Veterinary Medicines Directorate

Veterinary Pharmacovigilance in the United Kingdom

Annual Review 2017 – a summary

Introduction

Veterinary pharmacovigilance is the monitoring of all adverse event (AE) reports, both adverse reactions and suspected lack of expected efficacy (SLEE), for emerging patterns of undesirable effects, following the use of veterinary medicines.

Without the information submitted by reporters, we would not be able to continually make users better informed about the medicines they are using.

Within the UK, vets, animal owners and other people who work with animals administer many millions of doses of different types of veterinary medicine to animals every year. In a relatively small number of cases, an AE occurs. This may occur during, or sometime after, the use of a medicine.

During 2017, VMD received and assessed 6721 adverse event reports. This is an increase of only 2.5% on the previous year, compared to 15% from 2015 to 2016.

We required veterinary pharmaceutical companies to improve the product literature[1] of over 80 products, as a result of adverse event information received.

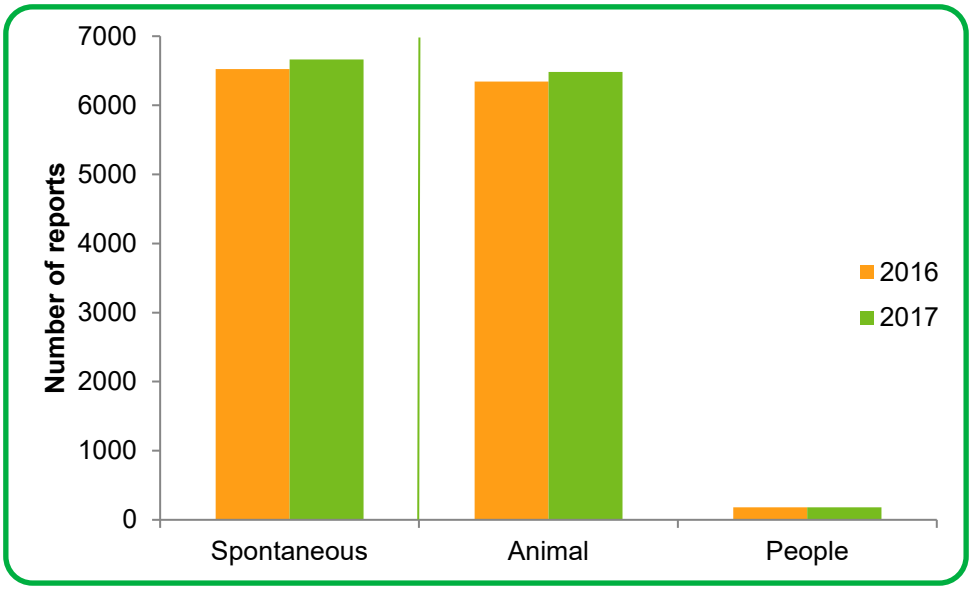
Most of the reports received described events that occurred in animals during or after the use of authorised veterinary or human medicines. Many reports involved the use of multiple products, some of which may not have been authorised medicines.

Some reports describe reactions experienced by humans exposed to products used to treat animals. Others involved the detection of the residues of veterinary medicines in a food product intended for human consumption, usually milk, before it enters the food chain.

This Summary provides an overview of the adverse events received in 2017, and a list of the product literature changes (See Annex).

[1] Also known as the Summary of Product Characteristics or SPC.

The overall number of adverse event reports received in 2017 increased compared to 2016.

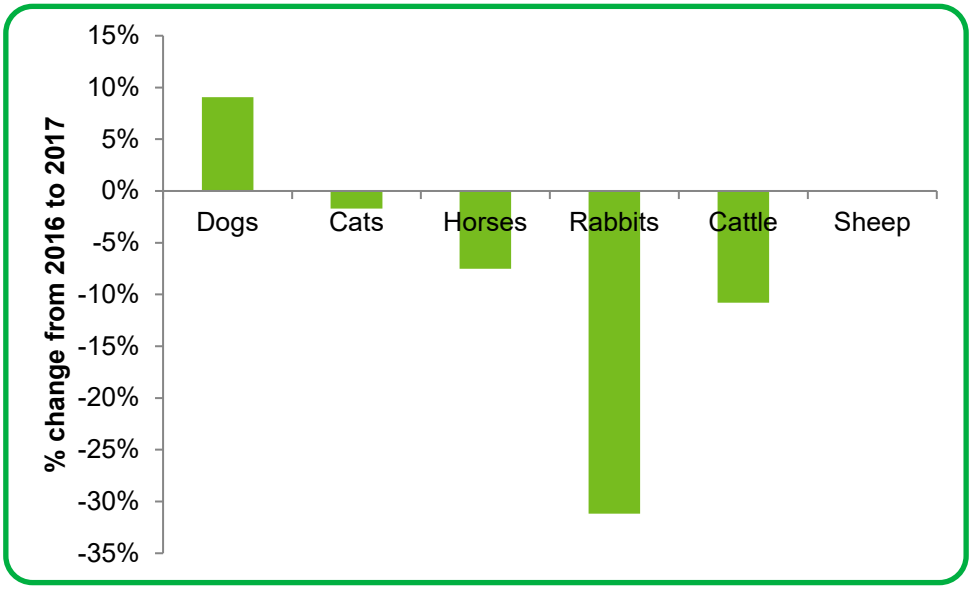


We received 'spontaneous'[2] reports following 'everyday' product use from many sources.

Fewer than 200 people reacted unfavourably after exposure to veterinary medicines.

The number of spontaneous reports increased by 2.1% overall.

