

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**Warnings**

This product is intended for use only by licensed medical personnel experienced in administering allergenic extracts and trained to provide immediate emergency treatment in the event of a life-threatening reaction. Allergenic extracts may potentially elicit a severe life-threatening systemic reaction, rarely resulting in death. Therefore, emergency measures and personnel trained in their use should 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.

Scratch, prick or puncture test first. Test intradermally only to those antigens giving negative or questionable reactions on scratch, prick or puncture testing.

This product should never be injected intravenously. Patients on non-selective beta blockers may be more reactive to allergens given for testing or treatment and may be unresponsive to the usual doses of antihistamines or epinephrine. Refer also to the Warnings, Precautions, and Adverse Reactions Sections below for further discussion.

**Description**

Extracts for intradermal testing are supplied in sterile multi-dose vials containing, in addition to the extract antigens and antigens, 0.5% sodium chloride, 0.25% sodium bicarbonate, up to 1% glycerin, 2% glycerin for APM products, and, as preservative, 0.4% phenol. The strength of these extracts may be expressed in terms of:

1. Weight to Volume (w/v)
2. Protein Nitrogen Units/mL (PNU/mL)
3. Allergy Units/mL (AU/mL)
4. Bioequivalent Allergy Units/mL (BAU/mL)
5. Concentrate

**Concentration**

**Concentration**

For regular extracts labeled in Allergy Units (AU)/mL is determined by in vitro preparation of standardized extracts and others 100,000 AU/mL. To avoid possible confusion about this change in the method of allergy unit assignment, the nomenclature changed for standardized extracts whose allergy units are assigned based on quantitative skin testing, and are labeled in Bioequivalent Allergy Units (BAU)/mL. References labeled 10,000 BAU/mL can be diluted one to a half million fold, and references labeled 100,000 BAU/mL can be diluted one to 5 million fold and produce a sum of erythema diameter of 50 mm when intradermal testing highly reactive subjects.

**Concentration**

“Concentrate” label terminology applies to allergenic extract mixtures, where the individual antigens being combined vary in strength or the designation of strength.

**Clinical Pharmacology**

Allergenic extracts for intradermal 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 result from the interaction of surface of basophil and mast cells, which initiates a series of biochemical events resulting in the production of histamine, slow-reacting substance of anaphylaxis and other mediators. These, in turn, produce the immediate-type “wheal and flare” skin reaction.

**Indications and Usage**

Certain diagnostics carry labeling which states: Allergenic Extract for Diagnostic Use Only. Data to support the therapeutic use of products labeled with this statement have not been established.1,3

In addition to a carefully taken history, the use of intradermal testing in allergic conditions is an accepted method in the diagnosis of allergic conditions.1,2,4,5 When scratch, prick or puncture reactions are small, or if the patient gives a history of allergic symptoms to a scratch, prick or puncture test, prick or puncture tests are inconclusive, intradermal tests may be indicated. However, ANTIGENS PRODUCING LARGE 3 TO 4+ SCRATCH, PRICK OR PUNCTURE TESTS SHOULD NOT BE TESTED INTRADERMALLY.

Excessively large local reactions or systemic reactions are more likely to occur giving negative or questionable results in intradermal testing. The intensity of the skin reaction produced will be determined by two factors: the degree of sensitivity of the patient and the nature of the antigen extract applied. In general, pollen extracts produce wheal reactions, whereas other intradermal tests produce wheals less often. Skin tests to foods seldom produce wheal reactions except for infrequent instances of sensitivity to fish, nuts or spices, and rarely other foods.

**Contraindications**

There are no known absolute contraindications to allergy skin testing. 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. These patients may also be more refractory to the normal allergy treatment regime.

**Warnings**

Scratch, prick or puncture test first. Test intradermally only to those antigens giving negative or questionable reactions on scratch, prick or puncture testing.

