The Facts about Bravecto

Bravecto Safety Profile and Adverse Event Reporting

- Following the approval of any drug, animal health companies are required by law, to report, assess and analyze all complaints, regardless of the volume.
    - The purpose of this post approval monitoring is to ensure that the label continues to accurately reflect the safety and efficacy profile of the drug.
    - The information, which is continuously collected from post-approval monitoring, is scientifically and objectively assessed to determine if changes to the product label are warranted.

- Merck Animal Health has conducted such monitoring in Bravecto with regard to the more than 34 million doses that have been dispensed since it was first approved for sale in 2014.
    - With regard to these 34 million doses, we have reported all adverse events either reported to us or Merck noticed in social media to the governing regulatory agencies.
    - We do this not only because it is a legal requirement but so that accurate safety and efficacy information is available for veterinarians prescribing our products.

- Based on the most recent assessment, which was conducted by the European Medicines Agency (EMA), the incidence of all worldwide Adverse Events remains categorized as "rare," which means occurring in between 1/10,000 (0.01%) and 1/1,000 (0.1%). The most common reported events are mild and transient gastrointestinal upset, which are noted on the product label.

- As is the case with any product, we also receive reports of serious adverse events including deaths. For Bravecto, the incidence of such events is in line with the most rare categorization used by to the EMA, which is "very rare" – occurring in less than 1/10,000 (less than 0.01%).

- As noted on the FDA website,
    - "For any given ADE report, there is no certainty that the reported drug caused the adverse event. The adverse event may have been related to an underlying disease, using other drugs at the same time, or other non-drug related causes. And, this listing does not include information about underlying diseases, other drugs used at the same time, other non-drug related causes, or the final outcome of the reaction."

- All findings are reported to regulatory agencies unfiltered, which means all reports are submitted as soon as they meet the criteria for a valid adverse event case (which is an identifiable reporter, an animal concerned, a product and a clinical sign after product use reported) irrespective of the potential causal relationship.
    - Cases subsequently determined not to be related to the product are still included in the overall reporting numbers and are never deleted from the reporting database.
    - It is important to note that a report does not mean that the product caused the suspected adverse event.

- Once we submit the adverse event reports, the FDA, EMA and regulatory agencies around the world conduct a robust review of the adverse event reports.

- Notwithstanding the "very rare" incidence rate for reports of death, we take very seriously every such report, regardless of whether there is any basis to believe the event may be related to Bravecto or not.

- With regard to the cases included in the Atlanta story, please note the following:
    - Ideally, to conduct a fair and accurate causality assessment of a reported adverse event, it is imperative that all existing information be examined by a trained veterinary professional, including pet heath records, veterinary and diagnostic findings, pet owner information and any other details relevant to an individual case.
    - In the cases noted in the Bravecto story, there were no necropsies performed and little to no diagnostic work conducted. Without this information, it is not possible to determine a dog's cause of disease and/or death.

Bravecto Topical Question

- As stated on the FDA-approved label, during the clinical trials, out of the 221 dogs treated with Bravecto Topical, two dogs experienced seizures. The label also notes that in 100 dogs treated with another product fipronil + (s)-methoprene, as as comparison, one dog had a seizure.

- With regard to the two dogs in the Bravecto Topical group, one dog had a seizure 76 days after its first dose of Bravecto Topical, and just three days following treatment with a different, concurrently administered medication known to cause seizures. This medication was discontinued and the dog experienced no additional seizures during the study.

- The second dog experienced two seizures a day apart, 18 days after its first dose of Bravecto Topical. This dog was started on antiepileptic medication and had no additional seizures during the study.

- In addition, five days after the first dose of Bravecto Topical, a third dog was reported to be "off balance" for approximately 30 minutes by its owner. No similar occurrence was observed for this dog during the study. None of the dogs were removed from the study and all were retreated with Bravecto Topical without recurrence of seizures.

- This information is clearly and fully presented on the Bravecto Topical label, along with an appropriate precautionary statement, so that veterinarians may discuss the available safety data with their clients and make a fully informed decision.

- There were no instances of seizures in the clinical program for Bravecto Chew.

Additional Resources
Just the Facts
BravectoFacts.com