Veterinary Medicines Directorate

Veterinary Pharmacovigilance in the United Kingdom

Annual Review 2018 – a summary

Pet owners, farmers, animal carers, vets and anyone else interested in animal welfare should read this review. It gives information about the reports of side effects we received during the year. These reports were usually about animals, but sometimes people had a side effect after giving a medicine to an animal, or after accidentally touching or taking an animal medicine.

The annex to this review lists the changes made to medicine information leaflets during the year.

Highlights

During 2018, we improved 50 of the medicine information leaflets included with animal medicines. The changes made were based on adverse event reports received or on request from product owners. They ensured that the benefits of using these medicines continued to outweigh any risks. They also

made users better informed about the medicines they are using.

The VMD received 7,159 adverse event reports during 2018, a 6.5% increase from the previous year. Consider the millions of doses of different types of veterinary medicines used whilst reviewing these reports.

The VMD would like to thank owners and veterinary professionals for continuing to report adverse events as without these reports, this valuable work would not be possible.

Detailed information about the reports received can be accessed through VMD's adverse events dashboard.

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.

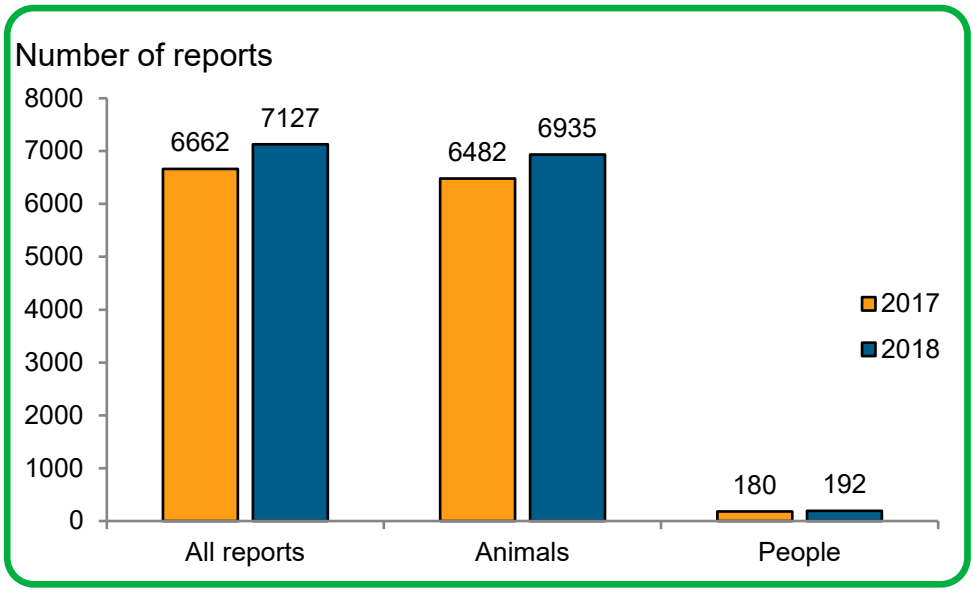
During 2018, VMD received and assessed 7,159 adverse event reports. This was an increase of 6.5% on the previous year, compared to a 2.5% increase from 2016 to 2017.

As a result of the adverse event information received; the product information leaflet enclosed with medicines was improved for 50 products.

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 described 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 entered the food chain.

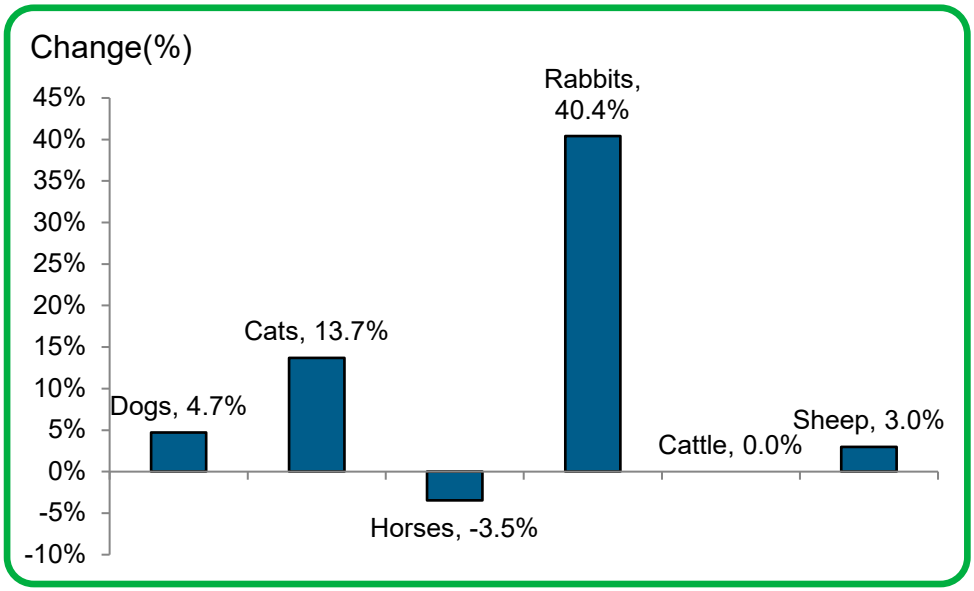
This Summary provides an overview of the adverse events received in 2018, and a list of the product information leaflet changes (See Annex).