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 he or she is sensitive. Therefore, use caution when applying pollen tests to patients during their active pollen season, or after an exposure to inhalant allergens to which he or she is sensitive. Therefore, use caution when applying pollen tests to patients during their active pollen season, or after an exposure to inhalant allergens to which he or she is sensitive. Therefore, use caution when applying pollen tests to patients during their active pollen season, or after an exposure to inhalant allergens to which he or she is sensitive. Therefore, use caution when applying pollen tests to patients during their active pollen season, or after an exposure to inhalant allergens to which he or she is sensitive. Therefore, use caution when applying pollen tests to patients during their active pollen season, or after an exposure to inhalant allergens to which he or she is sensitive. Therefore, use caution when applying pollen tests to patients during their active pollen season, or after an exposure to inhalant allergens to which he or she is sensitive.

**Adverse Reactions**

**Local Reactions**

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.

**Systemic Reactions**

With careful attention to dosage and administration, such reactions occur infrequently, 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.
Adverse reaction frequency data for allergenic extract administration for testing and treatment show that risk is low. It cannot be overemphasized that, under certain unpredictable combinations of circumstances, severe shock is a possibility. Other possible systemic reaction symptoms, in varying degrees of severity, are fainting, pallor, bradycardia, hypotension, angioedema, cough, wheezing, conjunctivitis, rhinitis and urticaria.

If a systemic or anaphylactic reaction does occur, apply a tourniquet above the site of 100 mm Hg. If tests are performed on the arms, and inject the 1:1000 epinephrine-hydrochloride intramuscularly or subcutaneously into the opposite arm. Loosen the tourniquet at least every 10 minutes. Do not obstruct arterial blood flow with the tourniquet.

**EPINEPHRINE: ADULT DOSAGE** 0.3 to 0.5 mL should be injected. Repeat in 5 to 10 minutes if necessary.

**PEDIATRIC DOSAGE:** The usual initial dose is 0.01 mg (mL) per kg body weight or 0.3 mL (mL) per square meter of body surface area. Suggested dosage for infants to 2 years of age is 0.05 mL to 0.1 mL; for children 2 to 6 years, 0.15 mL; and children 6 to 12 years, 0.2 mL. Single pediatric doses should not exceed 0.3 mg (mL). Doses may be repeated as frequently as every 20 minutes, depending on the severity of the condition and the response of the patient.

After administration of epinephrine, profound shock or vasomotor collapse should be treated with intravenous fluids, and possibly vasoactive drugs. Oxygen should be given by mask. Intravenous antihistamine, theophylline or adrenocorticosteroids may be used if necessary after adequate epinephrine and circulatory support have been given.

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. [Ref. J. Allergy Clin. Immunol. 77 (2): 271-273, 1986]

Rarely are all of the above measures necessary; the tourniquet and epinephrine usually produce prompt responses. However, the physician should be prepared in advance for all contingencies. Promptness in beginning emergency treatment measures is of utmost importance.

3. **Adverse Event Reporting**

Report all adverse events to Julliant HalsaSter Ster, LLC, Customer Technical Services Department at 1 (800) 992-1120. A voluntary adverse event reporting system for health professionals is available through the FDA MEDWATCH program. Preprinted forms (FDA Form 3500) are available from the FDA by calling 1 (800) FDA-1088. Completed forms should be mailed to MEDWATCH, 5600 Fisher Lane, Rockville, MD 20852-9787 or Fax to: (1) (800) FDA-0178.

4.  [OVERDOSAGE]

See ADVERSE REACTIONS Section.

5. **DOSE AND ADMINISTRATION**

1. **General**

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

2. **Intradermal Testing Methods**

Cleanse the rubber stopper of the vial with liquid antiseptic before withdrawing extract. A sterile tuberculin syringe with 26-gauge, short-bevel needle should be used for the injection. The anterior surface of the upper and lower arm is preferable for testing. Cleanse the skin with soap and water or wash with alcohol or other antiseptic. Introduce the needle between the superficial layers of the skin and inject 0.02 mL of the extract.

Test sites should be at least 2.5 cm apart, and no more than 10 to 20 antigens should be introduced at one time. This rule can be followed with additional groups of 10, providing the reactions are not numerous or strong. The same amount of extract should be injected in each site for proper comparison. It is advisable to avoid testing with more than one allergen in the same group in each series, i.e., nuts, fish, epidermals, etc.

