To report SUSPECTED ADVERSE REACTIONS contact Nielsen BioSciences, Inc. at (855) 855-1212 or MEDWATCH, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20852-7982. Telephone (800) 332-1088 or www.vaers.hhs.gov. (6.3)

DRUG INTERACTIONS

Corticosteroids and immunosuppressive drugs
Beta-blocking drugs. (7.0)

USE IN SPECIFIC POPULATIONS

Pediatric Use
Nursing Mothers

Corticosteroids and immunosuppressive drugs
Beta-blocking drugs

DOSE FORMS AND STRENGTHS

DOSAGE FORMS

Dose form.

Skin test strength

5.1 INDICATIONS AND USAGE

CANDIN® is indicated for a recall antigen for detecting cell-mediated hypersensitivity by intracutaneous (intradermal) testing. The potency of CANDIN® is measured by DTH skin tests in humans. The procedure involves concurrent (side-by-side) testing of production lots with an Internal Reference (IR), using sensitive adults who have been previously screened and qualified to serve as test subjects. The induration response at 48 hours elicited by 0.1 ml of a production lot is measured and compared to the response elicited by 0.1 ml of the IR. The test is satisfactory if the potency of the production lot does not differ more than ± 20% from the potency of the IR, when analyzed by the paired t-test (two-tailed) at a p value of 0.05. The potency of the IR is monitored by DTH skin testing. Persons included in the assay pool are qualified as test subjects by receiving four skin tests with the IR from which a mean induration response (mm) is calculated. The response of the four skin tests with the IR must show that the potency of the IR has not changed more than ± 20% from the mean qualifying response in the same test subject, when analyzed by the paired t-test (two-tailed) at a p value of 0.05. The required induration response at 48 hours to the IR is 15 mm ± 20%.

2 DOSE ADMINISTRATION

2.1 Parenteral drug products should be inspected visually for particulate matter and container leakages. Epinephrine and oxygen must be immediately available in the event of a serious systemic response.

6 ADVERSE REACTIONS

6.1 Local reactions to CANDIN® in included swelling, pruritus and vesiculation. Reactions involving necrosis and ulceration have not been observed, but such reactions are theoretically possible and might occur in persons with exquisite cellular hypersensitivity to the antigen. Local reactions may be treated with a cold compress and topical steroids. Severe local reactions may require additional measures as appropriate.

In a published study of 479 HIV positive adults tested with CANDIN®, adverse local reactions were observed in six subjects as follows: ecchymosis (three), vesiculation with edema (one), vesiculation and weeping edema (one). Pruritus and swelling cleared within 48 hours; vesiculation with edema required approximately 1 week to resolve. (6.1)

In two studies involving 171 persons discussed under CLINICAL STUDIES in Tables 1, 2, 3, and text, one adverse reaction was observed. This reaction consisted of induration 22 mm ± 54 mm at 48 hours which resolved in 5 days. (6.1)

Testing of CANDIN® for consistency of potency is performed in healthy human subjects who are known to be skin test positive to the antigen and unresponsive (see CLINICAL STUDIES) to Candida albicans. In cases of Type I allergy manifested as either generalized or adverse local reactions. One subject had induration with a central vesicle which subsided within a few days. (6.1)

FULL PRESCRIBING INFORMATION

Candida albicans Skin Test Antigen For Cellular Hypersensitivity - CANDIN® Intradermal Injection

Nielsen BioSciences, Inc.
Mfg. by AllerMed Laboratories, Inc.

WARNING

See full prescribing information for complete boxed warning.

The expected response to CANDIN® is a local area of inflammation at the site of the skin test. The reaction is usually done to determine reaching maximum diameter between 24 and 48 hours. Larger accelerated reactions can occur, which may require treatment with local cold compresses and anti-inflammatory medications. (2.3,6.1)

Systemic 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)

CANDIN® should never be given intravenously. (5)

To report SUSPECTED ADVERSE REACTIONS contact Nielsen BioSciences, Inc. at (855) 855-1212 or MEDWATCH, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20852-7982. Telephone (800) 332-1088 or www.vaers.hhs.gov. (6.3)

RECENT MAJOR CHANGES

INDICATIONS AND USAGE

CANDIN® is a solution for intradermal injection supplied in a 1 ml, multi-dose vial. (3.1)

The skin-test strength of CANDIN® has been determined from dose-response studies in healthy adults. 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)

DOSE FORMS AND STRENGTHS

CANDIN® is a solution for intradermal injection supplied in a 1 ml, multi-dose vial. (3.1)

The skin-test strength of CANDIN® has been determined from dose-response studies in healthy adults. 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)

CONTRAINDICATIONS

CANDIN® should not be used after a previous unacceptable adverse reaction to this antigen or to a similar product, i.e., extreme hypersensitivity/allergy. (4.0)

