



Controls on Veterinary Medicines

Summary

This document provides an overview of the broad range of regulatory controls that are in place governing the authorisation, supply and monitoring of veterinary medicinal products. These comprehensive controls ensure that safe, effective and quality veterinary medicines are available for the health and welfare of our animals, whilst safeguarding people and the environment.

Introduction

In the UK, the Veterinary Medicines Regulation (VMR) provides for legislative requirements concerning the manufacture, classification, supply, marketing and use of veterinary medicines (1). Additionally, there are a range of EU regulatory controls that also apply to veterinary medicinal products (VMPs) including controls on safety, licensing and monitoring (2).

In the UK, the national competent authority and independent regulator is the Veterinary Medicines Directorate (VMD) (3). At the EU level, the European Medicines Agency (EMA) is responsible for the scientific evaluation and monitoring of medicines (4).

All of the authorised veterinary medicines available in the UK for animals must undergo a strict regulatory approval process, before they gain a Marketing Authorisation (MA) or licence for sale and supply (5).

Scientific studies by animal medicine companies and subsequent evaluation, by independent regulatory authorities, ensure that each authorised veterinary medicinal product meets the required standard of safety, efficacy and quality. This ensures that animal medicines are safe to use, they are efficacious (effective) and they meet quality criteria.

In the UK, animal medicines can be classified based on their authorised supply route, which allows for control over the sale and distribution of medicines e.g. antibiotics are only available on prescription from a veterinary surgeon i.e. all antibiotics are POM-V

(prescription only medicines - through a veterinary surgeon).

On farm, there is a legal requirement, under the VMR, to record all veterinary medicines obtained and used in food-producing animals (1). When veterinary medicines are administered to farm animals, the safety of food from these animals and their products (e.g. meat, milk, eggs) is monitored through a statutory residue surveillance scheme (6). This scheme ensures that the UK meets an EU regulatory requirement to analyse samples for residues of veterinary medicines (7).

For all authorised veterinary medicines, there is an ongoing process of safety and efficacy monitoring – called pharmacovigilance – that ensures the continued safe use of effective medicines (8).

Only authorised veterinary medicines can legally be used in the UK. The enforcement division of the VMD proactively takes action, which can include prosecution, against any illegal marketing and use of unauthorised products in relation to breaches of the VMR (9).

The Authorisation of Veterinary Medicines

Before an animal medicine can be placed on the UK market it must be approved. This takes the form of a Marketing Authorisation (MA). Rigorous European and UK standards for the registration process ensures only those medicines that meet defined standard of quality, safety and efficacy are authorised.

The discovery, research and development of an animal medicine is a lengthy and very expensive process with successful products taking 5-11 years to reach the marketplace (10).

The process of applying for an MA includes the submission of an extensive and detailed dossier, which consists of data that supports the safety, quality and efficacy of the product in accordance with the legal

framework. This information helps the national and European regulators to carry out an independent scientific assessment to ensure that all the regulatory criteria have been met.

Safety, Quality and Efficacy

The aim of an independent scientific assessment, for a marketing authorisation, is to evaluate the safety profile, the quality of the manufactured product and the effectiveness of the product. The submitted dossier of data, which supports this assessment, is the end result of years of discovery, pre-clinical laboratory development and clinical field trials.

A marketing authorisation will only be granted if the experts, either at the VMD in the UK or EMA for products seeking EU-wide approach, and their advisory committees of independent experts (the Veterinary Products Committee (VPC) in the UK or Committee for Veterinary Medicinal Products (CVMP) in Europe), are fully satisfied (11, 12).

Safety

Stringent safety criteria are imposed during the evaluation of the medicine. Safety aspects of a medicine include its safety in animals; in those individuals administering the veterinary medicine e.g. farmers, pet owners, vets; and safety in the environment. In the case of farm animals, safety also means it will be safe for consumers to eat animal products e.g. meat, milk, eggs or honey from treated animals.