A site should be injected with 0.02 mL of the control solution. All skin tests should be validated by appropriate positive control tests (e.g., histamine) and negative control tests [e.g., Glycerin, Albumin Saline with Phenol (0.4%) or Buffered Saline with Phenol (0.4%)]. The negative control test should be the same material as is used as a diluting fluid in the test extracts. Diluting fluid is used in the same way as an active test extract. False positive reactions are sometimes encountered in intradermal testing, and the possibility of irritation reactions should always be taken into consideration.

In cases where the patient is known to be quite sensitive, screen testing by scratch, prick or puncture method is recommended, and intradermal testing should be done with caution.

The intradermal strength is usually safe for testing patients presenting with negative scratch, prick or puncture tests. It is recommended that a 1:10 dilution of the stock intradermal strength be used in preliminary testing of patients not previously screened by scratch, prick or puncture tests.

3. **Use of Antigen Mixes**

The use of complicated mixtures of unrelated pollens for testing is not recommended since in the case of a positive reaction it does not indicate which pollen (s) is responsible, and in the case of a negative reaction, it fails to indicate whether the individual pollens at full concentration would give a positive reaction.

4. **Reading Skin Test Reactions**

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 surrounding a central papule at least 5 mm in diameter. In some instances with 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.

5. **Standardized Products**

(a) **Mites:** The skin test concentrations of 30 AU/mL and 300 AU/mL in multiple dose vials are used for intradermal testing.

Intradermal skin tests in selected highly sensitive subjects are presented for reference purposes:

<table>
<thead>
<tr>
<th>Allergen</th>
<th>Number of Subjects</th>
<th>Mean Concentration (AU/mL)</th>
<th>Erythema Diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>D. farinae</td>
<td>12</td>
<td>0.0609</td>
<td>5-10</td>
</tr>
<tr>
<td>D. pteronyssinus</td>
<td>12</td>
<td>0.0333</td>
<td>5-10</td>
</tr>
</tbody>
</table>

Intradermal extracts should be used as follows:

1. **Patients with a negative scratch, prick or puncture test:** Patients who do not react to a valid scratch, prick or puncture test should be tested intradermally with 0.02 to 0.05 mL of a 30 AU/mL extract solution.

If this test is negative, a second intradermal test may be performed using a 300 AU/mL extract solution. The negative control used with this latter dilution should contain 0.5% glycerin.

2. **Patients tested only by the intradermal method:** Patients suspected of being highly allergic should be tested with 0.02 to 0.05 mL of a 30 AU/mL solution containing 0.03 AU/mL. A negative test should be followed by repeat tests using progressively stronger concentrations until the maximum recommended strength of 300 AU/mL is reached. The negative control used with this latter dilution should contain 0.5% glycerin.

(c) **Ragweed pollen (Short Ragweed or Giant and Short Ragweed Mixtures) Amb 1 (formerly known as Antigen E) Assayed:**

The intradermal strength for Short Ragweed extract is usually 5000 AU/mL, which by calculation contains approximately 0.7 to 3 units of Amb 1/mL. For Giant and Short Ragweed mix the suggested intradermal strength is 5000 AU/mL, which by calculation contains 0.4 to 1.5 units of Amb 1/mL. These strengths are usually safe for testing patients previously having negative scratch, prick or puncture test reactions. A 1:10 dilution of the stock intradermal strength should be used in preliminary testing of patients not previously screened by scratch, prick, or puncture tests.

A study of ragweed sensitive patients indicates that intradermal tests, using 0.05 mL of extract, produce positive reactions (1+ to 2+) at Amb 1 concentrations of from 2.7x10^4 to 2.7x10^5 units per mL. The equivalent PNU range was 100 to 0.001 PNU per mL.

Ragweed skin tests are graded in terms of the wheal and erythema response noted at 15 minutes. Wheal and erythema size may be recorded by actual measurement of the extent of both responses.

6. **Pediatric Use**

The dose is the same in patients of all age groups. Because the wheal size in response to allergen skin testing decreases with age, appropriate histamine positive control skin tests must be performed.

7. **Storage**

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

8. **LIMITED WARRANTY**

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; the health of the patient; the 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.

In no event will the Company be liable for any special, incidental, or consequential damages, or any damages whatsoever resulting from loss of use, data, or profits, whether or not such damages were foreseen, anticipated, or otherwise preventable.

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REFERENCES


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