The overall number of adverse event reports received in 2018 increased compared to 2017.

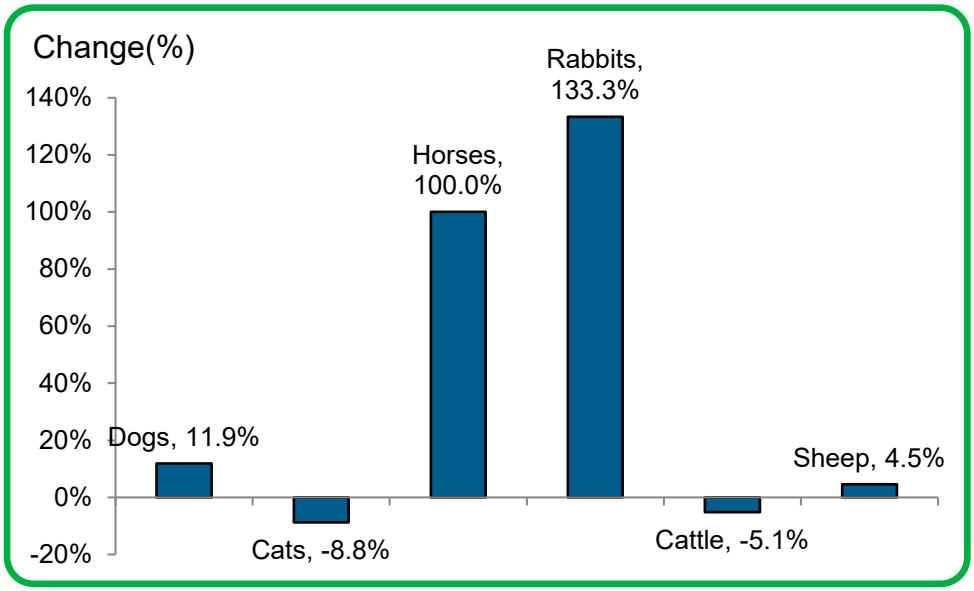
- The number of reports received in 2018 increased from 6,662 in 2017 to 7,127; an increase of 465 (7.0%).
- The number of animal reports in 2018 increased from 6,482 in 2017 to 6,935; an increase of 453 (7.0%).
- The number of reports involving people increased from 180 in 2017 to 192; an increase of 6.7%.

The size of the increase in animal reports varied from species to species.



- The number of reports involving dogs in 2018 increased by 4.7%.
- The number of reports involving cats in 2018 increased by 13.7%.
- The number of reports involving rabbits increased by 40.4%.
- The number of reports involving horses decreased by 3.5%.
- The number of reports involving cattle did not change.
- The number of reports involving sheep increased by 3.0%.

The number of suspected lack of expected efficacy (medicine not working) reports generally increased for the species most often reported but decreased for cats and cattle.