For farm animal medicines there has to be a Maximum Residue Limit (MRL) for the active ingredient (the highest level of residue that does not pose a risk to the consumer) and set withdrawal periods – the time that must elapse since the last treatment before the animal or its products can enter the food chain, which ensures any remaining residues are below the MRL (13, 14). Large additional safety factors are also applied during the establishment of the withdrawal period to ensure consumer safety (more information can be found in the NOAH briefing document – veterinary medicines and the safety of food from animals).

Quality

An animal medicines manufacturer must demonstrate the required quality standard of the final veterinary medicine, the consistent quality of the ingredients and the manufacturing processes that were used to make the product. Quality is very important to ensure that product safety and consistency is assured – meaning all batches of a product meet the required standards. The stability of the product is important to ensure that the product retains its quality and efficacy at least until the stated expiry date.

Efficacy

All medicines must do what they claim to do when used as per label instructions. The animal medicines

company must substantiate any and all claims for the effectiveness of the product. Field trials make sure that the product will work in practical ‘real life’ situations; demonstrating effectiveness in preventing or treating a particular medical condition – in agreement with the claims made on the product labelling or information sheet. More information on authorised veterinary medicinal products, including indications for use can be found on the SPC (Summary of Product Characteristics) in the VMD Product Information Database or in the NOAH compendium of datasheet (15, 16).

Only when the independent regulator is satisfied on all three criteria can a marketing authorisation be considered, which may then be used to legally place a veterinary medicinal product on the UK market in accordance with the VMR.

Veterinary Medicine Authorisation Routes

There are four different routes (national, centralised, mutual recognition and decentralised) for obtaining marketing authorisations, resulting in products that are nationally authorised, centrally authorised or mutually recognised (5):

Nationally authorised products: Applications are submitted to the national competent authority, which is the VMD in the UK. MA's granted under this procedure are valid in the UK only. This procedure does not involve any other member state.

Centrally authorised products: The centralised procedure is used when an applicant wants to market a product throughout the EU. Centrally Authorised Products (CAPs) are evaluated by the EMA and issued by the European Commission – therefore they are assessed and approved at community level involving all member states. The authorisation is pan-European and allows marketing and sale in all member states, including the UK. The centralised procedure is compulsory for certain biotechnology products and may be requested for other innovative products.

Mutually recognised products: These products are assessed and approved involving at least two member states via a mutual recognition procedure (MRP), where the product is already authorised in a least one member state and an authorisation is sought in one or more other member states. In this case, the reference member state (RMS) has authorised the product and submits their evaluation to the other concerned member states. The **decentralised procedure** (DCP) also results in a mutually recognised product. The decentralised route may be used if the product is not authorised in any member state and the applicant would like authorisation in several or all member states. This may occur where the centralised procedure is not mandatory, the product is not eligible for centralised procedure or where optional – the applicant does not wish to use the centralised procedure.

Regulatory Controls Post-Authorisation

The regulatory controls on veterinary medicines continue after the pre-authorisation and authorisation phases, when products are placed on market. These controls include restrictions on the supply and use of some products, depending on their classification. Controls also include the continued monitoring of safety and efficacy, through pharmacovigilance activities and the national statutory surveillance programme for residues in food from animals. To ensure our animals receive only those medicines that have been authorised and meet the strict criteria of quality, efficacy and safety, the illegal marketing and use of unauthorised products is monitored and action taken, where appropriate, by the VMD through its enforcement activities.

Classification and Distribution of Medicines

There are four legal categories of authorised veterinary medicines, which designates their distribution category and controls the supply route of these medicines.

1. POM-V: (Prescription Only Medicine – Veterinary Surgeon). These medicines can only be supplied on prescription by a veterinary surgeon. Products such as antibiotics will always be POM-V medicines.
2. POM-VPS: (Prescription Only Medicine – Veterinary Surgeon, Pharmacist, Suitably Qualified Person (SQP)). These medicines can only be supplied on prescription by a Registered Qualified Person (RQP) – i.e. a veterinary surgeon, a pharmacist or a Suitably Qualified Person (17). POM-VPS medicines include some wormers for livestock.
3. NFA-VPS: (Non-Food Animal - Veterinary Surgeon, Pharmacist, SQP). These medicines for companion animals may be supplied by a veterinary surgeon, a pharmacist or a Suitably Qualified Person provided the requirements for supply are met. They do not require a prescription.
4. AVM-GSL: (Authorised Veterinary Medicine – General Sales List). These medicines have no restrictions in the VMR and are commonly called ‘over the counter medicines’.

