



Pharmacovigilance: Monitoring the Safety & Efficacy of Animal Medicines

Summary

This document introduces the topic of pharmacovigilance, which includes the ongoing monitoring of the safety and efficacy of animal medicines after they have been authorised and placed on the market. Key pharmacovigilance areas are highlighted including the regulatory framework, responsibilities, reporting and assessment of adverse events. Animals, people and the environment benefit from these pharmacovigilance activities, which aim to ensure the continued safe use of effective medicines.

Introduction: Veterinary Pharmacovigilance

Veterinary pharmacovigilance broadly describes the science and activities relating to the monitoring and evaluation of adverse events and improving the safety of veterinary medicines (1, 2). Pharmacovigilance also considers suspected lack of expected efficacy (where the medicine has failed to work) and any problems with residues of veterinary medicines, in food derived from animals, where the appropriate withdrawal period and dose rate has been followed.

An **Adverse Event (AE)** is any observation in animals, humans or the environment, whether or not considered to be product-related, that is unfavourable and unintended and that occurs after any use of a veterinary medicine (3).

All authorised veterinary medicines have undergone a rigorous process of assessment that includes scrutiny of safety, quality and efficacy by the independent regulatory authorities. Safe medicines are approved for market when the benefits to animals outweigh any known potential risks. Potential risks or adverse events may also be mitigated though safety precautions included in the product documentation with appropriate advice on use and disposal.

There is also a process of on-going monitoring and assessment to further define and scientifically evaluate the safety and efficacy of the product. These pharmacovigilance activities allow for the detection of

any suspected adverse reactions that may occur, when medicines are used in a larger and more diverse population of animals i.e. under 'field conditions'.

A **Suspected Adverse Reaction (SAR)** is an adverse event that involves the development of side effects in animals or humans after any use of a veterinary medicine (3).

Reassuringly, the UK veterinary medicines regulator (the Veterinary Medicines Directorate or VMD) recently stated that *'the chance of an adverse event happening in any particular animal or person is very low'* (3).

Nevertheless, all those involved in the marketing and use of veterinary medicines, including vets, SQPs and the general public, have the opportunity to report adverse events. In fact, market authorisation holders (MAHs) (i.e. animal health companies that market animal medicines) have a legal obligation to record any information they receive about adverse events involving their veterinary medicinal products (4, 5).

Although animal medicines companies do incur significant costs to undertake all of these veterinary pharmacovigilance processes, e.g. in personnel expertise, time and resources, the end result is the provision of continued assurance, and a mechanism to allow for further improvements, in the safety profiles of our animal medicines.

Regulatory Framework

Veterinary pharmacovigilance activities in the UK are governed by a regulatory framework comprised of the UK Veterinary Medicines Regulations 2013 and Volume 9B guidelines – 'Pharmacovigilance for Medicinal Products for Veterinary Use' published by the European Commission in the context of (EC) No 726/2004 and Directive 2001/82/EC (5, 6, 7, 8). The legislation sets out the roles and responsibilities for both the MAHs and the regulators with respect to pharmacovigilance duties.

The comprehensive regulatory framework in place, which governs pharmacovigilance activities, ensures that animal and human health is robustly protected and available animal medicines continue to meet high standards of quality, safety and efficacy.

Pharmacovigilance: Responsibilities

MAHs and the Competent Authority together share important pharmacovigilance responsibilities.

The responsibilities of MAHs include having an appropriately Qualified Person responsible for Pharmacovigilance (QPPV), who will oversee the collection, recording and analysis of reports. The QPPV ensures that there is a suitable system in place for these tasks and co-ordinates with the competent authority in the submission of reports and during inspections. The precise details of these various processes, procedures and inspections that must occur are provided within the legislation and guideline.

MAHs must send all serious animal and all human AE reports to the VMD within a short specified period of time after they are notified (4, 5). These requirements ensure that adverse events, should they arise, are investigated and evaluated in a timely manner.

Additionally, MAHs provide Periodic Safety Update Reports (PSURs) to the Competent Authority for all authorised products as required. Generally, they are submitted six-monthly for the first 2 years after product authorisation, annually for the subsequent 2 years, and thereafter every 3 years (5).

A **Periodic Safety Update Report (PSUR)** is a periodical scientific report on adverse events and other issues within the scope of pharmacovigilance that have been reported to a MAH during a specific period (5, 6).

The report lists all the suspected adverse reactions reported to the company since the last PSUR. The report places suspected adverse events in context by looking at the incidence of reactions, taking account of the number of doses sold. PSURs provide a concise assessment and evaluation of the current safety profile of the product.

Reporting Suspected Adverse Reactions

The chances of an adverse event happening in any particular animal or person is very low (3). However, if an adverse reaction to an animal medicine is suspected, it should be reported to the VMD or to the animal medicine company, MAH, of the product involved (9).

The VMD is the independent regulator and Competent Authority (CA) for veterinary medicines in the UK. The VMD pharmacovigilance team receives and evaluates reports of adverse events and lack of efficacy in

animals and people, which can be submitted by anyone (9).

A **Suspected Lack of Expected Efficacy (SLEE)** is when a veterinary medicinal product is not thought to have worked as well as expected (3).

The purpose of pharmacovigilance is to help improve the safe and effective use of veterinary medicines. To achieve this, the VMD pharmacovigilance team examines each report and makes an assessment on the adverse event, if there has been any previous reports to the product, if any further information is needed and what follow up action is required.

Anyone can report an AE including vets, doctors, farmers, pharmacists and members of the public and they are actively encouraged to do so by both the VMD and NOAH (9, 10). Often, vets and farmers will contact the manufacturer directly to report a suspected adverse reaction. Companies are then under a legal obligation to report these to the VMD.

The mechanisms in place to report AEs ensures important information regarding the use of veterinary medicines in the community is scientifically appraised and used to inform appropriate actions. In some cases this may involve providing more advice to users of the medicine as to how to use it safely and/or changes to the product literature. Although the VMD has the authority to withdraw products or specific batches of medicines from the market if required, this is a very rare occurrence. Nevertheless, the possibility to do so provides further assurance of the safety and efficacy of animal medicines on the UK market.

Conclusions

- Authorised veterinary medicines undergo further monitoring for safety and efficacy after they are placed on the market.
- The process of detecting, evaluating, understanding and preventing adverse effects of medicines is known as pharmacovigilance.
- A comprehensive regulatory framework governs the roles and responsibilities of market authorisation holders and the Competent Authority with respect to veterinary pharmacovigilance duties.
- The VMD provides an adverse event reporting mechanism, and associated pharmacovigilance activities, which help to protect animals, people and the environment.
- NOAH and the VMD encourage anyone involved in prescribing and using animal medicines to report suspected adverse events to the VMD or the animal medicine company.

What is NOAH? The National Office of Animal Health Ltd represents the UK animal medicine industry: its aim is to promote the benefits of safe, effective, quality medicines for the health and welfare of all animals. For further information, including more briefing documents on animal medicines topics see www.noah.co.uk and follow @UKNOAH on Twitter.

(For more information see NOAH briefing documents on Controls on Animal medicines and Veterinary Medicines and the Safety of Food from Animals).

10. NOAH information on suspected adverse reactions:
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