

Therapeutic gaps in the Horse sector

Meeting of 19/10/21

Participants: Charles-François Louf (AVEF President, veterinary practitioner in Vosges), Laurent Mangold (AVEF Vice-President, antibiotic expert, veterinary practitioner in Argonny), Claire Scicluna (AVEF therapeutic commission, veterinary practitioner in Oise), Jean-Luc Cadoré (VetAgroSup Professor, CSMV representative)

Absent: Marie-Noëlle Lemouland (SNGTV representative), Pascal Boireau (Anses Manager of the Anses Maisons-Alfort – Dozulé laboratory)

for ANMV: L. Baduel, S. Barreteau, M. Salery, H. Ait Lbacha, S. Rougier, L. Fabry - **Excused absent:** JP Orand

Pathology	Problem* encountered *Economic: E / Cascade: C / Other: A	Problem type * (E/C/A)	Alternatives identified	PRIORITIES Major: M minor: m
Non-critical IV injectable antibiotics, in intensive care.	<p>Need for non-critical ATB (penicillin sodium or amoxicilline) that can be administered intravenously (IV). Marketing authorisation (MA) for CLAMOXYL 5G abandoned in 2009. No Mutual Recognition (MR) envisaged by the MA holder based on the MA of another European country. PENETAVET stopped.</p> <p>BELCOPENI 5 (Benzylpenicillin sodium + colistimethate (=colistine...)) authorised for all species, and slow IV, has not been marketed since 2017.</p> <p>"Cascade" use of Veterinary Medicinal Products (VMPs) for cattle not possible for different reasons:</p> <ul style="list-style-type: none"> - pénéthamate (STOP M, PENETHAMATE, PENETHAONE, PERMACYL, REVOZYN): indicated for Intramuscular (IM) route only and contraindicated in IV (suspensions). - Penicillin procaine and benzathine unusable: risk of neurological reactions (procaine), significant shock if the product passes into the blood during injection with a risk of a very violent reaction of the animal (unacceptable for any valuable horse), local reactions and pain ++ when IM use. 		<p>Use of critical antibiotics: marbofloxacin, EXCENEL or COBACTAN is forbidden.</p> <p>Access to "human" CLAMOXYL refused by Panpharma => regulatory reason to be clarified</p> <p>There should be a 1st line ATB that does not risk laying horses on the ground and could be injected through the IV route</p>	M n°1
Chondroprotection	<p>Triamcinolone is the only corticosteroid considered chondroprotective (with appropriate dose) for intraarticular injection. No corresponding VMP for horse. The VMP with triamcinolone diacetate, i.e CANITEDAROL for dogs and cats, is no longer marketed.</p>	E	<p>VMP with triamcinolone available in the US => why not in Eu? Human MP based on triamcinolone acetonide (Kenacort Unidose 40 or 80 mg accessible in pharmacies, 6-7 €)</p> <p>New VMPs with stem cells (Articell Forte and Horstem) have different indications (osteoarthritis), are very expensive and their interest has to be confirmed (variable results).</p>	M n° 2

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	<p>Synvet has been removed. => There is only one remaining VMP with hyaluronic acid (HYONATE): - in case of shortage, the only possible allowed alternative is a human MP <i>via</i> the “cascade” + problem of the HYONATE multipunctured bottle with intra-articular risks of infection. => VMPs with hyaluronic acid are less satisfactory than existing human medical devices that have undergone improvements in recent years</p>		<p>Wish of a MA for a single-dose HYONATE which could be administered through intra-articular, IV & IM route.</p> <p>Human medical devices in single-dose syringes are more satisfactory, less expensive but regulatory prohibited for a veterinary use.</p>	
Leptospirosis	<p>Vaccine exists in the US (Boehringer or Zoetis). A vaccine would avoid treatment with antibiotics. Increase in seropositive horses according to certain opinions from the field. This is a zoonosis, but with low zoonotic risk. Clinical expression of infection related to the direct action of leptospire, is rare according to ENV, and little detected in the acute phase.</p>		<p>Curative treatment: tetracyclins, penicillins. ⇒ Registration of the US vaccine to be promoted in the EU (market > West Nile vaccine) and (≈ ½ influenza market). See RESPE epidemiological data, EU & US figures</p>	m
Asthma	<p>Problems with the administration of the new VMP, ASERVO: => pharmacovigilance declarations to be made. Non-recyclable device + high cost... Wish for other solutions and clarification of so-called “asthma”</p>	A, E	<p>Autologous treatments (interleukin) => which devices and/or which molecules need to be further specified</p>	m
Lactation induction	<p>Need for a VMP (small market).</p>		<p>Domperidone is less effective but works. Human MP: sulpiride (injectable abandoned, only available in tablets)</p>	m
Botulism (very rare)	<p>No vaccine or equine serum available <i>Very rare.</i></p>		<p><i>Possible import of an ANTRAVAX bovine vaccine</i> Bovine serum</p>	m
Chemical castration	<p>Vaccine reactions with IMPROVAC (not reported because well-known and predictable reactions). There is currently no strong demand for VMPs but it could be further wished in a general context of taking animal welfare into account. Restricted market. Only IMPROVAC vial corresponding to 100 to 1000 doses (10*50 doses = 800 €) is available...</p>	E, A	<p>IMPROVAC. Report pharmacovigilance declarations. EQUITY is available in Australia and NZ (fewer AEs than IMPROVAC?).</p>	m