The magnitude of the change varied from species to species.



Of the major[3] species, dogs were the only ones with an increased number of reports.

The largest decrease was for rabbits, with a decrease of over 31%.

The number of sheep reports was unchanged.

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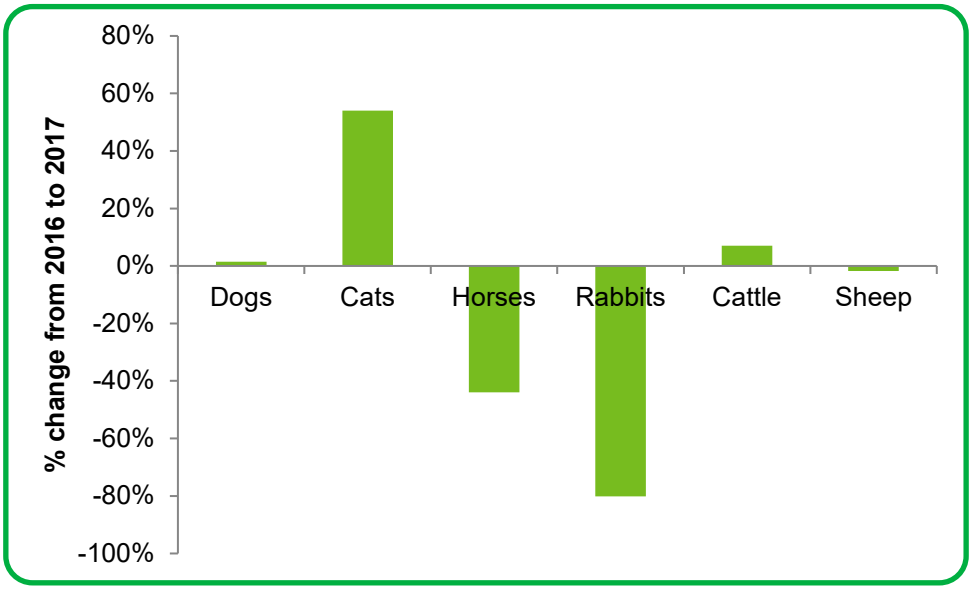
[2] Not including clinical trials.

[3] Major species are those for which we receive most reports.

The number of suspected lack of expected efficacy (medicine not working) reports increased for some major species and decreased for others.



There was a marked increase (54%) in the number of suspected lack of expected efficacy (SLEE) reports for cats compared to 2016. There was a 7% increase in SLEE reports for cattle.

Rabbits (80%) and horses (44%) showed the greatest decreases in SLEE reports compared to 2016.

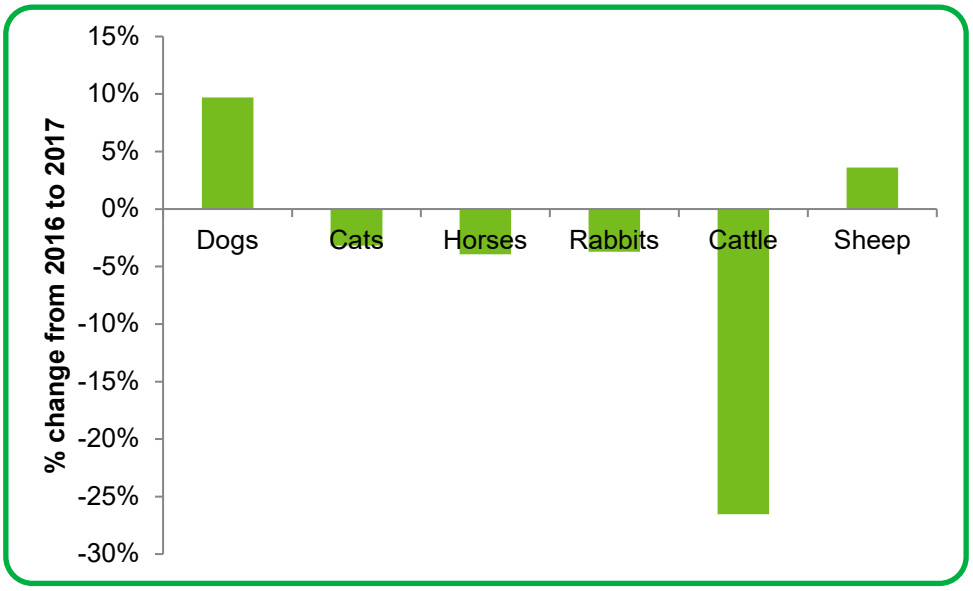
We received an increased number of SLEE reports in cats for products that affect the nervous system, including general anaesthetics, sedatives and analgesics. Products for reversal of sedation also showed an increase, as did combined treatments for the prevention of infestation by internal and external parasites.

For cattle, there was an increase in the number of SLEE reports for bovine viral diarrhoea (BVD) vaccines, products for reproductive cycle control, and products for the treatment of internal and external parasites containing eprinomectin or ivermectin in combination with another ingredient. There was also an increase in reports for products used against protozoal disease.

In 2017, the number of SLEEs reported in rabbits was less than a fifth of the number reported the previous year and less than half of those reported in 2015. Almost all of reports in each year were associated with vaccines for myxomatosis and/or rabbit haemorrhagic disease (RHD). There was a suspicion that a new variant of RHD had become endemic in the United Kingdom in 2016.

For horses, there was a decrease in the number of SLEE reports, mainly involving vaccines and sedatives.

The number of safety (adverse reaction) reports increased in only two major species.



