17 December 2021
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Veterinary Medicines Division

Pharmacovigilance-related regulatory recommendations for centrally authorised veterinary medicinal products during 2021 (Updated monthly)

Please note that the recommendations shown in this document may not reflect the exact final wording that will appear in the actual package leaflet that still needs to be implemented by the marketing authorisation holders.

Previous regulatory recommendations and ongoing procedures are outlined in Pharmacovigilance regulatory recommendations for centrally authorised veterinary medicinal products during 2020 (EMA/112926/2020)

Product (active substance(s))	**CVMP meeting date**	**Recommendation - SPC change** (additions to text **in bold**, deletions in ~~strikethrough~~)
Advocate (imidacloprid/moxidectin)	**13-15 July 2021**	**Section 4.6 of SPC for Advocate spot-on solution for dogs**: **Vomiting can occur on rare occasions.** Use of the product may result in transient pruritus in dogs. ~~Vomiting can occur on rare occasions.~~ Transient local skin sensitivity reactions including increased itching, hair loss, greasy fur and redness at application site have been reported in very rare cases~~ in spontaneous (pharmacovigilance) reports~~. These signs disappear without further treatment. ~~If the animal licks the application site after treatment, n~~**N**eurological signs~~, (most of which are transient)~~ **such as ataxia and muscle tremor (most of which are transient)** may be observed in very rare cases (see section 4.10).

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Bravecto (fluralaner)	**15-17 June 2021**	**Section 4.6 of SPC for Bravecto spot-on solution for cats**: Mild and transient skin reactions at the application site, such as erythema and pruritus or alopecia were commonly observed in clinical trials (2.2% of treated cats). The following other signs shortly after administration were uncommonly observed: apathy/tremors/anorexia (0.9% of treated cats) or vomiting/hypersalivation (0.4% of treated cats). **Convulsions have been reported very rarely based on post marketing safety experience (pharmacovigilance).**
Bravecto Plus (fluralaner/moxidectin)	**5-7 October 2021**	**Section 4.5 of SPC for Bravecto Plus (under Special precautions for use in animals):** Care should be taken to avoid contact with the eyes of the animal. Do not use directly on skin lesions. In the absence of available data, treatment of kittens less than 9 weeks of age and cats less than 1.2 kg bodyweight is not recommended. Treatment of male breeding animals is not recommended. This product is for topical use and should not be administered orally. Oral uptake of the product at the maximum recommended dose of 93 mg fluralaner + 4.65 mg moxidectin/kg body weight induced some self-limiting salivation or single incidences of vomiting immediately after administration. It is important to apply the dose as indicated to prevent the animal from licking and ingesting the product **(see sections 4.6 and 4.9)**. Do not allow recently treated animals to groom each other. Do not allow treated animals to come into contact with untreated animals until the

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		application site is dry. **Section 4.6 of SPC for Bravecto Plus:** Mild and transient skin reactions at the application site (alopecia, flaking skin, redness and pruritus) were commonly observed in clinical trials. ~~The following other adverse reactions were uncommonly observed in clinical trials shortly after administration: d~~**D**yspnoea after licking the application site, hypersalivation, emesis, haematemesis, diarrhoea, lethargy, pyrexia, tachypnoea~~,~~ **and** mydriasis **were uncommonly observed in clinical trials shortly after administration.** ~~Tremors and anorexia~~**Anorexia as well as neurological manifestations such as tremors and ataxia** have been reported very rarely after the use of this product based on post-marketing safety experience ~~(pharmacovigilance)~~.
Cerenia (maropitant)	**15-17 June 2021**	**Section 4.6 of SPC for Cerenia tablets for dogs**: Incidents of pre-travel vomiting, usually within two hours post-dosing were commonly reported after administration of the 8 mg/kg dose. **Lethargy has been reported in very rare cases, based on post-marketing safety experience.** **Section 4.6 of SPC for Cerenia injection for solution for dogs and cats** (additions to text in **bold**, deletions in ~~strikethrough~~): Pain at injection site may occur when injected subcutaneously. In cats, moderate to severe response to injection is very commonly observed (in approximately one third of cats). ~~In very rare cases, a~~**A**naphylactic type reactions (allergic oedema, urticaria, erythema, collapse, dyspnoea, pale mucous membranes) may occur **in very rare cases**.