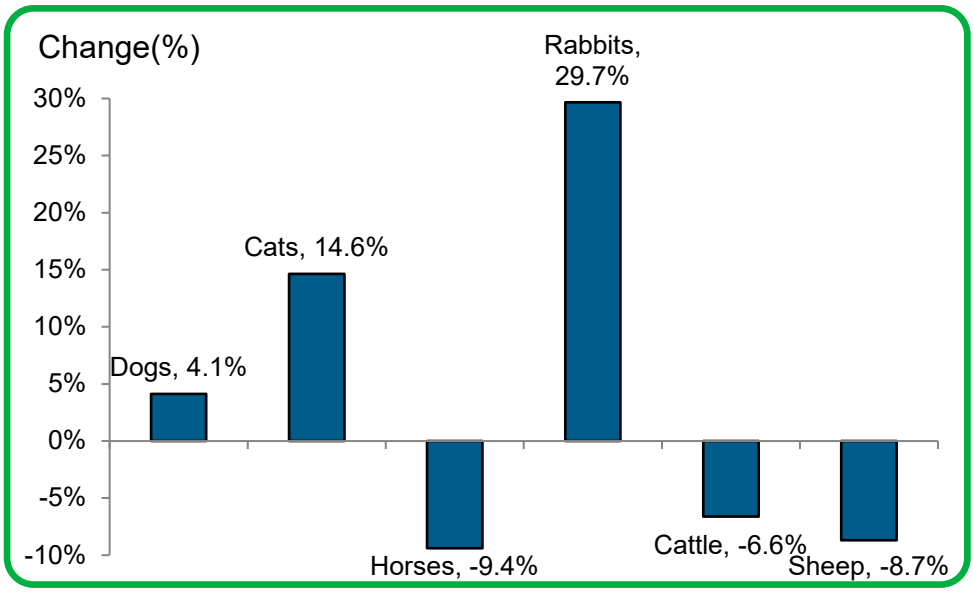


- There was a 12% increase in SLEE reports involving dogs compared to 2017.
- There was an 8.8% decrease in SLEE reports for cats.
- There was a 100% increase in SLEE reports for horses.
- There was a marked increase (133.3%) in the number of suspected lack of expected efficacy (SLEE) reports for rabbits.
- There was a 4.5% increase in SLEE reports for sheep.
- There was a 5.1% decrease in SLEE reports for cattle.

In 2018, the number of SLEEs reported in rabbits was more than twice the number reported in the previous year, but a similar number to those reported in 2015. Almost all reports in these years were associated with vaccines for myxomatosis and/or rabbit haemorrhagic disease (RHD).

For horses, most of the SLEE reports involved the use of euthanasia products.

The number of safety (adverse reaction) reports increased in three of the six most often reported species.



- The number of safety reports received involving dogs increased by 4.1%.
- Safety reports for cats increased by 14.6%.
- Safety reports for horses decreased by 9.4%.
- Safety reports for rabbits increased by 29.7%.
- The number of cattle safety reports decreased by 6.6%.
- The number of sheep safety reports decreased by 8.7%.

Most rabbit safety reports involved the use of one, or occasionally two, vaccines. Other types of product mentioned in rabbit safety reports in a decreasing order of prevalence were general anaesthetics, analgesics (predominantly buprenorphine), and sedatives (mostly medetomidine).

In cat reports, by far the most often reported products were live or inactivated viral vaccines. Far fewer anti-parasiticides were mentioned, with endectocides mentioned most often followed closely by ectoparasiticides, and anthelmintics and

anti-protozoal products mentioned least often. Products associated with thyroid therapy were also reported, with mentions of anti-thyroid preparations being 10-fold higher than steroid preparations.

For dogs, inactivated bacterial vaccines and live viral vaccines were most often reported. Vaccines with a combination of live viral and inactivated bacterial components, and those with a combination of live viral and live bacterial components were reported at a much lower, but not insignificant rate. As with cats, far fewer anti-parasiticides were mentioned, but of these, ectoparasiticides were mentioned most, followed by endectocides, anthelmintics and anti-protozoal products.

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

Vets are required to use veterinary medicines authorised in the UK to treat animals, unless there is no suitable medicine available. Using their clinical judgement, they can decide to use a:

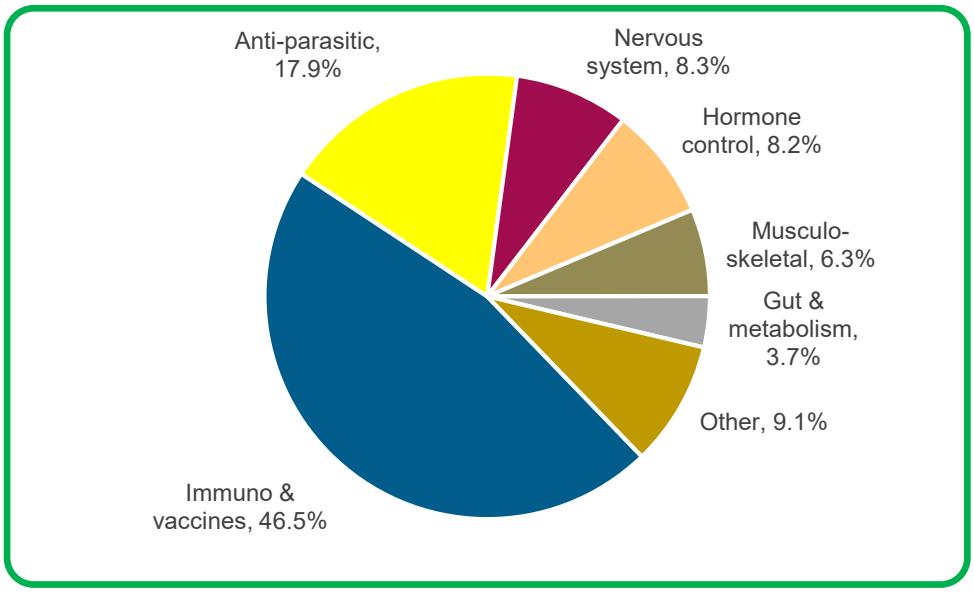
- medicine authorised in the UK for use in people
- veterinary medicine not authorised in the UK
- specially prepared (extemporaneous) medicine

