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Veterinary Medicines Division

Pharmacovigilance regulatory recommendations for centrally authorised veterinary medicinal products during 2020

This document is updated monthly with the recommendations of the Committee for Medicinal Products for Veterinary Use for regulatory action based on pharmacovigilance data. Please note that the recommendations shown in this document may not reflect the final wording which may change in the course of the review before implementation by marketing authorisation holders.
Previous regulatory recommendations and ongoing investigations are outlined in the Annual veterinary pharmacovigilance bulletin 2019 (EMA/CVMP/PhVWP/33617/2020).

CVMP meeting date	Product	Recommendation - SPC change
21-23 January 2020	**Advocate** (imidacloprid/moxidectin)	**Section 4.6 of SPC of Advocate for dogs** (additions to text in **bold**, deletions in ~~strikethrough~~): Use of the product may result in transient pruritus in dogs**.** ~~greasy hair, erythema and~~ Vomiting can occur on rare occasion~~s~~. **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. ~~The product may, in rare cases, cause local~~

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		~~hypersensitivity reactions.~~ If the animal licks the application site after treatment, neurological signs (most of which are transient) may be observed in very rare cases (see section 4.10). **Section 4.5 of the SPCs to both cat and ferret, and dog** (new text **in bold**, deletions in ~~strikethrough~~): The treatment of cats weighing less than 1 kg and ferrets weighing less than 0.8 kg should be based on a benefit-risk assessment. There is limited experience on the use of the product in sick and debilitated animals, thus the product should only be used based on a benefit-risk assessment for these animals. **Do not apply in the mouth, in the eyes or the ears of the animal.** **Care should be taken that the product** ~~content of the pipette or the applied dose~~ **is not ingested by animals and does not come into contact with the eyes or mouth of the recipient and/or other animals.** **Consider carefully the correct application method described in section 4.9, especially that the product should be applied to the site specified in order to minimise the risk for the animal to lick the product.** **Do not allow recently treated animals to groom each other. Do not allow treated animals to come into contact with untreated animals until the application site is dry.** **Section 4.7 of SPC** should be amended as follows (current text ~~strikethrough~~, new proposed text **bold**): ~~The safety of the veterinary medicinal product has not been established during pregnancy and lactation. Laboratory studies with either imidacloprid or moxidectin in rats and rabbits have not produced any evidence of teratogenic, foetotoxic or maternotoxic effects. Use only accordingly to the benefit-risk assessment by the responsible veterinarian.~~ **The safety of the veterinary medicinal product has not been established during pregnancy and lactation in the target species. Moxidectin caused foetal malformations and reduced pup survival in**

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		rats. Therefore, the use of the product is not recommended in animals intended for breeding or during pregnancy and lactation.
21-23 January 2020	**Credelio** (lotilaner)	**Credelio Chewable Tablets for Dogs** (additions to text **in bold,** deletions in ~~strikethrough~~): **Section 4.6 Adverse reactions** (frequency and seriousness) Mild, transient, gastrointestinal signs (vomiting; diarrhoea; **anorexia**), ~~neurological signs (convulsion; muscle tremor; ataxia)~~ **and lethargy** have been reported very rarely based on post-marketing safety experience. These signs typically resolve without treatment. **Neurological disorders such as tremor, ataxia or convulsion may occur in very rare cases. In most cases these signs are transient**. **Credelio Chewable Tablets for cats** (additions to text **in bold**, ~~deletions in strikethrough~~): **Section 4.6 Adverse reactions** (frequency and seriousness) **Vomiting has been reported very rarely based on post marketing safety experience and typically resolves without treatment.**
21-23 January 2020	**Metacam/Novem** (meloxicam)	**Metacam** (additions to text **in bold**, deletions in ~~strikethrough~~): **Section 4.5** in the SPC all Metacam oral suspensions as well as for all Metacam solutions for injection formulations. **This product can cause eye irritation. In case of contact with the eyes, immediately rinse thoroughly with water.** **Novem** (additions to text **in bold**, deletions in ~~strikethrough~~): **Section 4.5** in the SPC for all Novem® solution for injection formulations. **This product can cause eye irritation. In case of contact with the eyes, immediately rinse thoroughly with water.**

