Pulmonary thromboembolism is a primary concern for heartworm-infected dogs. Signs can be minimal yet rapidly fatal, and the lack of noninvasive tests can make diagnosis difficult. D-Dimers, by-products of fibrin protein, are produced when a blood clot is degraded, and d-dimer screening is often the first step in diagnosing pulmonary thromboembolism in humans. Researchers examined the use of this by-product to monitor arteries in dogs infected with *Dirofilaria immitis*. Results revealed that d-dimer levels were increased in plasma samples of infected dogs with pulmonary thromboembolism, and staining of tissue samples from those animals revealed d-dimer deposits in affected blood vessels. Naturally infected animals with d-dimer deposits in the pulmonary arteries always had plasma levels ≥0.2 µg/mL. Below that value, only 13% of animals had d-dimer deposits in their pulmonary arteries.

**Commentary**

Screening d-dimer plasma levels can be a useful method for monitoring the condition of heartworm-infected dogs. The presence of d-dimer levels >0.2 µg/mL adds strong support to a diagnosis of pulmonary thromboembolism, reducing the need for more invasive procedures and allowing prompt treatment with antiocoagulants. However, any result that conditions in the breakdow of blood clots can elevate d-dimer levels, so careful differential diagnosis is essential.—Carly Jordan, PhD

**Source**


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**FOCUS**

**D-Dimers for Dirofilaria Patients**

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**RESEARCH NOTE: Treating Cancer by Understanding Its Genetics**

Up to 10% of feline tumors are oral, specifically squamous cell carcinomas (SCCs). Feline oral SCCs are locally aggressive and cause high morbidity. They have an inherent insensitivity to radiation and chemotherapy. The cancer stem cell (CSC) theory suggests that cancer may be driven by a small subpopulation of primitive CSCs with the ability to form new tumors. These cells demonstrate resistance to cytotoxic drug treatment and/or radiotherapy. This study identified a stem cell population in a feline SCC cell line. Further study of the unique molecular processes and pathways of CSCs should enable development of novel therapies targeting this cell population.

**Source**


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**CAPSULES**

**Dirofilaria immitis**

**Topical Parasiticide for Dogs and Cats**

**BRIEF SUMMARY:** See package insert for full prescribing information.

**CAUTION:** US Federal law restricts this drug to use by or on the order of a licensed veterinarian.

**INDICATIONS:** Revolution is recommended for use in dogs six weeks of age and older and cats eight weeks of age and older for the following parasitic and infectious indications:

- **Dogs:** Revolution kills adult flukes and prevents fluke eggs from hatching for six months and is indicated for the prevention and control of fluke infections (*Clonorchis sinensis*), prevention of heartworm disease caused by *Dirofilaria immitis*, and the treatment and control of ear mites (*Otodectes cynotis*) infections. Revolution is also indicated for the treatment and control of sarcoptic mange (*Sarcoptes scabiei*) and intestinal hookworm (*Ancylostoma tubaeforme*) infestations in dogs.
- **Cats:** Revolution kills adult flukes and prevents fluke eggs from hatching for six months and is indicated for the prevention and control of fluke infections (*Clonorchis sinensis*), prevention of heartworm disease caused by *Dirofilaria immitis*, and the treatment and control of ear mites (*Otodectes cynotis*) infections. Revolution is also indicated for the treatment and control of roundworm (*Toxocara cati*) and intestinal hookworm (*Ancylostoma tubaeforme*) infestations in cats.

**WARNINGS:**

- **Nonsurgical use.** Keep out of the reach of children.
- In humans, Revolution may be irritating to skin and eyes. Reactions such as sneezing and skin rashness have been reported in humans in rare instances. Individuals with known hypersensitivity to Revolution should use the product with caution or consult a medical care professional. Revolution contains isopropyl alcohol and the preservative haloxyalin (BHT). Wash hands after use and wash off any product in contact with the skin immediately with soap and water. If contact with eyes occurs, flush eyes copiously with water. In case of ingestion by a human, contact a physician immediately. The material safety data sheet (MSDS) provides more detailed occupational safety information. For a copy of the MSDS or to report adverse reactions attributable to exposure to this product, call 1-800-366-2008.

