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Chapter 5. Reporting lack of efficacy

Contents

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Overview

Pharmacovigilance, as defined by the World Health Organization[1], is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem. Adverse effects in veterinary medicine are known as adverse events, which the Veterinary International Cooperation on Harmonisation (VICH) of Technical Requirements for Registration of Veterinary Medicinal Products defines as "*any observation in animals, whether or not considered to be product-related, that is unfavourable and unintended and that occurs after any use of veterinary medicinal product (VMP) (off-label and on-label uses). Included are events related to a suspected lack of expected efficacy according to approved labelling or noxious reactions in humans after being exposed to VMP(s)*". Adverse events may be undesirable side effects, such as adverse reactions, or a suspected lack of expected efficacy to a particular medicine. Adverse events may be seen, for example, in the animal being treated, in other animals, the person handling the medicine or in the environment (Veterinary Medicines Directorate, 2024a).

The Veterinary Medicines Directorate (VMD) is the regulatory authority responsible for pharmacovigilance in relation to veterinary medicines in the United Kingdom, including for Marketing Authorisations (MAs). Each Marketing Authorisation Holder (MAH) must have a suitable pharmacovigilance system in place for collecting, collating and evaluating information in relation to adverse events in respect of any veterinary medicinal product for which it holds an authorisation. They have a legal obligation to report all adverse event reports that they receive to the VMD within 30 days of awareness. Reports are anonymised to maintain reporter confidentiality, and procedures are in place to avoid duplication of reports. The VMD inspects MAHs to ensure that they have the personnel, systems, and facilities in place to comply with their pharmacovigilance obligations.

The Veterinary Medicines Regulations 2013 (as amended) sets out the legal framework for the pharmacovigilance of veterinary medicine products in Great Britain;

[1] https://www.who.int/

pharmacovigilance for products authorised in Northern Ireland is required to be in accordance with the European Union acquis (Veterinary Medicines Directorate, 2024a).

Adverse events

Adverse events, including lack of efficacy, can occur following administration of any veterinary medicinal product. Although the scope of this chapter relates to suspected lack of efficacy reports, it is also important to look out for, and report, any other types of adverse events that occur following administration of a veterinary medicinal product, such as adverse reactions. In some cases, a report will involve multiple types of adverse events, such as an adverse reaction and a lack of efficacy.

Lack of efficacy

Lack of efficacy is the apparent inability of an authorised veterinary medicinal product to have the expected efficacy in an animal, whether or not the product was used in accordance with the Summary of Product Characteristics (SPC) (Veterinary Medicines Directorate, 2024c).

In relation to anthelmintics, reasons to report a suspected lack of efficacy may include:

- Clinical disease or death due to a suspected or proven parasitic burden
- Insufficient faecal egg reduction test (FECRT) – (see Chapter 4. Testing for anthelmintic resistance for further information)
- Shortened egg reappearance period (ERP).

A lack of efficacy may be due to **an actual reduced efficacy** of the product due to:

- Incorrect storage
- Use of an expired product
- Batch quality problems (uncommon)
- Anthelmintic resistance.

Alternatively, apparent lack of efficacy may relate to a myriad of other, **non-product related factors**, such as:

- Unrealistic expectations (for example, expecting the faecal egg count to be zero after administration and throughout the administration interval of the active substance, or that a large cyathostomin larval burden will be completely removed by administration of an authorised product)
- Incorrect dose administration (commonly due to incorrect weight estimates)
- Failure to administer correctly (see Chapter 8. Behaviour Change for further information)
- Concurrent disease (for example short-term changes in the overall health of the animal can affect the quality of the faecal samples collected between pre- and post-treatment FEC tests which can impact the eggs per gram count).

(Veterinary Medicines Directorate, 2024b)

Why is it important to report a suspected lack of efficacy?

It is important to **report all cases where there is a suspected lack of efficacy**, including those which may already be detailed on the SPC (such as resistance to benzimidazoles in cyathostomins) (Veterinary Medicines Directorate, 2024b). Reporting of adverse events (including suspected lack of efficacy) is part of a prescriber's professional responsibility, as outlined in the RCVS code of conduct and SQP Code of Practice. Reporting provides real-time field information in relevant populations enabling the early identification of potential problems and appropriate action to be taken.