The number of safety reports received involving dogs increased by over 9%. Sheep safety reports increased by less than 4%.

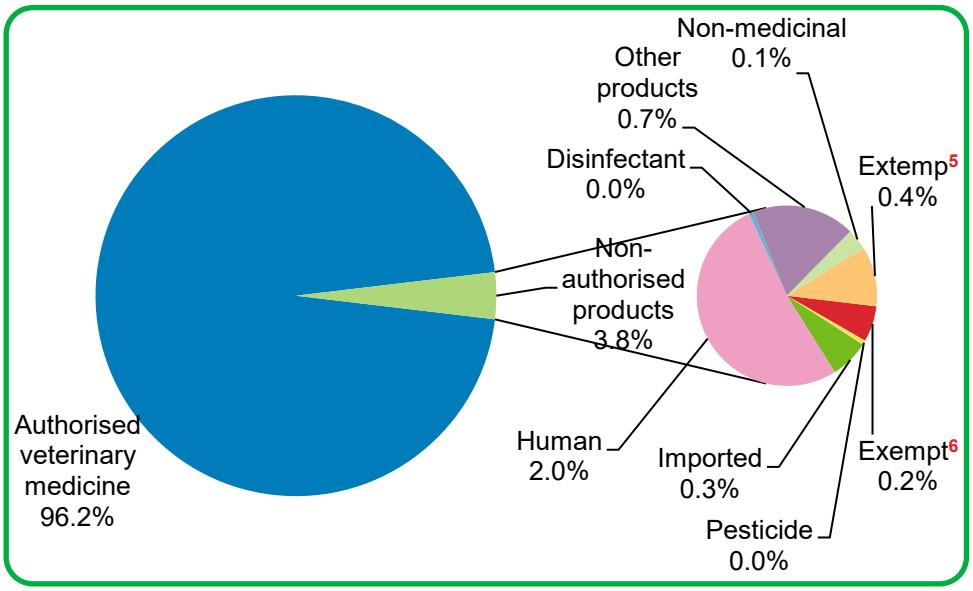
Cat, horse and rabbit safety reports all decreased by less than 4%. Cattle safety reports decreased by over 26%.

The increase in number of safety reports for dogs was due to more reports involving medicines for treating the intestines, the heart and circulation, the nervous system and the ears. There were also an increased numbers of reports for vaccines, products controlling the levels of systemic hormones and for the treatment and prevention of internal and/or external parasite infestations.

Half of the products involved in sheep safety cases were antiparasitics, with half of those medicines being wormers, and half of these contained levamisole in combination with another drug.

For cattle, the greatest decrease in number of reports was for vaccines, with a smaller decrease for medicines for controlling the reproductive cycle. There were much smaller increases in the number of reports involving systemic antiinfectives and non-steroidal anti-inflammatory medicines.

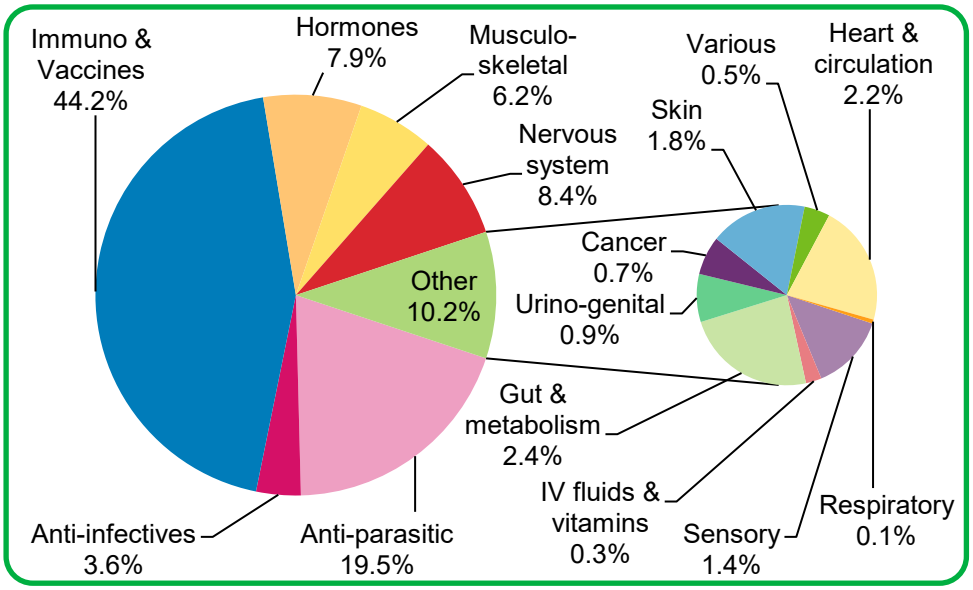
Most products involved in animal adverse event reports were authorised veterinary medicines[4].



Most products involved in animal adverse event reports were authorised veterinary medicines. This is to be expected as the non-authorised products should only be used where a suitable authorised product is not available.

Human medicines accounted for 2% of products mentioned in these reports.

Vaccinations and immunotherapy products were the veterinary medicines most often associated with animal adverse event reports.



As in 2016, anti-parasitic products for the treatment of internal and/or external parasites accounted for almost a fifth of all veterinary medicines referred to in adverse event reports.