In 2018 97% of the products mentioned in animal adverse event reports were UK authorised veterinary medicines.

Of the remaining 3% of products:

- 1.4% were UK medicines authorised for use in people
- 0.4% were extemporaneous medicines
- 0.3% were imported medicines

- 0.3% were veterinary medicines that are exempt from marketing authorisation requirements
- 0.6% of products were either unidentified products or those without medicinal value, such as microchips,



sutures, household pesticide sprays or disinfectants.

Immunological products were the veterinary medicines most often associated with animal adverse event reports.

- 46.5% of medicines were for aiding the immune system
- 17.9% were for the control of parasites
- 8.3% were for the nervous system, mostly anaesthetics
- 8.2% were for controlling hormone balance
- 6.3% were for treatment of bone and joint problems
- 3.7% were for treating digestive and metabolic problems

Other products included

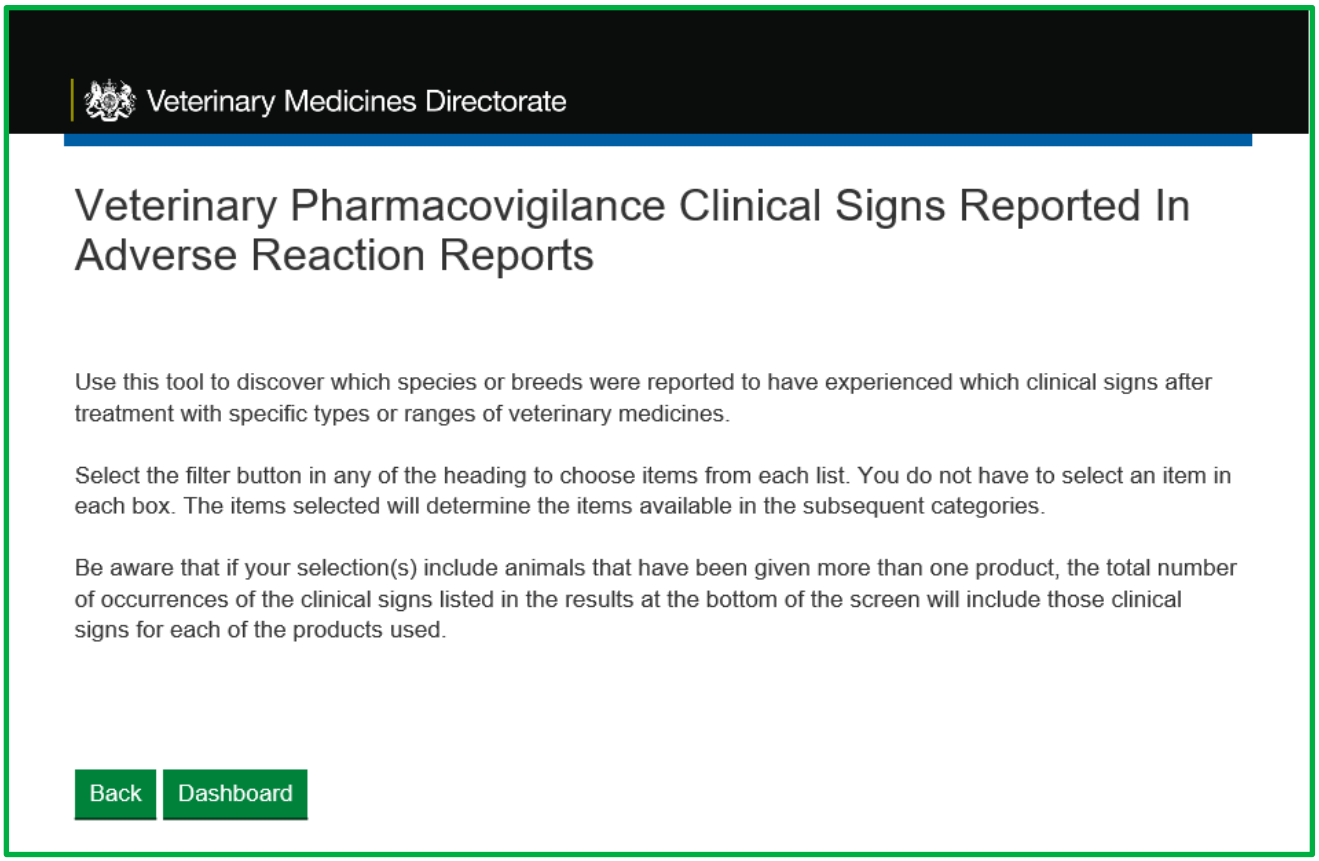
- 3.0% treatments to prevent or treat infection, other than vaccines

