16 December 2022
EMA/CVMP/PhVWP/48138/2022
Veterinary Medicines Division

Pharmacovigilance-related regulatory recommendations for centrally authorised veterinary medicinal products during 2022 (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. When the exact wording for the package leaflet is provided with the recommendations in this document, this needs to be implemented by the marketing authorisation holders accordingly.

Previous regulatory recommendations and ongoing procedures are outlined in (EMA/CVMP/PhVWP/105691/2021) and Pharmacovigilance regulatory recommendations for centrally authorised veterinary medicinal products during 2020 (EMA/112926/2020).

Product (active substance(s))	**CVMP meeting date**	**Recommendation – Summary of Product Characteristics (SPC)/Package Leaflet (PL) change** (additions to text **in bold**, deletions in ~~strikethrough~~)
Aservo EquiHaler (ciclesonide)	**10-12 May 2022**	**Section 4.5 of SPC for Aservo EquiHaler:** Special precautions for use in animals Safety of the veterinary medicinal product has not been established in horses weighing less than 200 kg body weight, or in foals. The prescribing veterinarian should assess if the horse has a temperament suitable for a safe and efficacious administration of the Aservo EquiHaler in agreement with good veterinary practice. Horses might not adapt to an easy and safe application of the Aservo EquiHaler within a couple of days. ~~In~~

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Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000
An agency of the European Union

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(active substance(s))</th><th>CVMP meeting date</th><th>Recommendation – Summary of Product Characteristics (SPC)/Package Leaflet (PL) change (additions to text in bold, deletions in ~~strikethrough~~)</th></tr>
<tr><td></td><td></td><td>~~such cases, a~~An alternative treatment should be considered if the horse does not adapt to the treatment with Aservo EquiHaler.

The onset of clinical improvement may take several days. The use of concomitant medication (such as bronchodilators) and environmental control may need to be considered in cases of severe clinical signs of respiratory obstruction, at the discretion of the attending veterinarian (see also section 4.8).

<u>Special precautions to be taken by the person administering the veterinary medicinal product to animals</u>

Follow closely the instructions for handling and use of the Aservo EquiHaler as provided in the package leaflet section “Other Information”.

A European survey showed that 16 out 84 horses could not be treated according to the product information due to horses not co-operating. In case a horse has a tendency towards defensive behavioural reactions, additional safety precautions could be considered (e.g., employ a second person to handle the horse). Acclimatising the horse with a training device prior to treatment start has in some cases shown to ease the administration of the veterinary medicinal product.</td></tr>
<tr><td>NEW
Bravecto
(fluralaner)
The text presentation has been adapted in line with changes mandated by Regulation (EU) 2019/6</td><td>6-8 December 2022</td><td>Section 3.6 of SPC for Bravecto <u>spot-on solution for dogs</u>:

Dog:
<table><tr><td>Very rare
(<1 animal / 10,000 animals treated, including isolated reports):</td><td>Muscle tremor, ataxia, convulsion</td></tr></table>
Section 7 of PL for Bravecto <u>spot-on solution for dogs</u>:

Dog:
<table><tr><td>Very rare (<1 animal / 10,000 animals treated, including isolated reports):</td></tr><tr><td>Muscle tremor, ataxia (incoordination), convulsion</td></tr></table></td></tr>
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BTVPUR (bluetongue-virus serotype-1 antigen/ bluetongue virus serotype 8 antigen)	**11-13 April 2022**	**Section 4.6 of SPC for BTVPUR:** **Hypersensitivity reactions may occur in very rare cases.** ~~In very rare cases it has been observed a~~ **A** small local swelling at the injection site (at most 32 cm^2 in cattle and 24 cm^2 in sheep) which becomes residual 35 days later ($\leq$ 1 cm^2) **has been observed in very rare cases**. ~~In very rare cases a~~ **A** transient increase in body temperature, normally not exceeding an average of 1.1°C, may occur within 24 hours after vaccination **in very rare cases**.
Cardalis (benazepril hydrochloride/ spironolactone)	**14-15 June 2022**	**Section 4.6 of SPC for Cardalis:** Vomiting, diarrhoea, pruritus, **lethargy, anorexia, ataxia, incoordination or signs of fatigue** have been reported very rarely ~~in spontaneous reports~~. **In dogs with chronic kidney disease, benazepril may increase plasma creatinine concentrations at the start of therapy very rarely. A moderate increase in plasma creatinine concentrations following administration of ACE inhibitors is compatible with the reduction in glomerular hypertension induced by these agents and is therefore not necessarily a reason to stop therapy in the absence of other signs.**
Cerenia (maropitant)	**10-12 May 2022**	**Section 4.6 of SPC for Cerenia:** Cerenia tablets Incidents of pre-travel vomiting, usually within two hours post-dosing were commonly reported after administration of the 8 mg/kg dose. **Neurological disorders such as ataxia, convulsion/seizure or muscle tremor have been reported in very rare cases.** Cerenia solution for injection

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<tr><td></td><td></td><td>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).