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17-18 March 2020	**Galliprant** (grapiprant)	**Section 4.6 of SPC of Galliprant** (additions to text in **bold**, deletions in ~~strikethrough~~): 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, whereas soft-formed faeces, diarrhoea and inappetence were commonly observed. In very rare cases, haematemesis or haemorrhagic diarrhoea was reported following clinical use ~~post-authorisation in the USA~~.
16-18 June 2020	**Purevax FeLV** [Feline leukaemia vaccine (live recombinant)]	**Section 4.6 of SPC of Purevax FeLV** (additions to text in **bold**, deletions in ~~strikethrough~~): A temporary small (< 2 cm) nodule**, which regresses within 1 to 4 weeks**, ~~may appear~~ **was very commonly observed** at the site of injection ~~which regresses within 1 to 4 weeks~~ **during safety and field studies**. Transient lethargy and hyperthermia ~~may occur for 1 day, exceptionally 2 days~~ **were very commonly observed during safety and field studies and lasted usually** for 1 day, exceptionally **for** 2 days. **Anorexia and emesis have been reported very rarely based on post marketing safety experience.** A hypersensitivity reaction may occur **in very rare cases**~~, which may require appropriate symptomatic treatment~~. **Such reactions may evolve to a more severe condition (anaphylaxis). If such reactions occur, appropriate treatment is recommended.** **The frequency of adverse reactions is defined using the following convention:** **- very common (more than 1 in 10 animals treated displaying adverse reaction(s))** **- common (more than 1 but less than 10 animals treated in 100 animals)** **- uncommon (more than 1 but less than 10 animals treated in 1,000 animals)** **- rare (more than 1 but less than 10 animals in 10,000 animals treated)** **- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).**
16-18 June 2020	**Vectra 3D**	**Section 4.6 of SPC of Vectra 3D** (additions to text in **bold**, deletions in ~~strikethrough~~):

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	(dinotefuran, pyriproxyfen, permethrin)	~~Transient e~~Erythema, pruritus or other signs of discomfort at the application site have been reported rarely~~ and usually disappear spontaneously, within 24 hours following administration of the product~~. **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.
14-16 July 2020	**Activyl Tick Plus** (indoxacarb, permethrin)	**Section 4.6 of SPC of Activyl Tick Plus** (additions to text in **bold**, deletions in ~~strikethrough~~): Transitory erythema, hair loss or itching at the application site were commonly observed in clinical studies. These effects will usually resolve without treatment. Gastrointestinal signs (e.g. emesis, diarrhoea or anorexia), reversible neurological signs (e.g. tremor or ataxia) or lethargy have been observed in very rare cases. These signs are usually transient and generally resolve within 24 – 48 hours. **If adverse reactions occur bathe the animal with mild soap and rinse with large amounts of water.** The application of the veterinary medicinal product may produce a local, temporary oily appearance or hair clumping at the application site. A dry white residue may be also observed. This is normal and will generally resolve within a couple of days after administration. These changes do not affect the safety or efficacy of the veterinary medicinal product.
14-16 July 2020	**Cardalis**	**Section 4.6 of SPC of Cardalis** (additions to text in **bold,** deletions in ~~strikethrough~~)**:**

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	(benazepril hydrochloride, spironolactone)	Vomiting, **diarrhoea and pruritus** ~~has~~**have** been reported very rarely in spontaneous reports.

14-16 July 2020	**Onsior** (robenacoxib)	**<u>Section 4.6 of SPC of Onsior 6mg Tablets for Cats</u>** (additions to text **in bold,** deletions in ~~strikethrough~~): Mild and transient diarrhoea, soft faeces or vomiting were commonly reported in clinical trials with treatment up to 6 days. ~~In very rare cases, l~~**L**ethargy may be observed in very rare cases. ~~Vomiting was very commonly reported, and anorexia, diarrhoea, lethargy and inappropriate defecation were commonly reported in field studies with treatment up to 12 weeks in cats with chronic musculoskeletal disorder, with similar frequencies in the Onsior and placebo treated cats.~~ **In addition, elevated renal parameters (creatinine, BUN and SDMA), and renal insufficiency have been reported very rarely in post marketing safety experience, more commonly in older cats and with concomitant use of anaesthetic or sedative agents (see also Sections 4.5 Special precautions for use, 4.8 Interaction with other medicinal products and forms of interaction, and 4.9 Amounts to be administered and administration route).**
8-9 September 2020	**Convenia** (cefovecin)	**<u>Section 4.5 of SPC of Convenia</u>** (additions to text in **bold,** deletions in ~~strikethrough~~): **Occasionally, cephalosporins have been associated with myelotoxicity, thereby creating a toxic neutropenia. Other haematological reactions seen with cephalosporins include neutropenia, anaemia, hypoprothrombinemia, thrombocytopenia, prolonged prothrombin time (PT) and partial thromboplastin time (PTT), platelet dysfunction.** **<u>Section 4.6 of SPC of Convenia</u>** (additions to text in **bold,** deletions in ~~strikethrough~~): ~~On very rare occasions g~~**G**astrointestinal signs, including emesis, ~~and/or~~ diarrhoea **and/or anorexia** have been observed **on very rare occasions**. ~~In very rare cases n~~**N**eurological signs **(ataxia, convulsion or seizure)** and injection site reactions have been reported **in very rare cases** after the use of the product. **Hypersensitivity reactions (e.g. anaphylaxis, dyspnoea, circulatory shock) may occur very rarely. If such a reaction occurs, appropriate treatment should be administered without delay (see also 4.5 Special precautions for use in animals).**