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Other Questions/Requests:

- **Difficulties in the veterinary use of products without MA, legally not authorised in the first line** when veterinary medicinal products exist, e.g.:
 - Hyaluronic acid in single-dose syringe (medical devices for humans – see above)
 - Sarapin used as an analgesic for neuralgia, back pain (used for humans in the US)
 - Athramid Vet (medical device in the US – polyacrylamide hydrogel), without MA in EU
- Use of homeopathic drugs to be clarified / recent positioning of CNOV
- Access to BCG in pharmacies for sarcoids
- RELAQUINE: administration difficulties with the bottle, which replaced the syringes (although much more suitable, even if air bubbles were found during quality controls on the market, knowing that such bubbles were without consequences in this case). It is important to consult the AVEF prior to initiate such packaging changes. It is reminded that it is a very useful product (must be kept).
- Undeclared / anticipated shortages
ANMV post-meeting note => information to be systematically reported to the ANMV as soon as possible (e-mail address: DQ_ANMV@anses.fr) by MA holders but also by vets, if necessary.
- Doxycycline: bioavailability/efficacy in horses? long oral treatment practices (Lyme) => substantive work to be planned on this subject
- Issues with borderline claims on non-VMPs
ANMV post-meeting note => to be declared to ANMV (Market Surveillance Unit) – e-mail address: usm@anses.fr
- Difficult access to details on VMPs registered through the centralised MA *via* iRCP : transfer to the EMA site which is not very user friendly
ANMV post-meeting note => detailed procedure is available by clicking on the top right of the screen (to the left of the question mark) on “[RCP of centralised AMMs](#)”

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Resolution in progress	EXISTING solution			
Rhodococcosis	Expected vaccine. Avoid the use of critical antibiotics. Veterinary erythromycin not always effective and risk of diarrhoea in the foal. Efficacy of auto-vaccines to be evaluated. <i>Pay attention to the diagnosis</i>		See AVEF recommendations => Peni-Gentamicin. According to ATB Gram. Framework reviewed in the antibiotherapy Good Practices In curative mode: human MP: azithromycin/ tulathromycin + rifampicin.	m
Piroplasmosis	CARBESIA: the withdrawal time of 213 days is not applicable in practice.	C		
Myositis	Vit E not very effective. A dantrolene-based VMP would be a plus.		Increasingly rare myositis (thanks to food supplements) Veterinary vitamine E or human MP with Dantrolene (DANTRIUM)	
Antibiotic against anaerobes (pleuropneumonia)	Need for a metronidazole (IV?) based VMP <i>Only in horses not intended for human consumption</i>	Inspection	OK for oral route (50 mg/kg/3x per day) Active substance (powder) could be purchased at vet distributors for extemporaneous preparations Human MP (tablets)	
Mycotic keratitis	Need for a VMP suitable for ophthalmic application. Rare problems		Human injectables MP: natamycin or fungizone	
Alpha2agonist antagonist (detomidine)	A VMP would be welcome. (interest?)		Atipamezole OK	
Immunostimulator	Alternative to antibiotic use. Wish for VMP in Europe. Control of illegal importation, including through internet		Parapox-type immunomodulator (no longer available abroad)	