

Name: Isoxazoline inquiries

DATE:10/1/2018

This serves as the response to your Freedom of Information Act (FOIA) request for records regarding adverse event reports received for afoxolaner, fluralaner, lotilaner and sarolaner.

A search of CVM's Adverse Drug Event (ADE) database was performed on 10-01-2018.

The search parameters were:

Active ingredient(s): afoxolaner, fluralaner, lotilaner and sarolaner

Reports received: From 09-04-2013 through 07-31-2018

Case type: Spontaneous ADE report

Species: All

Route of administration: All

For each drug (active ingredient), we have provided the '**CVM ADE Comprehensive Clinical Detail Report Listing**', which is a cumulative listing of adverse experiences in reports submitted to CVM.

General Information about CVM's ADE Database

The primary purpose for maintaining the CVM ADE database is to provide an early warning or signaling system to CVM for adverse effects not detected during pre-market testing of FDA-approved animal drugs and for monitoring the performance of drugs not approved for use in animals. Information from these ADE reports is received and coded in an electronic FDA/CVM ADE database. CVM scientists use the ADE database to make decisions about product safety which may include changes to the label or other regulatory action. CVM's ADE reporting system depends on detection and voluntary reporting of adverse clinical events by veterinarians and animal owners.

The Center's ADE review process is complex, and for each report takes into consideration confounding factors such as:

Dosage

Concomitant drug use

The medical and physical condition of animals at the time of treatment

Environmental and management information

Product defects

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Extra-label (off label) uses

The specifics of these complex factors cannot be addressed in the CVM ADE Comprehensive Clinical Detail Report Listing.

How to Use the CVM ADE Comprehensive Clinical Detail Report Listing

Clinical signs reported for an active ingredient are listed in order from most frequently reported to least frequently reported, grouped by species and route of administration.

More than one clinical sign may have been reported per ADE case report, so the Number of times reported column is not additive and does not necessarily represent the total number of reports received. Also, if a manufacturer reports multiple products in a single ADE case report, clinical signs are associated with each of the manufacturer's products.

Afoxolaner, fluralaner, lotilaner and sarolaner tablets are approved for oral use in **dogs** only. Fluralaner topical solution is approved for topical use in **cats and dogs**. For the time period of the ADE database search (09-04-2013 to 07-31-2018), there were a total of 24111 ADE reports received for afoxolaner for dogs, a total of 22626 ADE reports received for fluralaner for dogs, a total of 2222 ADE reports received for fluralaner in cats, a total of 229 ADE reports received for lotilaner for dogs and a total of 3819 ADE reports received for sarolaner for dogs.

The following shows the number of reports broken down by all species for which reports have been received during this time period:

DRUG: AFOXOLANER

Number of reports in dogs: 24111

Number of reports in cats: 27

Number of reports in other species: 7

Number of reports in humans, accidental exposure: 44

Total number of Adverse Drug Events in all species: 24189

DRUG: FLURALANER

Number of reports in dogs: 22626

Number of reports in cats: 2222

Number of reports in other species: 12

Number of reports in humans, accidental exposure: 282

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Total number of Adverse Drug Events in all species: 25142

DRUG: LOTILANER

Number of reports in dogs: 229

Number of reports in cats: 0

Number of reports in humans, accidental exposure: 0

Total number of Adverse Drug Events in all species: 229

DRUG: SAROLANER

Number of reports in dogs: 3819

Number of reports in cats: 59

Number of reports in humans, accidental exposure: 5

Total number of Adverse Drug Events in all species: 3883

When reviewing the CVM ADE Comprehensive Clinical Detail Report Listing, the reader should be aware that:

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. The clinical detail 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.

The accuracy of information regarding the ADE is dependent on the quality of information received from the reporting veterinarian or animal owner.

Accumulated ADE reports should not be used to calculate incidence rates or estimates of drug risk, because there is no accurate way to determine how many animals were actually given the drug, which is needed as the denominator in calculations of incidence and relative risk.

It is inappropriate to make use of adverse event data to compare the safety of different products. For example, if a drug is widely used to treat certain conditions, there may be more ADEs for that drug than another product that is not used as often. This would not mean that the first drug was more unsafe than the second. The number of reports simply represents the number of ADEs received for a particular drug and should not be used for any type of comparison purposes.

Underreporting occurs with most adverse event reporting systems. The frequency of reporting for a given drug product varies over time, and may be greater when the drug is newly marketed, or when media publicity occurs.

Information on how the drugs were used (for indications on the product label or in an extra label manner) is not provided in the clinical detail listing.

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More information about CVM's ADE Reporting System can be found on our web site at: [FDA, Animal and Veterinary, Safety and Health page](#)