FULL PRESCRIBING INFORMATION: CONTENTS:

1 INDICATIONS AND USAGE

CANDIN® is indicated for use as a recall antigen for detecting cell-mediated hypersensitivity by intracutaneous (intradermal) testing. The product is intended to elicit an induration response ≥5 mm in immunologically competent persons with cellular hypersensitivity to the antigen (see DOSAGE AND ADMINISTRATION). (3.2)

2 DOSAGE AND ADMINISTRATION

2.1 Intracutaneous (intradermal) Injection

The skin-test strength of CANDIN® has been determined from production lots with an Internal Reference (IR), using sensitive adults (see DOSAGE FORMS AND STRENGTHS).

3 DOSAGE FORMS AND STRENGTHS

DOSAGE FORMS AND STRENGTHS

3.1 Dosage form.

CANDIN® skin test dose is 0.1 mL administered intradermally.

2.3 Mechanism of Action

Mediated hypersensitivity by intracutaneous (intradermal) testing. The antigen (C. albicans) is injected intracutaneously. (6.2)

4 CONTRAINDICATIONS

5.2 Geriatric Use

The expected response to CANDIN® is a local area of inflammation at the site of the skin test. The size of reaction depends upon the sensitivity of the person receiving the test. The reaction size is not a measure of cellular immune response.

5 WARNINGS AND PRECAUTIONS

5.1 Administration

Adverse reactions can occur with skin test antigens and in certain individuals these reactions may be life-threatening or cause death. Emergency measures and personnel trained in their use should be immediately available. Patients should be observed for at least 20 minutes following the administration of a skin test. (6.2)

5.2 Serious adverse reactions to CANDIN® should be reported to Nielsen BioSciences, Inc. at (855) 855-1212 or MEDWATCH, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20852-9782. Telephone: (800) 332-1088 or www.vaers.hhs.gov. (5)

5.3 Response to CANDIN® in adults with cancer who have been previously screened and qualified to serve as test volunteers: 6 patients, 5 responses. (5.5)

6 ADVERSE REACTIONS

6.1 Immediate hypersensitivity local reactions

The time required for the induration response to reach maximum intensity varies with the individual. The reaction usually begins within 24 hours and peaks between 24 and 48 hours. The skin test should be read at 48 hours by visually inspecting the test site and palpating the indurated area. Most reactions should be made across two diameters as shown in the figure below. The mean of the longest and midpoint orthogonal diameters of the indurated area should be reported as the DTH reaction. For example, a reaction that is 10 mm in diameter by 8 mm (midpoint orthogonal diameter) has a sum of 18 mm and a mean of 9 mm. The DTH response is therefore 9 mm.

6.2 Systemic reactions

Systemic reactions can occur with skin test antigens and in certain individuals these reactions may be life-threatening or cause death. Patients should be observed for at least 20 minutes following the administration of a skin test. Emergency measures and personnel trained in their use should be immediately available in the event of a serious systemic reaction. See WARNINGS AND PRECAUTIONS. (5)

6.3 Local reactions

Local reactions can occur following administration. See WARNINGS AND PRECAUTIONS. (5)

7 DRUG INTERACTIONS

7.1 Corticosteroids and immunosuppressive drugs

Beta-blockers drugs. (7.0)

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1 allergy manifested as either generalized or adverse local reactions. One subject had induration with a central vesicle which subsided within a few days.

Severe local reactions, including rash, vesication, bullae, dermal and cellular induration are possible in highly allergic persons.

6.2 Systemic reactions to CANDIN® have not been observed. However, all foreign antigens have the remote possibility of causing Type 1 anaphylaxis and even death when injected intradermally.9 Systemic allergic reactions usually occur within 30 minutes after the injection of antigen. In Table 2, the response to CANDIN® in adults with HIV infection (no-AIDS-indicator conditions) and adult control subjects (Table 2). Response to CANDIN® in Adults with HIV Infection: In one study (Table 2), the skin test responses of adults with HIV infection were compared to those of healthy control subjects (age range 22 - 65). In this study, 60% of males tested positive compared to 53% of females; the mean induration in responding males was 12.8 mm and in responding females was 13.0 mm.

14 CLINICAL STUDIES

14.1 Response to CANDIN® in Healthy Adults (Table 1). In a group of 18 subjects, 14 (78%) of the individuals tested to CANDIN® with an induration response ≥ 5 mm at 48 hours. In a second study of 35 subjects, 21 (60%) had induration responses ≥ 5 mm at 48 hours. In this study, 65% of males tested positive compared to 53% of females; the mean induration in responding males was 12.8 mm and in responding females was 13.0 mm.