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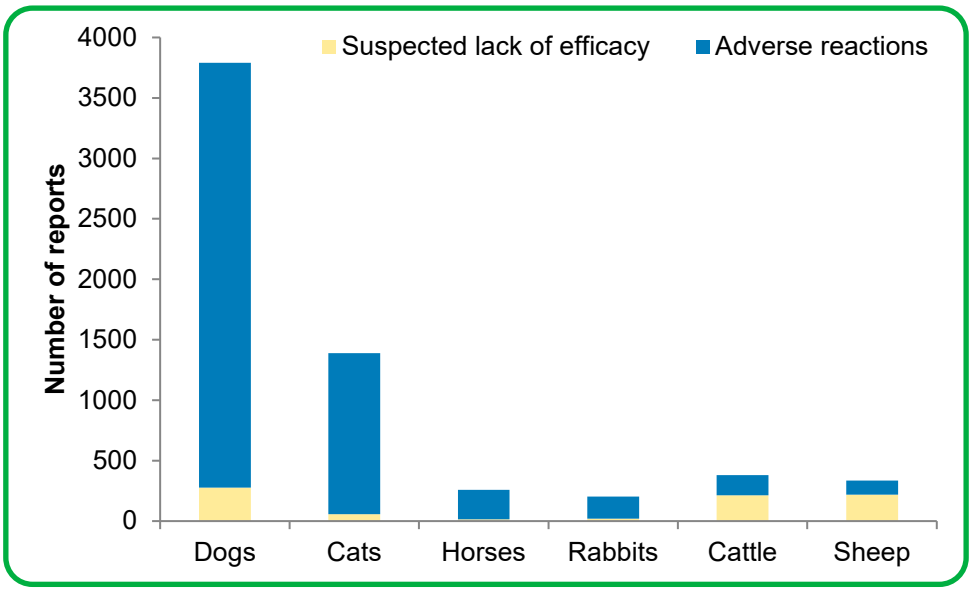
[4] www.gov.uk/guidance/the-cascade-prescribing-unauthorised-medicines

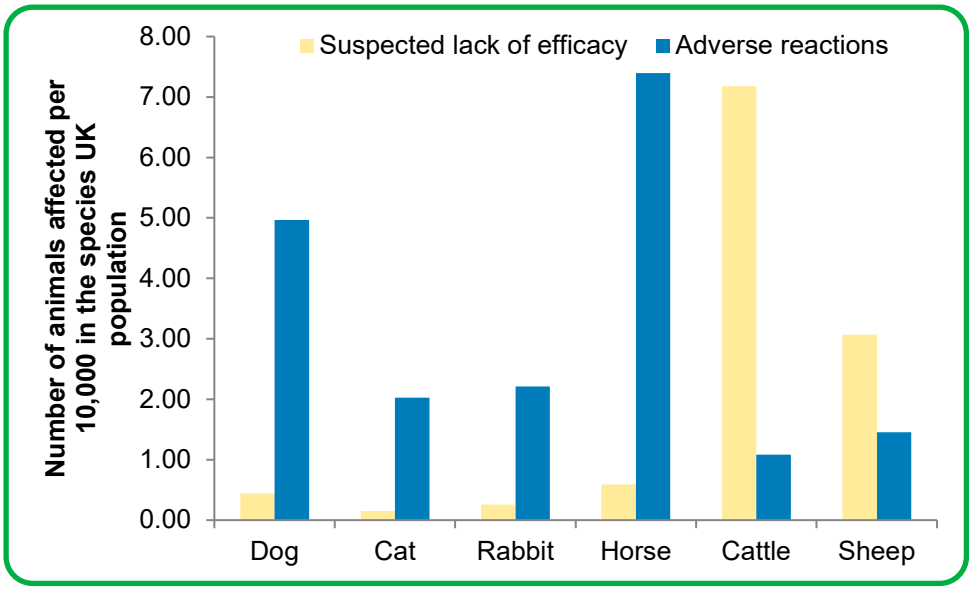
[5] Extemp = extemporaneous medicines, which are not authorised medicines but specifically prepared for an individual patient in accordance with a veterinary prescription

[6] Exempt products do not have a marketing authorisation because the animals they treat are kept exclusively as pets and are not intended to produce food for human consumption.

The number of reports of suspected lack of expected efficacy was much smaller than the number of reports of adverse reaction for all major species, except cattle and sheep.



Fewer than 8 animals per 10,000 in the UK population of the major species were affected by adverse reactions or medicines not working.



You can find further detail about the species and medicines involved in these 2017 reports in the dashboard at www.vmd.defra.gov.uk/PharmacovigilanceAdverseEventData

Important messages

For anyone administering veterinary medicines

- Obtain veterinary medicines from a reputable source. Look for the VMD Accredited Internet Retailer Scheme logo if you are buying medicines online.
- Report a problem with an authorised veterinary medicine to the Marketing Authorisation Holder or to us[7]. We cannot take regulatory action in relation to a medicine without sufficient evidence of a problem. Social media does not provide the evidence we need.
- Use appropriate safety equipment when administering medicines that may be harmful to your own health.
- Use appropriate personal protective safety equipment or animal restraints when administering medicines to animals that may harm you or cause you to harm yourself with a needle if they move unexpectedly.
- Seek immediate medical attention if you accidentally inject yourself with an oil-based vaccine. Also report the incident to us, with as much information as possible.
- Be aware of the hazards posed by some surgery-only medicines, e.g. inhaled anaesthetics are a risk to unborn children.
- If you are planning to euthanase a horse, have a secondary plan available, in case the original method does not achieve the required outcome. Wear head protection.
- Reduce the chance of accidental exposure by keeping animal medicines out-of-sight and reach of children (and animals) and separate from personal medicines.
- Clean and dry any dosing equipment thoroughly between uses, particularly if used with different medicines.
- Dispose of empty medicine containers promptly, in accordance with labelling instructions. Oral horse medicine syringes are attractive to dogs, and discarded ‘empties’ ingested by dogs can have serious or fatal consequences.
- If you suspect your animal has been poisoned by a veterinary medicine, seek advice from the Veterinary Poisons Information Service[8], then report[7] the adverse event to us. If you have been affected, seek medical advice first, and then report to us.