Anaphylactic type reactions (allergic oedema, urticaria, erythema, collapse, dyspnoea, pale mucous membranes) may occur in very rare cases.

Neurological disorders such as ataxia, convulsion/seizure or muscle tremor have been reported in very rare cases.</td></tr>
<tr><td>Equilis Prequenza
(equine influenza-virus strains: A/equine-2/South Africa /4/03, A/equine-2/Newmarket/2/93)
The text presentation has been adapted in line with changes mandated by Regulation (EU) 2019/6</td><td>8-10 November 2022</td><td>Section 4.6 of SPC for Equilis Prequenza:
<table><tr><td>Very rare
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Section 6 of PL for Equilis Prequenza:
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<tr><td>Equilis Prequenza Te
(equine influenza-virus strains: A/equine-2/South Africa/4/03, A/equine-2/Newmarket/2/93, tetanus toxoid)
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<tr><td>NEW Felpreva
(emodepside, praziquantel, tigolaner)</td><td>6-8 December 2022</td><td>Section 4.6 of SPC for Felpreva:
`...
Neurological disorders such as ataxia and tremor may occur in very rare cases. Mild and transient digestive tract disorders such as hypersalivation or vomiting may occur in very rare cases. These effects are thought to occur as a result of the cat licking the application site immediately after</td></tr>
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		treatment. In individual cases these signs can be accompanied by non-specific signs such as agitation, vocalisation or inappetence …' **Section 6 of PL for Felpreva:** '… **Neurological disorders such as ataxia (incoordination) and tremor may occur in very rare cases**. Mild and transient digestive tract disorders such as hypersalivation or vomiting may occur in very rare cases. These effects are thought to occur as a result of the cat licking the application site immediately after treatment. In individual cases these signs can be accompanied by non-specific signs such as agitation, vocalisation or inappetence …'
Hiprabovis IBR Marker Live (Infectious bovine rhinotracheitis vaccine (live))	**12-14 July 2022**	**Section 4.6 of SPC for Hiprabovis IBR Marker Live:** **Hypersensitivity reactions, including anaphylaxis (sometimes fatal), have been reported rarely**. ~~Vaccination might very rarely cause hypersensitivity reactions.~~ In such cases, an appropriate symptomatic treatment should be administered.
NEW **Improvac** (Synthetic peptide analogue of GnRF conjugated to diphtheria toxoid)	**6-8 December 2022**	**Section 3.5 of SPC (Special precautions for use/Other precautions) and section 6 of the PL (Special Warnings/Other precautions) for Improvac:** **The safety and efficacy of the veterinary medicinal product in non-target species such as horses has not been evaluated. Adverse events have been observed in horses including serious anaphylactic type reactions which have led to fatalities.**
Librela (bedinvetmab)	**10-12 May 2022**	**Sections 4.5 and 4.6 of SPC for Librela:** 4.5 Special precautions for use Special precautions for use in animals

Product (active substance(s))	**CVMP meeting date**	**Recommendation – Summary of Product Characteristics (SPC)/Package Leaflet (PL) change** (additions to text **in bold**, deletions in ~~strikethrough~~)
		~~None.~~ **Where a dog has not been able to properly exercise prior to treatment due to its clinical condition, it is recommended that the dog is gradually (over a few weeks) allowed to increase the amount of exercise they take (to prevent overexercise by some dogs).** 4.6 Adverse reactions (frequency and seriousness) Mild reactions at the injection site (e.g. swelling and heat) may ~~uncommonly~~ be observed **uncommonly**. **Polydipsia and/or polyuria have been reported rarely.** Hypersensitivity-type reactions **(e.g. anaphylaxis, pruritus, facial swelling)** have been reported very rarely. In case of such reactions, appropriate symptomatic treatment should be administered. **Clinical signs of immune-mediated diseases, such as haemolytic anaemia or thrombocytopenia, have been reported very rarely.**
Mhyosphere PCV ID (Mycoplasma hyopneumoniae, strain 7304 (Nexhyon), expressing the capsid protein of porcine circovirus type 2a, inactivated)	**15-16 March 2022**	**Section 4.6 of SPC for Mhyosphere PCV ID:** Mild transient local reactions consisting of non-painful skin inflammations, of less than 3 cm in diameter are very common. Moderate inflammation (between 3-5 cm) at day 1 post-vaccination is commonly observed, which generally decrease to less than 3 cm the next day. These local reactions can be observed during the first week after vaccination and last for 1 to 3 days. One or two weeks later, these local reactions can reappear lasting for 1 to 7 days. Local reactions disappear completely within approximately 3 weeks after vaccination without treatment. A slight transient increase in body temperature (mean 0.3ºC, in individual pigs less than 1.5ºC) occurred commonly in field studies. This slight increase subsided spontaneously within 48 hours without treatment. **Anaphylactic-type reactions (e.g. vomiting, circulatory disorders, dyspnoea) which might be life-threatening, may occur very rarely in some sensitive animals based on post-**

