6. As with many vaccines, anaphylaxis may occur after use. Initial antidote of epinephrine is recommended and should be followed with appropriate supportive therapy.
7. This product has been shown to be efficacious in healthy animals. A protective immune response may not be elicited if animals are incubating an infectious disease, are malnourished or parasitized, are stressed due to shipment or environmental conditions, are otherwise immunocompromised, or the vaccine is not administered in accordance with label directions.

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Technical inquiries should be directed to Zoetis Inc. Veterinary Services, (888) 963-8471 (USA), (800) 461-0917 (Canada).

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Zoetis Inc.
Kalamazoo, MI 49007, USA

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Printed in USA

Feline Leukemia Vaccine

Killed Virus

Leukocell® 2

PRODUCT DESCRIPTION: Leukocell 2 is a multiple viral antigen vaccine for vaccination of healthy cats 9 weeks of age or older as an aid in preventing persistent viremia, lymphoid tumors caused by feline leukemia virus (FeLV), and diseases associated with FeLV infection. Leukocell 2 is prepared by propagating FeLV, subgroups A, B, and C, in FeLV-transformed lymphoid cells. Viral antigens are chemically inactivated, combined with a sterile adjuvant to enhance the immune response, and packaged in liquid form.

Leukocell 2 is prepared from an FeLV-transformed lymphoid cell line that releases FeLV viral particles which are soluble in a cell culture medium.[1] The practical benefit of this unique, patented feature is that production of immunosuppressive effects characteristic of fully assembled FeLV antigens, whether live or killed, is reduced.[2–4] (See SAFETY AND EFFICACY)

Leukocell 2 is a second generation vaccine derived from and comparable to Leukocell, the first federally licensed FeLV vaccine. Licensed in the United States in November 1984, Leukocell originally was indicated for 3 intramuscular (IM) doses, a regimen demonstrated to be efficacious in preventing

persistent viremia, lymphoid tumors, and FeLV-associated diseases. After basic development studies were performed to demonstrate suitability for licensing, additional data has been published attesting to the vaccine's safety and efficacy. Lymphocyte blastogenesis assays (LBA) showed that soluble vaccine proteins produced no significant effect on LBA of cat lymphocytes when compared with control samples,[5,6] an indication that the vaccine is not immunosuppressive. In a related test, cats were vaccinated with a 10-fold concentration of enhanced vaccine, and lymphocytes from these cats showed no change in LBA response, nor did their LBA values differ appreciably from those of nonvaccinated cats.[5,6] Other studies showed that Leukocell was an aid in protecting vaccinated cats from latent FeLV infection, even when repeated immunosuppressive treatment was administered.[5,7,8] Another series of tests showed that Leukocell consistently elicited marked levels of complement-dependent cytotoxic (CDC) antibodies, demonstrating that the vaccine's immunizing properties are not limited to its ability to stimulate anti-gp70 and anti-feline oncornavirus-associated membrane antigen (FOCMA) antibodies.[5,9,10] Clinical reports by independent practitioners have demonstrated that the vaccine protected cats in high-risk environments where frequent or continuous contact with known leukemic cats occurred.[11]

Leukocell 2 was licensed with a 2-dose subcutaneous (SC) indication. In multiple tests conducted to determine suitability for licensing, using minimal potency vaccine, Leukocell 2 was shown to be:

- Highly immunogenic, producing and priming for antibody responses to gp70, FOCMA, and virus neutralizing (VN) antigens.
- Highly efficacious, protecting more than 70% of artificially immunosuppressed vaccinates against persistent viremia after challenge.
- Safe, as no change in normal blood cell values of vaccinated cats was observed during the vaccination period.

DISEASE DESCRIPTION: FeLV is associated with a complex of feline diseases. These include 2 forms of cancer: (1) lymphosarcoma, characterized by presence of tumors, and (2) leukemia, characterized by presence of malignant cells in the bloodstream. In addition, FeLV is associated with a variety of non-neoplastic diseases, including aplastic anemia, reproduction failure, stomatitis, Fading Kitten Syndrome (thymic atrophy), and upper respiratory infections. The pathological process is enhanced by the virus's role as an immunosuppressive agent. Following chronic infection, immunosuppression persists until cancer or disease of microbial origin develops, usually after a period of months or years.