- 1.9% treatments for skin problems
- 1.3% treatments for heart or circulation problems
- 1.2% for eye or ear problems
- 0.9% for bladder problems
- 0.8% for cancer treatments, fluids, vitamins and treatments for breathing problems

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

Animal	Number of Adverse Reaction reports (species %)	Number of SLEE reports (species %)
Dogs	3659 (92.2%)	309 (7.8%)
Cats	1527 (96.7%)	52 (3.3%)
Horses	222 (88.8%)	28 (11.2%)
Rabbits	236 (82.8%)	49 (17.2%)
Cattle	155 (43.3%)	203 (56.7%)
Sheep	105 (31.3%)	230 (68.7%)

Use our interactive data dashboard to explore the data.



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. 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.

- Report a problem with a medicine especially prepared for your animal (an extemporaneous product) to the pharmacist/vet/manufacturer of that medicine or to us.
- 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, follow the product leaflet guidance and 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 your vet or the Veterinary Poisons Information Service, then report 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 share a bed 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. These animals can excrete medicine residues that could be harmful to your dog, if ingested.
- Do not allow animals recently treated with topical medicines to enter streams, rivers or other water courses, as these medicines can be fatal to water life.

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 2018. Information received prior to 2018 will have contributed to the evidence leading to the initiation of these actions.

For food-producing and other large animals

Product name	Marketing Authorisation Holder	Active ingredient(s)	Change
Apiguard Gel (25% Thymol) for beehive use	Vita (Europe) Ltd	Thymol	Section 4.6 of the SPC has been updated to include; 'A slight agitation of the colony during the treatment is possible. Occasionally at high temperature some slight reduction in young brood can occur during the treatment period; this is transient and has no effect on the development of the colony. Localised bee brood removal can sometimes occur in treated colonies. Normal bee behaviour involves removing or cleaning the gel from the tray above the brood frames with no effect on the colony; however, especially with more hygienic strains, some bees may occasionally remove uncapped bee brood from the vicinity of the product also. If this is observed, remove the product from the colony.'
Bluevac BTV8 suspension for injection for cattle and sheep	CZ Veterinaria S.A.	Bluetongue virus	Section 4.6 of the SPC has been updated to include: 'An average increase in body temperature varying between 0.5 and 1.0 ºC is a common reaction observed in sheep and cattle. It lasted not longer than 24 to 48 hours. Transient fever was observed in rare cases. Temporary local reactions can occur very rarely at the injection site in the form of a nodule of 0.5 to 1 cm in sheep and of 0.5 to 3 cm in cattle which disappears within 14 days, at the latest and which may be painful. Loss of appetite can occur in very rare cases. Hypersensitivity reactions are very rarely observed.'

Enzaprost 5 mg/ml solution for injection for cattle and pig	Ceva Animal Health	Dinoprost	Section 4.6 of the SPC has been updated to include the following: Cattle Increased rectal temperature (hyperthermia) has been reported very rarely. However, rectal temperature changes have been transient in all cases observed and have not been detrimental to the animal. Limited salivation has been seen in some instances. The side-effects disappear within one hour after the administration of PGF2α. In cattle, if used for induction of parturition, retained foetal membranes may occur more frequently, depending on the time of use of the product. Pigs Transient side-effects consisting of increased body temperature, signs of pain at the site of injection increased respiratory rate, increased salivation, stimulation of defecation and urination, flushing of skin, dyspnea, slight ataxia, abdominal muscle spasms and vomiting occur occasionally following the administration of dinoprost in pregnant sows and gilts. These effects tend to parallel the signs exhibited by sows prior to normal parturition, only they appear to be condensed in time. These effects are usually seen within 10 minutes of injection and disappear within 3 hours. Nest building is a common behaviour 5 to 10 minutes after the administration of prostaglandin in sows that are housed in pen or pasture. In very rare occasions, anaphylactic-type reactions, hyperactivity (restlessness – arching of back, pawing, and rubbing and gnawing the crate) and pruritus have been reported.
Gallivac IB88 NEO effervescent tablet for suspension for nebulisation for chickens	Merial Animal Health Ltd	Infectious bronchitis virus	Section 4.6 of the SPC has been revised to add that mild respiratory signs have been reported very commonly in studies and signs may persist for up to 23 days.