There are specific requirements, in terms of qualification and supply of medicines, for Registered Qualified Persons (RQP) – vets, pharmacists and SQPs (18).

The distribution of animal medicines in the UK is strictly controlled by legislation including the VMR (1). Wholesalers are inspected and authorised by the VMD and are required to hold a marketing authorisation, a manufacturer’s authorisation or a wholesale dealer’s authorisation (WDA) (19).

Manufacturers are required to comply with Good Manufacturing Practice (GMP) for the authorised veterinary medicinal products they produce. Additionally, they must hold a Manufacturing Authorisation for those products, unless they are for small non-food producing pet animals (20). Registered manufacturing facilities and processes are regularly inspected by the VMD with ongoing re-inspection at a risk-based frequency.

The inspectors check the premises are suitable for the production of safe, effective medicines of a consistently high quality, and that they are being manufactured in accordance with their marketing authorisations. Vets’ and merchants’ premises and pharmacies are also all regularly inspected to ensure they meet the required standards.

Veterinary Medicines and the Safety of Food

Animal medicines for food producing animals are strictly controlled by the UK national law (VMR) and European law (13). Requirements on farm include the recording of all medicines bought and administered. To ensure consumers are provided with safe food from animals when medicines are used, farmers and vets must observe the withdrawal period for all medicines. This is the time that must elapse from last dose, until the animal or its products are allowed to enter the food chain. This scientifically assessed time period, which includes large safety margins, ensures that any residues that may be present have depleted to levels below the Maximum Residue Limit (MRL), meaning animal products are safe to consume.

In the UK, the VMD oversees a statutory residue surveillance scheme that analyses samples from animal foodstuff and publishes results annually (6). The surveillance reports from the VMD show that the vast majority of samples tested are compliant. This provides assurance that the regulatory control measures and actions are safeguarding our food from animals. More information on this topic can be found in the NOAH briefing document: veterinary medicines and the safety of food from animals.

Pharmacovigilance

The ongoing post-authorisation monitoring of safety and efficacy of veterinary medicines is termed ‘pharmacovigilance’. 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 from animals, where the appropriate withdrawal period and dose rate has been followed.

The monitoring and evaluation of Adverse Events (AEs) - 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

– provides an opportunity to continually improve the safety profile of veterinary medicines.

The VMD, as part of their pharmacovigilance activities, receive and evaluate reports of adverse events and lack of efficacy in animals and people (21). The most recent VMD annual review of pharmacovigilance in the UK reassuringly stated that *'the chance of an adverse event happening in any particular animal or person is very low'* (22). Nevertheless, the controls and surveillance monitoring in place continue to safeguard animals, people and the environment as well as continually improving the safety profile of veterinary medicines. More information on this topic can be found in the NOAH briefing document: pharmacovigilance, monitoring the safety and efficacy of animal medicines.

Conclusions

- UK and EU regulatory controls on veterinary medicines cover activities in the discovery, research and development phases, through authorisation of medicines and extend throughout the post-authorisation phase.
- Before medicines are authorised, they must meet strict safety, quality and efficacy standards to gain a marketing authorisation.
- There are a number of authorisation routes for veterinary medicines, which govern the countries where the animal medicine may be marketed and sold.
- In the UK, the classification of authorised veterinary medicines designates the supply and distribution of these medicines.
- Strict controls on medicines for food-producing animals, including record keeping and observance of withdrawal periods, ensures the safety from residues of veterinary medicines in food from treated animals.
- Pharmacovigilance and the monitoring and evaluation of adverse events allows for the ongoing improvement of the safety profile of medicines on the market.

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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 on authorised veterinary medicines see NOAH briefing documents on Veterinary Medicines and the Safety of Food from Animals and Pharmacovigilance).

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