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Committee for Medicinal Products for Veterinary Use

Questions and answers on adverse event reporting

This question and answer document on adverse event reporting was originally developed following the Committee for Medicinal Products for Veterinary Use Pharmacovigilance Working Party (PhVWP-V) interested parties meeting on implementation of Volume 9B of The Rules Governing Medicinal Products in the European Union – Guidelines on Pharmacovigilance for Medicinal Products for Veterinary Use held on 26 September 2012 based on questions submitted by participants. The document aims to facilitate the understanding of the guidance in Volume 9B and to strengthen and harmonise the approach to adverse event reporting. The document was updated in November 2015 to include a new question (3) on reporting lack of expected efficacy following use of euthanasia products.

1. Should lack of expected efficacy (LEE) reports be reported in the same way as for adverse events?

Lack of expected efficacy (LEE) events should always be reported. Even if 100% efficacy is not claimed, unless LEE is reported there is no indication as to what the actual level of efficacy is. If the condition has been misdiagnosed and the product would not be expected to be effective, the report should be coded as causality N-Unlikely. If the product had been used off-label, depending on the type of off-label use (e.g. overdose) the causality assessment could be adjusted to reflect this.

The VICH definition of an adverse event includes LEE, therefore it follows that LEE reports which result in death, are life-threatening, or which result in persistent or significant disability/incapacity, or congenital anomalies or birth defects should be reported expeditedly to the relevant competent authority within 15 days.

2. Should lack of expected efficacy (LEE) events be reported when the product is used off-label?

Reports of LEE can provide useful information on the safety of the veterinary medicinal product. LEE events should be recorded by the person responsible for pharmacovigilance and reported to the competent authorities in the same way as for all adverse events. Off label use in antimicrobials is of particular importance.

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3. **How should lack of expected efficacy (LEE) events be coded following use of euthanasia products?**

   These events should be coded using only the VeDDRA low level terms 'lack of efficacy' and 'unrelated death' (as the death was unrelated to the adverse event 'lack of efficacy'). No other clinical signs observed should be coded using VeDDRA. In all cases, however, such reports are considered serious adverse events and should be reported accordingly.

4. **Volume 9B (Part I Section 4.2.2.) states the following: the MAH should report all serious and unexpected adverse events in animals (both criteria must apply), all human adverse reactions and any suspected transmission of an infectious agent relating to the use of VMPs which have occurred outside the territories of EEA (i.e. third country reports) and which are brought to his attention or of which he can reasonably be expected to have knowledge. What does the phrase '.....or of which he can reasonably be expected to have knowledge' mean?**

   Some marketing authorisation holders (MAHs) have reported that they cannot be expected to have knowledge of adverse events reported to distributors or other MAHs with whom they have marketing agreements and that the 15-days for expedited reporting should not start until the 'parent' MAH receives the information. However, MAHs should ensure that any such agreements account for the immediate transfer of adverse event reports to the 'parent' MAH.

5. **Have suspected adverse reaction (SAR) reports from literature highlighted safety or efficacy issues that were not picked up by spontaneous reporting previously? Are there any examples that would support a periodicity of literature searches higher than the periodic safety update report (PSUR) periodicity for a veterinary medicinal product (VMP)?**

   There has been a published reference confirming existing resistance patterns of *Brachyspira hyodysenteriae* against commonly used macrolide and pleuromutilin antimicrobials. This is relevant to a centrally authorised product.

   It is good pharmacovigilance practice for literature searches to be conducted more frequently than the PSUR periodicity, particularly when the 3-year PSUR interval has been reached or depending on the potential 'risk' associated with the product.

References

- European Commission (2011): Volume 9B of the Rules Governing Medicinal Products in the European Union Guidelines on Pharmacovigilance for Medicinal Products for Veterinary Use (http://ec.europa.eu/health/documents/eudralex/vol-9/index_en.htm)
- European Parliament and the Council. Directive 2001/82/EC of 6 November 2001 on the Community Code Relating to Medicinal Products for Veterinary Use, as amended by Directives 2004/28 EC, 2009/9/EC and 2009/53/EC in European Commission: The Rules Governing Medicinal Products in the European Union – Volume 5 – EU pharmaceutical legislation for medicinal products for veterinary use (http://ec.europa.eu/health/documents/eudralex/index_en.htm)
- European Parliament and the Council. Regulation (EC) No 726/2004 of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, in European Commission: The Rules Governing Medicinal Products in the European Union – Volume 5 – EU pharmaceutical legislation

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- Committee for Medicinal Products for Veterinary Use (2016) Guidance notes on the use of VeDDRA terminology for reporting suspected adverse reactions in animals and humans – EMA/CVMP/PhVWP/288284/2007-Rev.9 *(when available)*