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<tr><td></td><td></td><td>marketing safety experience. Under these circumstances, appropriate symptomatic treatment should be administered.</td></tr>
<tr><td>Nasym
(live attenuated bovine respiratory syncytial virus (BRSV), strain Lym-56)</td><td>10-12 May 2022</td><td>Section 4.6 of SPC for Nasym:

Slight alteration of faecal consistency may be commonly observed post-vaccination.

Calves may uncommonly display a peak in temperature of at least 1.7°C two days after vaccination that resolves the next day without treatment.

Anaphylactic-type reactions which may be serious (including fatal) have been reported very rarely. In case of such reactions, appropriate symptomatic treatment should be administered.</td></tr>
<tr><td>Neptra
(florfenicol/terbinafine hydrochloride/mometasone furoate)</td><td>15-16 February 2022</td><td>Section 4.6 of SPC for Neptra:

Deafness or impaired hearing have been reported in very rare cases in dogs, mainly in elderly animals, in post authorisation experience.

Vocalisation, head shaking and application site pain shortly after product application have been reported in very rare cases in post authorisation experience ~~very rarely in spontaneous (pharmacovigilance) reports~~.

Ataxia, internal ear disorder, nystagmus, emesis, application site erythema, hyperactivity, anorexia and application site inflammation and eye disorders (such as eye irritation, blepharospasm, conjunctivitis, corneal ulcer, keratoconjunctivitis sicca) ~~were~~ have been reported in very rare cases in post authorisation experience ~~very rarely in spontaneous (pharmacovigilance) reports~~.</td></tr>
<tr><td>Nobivac DP Plus
(live attenuated (weakened) canine distemper virus (CDV) and canine parvovirus (CPV))
The text presentation has been adapted in line with</td><td>8-10 November 2022</td><td>Section 4.6 of SPC for Nobivac DP Plus:

<table><tr><td>Very rare
(<1 animal / 10 000 animals treated, including isolated reports):</td><td>Hypersensitivity reaction[1]</td></tr></table></td></tr>
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changes mandated by Regulation (EU) 2019/6		**[1]including anaphylaxis (sometimes fatal). If such a reaction occurs, appropriate treatment should be administered without delay.** **Section 6 of PL for Nobivac DP Plus:** **Very rare (<1 animal / 10 000 animals treated, including isolated reports):** **Hypersensitivity reaction[1]** **[1]including anaphylaxis (sometimes fatal). If such a reaction occurs, appropriate treatment should be administered without delay.**
Nobivac Myxo-RHD Plus (Live myxoma vectored RHD virus strain 009/Live myxoma vectored RHD virus strain MK1899)	**15-16 February 2022**	**Section 4.6 of SPC for Nobivac Myxo-RHD Plus:** A transient temperature increase of 1 – 2 °C can commonly occur. A small, non-painful swelling (maximum 2 cm diameter) at the injection site is commonly observed within the first two weeks after vaccination. The swelling will resolve completely by 3 weeks after vaccination. In pet rabbits, local reactions at the injection site such as necrosis, scabs, crusts or hair loss may occur in very rare cases. Serious hypersensitivity reactions, which may be fatal, may occur after vaccination in very rare cases. The appearance of mild clinical signs of myxomatosis may occur within 3 weeks of vaccination in very rare cases. Recent or latent infection with field myxoma virus seems to play a role in this to a certain extent. **Anorexia and lethargy may occur in very rare cases.**