14.2 Cellular hypersensitivity response to CANDIN® in adults with AIDS, adults with HIV infection (no-AIDS-indicator conditions) and adult control subjects (Table 2). In a second study involving 20 male patients (age range 26 – 57) diagnosed with AIDS based on clinical criteria only, one subject responded to CANDIN®. In the same study 65% of the male control subjects had DTH reactions ≥ 5 mm to CANDIN® (Table 1, Study 2). The mean induration response at 48 hours for control subjects was 8.5 mm compared to 1.78 mm for AIDS subjects. AIDS vs. control responses were p < 0.01 mean induration and ≥ 0.01 induration ≥ 5 mm.

Because HIV infection can modify the DTH response to tuberculin, it is advisable to skin test HIV-infected patients at high risk of tuberculosis in addition to tuberculin.20 In a published study, 479 subjects (334 males and 145 females) infected with HIV and who were skin tested for tuberculosis had several additional antigens, including CANDIN® supplied under IND to the investigators. Only 12% reacted to tuberculin (≥ 5 mm), 57% reacted to CANDIN® (≥ 3 mm) and 60% reacted to either tuberculin or CANDIN® or both. In this study, a 3 mm induration response to CANDIN® was considered positive. The authors concluded that in HIV-infected subjects, testing with other DTH antigens increases the accuracy of interpretation of negative tuberculin reactions.

Table 2. Cellular hypersensitivity response to CANDIN® in adults with AIDS, adults with HIV infection (no-AIDS-indicator conditions) and adult control subjects. Range and mean of CD4 T-cell counts shown in the shaded area of the table.

<table>
<thead>
<tr>
<th>Group</th>
<th>Classifi-</th>
<th>Zidovudine Use</th>
<th>CD4 Range</th>
<th>Mean Indur. (mm)</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS</td>
<td>A3,B3,C</td>
<td>12</td>
<td>4-483</td>
<td>145</td>
<td>3.313</td>
<td>9</td>
</tr>
<tr>
<td>HIV</td>
<td>A1,A2</td>
<td>28</td>
<td>101-1065</td>
<td>455</td>
<td>5.67</td>
<td>15</td>
</tr>
<tr>
<td>HIV</td>
<td>B1,B2</td>
<td>23</td>
<td>101-1065</td>
<td>455</td>
<td>5.67</td>
<td>15</td>
</tr>
</tbody>
</table>

*reference (5)
(a) p = 0.01 compared to Control. (b) p < 0.01 compared to Control.
(c) See Control Group in Table 1.

14.3 Cellular hypersensitivity response to CANDIN® in adults with cancer (Table 3). In one study of 18 patients with lung cancer, CANDIN® elicited a positive DTH response in 17 of 18 patients. In a second study of 20 patients with metastatic cancer, no reactions ≥ 5 mm were observed (Table 3).

Table 3. Cellular hypersensitivity response to CANDIN® in adults with cancer.

<table>
<thead>
<tr>
<th>Age Range (years)</th>
<th>Number reactions ≥ 5 mm at 48 hours</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 1</td>
<td>18</td>
<td>52 – 75</td>
</tr>
<tr>
<td>Study 2</td>
<td>20</td>
<td>47 - 81</td>
</tr>
</tbody>
</table>

15 REFERENCES


6. HOW SUPPLIED/STORAGE AND HANDLING

CANDIN® is supplied in a 1 ml multidose vial containing 10 ml doses. Storage

Store between 2 - 8°C. Do not freeze.

7. PATIENT COUNSELING INFORMATION

Local reactions to CANDIN® can include redness, swelling, pruritus, paresthesia and discoloration of the skin. These reactions usually subside within hours or days after administration of the skin test. In some patients, skin discoloration may persist for several weeks. Progression of the DTH reaction to vesication, necrosis and ulceration is possible. Patients should be informed that all foreign antigens have the remote possibility of causing Type 1 anaphylactic reactions that may require the administration of epinephrine and other drugs or emergency procedures and may be life threatening in some cases. Patients should report any serious adverse reactions to their health care provider.

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

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Candida albicans Skin Test Antigen for Cellular Hypersensitivity
CANDIN®

Mfg. by Allermed Laboratories, Inc.
San Diego, CA. 92111