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		Lethargy has been reported in very rare cases, based on post-marketing safety experience.
Comfortis (spinosad)	**16-18 March 2021**	**Section 4.6 of SPC for Comfortis (under subsection for cats)**: Cats Other commonly observed adverse reactions in cats were diarrhoea and anorexia. Lethargy, loss of condition and salivation were uncommon. Seizures**, ataxia and muscle tremor** were rare adverse reactions.
Cytopoint (lokivetmab)	**10-12 May 2021**	**Section 4.6 of SPC for Cytopoint**: Hypersensitivity reactions (anaphylaxis, facial oedema, urticaria) have been reported to occur in rare cases from spontaneous reports. In such cases appropriate treatment should be administered immediately. Vomiting and/or diarrhoea have been reported to occur in rare cases from spontaneous reports and may occur in connection with hypersensitivity reactions. Treatment should be administered as needed. Neurological signs (seizure, convulsion or ataxia) have been rarely observed in spontaneous reports following use of the veterinary medicinal product. **Application site disorders (injection site pain, injection site swelling) have been reported very rarely in spontaneous reports.** **Clinical signs of immune-mediated diseases, such as haemolytic anaemia or thrombocytopenia, have been reported very rarely in spontaneous reports.**
Draxxin (tulathromycin)	**10-12 May 2021**	**Section 4.5 of SPC for Draxxin**: Tulathromycin is irritating to eyes. In case of accidental eye exposure, flush the eyes immediately with clean water. Tulathromycin may cause sensitisation by skin contact **resulting in e.g. reddening of**

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		the skin (erythema) and/or dermatitis. In case of accidental spillage onto skin, wash the skin immediately with soap and water. Wash hands after use. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician. **If there is suspicion of a hypersensitivity reaction following accidental exposure (recognised by e.g. itching, difficulty in breathing, hives, swelling on the face, nausea, vomiting) appropriate treatment should be administered.** **Seek medical advice immediately and show the package leaflet or the label to the physician.**
Felisecto Plus (selamectin/sarolaner)	**15-17 February 2021**	**Section 4.6 of SPC for Felisecto Plus**: Use of the veterinary medicinal product may result in mild and transient pruritus at the application site. Mild to moderate alopecia at the application site, erythema and drooling have been uncommonly observed. **Neurological signs (convulsions, ataxia) and gastrointestinal signs (emesis, diarrhoea) have been reported very rarely based on post-marketing safety experience. In most cases these signs are transient.**
NEW **Fevaxyn Pentofel** (inactivated feline rhinotracheitis virus, inactivated feline calicivirus, inactivated feline *Chlamydophila felis*, inactivated feline leukaemia virus, inactivated feline panleukopenia virus)	**7-9 December 2021**	**Section 4.6 of SPC for Fevaxyn Pentofel:** Vaccinated cats may develop post-vaccinal reactions including transient fever, vomiting, anorexia and/or depression which usually disappear within 24 hours. A local reaction with swelling, pain, pruriti~~t~~us or hair loss at the injection site may be observed. ~~In very rare cases an a~~**A**naphylac**ti**~~coid~~ reaction**s** with oedema, pruriti~~t~~us, respiratory and cardiac distress, severe gastrointestinal signs **(including haematemesis and**

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		haemorrhagic diarrhoea) or shock ha**ve**~~s~~ been seen during the first hours after vaccination **in very rare cases**. See section 4.5 for guidance about treatment.
Galliprant (grapiprant)	**13-15 April 2021**	**Section 4.6 of SPC for Galliprant**: ~~In clinical studies, the following mild and generally transient adverse reactions have been observed: vomiting, soft-formed faeces, diarrhoea and inappetence.~~ Vomiting was observed very commonly **in clinical studies.** ~~whereas s~~ Soft-formed faeces, diarrhoea and inappetence were commonly observed **in clinical studies. These signs were generally transient.** ~~In very rare cases, haematemesis or haemorrhagic diarrhoea was reported following clinical use post authorisation.~~ **Elevated liver enzymes, elevated BUN, elevated creatinine, haematemesis and haemorrhagic diarrhoea have been reported very rarely following use post authorisation.**
Kexxtone (monensin)	**13-15 April 2021**	**Section 4.5 of SPC for Kexxtone, under 'Other precautions'**: 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 veterinary medicinal products containing monensin. Due to the risk of bolus regurgitation, do not allow these species access to areas where treated cattle have been kept. **Keep dogs away from treated animals. Accidental ingestion of active ingredient by dogs has resulted in fatal consequences. In case of suspected ingestion by dogs, seek veterinary advice immediately.**
Kriptazen (halofuginone)	**13-15 July 2021**	**Section 4.6 of SPC for Kriptazen**: An increase in the level of diarrhoea has been observed in ~~very~~ rare cases, in treated animals.