For people who work or play with treated animals

- Never allow animals recently treated with topical medicines e.g. spot-ons, collars, to sleep with people.
- Always ensure that spot-on anti-parasitic products are completely dry before allowing anyone, including other pets, to kiss, cuddle or groom the treated animal.
- Do not allow your dog to run free in areas inhabited by farm animals or horses. They can excrete medicine residues that could be harmful to your dog, if ingested.
- Do not let animals recently treated with topical medicines to enter streams, rivers or other water courses, as these medicines can be fatal to water life.

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[7] Report a problem with a veterinary medicine - www.gov.uk/report-veterinary-medicine-problem
[8] Veterinary Poison Information Service – www.vpisglobal.com – membership required

ANNEX

Product information changes relating to pharmacovigilance

The following table lists the changes made to product literature as a result of information received in Adverse Event reports. Without the information submitted by reporters, we would not be able to continually make users better informed about the medicines they are using, and reduce some of the risks associated with the use of those medicines.

We thank all reporters for their continuing support in providing us with the essential information we need to monitor medicine safety.

This table lists all pharmacovigilance-related regulatory actions taken during 2017. Information received prior to 2017 will have contributed to the evidence leading to the initiation of these actions.

Key:

Product name
Active ingredient(s)
Marketing Authorisation Holder

Products	**Change**
Animeloxan 5 mg/ml solution for injection for dogs and cats *Meloxicam* aniMedica GmbH	Section 4.6 of the SPC has been updated to include injection site pain as an adverse event.
Bob Martin Clear 3 in 1 Wormer 150/144/50 mg tablets for dogs XL 525/504/175 mg tablets for dogs **Drontal Plus** Flavour bone shaped tablets Flavour tablets for dogs XL Flavour tablets for dogs *Febantel, pyrantel embonate, praziquantel* Bayer plc	Section 4.6 of the SPC has been updated to state: 'In very rare cases slight and transient digestive tract disorders such as vomiting and/or diarrhoea may occur. In individual cases these signs can be accompanied by nonspecific signs such as lethargy, anorexia or hyperactivity'.

Bob Martin Clear Flea 11.4 mg tablets for cats, small dogs and puppies 57 mg tablets for large dogs **Johnson's 4fleas** 11.4 mg tablets for cats and kittens 11.4 mg tablets for small dogs and puppies 57 mg tablets for dogs *Nitenpyram* Elanco Europe Ltd	Section 4.6 of the SPC has been updated to include: 'For the first hour after administration, the pet may scratch more than normal. This effect is caused by the fleas reacting to the product. In very rare cases this may present as transient signs of hyperactivity, panting, vocalization and excessive grooming/licking. Transient neurological sings such as muscle tremors, ataxia and convulsions have also been reported in very rare occasions.'
Bovela Lyophilisate and Solvent for suspension for injection for cattle *Bovine viral diarrhoea virus* Boehringer Ingelheim Vetmedica GmbH	Sections 4.4 and 4.7 of the SPC have been updated following a routine Periodic Safety Update Report (PSUR) including information on definitive diagnosis of persistent infection of BVD.
Bravecto 112.5 mg chewable tablets for very small dogs (2–4.5 kg) 250 mg chewable tablets for small dogs (>4.5 –10 kg) 500 mg chewable tablets for medium-sized dogs (>10–20 kg) 1000 mg chewable tablets for large dogs (>20–40 kg) 1400 mg chewable tablets for very large dogs (>40–56 kg) *Fluralaner* Intervet International BV	Section 4.6 of the SPC has been updated to add: 'Lethargy has been reported very rarely in spontaneous (pharmacovigilance) reports.'

Bravecto 112.5 mg chewable tablets for very small dogs (2–4.5 kg) 250 mg chewable tablets for small dogs (>4.5 –10 kg) 500 mg chewable tablets for medium-sized dogs (>10–20 kg) 1000 mg chewable tablets for large dogs (>20–40 kg) 1400 mg chewable tablets for very large dogs (>40–56 kg) 112.5 mg spot-on solution for small cats (1.2-2.8 kg) 112.5 mg spot-on solution for very small dogs (2-4.5 kg) 250 mg spot-on solution for medium sized cats (2.8-6.25 kg) 250 mg spot-on solution for small dogs (>4.5-10 kg) 500 mg spot-on solution for medium dogs (>10-20 kg) 1000 mg spot-on solution for large dogs (>20-40 kg) 1400mg spot-on solution for very large dogs (>40-56 kg) *Fluralaner* Intervet International BV	The following warning has been added to section 4.5 of the SPC: 'Use with caution in dogs with epilepsy.' The following warnings have been added to section 4.6 of the SPC: 'Commonly observed adverse reactions in clinical trials (1.6% of treated dogs) were mild and transient gastrointestinal effects such as diarrhoea, vomiting, inappetence, and drooling. Convulsions and lethargy have been reported very rarely in spontaneous (pharmacovigilance) reports.'
Broadline Spot-on solution for cats < 2.5 kg 2.5-7.5 kg *Fipronil, (S) - methoprene, praziquantel, eprinomectin* Merial	The following has been added to section 4.5 of the SPC: Muscle tremors have been reported in very rare cases based on post marketing safety experience. These signs usually resolve spontaneously within 24 hours. Also added to section 4.6 of the SPC: A temporary clumping or spiking of the hair and mild and transient skin reactions at the application site (itching, hair loss) have been commonly observed at the application site after treatment in clinical studies. If the cat licked the application site after treatment, common temporary excessive salivation was observed in clinical trials. Oral ingestion of the product may result in digestive tract and/or in neurological disorders (see section 4.5). Symptomatic treatment can be required if these signs do not resolve spontaneously within 24 hours. Correct application will minimise the occurrence of such events (see section 4.9).