- **Flammability:** Keep away from heat, sparks, open flames or other sources of ignition.
- Do not use in sick, debilitated or underweight animals. (see SAFETY)

**PRECAUTIONS:**

Prior to administration of Revolution, dogs should be tested for existing heartworm infections, and the discretion of the veterinarian should be used to determine whether a patient should be treated to remove adult heartworms. Revolution is not effective against adult *D. immitis* and, while the number of circulating microfilariae may decrease following treatment, Revolution is not effective for microfilaricidal clearance.

Hypersensitivity reactions have not been observed in dogs with patent heartworm infections administered three times the recommended dose of Revolution. Higher doses were not tested.

**ADVERSE REACTIONS:**

**Pre-approval clinical trials:**

Following treatment with Revolution, transient localized alopecia with or without inflammation at or near the site of application was observed in approximately 1% of cats treated. Other signs observed rarely (<0.5% of 1743 treated cats and dogs) included vomiting, muscle tremors or diarrhea in cats or dogs, anorexia, alopecia, dermatitis, hypopigmentation, and muscle tremors.

**Post-approval experience:**

In addition to the aforementioned clinical signs that were reported in non-approval clinical studies, there have been reported pathological or clinical observations in cats, dogs, liver and renal reports of death. There have also been rare reports of seizures in dogs. (see WARNINGS)

**SAFETY:**

Revolution has been tested safely in over 100 different pure and mixed breeds of healthy dogs and over 15 different pure and mixed breeds of healthy cats, including pregnant and lactating females, breeding males and females, puppies six weeks of age and older, kittens eight weeks of age and older, and avermectin-sensitive collies. A kitten, estimated to be 5–6 weeks old (2.3 kg), died 8–12 hours after receiving a single treatment of Revolution at the recommended dosage. The kitten displayed clinical signs of which included mucous sneezing, salivation and neurological signs. The kitten was a stray with an unknown history and was malnourished and underweight. (see WARNINGS)

**DOGS:** In safety studies, Revolution was administered at 1, 3, 5, and 10 times the recommended dose to six-week-old puppies, and no adverse reactions were observed. The safety of Revolution administered orally was tested in cases of accidental oral ingestion. Oral administration of Revolution at the recommended topical dose in 5–6 month-old puppies did not cause any adverse reactions. In a pre-clinical study saline-injected dogs did not cause any adverse reactions. In a pre-clinical study saline-injected dogs did not cause any adverse reactions. Oral administration of 2.5, 10, and 15 mg/kg for 6 doses for 2 days did not cause any adverse reactions. In a pre-clinical study saline-injected dogs did not cause any adverse reactions. However, eight hours after receiving 5 mg/kg orally, on avermectin-sensitive collies became weak for several hours, but did not show any other adverse reactions after receiving subsequent doses of 10 and 15 mg/kg orally. In a topically safety study conducted with avermectin-sensitive collies at 1, 3, and 5 times the recommended dose of Revolution, salivation was observed in all treatment groups, including the vehicle control. Revolution also was administered at 3 times the recommended dose to heartworm infected dogs, and no adverse effects were observed. (see SAFETY)

**CATS:** In safety studies, Revolution was applied at 1, 3, 5, and 10 times the recommended dose to six-week-old kittens. No adverse reactions were observed. The safety of Revolution administered orally was also tested in case of accidental oral ingestion. Oral administration of the recommended topical dose of Revolution to cats caused salivation and intermittent vomiting. Revolution also was applied at 4 times the recommended dose to patent heartworm infected cats, and no adverse reactions were observed.

In well-controlled clinical studies, Revolution was used safely in animals receiving other frequently used veterinary products such as vaccines, anthelmintics, antibiotics, steroids, diuretics, antihypertensives, and anti-inflammatories. (see WARNINGS)

**ADVERSE REACTIONS:**

A severe reaction has been reported in a cat. The cat died after oral administration of 2.5 mg/kg in a targeted study. No adverse reactions were observed in the targeted study. (see WARNINGS)

**STORAGE CONDITIONS:** Store below 30°C (86°F).

**HOW SUPPLIED:** Available in eight separate dose strengths for dogs and cats of different weights: Revolution for parasites and tick infestations is available in cartons containing 3 single dose tubes. Revolution for cats and dogs is available in cartons containing 3 or 6 single dose tubes.

**NADA 141-152. Approved by FDA**

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