Cats with MDR1 mutation at risk of severe reactions to popular medication

March 28 2024, by Devin Roktya

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More than half a million cats in the United States could be at risk of a severe or even fatal neurological reaction to the active ingredient in some top-selling parasite preventatives for felines.

While the ingredient eprinomectin, which is found in products like NexGard COMBO and Centragard, appears safe and effective for the significant majority of cats when used at label doses, a study conducted by Washington State University's Program for Individualized Medicine identified a risk of severe adverse effects in cats with the MDR1 genetic mutation.

Genetically affected cats lack a protective mechanism that prevents certain drugs, including eprinomectin, from entering the brain and causing serious neurological toxicity.

"Almost every week, we receive reports about someone's pet cat having serious reactions to eprinomectin. This is not an issue with the drug itself—the problem lies in the genes of 1% of cats. That is a sizeable number considering there are over 60 million pet cats in the U.S., and we're trying to increase general awareness of these risks," said Dr. Katrina Mealey, a WSU veterinarian and pharmacologist who led the research.

Mealey and her team initiated their investigation in response to an uptick in reports of adverse neurological reactions following the marketing of eprinomectin-containing products in the U.S. The team reviewed medical records from 33 cats that became extremely ill or died after treatment with products containing eprinomectin to rule out any other potential cause of neurological toxicity. In fourteen cases, no other reasonable cause was identified.

Eight of these 14 cats were homozygous—having two copies of the same gene—for the MDR1 mutation. Three of those cats died. The findings were published in the Journal of Veterinary Pharmacology and Therapeutics.

"While this appears like a small number of cases, we consistently receive

new reports. If this were happening in human patients, federal agencies would be issuing regulatory actions immediately," Mealey said. "The results indicate cats with the MDR1 mutation are at high risk for experiencing serious adverse effects from products containing eprinomectin, and they should not be treated with these products."

Mealey is hopeful the findings will lead the U.S. Food and Drug Administration to evaluate and consider warning labels on products containing eprinomectin.

"Pet owners really should be aware of the risk to their pets. Based on the data in this study, I hope the FDA acts to conduct a timely review of the current labeling standards and adopts the modifications necessary to protect the health and lives of cats with the feline MDR1 mutation treated with this product," Mealey said.

Genetic testing is the only reliable way to know if a cat has the MDR1 mutation. Mealey, who initially discovered the MDR1 mutation and invented the first test to detect the condition, noted that MDR1 genotyping could have identified at-risk cats and prevented serious adverse events in more than half the cases in the study.

"I recommend the test for all cats, preferably when they are kittens," Mealey said. "If your veterinarian knows your pet has the MDR1 mutation, he or she can ensure only safe medications and doses are administered."

Cats having adverse reactions to eprinomectin can display many symptoms, including loss of coordination, increased salivation, tremors, partial paralysis, dilated pupils, coma, seizures, and death. Additionally, some cats in the study were unable to retract or use their tongue completely for days to weeks after eprinomectin application.

Mealey noted clinical signs often do not occur for several hours since these products are applied topically with delayed systemic absorption, so cats should be observed for up to 12 hours after the product is applied.

More information: Katrina L. Mealey et al, Application of eprinomectin-containing parasiticides at label doses causes neurological toxicosis in cats homozygous for ABCB11930_1931del TC, *Journal of Veterinary Pharmacology and Therapeutics* (2024). DOI: 10.1111/jvp.13431

Provided by Washington State University