Buprevet Multidose 0.3 mg/ml solution for injection for dogs and cats *Buprenorphine* Richter Pharma AG	Section 4.6 of the SPC has been updated to include: 'Local discomfort or pain at the injection site, resulting in vocalisation, may occur very rarely. The effect is normally temporary.'
Canigen DHPPi lyophilisate for suspension for injection *Canine adenovirus, distemper virus, parainfluenza virus, parvovirus* Intervet UK Ltd	Section 4.6 of the SPC had been updated to include: 'In very rare cases, a diffuse swelling, up to 5 mm in diameter, may be observed at the site of injection. Occasionally this swelling may be hard and painful and last for up to 3 days post injection. In the very rare event of hypersensitivity reaction occurring following vaccination, administer an antihistamine, corticosteroid or adrenaline, without delay and by the most immediate route.'
Canigen L4 suspension for injection for dogs *Leptospira australis; L. canicola; L. grippotyphosa; L. icterohaemorrhagiae* Intervet International BV	The following has been added to section 4.6 of the SPC: A mild and transient increase in body temperature (≤ 1°C) has been observed very commonly in clinical studies for a few days after vaccination, with some pups showing less activity and/or a reduced appetite. A small transient swelling at the site of injection (≤ 4 cm), which can occasionally be firm and painful on palpation, has been observed very commonly in clinical studies. Any such swelling will either have disappeared or be clearly diminished by 14 days post-vaccination. In very rare cases, clinical signs of immune-mediated haemolytic anaemia, immune-mediated thrombocytopenia, or immune-mediated polyarthritis have been reported. In very rare cases a transient acute hypersensitivity reaction may occur. Such reactions may evolve to a more severe condition (anaphylaxis), which may be life-threatening. If such reactions occur appropriate treatment is recommended.
Canigen Pi *Canine parainfluenza virus* Intervet UK Ltd	Section 4.6 of the SPC has been updated to include: 'In very rare cases, some dogs may show discomfort during injection. In very rare cases, a diffuse swelling, up to 5 mm in diameter, may be observed at the site of injection. Occasionally this swelling may be hard and painful and last for up to 3 days post injection. In very rare cases, hypersensitivity reactions may occur. In the event of an anaphylactic reaction appropriate treatment such as adrenaline should be administered without delay.'

Capstar 11.4 mg tablets for cats and small dogs 57 mg tablets for large dogs *Nitenpyram* Elanco Europe Ltd	Section 4.6 of the SPC has been updated to state: 'For the first hour after administration, the pet may scratch more than normal. This effect is caused by the fleas reacting to the product. In very rare cases this may present as transient signs of hyperactivity, panting, vocalization and excessive grooming/licking. Transient neurological sings such as muscle tremors, ataxia and convulsions have also been reported in very rare occasions'.
Cardalis 2.5 mg/20 mg chewable tablets for dogs 5 mg/40 mg chewable tablets for dogs 10mg/80mg chewable tablets for dogs *Spironolactone, benazepril hydrochloride* Ceva Sante Animale	Section 4.6 of the SPC has been updated to add: 'Vomiting has been reported very rarely in spontaneous reports'.
Cazitel Plus XL tablets for dogs **Prazitel Plus XL tablets for dogs** **Strantel Plus XL tablets for dogs** *Febantel, praziquantel, pyrantel embonate* Chanelle Pharmaceuticals Manufacturing Ltd	Section 4.6 of the SPC has been updated to add: 'In very rare cases, gastrointestinal disorders (diarrhoea, emesis) have been observed.'
Coxevac suspension for injection for cattle and goats *Coxiella burnetii* Ceva Animal Health Ltd	Section 4.6 of the SPC has been updated following a Periodic Safety Update Report PSUR) stating that following vaccination in goats systemic signs like lethargy, malaise and / or anorexia have been uncommonly observed and diarrhoea rarely observed in post marketing safety experience.
Dexadreson 2 mg/ml solution for injection *Dexamethasone* Intervet UK Ltd	Section 4.6 of the SPC has been updated to include the following: 'In very rare cases hypersensitivity reactions might occur.'
Dexa-ject 2 mg/ml solution for injection for cattle, horses, pigs, dogs and cats *Dexamethasone* Dopharma Research BV	Section 4.6 of the SPC has been updated with the addition of the following: 'Corticosteroid use may increase the risk of acute pancreatitis. Other possible adverse reactions associated with corticosteroid use include laminitis and reduction in milk yield.'
Duowin, cutaneous spray solution *Permethrin* Virbac S A	Section 4.3 of the SPC has been updated to include: 'Do not use on cats as adverse reactions and even death can occur'. Additional warnings pertaining to accidental exposure in cats have been added to section 4.5 of the SPC.

