Simparica Chewables and Simparica Trio Response Statement for All Audiences – Safety

- Zoetis colleagues, many of us pet owners, care about the well-being of pets, and we are committed to providing safe and effective products to veterinarians, pet owners and the animals in their care. We all sympathize with the frustration and concerns of pet owners when their pets are sick.

- Our products, Simparica®(sarolaner) Chewables, introduced in 2016, and Simparica Trio® (sarolaner, moxidectin, and pyrantel chewable tablets), introduced in 2020, are two of seven medications in the isoxazoline class currently on the market for dogs. Other products in the isoxazoline class include Bravecto 1 month, Bravecto 3 month, Bravecto Topical, Credelio, and NexGard.

- Simparica Chewables protect dogs from ticks and fleas, while Simparica Trio delivers all-in-one protection from heartworm disease, ticks and fleas, roundworms and hookworms.

- The labeling for both Simparica Chewables and Simparica Trio is approved by the FDA. Our product labels and promotional materials have always included information about neurologic signs such as tremors, unsteadiness, and/or seizures that have been associated with use of medicines in the isoxazoline class in some dogs.

- Our product labeling was updated in June 2019 to reflect a statement on potential neurologic events associated with all products in the isoxazoline class. Here is the website with prescribing and safety information for Simparica Chewables. You can click through from here for more detailed information that is shared in the packaging as well.
https://www.zoetisus.com/products/dogs/simparica/prescribing-information.aspx

- We are confident that both Simparica Chewables and Simparica Trio remain effective and safe parasite preventative options for dogs. More than 200,000,000 doses of Simparica Chewables and nearly 100,000,000 doses of Simparica Trio have been distributed globally. The overall global reporting rate for any clinical sign reported for Simparica Chewables or Simparica Trio (including vomiting, lethargy, diarrhea, or any neurologic sign), is classified as very rare as defined by international regulatory authorities. The adverse event profile for both products continues to be predictable and consistent with pre-approval studies and looks similar to other isoxazoline products on the market.

- Click here to see the full Prescribing Information for Simparica Trio: http://simparicatriopi.com/

- We focus on ensuring veterinarians have the proper education, prescribing and safety information to share with pet owners, so that they can best advise each pet owner which products are the best choice for their individual pet and best suited to each pet's medical needs. We also encourage pet owners to have regular conversations with veterinarians about their pet's health.

- All adverse events reported to Zoetis are handled by our internal teams, and also reported to the FDA as part of our standard procedures and in compliance with U.S. regulations.

- Unfortunately, all medicines come with some potential risks and side effects and that is why their use should always be taken in consultation with a veterinarian. For the vast majority of pets, preventative medicines are safe, effective and help greatly reduce health risks that can come from parasites, such as Lyme disease, anaplasmosis and other infectious diseases. These are serious

health concerns for all dogs and regular use of tick, flea, and heartworm medicines is recommended by veterinarians throughout the United States.

*December 2019 -- Notice to Applicants of Veterinary Medicinal Products, Volume 6C, Guideline on the Summary of Product Characteristics for Pharmaceutical Veterinary Medicinal Products, section 4.6.

Approval background timeline

- Simparica Chewables was approved in Nov 2015 in the EU, product was shipped starting in Q2 2016
- Simparica Chewables was approved in the US in Feb 2016, product was shipped starting in April 2016
- Simparica Trio was approved in the US in February 2020, product was shipped in Q1 2020
- Simparica Trio was approved in the EU and Canada in Q4 2019

Response on U.S. Food and Drug Administration (FDA) Communication about labeling for neurologic events

- The FDA published an Animal Drug Safety Communication on September 20, 2018 to alert pet owners and veterinarians to be aware of the potential for neurologic adverse events in animals when treated with drugs in the isoxazoline class.
    - The FDA carefully reviewed studies and other data on isoxazoline products prior to their respective approvals, and the FDA reminded pet owners and veterinarians that these products continue to be safe and effective for most animals.
    - All medicines come with potential risks and side effects. The FDA states that veterinarians should use their specialized training to review their patients' medical histories and determine, in consultation with pet owners, whether a product in the isoxazoline class is appropriate for the pet.
    - Zoetis worked closely with the FDA to include the new class statement on the label for Simparica Chewables. The Simparica Trio label also includes the class labeling information
- In August 2021, The FDA provided a Fact Sheet for Pet Owners and Veterinarians about Potential Adverse Events Associated with Isoxazoline Flea and Tick Products reflecting advice consistent with that provided in 2018.

Was Zoetis aware of the risk of seizures when it began marketing Simparica Chewables and Simparica Trio?

- The labeling, educational and promotional materials for Simparica Chewables and Simparica Trio have always included information about neurologic signs such as tremors, unsteadiness, and/or seizures that have been associated with use of these products in some dogs. This information appears on all materials that include the indications of the products—including the package insert, product box, and promotional materials.