Ketodolor 100 mg/ml Solution for Injection for Horses, Cattle, Pigs	Le Vet Beheer B.V	Ketoprofen	The following statement has been added to section 4.6 of the SPC: 'In common with all NSAIDs, due to their action of inhibition of prostaglandin synthesis, cases of gastric or renal intolerance have been observed very rarely'.
Linco Sol 400 mg/g powder for use in drinking water for pigs and chickens	Lavet Pharmaceuticals Ltd	Lincomycin	Section 4.6 of the SPC has been updated to read; 'On rare occasions, pigs given lincomycin-medicated water may develop diarrhoea/ soft stools and/or mild swelling of the anus within the first two days after onset of treatment. On rare occasions some pigs may show reddening of the skin and mild irritable behaviour. These conditions are usually self-correcting within 5-8 days without discontinuing the lincomycin treatment. Allergic/hypersensitive reactions occur on rare occasions.'
MAQS formic acid 68.2g beehive strips for honey bees	NOD Europe Ltd	Formic acid	The SPC has been updated as follows: Section 4.6: 'Insufficient ventilation, high ambient temperatures and insufficient hive volume have been identified as particular risk factors for build-up of formic acid concentrations beyond easily tolerated levels. Specific requirements of section 4.3 and 4.5 should be carefully observed as there is an increased risk of adverse events if these are not followed. In uncommon cases, increased adult bee mortality, brood mortality and/or queen loss have been observed. Secondary signs including bees absconding, reduced reproduction and/or total colony loss have been noted in consequence. Moribund bees (e.g. those suffering from a viral infection or a high mite infestation) are more susceptible to toxic effects. Formic acid will initially disturb colony activities and may, within one day of application, result in queen rejection, triggering queen supersedure activities. Colonies are expected to expand the cluster as part of controlling vapour concentration during the first 3 days of treatment. Bearding behaviour may be observed.

Ocnil 400 mg/g powder for use in drinking water	Vetpharma Animal Health, S.L	Lincomycin	Section 4.6 of the SPC has been updated to include; 'On rare occasions, pigs given lincomycin-medicated water may develop diarrhoea/soft stools and/or mild swelling of the anus within the first 2 days after onset of treatment. On rare occasions some pigs may show reddening of the skin and mild irritable behaviour. These conditions are usually self-correcting within 5-8 days without discontinuing the lincomycin treatment. Allergic/hypersensitive reactions occur on rare occasions.'
Porcilis PCV emulsion for injection for pigs	Intervet International BV	Porcine circovirus2	Section 4.6 of the SPC has been updated to include: 'In laboratory studies and field trials: Transient local reactions at the injection site were very commonly observed after vaccination mainly in the form of a hard, warm and sometimes painful swelling (diameter up to 10 cm). These reactions resolve spontaneously over a period of approximately 14–21 days without any major consequence on the general health status of the animals. Immediate systemic hypersensitivity-like reactions were commonly observed after vaccination, resulting in minor neurological symptoms such as tremors and/or excitation, which normally resolve within minutes without requiring treatment. A transient increase in body temperature, normally not exceeding 1°C, was very commonly observed until 2 days after vaccination. In individual animals, an increase of rectal temperature of 2.5°C lasting less than 24 hours was uncommonly observed. In some piglets, depression and a reduced feed intake for up to 5 days were uncommonly observed. Vaccination may result in a transient impairment of growth rate in the immediate period after administration of the vaccine. In post marketing experience: In very rare cases anaphylactic-type reactions can occur, which may be life-threatening. In the event of such reactions, treatment may be needed.