Easotic ear drops suspension for dogs multidose / single dose *Miconazole, hydrocortisone aceponate, gentamicin* Virbac S A	Section 4.6 of the SPC has been updated to include the following warning: 'In very rare cases, the use of the veterinary medicinal product has been associated with hearing impairment (partial hearing loss or deafness), usually temporary, and primarily in geriatric dogs. If this occurs, treatment should be stopped. See section 4.5 of the SPC.'
Equipramox 19.5 mg/g + 121.7 mg/g oral gel *Praziquantel, moxidectin* Continental Farmaceutica	Additional warning added to section 4.6 of the SPC: 'Anorexia and lethargy have been reported in very rare cases.'
Excenel Flow, 50 mg/ml, suspension for injection for pigs and cattle *Ceftiofur* Zoetis UK Ltd	Section 4.6 of the SPC has been updated and includes: 'Injection site reactions have been reported from the field in very rare cases.'
Extrontel Plus tablets for dogs *Febantel, praziquantel, pyrantel* C&H Generics Ltd	Section 4.6 of the SPC has been updated to include the following: 'In very rare cases, gastrointestinal disorders (diarrhoea, emesis) have been observed.'
EziWormer Cats & Kittens 230/20mg flavoured tablets *Pyrantel embonate,* p*raziquantel* Chanelle Pharmaceuticals Manufacturing Ltd	Section 4.6 of the SPC has been updated to include: 'Mild and short-lived digestive tract disorders such as excessive salivation and/or vomiting and mild and short-lived disorders of the nervous system such as loss of balance may occur in extremely rare cases.'
Genestran 75 micrograms/ml solution for injection for cattle, horses and pigs *Cloprostenol* aniMedica GmbH	Section 4.6 of the SPC has been updated and includes: 'Anaerobic infections may occur if anaerobic bacteria are introduced into the tissue by the intramuscular injection'.
Kexxtone 32.4 g continuous-release intraruminal device for cattle *Monensin* Eli Lilly and Company Ltd	The final paragraph in section 4.5 of the SPC has been updated to read as follows: 'Ingestion or oral exposure to monensin can be fatal in dogs, horses, other equines or guinea fowl. Do not allow dogs, horses, other equines or guinea fowl access to formulations containing monensin. Due to the risk of bolus regurgitation, do not allow these species access to areas where treated cattle have been kept.' Section 4.6 of the SPC has been updated to include: 'In rare cases digestive signs (e.g. diarrhoea, ruminant stomach disorder) have been observed. In very rare cases, oesophagus obstruction has been observed.'

Metacam 0.5 mg/ml oral suspension for cats 2 mg/ml solution for injection for cats 5 mg/ml solution for injection for cats and dogs *Meloxicam* Boehringer Ingelheim Vetmedica GmbH	Section 4.6 of the SPC has been updated to advise that, in very rare cases, gastrointestinal ulceration has been reported in the target species.
Metricure 500 mg intrauterine suspension *Cefapirin* Intervet UK Ltd	Section 4.6 of the SPC has been updated to include the following: 'Allergic reactions have been observed in very rare cases.'
Nobivac L4 suspension for injection for dogs *Leptospira australis; L. canicola; L. grippotyphosa; L. icterohaemorrhagiae* Intervet International BV	Section 4.6 of the SPC has been updated: 'A mild and transient increase in body temperature (≤ 1 °C) has been observed very commonly in clinical studies for a few days after vaccination, with some pups showing less activity and/or a reduced appetite. A small transient swelling at the site of injection (≤ 4 cm), which can occasionally be firm and painful on palpation, has been observed very commonly in clinical studies. Any such swelling will either have disappeared or be clearly diminished by 14 days post-vaccination. In very rare cases, clinical signs of immune-mediated haemolytic anaemia, immune-mediated thrombocytopenia, or immune-mediated polyarthritis have been reported. In very rare cases a transient acute hypersensitivity reaction may occur. Such reactions may evolve to a more severe condition (anaphylaxis), which may be life-threatening. If such reactions occur appropriate treatment is recommended.'
Optimmune 2 mg/g eye ointment *Ciclosporin A* Intervet UK Ltd	Section 4.6 of the SPC has been updated to read as follows: 'Slight eye irritation (e.g. eye redness, blepharospasm, conjunctivitis) has been reported in rare cases in the first days of treatment. If the irritation persists beyond 7 days, treatment should be discontinued. Inflammation and swelling of the skin of the eyelids have been observed in very rare cases. Furthermore, cases of pruritus, partly with strong scratching and skin lesions, and hair loss in the area around the eyes have been reported in very rare cases. This might be associated with overflow of excess ointment. Systemic reactions such as increased salivation, lethargy, inappetence and vomiting have been observed in very rare cases for which no confirmed conclusions concerning the causal relationship are available.'

Osphos 51 mg/ml solution for injection for horses *Clodronic acid* Dechra Ltd	Section 4.5 of the SPC has been updated with the following additional warning: 'Adequate access to drinking water should be provided when using the product. If uncertainty exists about renal function, renal parameters should be assessed before administration of the product. Water consumption and urine output should be monitored after administration.' Section 4.6 of the SPC has been updated to include: 'In a clinical field study, administration of clodronic acid at 1.19 mg/kg to 142 horses resulted in the following frequency of adverse reactions: nervousness, lip licking, yawning and colic were common; head bobbing, transient swelling and/or pain at the injection site, pawing the ground, hives and pruritus were uncommon. Episodes of renal insufficiency have been reported, rarely, during the post-authorisation period, and were more frequently observed in animals concurrently exposed to NSAIDs. In these cases, appropriate fluid therapy should be instituted and renal parameters monitored.' Section 4.8 of the SPC has been updated with the addition of the following warning: 'Concurrent administration of potentially nephrotoxic drugs, such as NSAIDs, should be approached with caution and renal function should be monitored.'
Osurnia ear gel for dogs *Florfenicol, terbinafine, betamethasone* Elanco Europe Ltd	Section 4.6 of the SPC has been updated to include: 'Post authorisation experience indicates that very rare cases of deafness or impaired hearing, usually temporary, in dogs have been reported after use, mainly in elderly animals.'
Porcilis ColiClos *Escherichia coli* ,*Clostridium perfringens* Intervet International BV	Section 4.6 of the SPC updated with the frequencies and the source of all adverse reactions and that hypersensitivity reactions may occur in very rare cases.
Porcilis PCV M Hyo Emulsion for injection for pigs *Porcine circovirus-2, Mycoplasma hyopneumoniae* Intervet International BV	Section 4.6 of the SPC has been updated to reflect frequency and types of adverse reactions reported including that in very rare cases anaphylactic-type reactions can occur, which may be life threatening.