WARNINGS AND PRECAUTIONS

The antigen must be injected intradermally as superficially as possible, causing a distinct, sharply defined bleb at the skin test site. An unacceptable adverse reaction that may result in the product is injected subcutaneously. It must not be given intravenously; care should be taken to avoid injection into a blood vessel. A separate sterile syringe and needle should be used for each patient to prevent cross-contamination by other licensed agents. Needles should be disposed of properly and should not be recapitated. (5)

It is possible that some patients may have exquisite immediate hypersensitivity to CANDIN®. In persons with bleeding tendency, bruising and non-specific induration may occur due to the trauma of the skin test. As with all skin test antigens, local and systemic allergic reactions can occur following intradermal injection. (5.2)

Physicians using this product must have facilities, equipment and medication necessary to treat potential side effects. Epinephrine and oxygen must be immediately available in the event of a serious systemic response. (5.3)

ADVERSE REACTIONS

Immediate hypersensitivity local reactions can include itching, swelling, pain and blistering at the test site occurring 15-20 minutes after administration. Necrosis is possible. (6.1)

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. (6.2)

Full prescribing information for complete boxed warning. (6.3)

CANDIN® is intended for use by physicians who are experienced in the intradermal administration of a skin test antigen. (6.4)

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, but is usually defined reaching maximum diameter between 24 and 48 hours. Larger accelerated reactions can occur which may require treatment with local cold compresses and anti-inflammatory medication. (2.3,6.1)

Systemic 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)

CANDIN® should never be given intravenously. (5)

To report SUSPECTED ADVERSE REACTIONS contact Nielsen BioSciences, Inc. at (855) 855-1212 or MEDWATCH, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20852-7982. Telephone (800) 332-1088 or www.vaers.hhs.gov. (6.3)

WARNING

See full prescribing information for complete boxed warning.

CANDIN® is intended for use by physicians who are experienced in the intradermal administration of a skin test antigen. (6.4)

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, but is usually defined reaching maximum diameter between 24 and 48 hours. Larger accelerated reactions can occur which may require treatment with local cold compresses and anti-inflammatory medication. (2.3,6.1)

Systemic 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)

CANDIN® should never be given intravenously. (5)

To report SUSPECTED ADVERSE REACTIONS contact Nielsen BioSciences, Inc. at (855) 855-1212 or MEDWATCH, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20852-7982. Telephone (800) 332-1088 or www.vaers.hhs.gov. (6.3)
Severe local reactions, including rash, vesiculation, bullae, dermal exfoliation and cellulitis are possible in highly allergic persons.

6.2 Systemic reactions to CANDIN® have not been observed. However, it is not known whether CANDIN® may be diminished in geriatric patients, women, patients with metastatic cancer, or patients with HIV infection. Therefore, the recommended dose for CANDIN® in adults with AIDS and HIV infection in HIV-infected patients (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 response of adult patients with HIV infection (no-AIDS-indicator conditions) and adult control subjects was compared to those of healthy control subjects (age range 22 - 65, HIV positive 20 - 45, Controls 25 - 69). When HIV-infected subjects were classified by the CDC's 1993 revised surveillance case definition for AIDS and the CD4 lymphocyte count at 1.000 cells/µl should be made available immediately as well as oxygen and emergency equipment.

Because individuals differ in their sensitivity to CANDIN®, the response to the recommended dose of 0.1 ml can vary in size and intensity. In highly sensitive persons, the result of overdose, or a mistake in the administration of CANDIN® may result in a more pronounced local or systemic outcome.

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 8.33 mm compared to 1.78 mm for the AIDS subject. AIDS vs control p-values were < 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 infection, in addition to tuberculosis vaccination. In a published study of DTH anergy, 479 subjects (334 males and 145 females) infected with HIV and being screened for tuberculosis were skin tested with several additional antigens to determine their entire immune status prior to the initiation of antiretroviral therapy. 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 mean of CD4 T-cell count shown in the shaded area of the table.

Table 1. Induration response to CANDIN® in healthy adults.

| Group | Classifi
cation* | Zidovu
dine Use | CD4 Range | Mean Indur. (mm) | % |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS</td>
<td>A1,B1,C1</td>
<td>12</td>
<td>14</td>
<td>4 - 68</td>
<td>15.35± 9</td>
</tr>
<tr>
<td>HIV</td>
<td>A1,A2</td>
<td>13</td>
<td>20</td>
<td>45</td>
<td>5</td>
</tr>
<tr>
<td>Control</td>
<td>---</td>
<td>18</td>
<td>0</td>
<td>555 - 1876</td>
<td>869 ± 03</td>
</tr>
</tbody>
</table>