Porcilis PCV M Hyo emulsion for injection for pigs	Intervet International BV	Mycoplasma hyopneumoniae, porcine circovirus 2	Section 4.6 of the SPC has been updated including that in very rare cases anaphylactic-type reactions can occur. In the event of such reactions, treatment may be needed.
Rhiniseng suspension for injection for pigs	Laboratorios Hipra SA	Inactivated Bordetella bronchiseptica strain 833CER, recombinant Type D Pasteurella multocida toxin (PMTr)	Section 4.6 of the SPC has been updated to include a reference to the occurrence of anaphylactic type reaction following use of product.
Startvac emulsion for injection for cattle	Laboratorios Hipra SA	Escherichia coli, Staphylococcus aureus	Section 4.6 of the SPC has been updated as follows: Very rare adverse reactions: Slight to moderate transient local reactions may occur after the administration of one dose of vaccine based on post-authorisation pharmacovigilance reporting. They would mainly be: swelling (up to 5 cm2 on average), which disappears within 1 or 2 weeks at most. In some cases, there may also be pain at the inoculation site that spontaneously subsides in a maximum of 4 days. A mean transient increase in body temperature of about 1 °C, in some cows up to 2 °C, may occur in the first 24 hours after injection based on post-authorisation pharmacovigilance reporting. Anaphylactic-type reactions may occur in some sensitive animals which might be life-threatening based on post-authorisation pharmacovigilance reporting. Under these circumstances, appropriate and rapid symptomatic treatment should be administered.

For pet animals

Cyclavance 100 mg/ml oral solution for dogs and cats	Virbac	Ciclosporin A	The following has been added to section 4.6 to reflect the addition of cats as a target species: Cats: In cats treated with ciclosporin the following undesirable effects were observed: Very common: gastrointestinal disturbances such as vomiting and diarrhoea, accompanied by weight loss. These are generally mild and transient and do not require the cessation of the treatment. Increased appetite was also commonly observed. Common: lethargy, anorexia, hypersalivation, hyperactivity, polydipsia, gingival hyperplasia and lymphopaenia. These effects generally resolve spontaneously after treatment is stopped or following a decrease in the dosing frequency. Side effects may be severe in individual animals.
Drontal cat film-coated tablets **XL film-coated tablets** **Bob Martin clear wormer 20/230mg tablets for cats & kittens**	Bayer plc	Praziquantel, pyrantel embonate	Section 4.6 of the SPC has been updated as follows: 'Mild and transient digestive tract disorders such as hypersalivation and/or vomiting and mild and transient neurological disorders such as ataxia may occur in extremely rare cases'.
Eravac emulsion for injection for rabbits	Laboratorios Hipra SA	Rabbit haemorrhagic disease virus type 2	Eravac has been demonstrated to be safe to use in dwarf rabbits (pet rabbits) and the SPC section 4.6 has been updated with additional information on adverse events.

Exitel 230/20 mg flavoured film-coated tablets for cats	Chanelle Pharmaceuticals Manufacturing Ltd	Praziquantel, pyrantel embonate	Section 4.6 of the SPC has been updated to include the following warning: 'In very rare cases, gastrointestinal disorders (vomiting) & neurological signs such as ataxia and muscle tremors have been observed.'
Feligen RCP	Virbac	Feline calicivirus, panleukopenia virus, viral rhinotracheitis virus	Section 4.6 of the SPC had been updated to include: 'Some transient post-vaccinal digestive disturbances were very commonly observed in safety studies. A slight and transient oedema which disappears spontaneously within 2 days was commonly observed during the days following vaccination in safety studies. Some transient and self-resolving post-vaccinal signs such as a slight hyperthermia and lethargy were commonly observed in safety studies. Hypersensitivity reactions (e.g. emesis, diarrhoea, dyspnoea, allergic oedema) have been reported in very rare cases from spontaneous reports. In case of such an allergic or anaphylactic reaction, appropriate symptomatic treatment should be administered. As reported in the literature, after the use of any vaccine containing a Feline calicivirus component, febrile limping syndrome reactions may occur very rarely in kittens.'

Frontline Combo spot-on cat	Merial Animal Health Ltd	(S)-Methoprene, fipronil	Section 4.6 of the SPC has been revised to include an instruction not to overdose. The adverse reactions stated are now considered to be applicable to ferrets (as well as cats): 'Among the very rare suspected adverse reactions, transient skin reactions on the application site (scaling, local hair loss, itching, redness) and general itching or hair loss have been reported after use. Excessive salivation, reversible nervous signs (increased sensitivity to stimulation, depression, other nervous signs) or vomiting have also been observed after use. If licking occurs, a brief period of excessive salivation may be observed due mainly to the nature of the carrier.'
Iso Vet 1000 mg/g inhalation vapour, liquid	Piramal Critical Care Ltd	Isoflurane	Section 4.6 of the SPC has been amended to include: 'Isoflurane produces hypotension and respiratory depression in a dose-related manner. Cardiac arrhythmias and transient bradycardia have been reported only rarely. Malignant hyperthermia has been reported very rarely in susceptible animals.
Milbemax tablets **for small dogs and puppies** **for dogs** **Milbemax chewable tablets** **for small dogs and puppies** **for dogs** **Milbemax film-coated tablets** **for small cats and kittens** **for cats**	Elanco Europe Ltd	Milbemycin oxime (A3 and A4), praziquantel	Section 4.6 of the SPC has been updated to advise that hypersensitivity reactions have been observed in very rare cases (less than 1 animal in 10,000 animals treated, including isolated reports).