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<tr><td>NEW
Procox
(emodepside, toltrazuril)
The text presentation has been adapted in line with changes mandated by Regulation (EU) 2019/6</td><td>6-8 December 2022</td><td>Section 3.6 of SPC for Procox:
Dogs:<table><tr><td>Very rare
(<1 animal / 10,000 animals treated, including isolated reports):</td><td>Lethargy
Muscle tremor, ataxia, convulsion
Vomiting, loose stool</td></tr></table>Section 7 of PL for Procox:
Dogs:<table><tr><td>Very rare (<1 animal / 10,000 animals treated, including isolated reports):</td></tr><tr><td>Lethargy
Muscle tremor, ataxia (incoordination), convulsion Vomiting, loose stool</td></tr></table></td></tr>
<tr><td>NEW
Proteq West Nile
(West Nile recombinant canarypox virus (vCP2017 virus))
The text presentation has been adapted in line with changes mandated by Regulation (EU) 2019/6</td><td>6-8 December 2022</td><td>Section 3.6 of SPC for Proteq West Nile:
Horses:<table><tr><td>Very rare
(<1 animal / 10,000 animals treated, including isolated reports):</td><td>Injection site abscess</td></tr></table>Section 7 of PL for Proteq West Nile:
Horses:<table><tr><td>Very rare (<1 animal / 10,000 animals treated, including isolated reports):</td></tr><tr><td>Injection site abscess</td></tr></table></td></tr>
<tr><td>Solensia
(frunevetmab)</td><td>8-10 November 2022</td><td>Section 4.6 of SPC and section 6 of PL for Solensia:
Mild reactions at the injection site (e.g., pain and alopecia) may be observed rarely.</td></tr>
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Stelfonta (tigilanol tiglate)	**11-13 April 2022**	**Sections 4.2, 4.5, 4.6 and 4.9 of SPC for Stelfonta:** 4.2 Indications for use, specifying the target species For the treatment of non-resectable, non-metastatic (WHO staging) ~~subcutaneous~~ mast cell tumours **of the following types in dogs:** **- Cutaneous mast cell tumours** (located anywhere on the dog)~~at or distal to the elbow or the hock~~, and **- Subcutaneous mast cell tumours located at or distal to the elbow or the hock**.~~non-resectable, non-metastatic cutaneous mast cell tumours in dogs.~~ Tumours must be less than or equal to 8 cm^3 in volume, and must be accessible to intratumoral injection. 4.5 Special precautions for use <u>Special precautions for use in animals:</u> Treating tumours in mucocutaneous locations (eyelids, vulva, preputial opening, anus, mouth) and at the extremities (e.g. paws, tail) could impair functionality**,** ~~due to the loss of tissue associated with the treatment.~~ **and at extremities may result in localised impairment of circulation due to a local inflammatory response at the treatment site leading to tissue loss and possible requirement for amputation**. … Tumours that lie completely in the subcutaneous tissue with no dermal involvement may have difficulty in creating an exit site for necrotic tissue removal. This may necessitate an incision to allow for drainage of necrotic tissue. **Ingestion of tumour remnants should be prevented.** The product is to be administered only by a veterinarian.

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		4.6 Adverse reactions (frequency and seriousness) <u>Uncommon</u> Severe: Infection/cellulitis, wound slough. Anorexia, reduced appetite, somnolence, tachycardia, neuropathy and pruritis. Leucocytosis, increased band neutrophils, thrombocytopenia and elevated ALT. Seizures, **compromised circulation, loss of essential tissue**. 4.9 Amount(s) to be administered and administration route When the total dose of the veterinary medicinal product has been administered, pause for up to 5 seconds to allow tissue dispersion before removing the needle from the tumour. The site of application should be covered for the first day after treatment in order to prevent direct contact with**, as well as licking of** residual or leaking product. Handle the cover with gloves to avoid contact with the product. In case of severe leakage of wound debris, which may occur in the first weeks following administration of the product, the wound should be covered.
Suprelorin (deslorelin acetate)	**14-15 June 2022**	**Section 4.6 of SPC for Suprelorin:** In humans and animals, testosterone modulates seizure susceptibility. ~~On very rare occasions (<0.01%) transient occurrence of seizure has been reported shortly after implantation, though the casual relationship with the application of the implant has not been established~~. **Epileptic seizures have been observed very rarely and have been reported on average 40 days after implantation, the median time to onset of signs was 14 days after implantation, on the same day of implantation at the earliest, and 36 weeks after implantation at the latest.** ~~In some cases, the dog had displayed epileptic seizure prior to the implant administration or was diagnosed as suffering from epilepsy.~~
Suvaxyn Circo (Inactivated recombinant chimeric porcine circovirus type 1 containing the	**18-19 January 2022**	**Section 4.5 of SPC for Suvaxyn Circo (under <u>Special precautions to be taken by the person administering the veterinary medicinal product to animals</u>):** ~~Not applicable.~~

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<tr><td>porcine circovirus type 2 ORF2 protein)</td><td></td><td>In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.</td></tr>
<tr><td>NEW
Zuprevo
(tildipirosin)
The text presentation has been adapted in line with changes mandated by Regulation (EU) 2019/6</td><td>6-8 December 2022</td><td>Section 3.6 of SPC for Zurpevo:

Pigs:
<table><tr><td>Very common
(>1 animal / 10 animals treated):</td><td>Injection site swelling (may be present up to 6 days post-treatment)
Injection site pain</td></tr><tr><td>Rare
(1 to 10 animals / 10,000 animals treated):</td><td>Anaphylaxis (may be fatal)</td></tr><tr><td>Very rare
(<1 animal / 10,000 animals treated, including isolated reports):</td><td>Lethargy</td></tr></table>
Section 7 of PL for Zuprevo:

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