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Letifend (Recombinant protein Q from Leishmania infantum MON-1)	**5-7 October 2021**	**Section 4.6 of SPC for Letifend:** After vaccination, scratching at the injection site has been observed very commonly in dogs. Spontaneous resolution of such reaction was observed within 4 hours. **Hypersensitivity reactions (e.g. anaphylaxis, skin manifestations such as oedema, urticaria, pruritus) have been reported in very rare cases. In case of such an allergic or anaphylactic reaction, appropriate symptomatic treatment should be administered.** Lethargy, vomiting, diarrhoea and hyperthermia following vaccination have each been reported to occur very rarely based on post-marketing safety experience. Treatment should be administered as needed.
Librela (bedinvetmab)	**3-4 November 2021**	**Section 4.6 of SPC for Librela:** Mild reactions at the injection site (e.g. swelling and heat) may uncommonly be observed. **Hypersensitivity-type reactions have been reported very rarely. In case of such reactions, appropriate symptomatic treatment should be administered.**
Osurnia (terbinafine/florfenicol/betamethasone)	**10-12 May 2021**	**Section 4.6 of SPC for Osurnia**: Deafness or impaired hearing, usually temporary, have been reported after use in very rare cases in dogs, mainly in elderly animals, in post authorisation experience. **Application site reactions (i.e. erythema, pain, pruritus, oedema and ulcer) have been reported in very rare cases, in post authorisation experience.** **Hypersensitivity reactions including facial oedema, urticaria and shock have been reported in very rare cases, in post authorisation experience.**
Prevomax (maropitant)	**15-17 June 2021**	**Section 4.6 of SPC for Prevomax**: Pain at injection site may occur when injected subcutaneously. In cats, moderate to severe response to injection is very commonly observed (in approximately one third of

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		cats). ~~In very rare cases, a~~Anaphylactic type reactions (allergic oedema, urticaria, erythema, collapse, dyspnoea, pale mucous membranes) may occur **in very rare cases.** **Lethargy has been reported in very rare cases, based on post-marketing safety experience.**
Purevax RC (Attenuated feline rhinotracheitis herpesvirus (FHV F2 strain)/Inactivated feline calicivirus (FCV 431 and G1 strains) antigens) **Purevax RCP** (Attenuated feline rhinotracheitis herpesvirus (FHV F2 strain)/Inactivated feline calicivirus (FCV 431 and G1 strains) antigens)/Attenuated feline panleucopenia virus (PLI IV)) **Purevax RCP FeLV** (Attenuated feline rhinotracheitis herpesvirus (FHV F2 strain)/Inactivated feline calicivirus (FCV 431 and G1 strains) antigens/Attenuated feline panleucopenia virus (PLI IV)/FELV recombinant canarypox virus (vCP97)	**5-7 October 2021**	**Section 4.6 of SPC for Purevax RC, Purevax RCP, Purevax RCP FeLV:** Transient apathy and anorexia as well as hyperthermia (lasting usually for 1 or 2 days) were commonly observed during safety and field studies. A local reaction (slight pain at palpation, itching or limited oedema) that disappears within 1 or 2 weeks at most was commonly observed during safety and field studies. A hypersensitivity reaction has been observed uncommonly in field studies, which may require appropriate symptomatic treatment. **Emesis (mostly within 24 to 48 hours) has been observed in very rare cases based on post-marketing safety experience.**
Purevax RCPCh (Attenuated feline rhinotracheitis herpesvirus (FHV F2 strain)/Inactivated feline calicivirus (FCV 431 and G1 strains) antigens/Attenuated Chlamydophila felis (905 strain)/Attenuated feline panleucopenia virus (PLI IV) **Purevax RCPCh FeLV** (Attenuated feline rhinotracheitis	**5-7 October 2021**	**Section 4.6 of SPC for Purevax RCPCh, Purevax RCPCh FeLV:** Transient apathy and anorexia as well as hyperthermia (lasting usually for 1 or 2 days) were commonly observed during safety and field studies. A local reaction (slight pain at palpation, itching or limited oedema) that disappears within 1 or 2 weeks at most was commonly observed during safety and field studies. A hypersensitivity reaction has been observed uncommonly in field studies, which may require appropriate symptomatic treatment.