The causative agent of FeLV disease is a retrovirus, which was named "feline leukemia virus" after its discovery in 1964. The designation is somewhat inaccurate in view of the variety of clinical conditions that result from FeLV infection, only a minority of which are leukemic. Three FeLV subgroups, designated A, B, and C, have been identified, with subgroup A predominating. Structurally, the FeLV envelope consists of 2 proteins, gp70 and p15e. The gp70 protein is the more prominent. It is considered to be the primary immunogenic antigen inasmuch as gp70 antibodies will neutralize FeLV. A variety of other FeLV proteins have been identified (including p10, p12, p15, and p27) although their correlation with FeLV disease has not been established.

Lymphosarcoma is the most common form of cancer caused by FeLV. Lymphosarcomas resulting from FeLV infections express a nonviral antigen on the surface of the malignant cells. This tumor-specific antigen is designated feline oncornavirus-associated cell membrane antigen (FOCMA). Postexposure antibodies to FOCMA have been shown to confer immunity to FeLV-induced lymphosarcoma and are an important factor in successful resistance to tumor development.[12] Studies have shown that cats that develop FeLV malignancies do not have high FOCMA antibody titers,[12] and that inadequate anti-FOCMA response is a cause, rather than an effect, of ensuing FeLV lymphosarcoma.[13]

SAFETY AND EFFICACY: The vaccine's safety and lack of immunosuppression have been demonstrated by the lymphocyte blastogenesis assay (LBA), differential and complete blood counts (CBC). Leukocell 2 stimulates and primes for antibody responses to gp70 glycoprotein, the tumor-specific antigen FOCMA (see DISEASE DESCRIPTION), as well as VN antigens.

In an immunogenicity study, 25 specific pathogen free (SPF) cats were vaccinated with a 2-dose primary regimen (2 doses were given 3 weeks apart). After the second dose, significant levels of antibodies to gp70 and FOCMA were detected as well as VN antibodies.

After challenge with the Rickard strain of FeLV, which infected 100% of the control cats, more than 70% of the vaccinates were protected against establishment of persistent viremia. In contrast, 60% of nonvaccinated control cats developed persistent viremia.

In assessing these results, it should be noted that test cats were subjected to a far more rigorous challenge regimen than could be expected under normal exposure conditions (normal FeLV incidence after exposure is 30%[14,15]). All test cats (including vaccinates) were artificially immunosuppressed before challenge to enhance susceptibility to FeLV infection and tumor development. Challenge virus was administered intranasally to ensure uniform exposure that conforms to the natural route of infection, and assures optimum delivery of challenge virus.

Demonstrated safety is particularly critical in the case of an FeLV vaccine. Whole FeLV (live or killed) contains a specific envelope protein, designated p15e, that is responsible for host immunosuppression.[2–4,16,17] Rigorous safety tests of Leukocell 2 did not demonstrate any immunosuppressive effects. Kittens vaccinated with Leukocell 2 had normal postvaccination white blood cell (WBC) counts, did not become viremic, remained clinically normal, and developed gp70, FOCMA, and VN antibodies.

Postvaccination reactions have been observed in about 2% of vaccinated cats. These included stinging on injection, transient listlessness, depression, and brief temperature elevations. Hypersensitivity evidenced by myxedema and gastrointestinal distress (vomiting and bowel evacuation) occasionally has been reported.

Although a diagnostic test for FeLV antigen is not required prior to vaccination with Leukocell 2, such a test may be beneficial in evaluating candidates for vaccination. Vaccination is of no known therapeutic value in cats with existing FeLV infection, nor will it alter the natural course of disease.

DIRECTIONS:

1. *General Directions:* Shake well. Aseptically administer 1 mL subcutaneously.
2. *Primary Vaccination:* Healthy cats 9 weeks of age or older should receive 2 doses administered 3–4 weeks apart.
3. *Revaccination:* Annual revaccination with a single dose is recommended.

PRECAUTIONS:

1. Store at 2°–7°C. Prolonged exposure to higher temperatures may adversely affect potency. Do not freeze.
2. Use entire contents when first opened.
3. Sterilized syringes and needles should be used to administer this vaccine.
4. Contains gentamicin as preservative.
5. Certain postvaccination reactions may occur. (See SAFETY AND EFFICACY)

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