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 July 2020 to include question 10 on identifiable sources for adverse events reported in social media.

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

   Yes - lack of expected efficacy (LEE) events should always be reported in the same way as for other adverse events. 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 expediently to the relevant competent authority within 15 days, if the event occurred in the EU/EEA or to EudraVigilance Veterinary (EV Vet) for third country events. LEE events not eligible for expedited reporting should be reported in the periodic safety update report (PSUR).

   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.

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.
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)?**

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.

An example of a publication supporting the need for regular literature monitoring, would be one confirming existing resistance patterns of *Brachyspira hyodysenteriae* against commonly used macrolide and pleuromutilin antimicrobials. This publication was relevant to a centrally authorised product.

6. **How should events relating to medication/prescription errors which do not result in adverse events be managed? e.g. intercepted errors or circumstances or information with the potential to lead to medication errors**

Where there is no adverse event associated with medication/prescription errors, it is recommended that the MAH keep a record of such events in their own database but these should not be reported as adverse events to EudraVigilance Veterinary (EVVet) or PSURs. However, where potential risks are identified as a result of medication errors without adverse events e.g. intercepted errors, the information should be summarised in the PSUR together with recommendations for addressing the issue. This is valuable information which may lead to improvements in the product information and the overall safety associated with the use of the product. Where such events have safety implications, impacting on the benefit-risk balance of the medicinal product, they should also be notified to the competent authorities.
7. For some products, section 4.1 of the summary of product characteristics (SPC) indicates a given target species, and in other sections of the same SPC (such as indications, contraindications, special precautions for use) there is a restriction of use within this target species (i.e. restriction to a category of age, weight, physiological status, type of production etc.). Should the use of a product occurring within the target species but outside the restriction of use mentioned in the SPC be classified as recommended use or off-label use?

Adverse events in animals belonging to the target species, but not to the subgroup of animals to which the use is restricted within the target species, should be considered as off-label use in the target species. Consequently:

In EudraVigilance Veterinary (EVVet) for the product the field “use according to label” should mention “No”; and the field “off-label use” should mention “Unauthorised species/species subgroup”.

In PSURs, these adverse events should be analysed in the section relating to adverse events after non recommended use in the target species. However they should be taken into account for the calculation of incidence of adverse reactions.

8. How should I report a case where the medicinal product was prescribed by a veterinarian, but on purpose not according to label?

Report the adverse event as ‘off label’ for the specific veterinary medicinal product.

9. How should I report a case where the medicinal product was prescribed according to the recommendations but the animal owner administered it in the wrong way?

Report the event as ‘off label’ for the specific veterinary medicinal product and add the VeDDRA term ‘medication error’ for the report.

10. What is considered an ‘identifiable source’ for adverse events reported via social media?

Volume 9B Part III Section 4.5 states that an identifiable source is part of the minimum information required for a valid adverse event report. Wherever possible this should include the name and address of the primary reporter, which may be a contactable email address.

For adverse events identified in social media channels or platforms (i.e. without a known reporting source) reasonable efforts should be made to contact the ‘notifier’ or ‘author’ to obtain a contactable email address (i.e. not just a social media nickname) and encourage the ‘notifier’ to complete an adverse event reporting form, e.g. MAH or national competent authority (NCA) form, to ensure the event is captured and reported within the pharmacovigilance system.

References