Rabigen SAG2 oral suspension, for Red foxes and Raccoon dogs *Rabies virus* Virbac S A	Section 4.6 of the SPC amended to read: 'No adverse events have been reported in the target species. As this vaccine presentation contains traces of gentamicin and contains tetracycline as biomarker, occasional hypersensitivity reactions may be observed in domestic animals that have accidentally ingested the bait. Vomiting due to gastric intolerance (potentially due to the aluminium/PVC sachet as part of the bait vaccine), in dogs which have accidentally ingested the bait, has been reported.'
Simparica 5mg, 10mg, 20mg, 40mg, 80mg, 120mg tablets for oral use in dogs *Sarolaner* Zoetis Belgium	Section 4.6 of the SPC has been updated: 'In very rare cases adverse reactions associated with mild and transient gastrointestinal effects such as vomiting and diarrhoea may occur. In very rare cases transient neurological disorders such as tremor, ataxia or convulsion may occur. These signs typically resolve without treatment.'
Strenzen 500/125 mg/g powder for use in drinking water for pigs *Amoxicillin, clavulanic acid* Elanco Europe Ltd	Section 4.6 of the SPC has been updated with the addition: 'Anal and perineal erythema, irritation and diarrhoea occur rarely.'
Versican Plus (DHPPi+L4R) **Versican Plus DHP lyophilisate and solvent for suspension for injection for dogs** **Versican Plus DHPPi lyophilisate and solvent for suspension for injection for dogs** **Versican Plus DHPPi/L4** **Versican Plus lyophilisate and solvent for suspension for injection for dogs** Various combinations of *canine distemper virus, canine adenovirus, canine parvovirus, canine parainfluenza virus, Leptospira icterohaemorrhagiae, L. bratislava, L. kerschneri, L. canicola, rabies virus* Zoetis Belgium	The wording in section 4.6 of the SPC has been clarified regarding expected hypersensitivity reactions (i.e. anaphylaxis, angioedema, dyspnoea, circulatory shock, collapse).
Versiguard Rabies *Rabies virus* Zoetis UK Ltd	Section 4.8 of the SPC has been updated to describe the possible reactions that could be seen after use with the Vanguard Plus range of vaccines.

Vetlflea 2.5 mg/ml cutaneous spray, solution for cats and dogs *Fipronil* Alfamed	Section 4.6 of the SPC has been updated to include: 'Very rarely, transient cutaneous reactions (erythema, pruritus or alopecia) have been reported after use. Hypersalivation, reversible neurological signs (hyperaesthesia, depression, nervous symptoms), vomiting or respiratory signs have also been observed very rarely after use.'
VIMCO emulsion for injection for ewe and goat *Staphylococcus aureus* Laboratorios Hipra SA	Section 4.6 had been updated with the addition of the following: 'Slight swelling at the injection site of less than 2 cm in diameter, which disappears within 12 days at most, occurred very commonly during clinical studies. Swelling at the injection site higher than 5 cm in diameter, which resolves within 3 days at most, occurred commonly during clinical studies. Transient increase in body temperature of up to 1.8 ºC occurred commonly between the first 4 hours and 3 days after injection during clinical studies, which spontaneously resolves within some days without compromising animal health status. Anaphylactic-type reactions, which might be life-threatening and/or cause abortion occurred very rarely based on post-authorisation pharmacovigilance reporting. Under these circumstances, appropriate and rapid symptomatic treatment should be administered. Mild apathy, anorexia and/or recumbency occurred very rarely after administration of the vaccine based on post-authorisation pharmacovigilance reporting.'
Vitamin K1 Laboratoire TVM 50 mg film-coated tablets for dogs *Phytomenadione* Laboratoire TVM	Section 4.6 has been updated to include: 'Very rarely, vomiting and skin disorders, as erythema and dermatitis, or allergic oedema have been reported.'
Zobuxa 15 mg tablets for cats and small dogs 50 mg tablets for cats and dogs *Enrofloxacin* Elanco Europe Ltd	Section 4.6 of the SPC has been updated to include the following warnings: 'In very rare cases hypersensitivity reactions (allergic skin reactions, anaphylaxis) can occur. In these cases, administration should be discontinued and a symptomatic treatment given. Cats: In rare cases, mild gastrointestinal symptoms (diarrhoea and vomiting) may occur after administration of the product.'
Zobuxa 100 mg tablets for dogs 150 mg tablets for dogs *Enrofloxacin* Elanco Europe Ltd	Section 4.6 of the SPC has been updated to include the following warnings: 'In very rare cases hypersensitivity reactions (allergic skin reactions, anaphylaxis) can occur. In these cases, administration should be discontinued and a symptomatic treatment given.'

Veterinary
Medicines
Directorate