Monitoring for anthelmintic resistance is a moving target where data from field populations is invaluable in determining the current situation in different geographical regions. Consistent and stringent reporting of lack of efficacy cases enables interventions at an individual, local and country level. In addition, the international movement of horses means that resistance to a class of anthelmintic can be easily distributed internationally, therefore monitoring for lack of efficacy is of global importance (Nielsen *et al.*, 2020).

The VMD does not give clinical advice or individual feedback on reports. However, MAHs have extensive knowledge of their products and can assist with advice and logistics of the follow-up of suspected lack of efficacy reports. In some cases, this may lead to a specific diagnosis or change in management which can be immediately implemented. If there is a repeating pattern or concern with a particular product and parasite species, further investigations are warranted which may result in further regulatory actions, such as amendment of the SPC or informing prescribers of specific concerns.

How to report suspected lack of efficacy

If, following administration of a veterinary medicine in the UK, a prescriber becomes aware of any adverse events including a lack of efficacy involving an animal, they should record what happened in as much detail as possible and make a report to the MAH, who is legally obliged to forward such reports to the VMD (The Veterinary Medicines Regulations 2013 [as amended]).

Reporting a suspected lack of efficacy

- Anyone who is made aware of a lack of efficacy can report, for example, the prescriber, the owner, the animal handlers, etc.
- Horse owners can contact their prescriber to report a suspected lack of efficacy.
- Reports of suspected lack of efficacy for authorised veterinary medicines should be made directly to the MAH. The MAH contact details can be found on the product leaflet or on the VMD's Product Information Database.
- Further information on how to report a suspected problem with a veterinary medicine is available here.

The VMD is developing an advanced online adverse event reporting portal[2], with implementation targeted for early 2026.

[2] https://www.gov.uk/government/news/vmd-strengthens-pharmacovigilance-framework-whilst-addressing-reporting-concerns

Prescribers and animal owners can contact the VMD (adverse.events@gov.uk) for cases where MAH identification is challenging or if the animal has been given a human medicine or a medicine that is not authorised for use in animals. Questions on how to report or other queries can be sent to adverse.events@vmd.go.uk with the case reference number if the enquirer has already reported it.

It is not necessary for the reporter to first determine if there was a problem with the product before submitting a suspected lack of efficacy report. Reports received by the VMD are monitored and statistically analysed to determine the likelihood of a product problem (Veterinary Medicines Directorate, 2024b).

Prior to reporting to the VMD, the MAH is expected to validate all cases reported by veterinary surgeons, other health-care professionals and the general public to ensure that the minimum information required is included in the report (see box below). All available information relevant to the evaluation of the suspected lack of efficacy should be provided (Veterinary Medicines Directorate, 2024b).

Minimum information required for reporting:

- **An identifiable source or primary reporter:** wherever possible, this should include the name and address of the primary reporter. Initials, geographic location or other unique identifier should be provided to allow the collection of further information and to avoid any duplication of reports whilst fully complying with relevant data protection laws, for example, the General Data Protection Regulation (GDPR) and privacy legislation.
- **Patient details:** species (including additional information such as animal age, sex, and weight is beneficial).
- **Veterinary medicine concerned:** product name.
- **Adverse event details:** it is recommended to record in the case narrative the opinion of the primary reporter and attending veterinary surgeon, identifying which products or active substances are suspected.

All reports of suspected lack of efficacy reported to the MAH, regardless of whether the product was used in accordance with the SPC, will be recorded by the person

responsible for pharmacovigilance and reported to the VMD in the same way as for other adverse event reports.

Anyone who is made aware of a Suspected Lack of Expected Efficacy (SLEE) can report it by:

- Telling their prescriber
- Contacting the MAH directly using the contact details on the product leaflet – you can check if a product is an approved animal medicine and who the MA holder is on the VMD product information database.

Additional tools which are over and above the required VMD reporting, are also being developed to facilitate collating of adverse events and suspected lack of efficacy cases. EVSNET (Equine Veterinary Surveillance Network) is an initiative from the University of Liverpool, funded by The Horse Trust, which provides equine health and disease information to veterinary practitioners, laboratories and owners of equines. EVSNET aims to be a system for syndromic surveillance and research on a large, real-time and continuous scale in the UK equine population and enables veterinary practices to link their clinical management systems with adverse event reports for equines. For more information on how your veterinary practice can take part, contact EVSNET here.