Molecare dog wormer tablets **Beaphar WORMclear tablets for dogs** **EziWormer Plus tablets for dogs** **Ridaworm Plus tablets for dogs** **TermaWorm** **tablets for dogs** **XL tablets for dogs** **VetUK Dog Wormer flavoured tablets**	C&H Generics Ltd	Febantel, praziquantel, pyrantel	Section 4.6 of the SPC has been updated: 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.
NexGard chewable tablets **11mg for dogs 2-4kg** **28mg for dogs 4-10kg** **68mg for dogs 10-25kg** **135mg for dogs 25-50kg**	Merial Animal Health Ltd	Afoxolaner	Section 4.6 of the SPC has been updated to include neurological signs (convulsions, ataxia and muscle tremors) as adverse reactions which have been reported very rarely.

Sevotek 1000 mg/g inhalation vapour, liquid for dogs and cats	Laboratorios Karizoo S.A	Sevoflurane	Cats have been included as a target species. Section 4.6 of the SPC has been updated to read; 'Hypotension, tachypnoea, muscle tenseness, excitation, apnoea, muscle fasciculations and emesis have been reported as very common adverse reactions, based on post-authorisation spontaneous reporting experience. Dose-dependent respiratory depression is commonly observed while using sevoflurane, therefore respiration should be closely monitored during sevoflurane anaesthesia and the inspired concentration of sevoflurane adjusted accordingly. Anaesthetic-induced bradycardia is commonly observed during sevoflurane anaesthesia. It may be reversed by administration of anticholinergics. Paddling, retching, salivation, cyanosis, premature ventricular contractions and excessive cardiopulmonary depression have been reported very rarely based on post-authorisation spontaneous reporting experience. In dogs, transient elevations in aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), bilirubin and white blood cell counts may occur with sevoflurane, as with the use of other halogenated anaesthetic agents. In cats, transient increases in AST and ALT may occur with sevoflurane, however, hepatic enzymes tend to remain within the normal range. Hypotension during sevoflurane anaesthesia may result in decreased renal blood flow. The possibility of sevoflurane triggering episodes of malignant hyperthermia in susceptible dogs and cats cannot be ruled out.'

Tardak 10 mg/ml suspension for injection	Zoetis UK Ltd	Delmadinone acetate	Section 4.6 has been updated to include the following: 'Manifestation of latent diabetes mellitus, elevated plasma liver enzymes (ALT, alkaline phosphate), changes in teats (tumours, hyperplasia, cysts, galactorrhoea) may occur. In rare cases, transient digestive disorders have been reported. Delmadinone acetate may cause adrenal suppression. In stress situations, the treated animal is then at risk of developing adrenocortical insufficiency during or after treatment.' Section 4.7 has been updated to read: 'Studies to investigate the return of fertility in breeding male dogs and cats have not been carried out. See also section 4.6.'
Versican Plus **DHPPi/L4R** **DHPPi/L4** **L4 suspension for injection for dogs** **Pi/L4 lyophilisate and solvent for suspension for injection for dogs** **Pi/L4R lyophilisate and solvent for suspension for injection for dogs**	Zoetis Belgium	Canine adenovirus, distemper virus, parainfluenza virus, parvovirus Leptospira bratislava, canicola, icterohaemorrhagiae, kirschneri Rabies virus	Section 4.6 of the SPC had been updated to cover transient swelling, anorexia, hypersensitivity reactions, systemic reactions and clinical signs.

Vetflea spot-on solution 67 mg for small dogs 134 mg for medium dogs 268 mg for large dogs 402 mg for very large dogs	Alfamed	Fipronil	Section 4.6 of the SPC has been updated to include, 'If licking occurs, a brief period of hypersalivation may be observed due mainly to the nature of the carrier. Very rarely, transient cutaneous reactions on the application site (skin discolouration, local alopecia, pruritus, erythema) and general pruritus or alopecia have been reported after use. Anorexia, hypersalivation, lethargy, reversible neurologic symptoms (hyperesthesia, depression, nervous symptoms), vomiting or respiratory symptoms have also been observed very rarely after use.'
VetWorm Plus tablets for dogs	Healthspan UK Ltd	Febantel, Praziquantel, Pyrantel embonate	Addition of the following warning to section 4.6 of the SPC: '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.'