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herpesvirus (FHV F2 strain)/Inactivated feline calicivirosis (FCV 431 and G1 strains) antigens/Attenuated Chlamydophila felis (905 strain)/Attenuated feline panleucopenia virus (PLI IV)/FeLV recombinant canarypox virus (vCP97)		**Emesis (mostly within 24 to 48 hours) has been observed in very rare cases based on post-marketing safety experience.** Transient hyperthermia and lethargy, sometimes associated with lameness, have been observed 1 to 3 weeks following booster vaccination in adult cats, in very rare cases, based on post marketing safety experience.
Simparica Trio (moxidectin/sarolaner/pyrantel embonate)	**13-15 April 2021**	**Section 4.6 of SPC for Simparica Trio**: ~~None known.~~**Gastrointestinal signs such as vomiting and diarrhoea, and systemic disorders such as lethargy, anorexia/inappetence may occur in very rare cases based on post-marketing safety experience. In most cases these signs are mild and transient.** **Neurological signs such as tremor, ataxia or convulsion may occur in very rare cases based on post-marketing safety experience. In most cases these signs are transient.**
Stronghold Plus (selamectin/sarolaner)	**15-17 February 2021**	**Section 4.6 of SPC for Stronghold Plus**: Use of the veterinary medicinal product may result in mild and transient pruritus at the application site. Mild to moderate alopecia at the application site, erythema and drooling have been uncommonly observed. **Neurological signs (convulsions, ataxia) and gastrointestinal signs (emesis, diarrhoea) have been reported very rarely based on post-marketing safety experience. In most cases these signs are transient.**
Ubac (Lipoteichoic acid (LTA) from Biofilm Adhesion Component (BAC) of Streptococcus uberis, strain 5616)	**5-7 October 2021**	**Section 4.6 of SPC for Ubac:** Local swelling more than 5 cm in diameter at the injection site is a very common reaction after administration of the vaccine. This swelling will have disappeared or be clearly reduced in size by 17 days post vaccination. However, in some cases, swelling may persist for up to 4 weeks.

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		A transient increase in rectal temperature (mean increase of 1 °C but may be up to 2 °C in individual animals) may very commonly occur in the first 24 hours after injection. **Anaphylactic-type reactions (e.g. oedema) which might be life-threatening, may occur very rarely in some sensitive animals based on post-marketing safety experience. Under these circumstances, appropriate symptomatic treatment should be administered.**
Vectra Felis (pyriproxyfen/dinotefuran)	**15-17 June 2021**	**Section 4.6 of SPC for Vectra Felis**: Slight scales, transient erythema and alopecia can be observed in rare cases, which usually disappear spontaneously without treatment. **Transient neurological signs such as muscle tremors or lethargy may occur very rarely and in particular after application site licking.**
Vectra 3D (pyriproxyfen/dinotefuran/permethrin)	**13-15 July 2021**	**Section 4.5 of SPC for Vectra 3D, under 'Special precautions to be taken by the person administering the veterinary medicinal product to animals'**: Do not eat, drink or smoke while handling the veterinary medicinal product. People with known hypersensitivity to any of the ingredients should avoid contact with the veterinary medicinal product. **Because the excipient N-methylpyrrolidone has shown evidence of foetal malformations in rabbits and rats in laboratory studies, pregnant women and women suspected of being pregnant should not administer the product and should avoid direct contact with the application site until the application site is no longer noticeable.**
NEW	**7-9 December 2021**	**Section 4.6 of SPC for Vectra 3D:** Erythema, pruritus or other signs of discomfort at the application site have been reported

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		rarely. These signs may be mild and transient. If signs persist or worsen, veterinary advice should be sought. Behavioural disorders such as hyperactivity, vocalisation or anxiety, systemic signs such as lethargy or anorexia, and neurological signs such as muscle tremor have been reported in rare cases. Signs of ataxia such as unsteady movement have been reported in very rare cases. Gastrointestinal signs such as vomiting or diarrhoea have also been reported very rarely. Transient cosmetic effects (wet appearance, spiking of hair coat and deposits) at the application site have been reported very rarely, however**,** these effects are usually not noticeable after 48 hours. **In addition, isolated reports on convulsions have been received.**
Vepured (Recombinant verotoxin 2e of E. coli)	**7-9 September 2021**	**Section 4.6 of SPC for Vepured**: Very common adverse reactions: - Mild inflammation at the injection site (< 5 cm in diameter) that typically resolves within three days post-vaccination without treatment. - Mild depression during the day of vaccination. - Temperature rise of maximum 1.1 °C was observed. Temperatures returned to normal within 24 hrs. **Emesis, recumbency, convulsion, lethargy and loss of consciousness occur in very rare cases within a few minutes after vaccination. The animals mostly start to recover within around 15 minutes. In case of severe anaphylactic-type reactions appropriate treatment is recommended.**