HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Transcript of the presentation entitled 'Pharmacovigilance and adverse event reporting for veterinarians, veterinary nurses and animal healthcare professionals'

SLIDE 1

Hello everyone and welcome to this presentation which will cover the topic of pharmacovigilance and adverse event reporting for veterinarians, veterinary nurses and other animal healthcare professionals. Adverse events include side effects, safety concerns or if a medicine is not working as expected following the use of a veterinary medicine and are most likely to be observed by veterinarians or pet owners. The HPRA uses information on reported adverse events to monitor the safety and effectiveness of veterinary medicines available for use in Ireland.

This is one of a series of presentations we have available, so if you would like to learn more about the monitoring of the safety and effectiveness of veterinary medicines (also known as veterinary pharmacovigilance), or a better insight into the work of the Health Products Regulatory Authority (HPRA), please feel free to access any of our published presentations.

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This presentation has been designed for veterinarians, veterinary nurses and other animal healthcare professionals.

The aim is to explain what pharmacovigilance is, what an adverse event is and how to report it, how adverse events arising from veterinary medicines are processed by the HPRA and also the importance of reporting adverse events.

We hope it will be informative and by the end you will have a better understanding of veterinary pharmacovigilance and how to report an adverse event to the HPRA.

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Before we go any further, allow me to give a brief introduction to the HPRA. We were formerly known as the Irish Medicines Board and in July 2014 our name was changed to the Health Products Regulatory Authority to better reflect the scope of our work. The HPRA regulates both human and veterinary medicines and our vision is "Excellence in health product regulation through science, collaboration and innovation."

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So what is Pharmacovigilance? The World Health Organisation definition is "The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem". This also applies to veterinary medicines.

There is a legal framework for pharmacovigilance of veterinary medicines in the European Union and also at a national level in Ireland.

The HPRA is what is known as a National Competent Authority and has responsibility for the pharmacovigilance of veterinary medicines that have been authorised for use in Ireland. Every EU Member State has their own competent authority.

The HPRA monitors the quality, safety and efficacy of veterinary medicines by recording and assessing reports of adverse events.

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We will now discuss adverse events, first - what is an adverse event? An adverse event is defined as any observation that is unfavourable and unintended and that occurs after the use of a veterinary medicine. This may relate to:

- adverse reactions in the treated animal following recommended use of the product – e.g., an anaphylactic reaction following a routine vaccination in a puppy;
- adverse reactions in the treated animal following off-label use (not used as recommended) – for example, an overdose of a product;
- lack of expected efficacy - the product not working as intended;
- effects in humans following accidental exposure to a veterinary medicine – for example, accidental self-injection or spilling a product onto the skin;
- violations of maximum residue limits - it is important to note here that some tests will detect residues in foodstuffs of treated animals; however the levels found may still be below the legal maximum residue limit permitted for the product;
- impact on the environment – for example, use of sheep dips near watercourses and safe disposal of spent sheep dip.

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Just to mention at this point that during this presentation you will hear the term adverse reaction as well as adverse event, so what is the difference?

An adverse reaction is one type of adverse event and is defined as a reaction to a veterinary medicine which is harmful and unintended and which occurs at doses normally used in animals for the prophylaxis (i.e. prevention), diagnosis or treatment of a disease or to restore, correct or modify a physiological function.

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A serious adverse reaction is one which results in death, or which is life-threatening, or which results in significant disability or incapacity, is a congenital anomaly/birth defect, or which results in permanent or prolonged signs in the animals treated.

So, an adverse reaction is one type of adverse event but not all adverse events are adverse reactions.

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Another type of adverse event is lack of expected efficacy. This is defined as the apparent inability of an authorised product to have the recognised expected efficacy in an animal, according to the claims of the Summary of Product Characteristics (SPC) and following use of the product in accordance with the SPC.

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When submitting an adverse event report, it is important to indicate if the product was used as recommended or if 'off-label' use occurred (either intentionally or in error). This can be done in the free text section of the description of the adverse event.

Off-label use is the use of a veterinary medicine that is not in accordance with it's Summary of Product Characteristics, including the misuse and serious abuse of the product. Examples could include administration of an incorrect dose, administration to a non-authorised target species, use of an incorrect route of administration or not respecting the recommended timing of vaccinations.

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We will now take a closer look at the Summary of Product Characteristics or the SPC. This is approved for each veterinary medicine that is granted a marketing authorisation.

The SPC approved for a product at the time of first granting a marketing authorisation is based upon the information presented in the application dossier for marketing authorisation.

The SPC contains information regarding the dosage, indications, safety, use, storage and disposal of the product and is intended to be used by healthcare professionals.

The most up to date versions of SPCs for products authorised nationally are available on the HPRA website, while the SPCs for centrally-authorised products (authorised by the European Medicines Agency) are available on the EMA website.

SPCs for veterinary medicines that have been authorised in any Member State will be available from the Union Product Database which can be accessed from the EMA website.

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This slide shows you how to search for an authorised veterinary medicine. Firstly, click on the 'VETERINARY' tab at the top of the HPRA's homepage and then you can select a product, active substance or marketing authorisation number to search for. There is also an 'advanced search' function available. Once you have selected a vaterinary medicine, there will be a link to the SPC to the right hand side.

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Just to mention some sections of relevance for pharmacovigilance in the SPC. It is also important to note that with the introduction of the new veterinary regulation (2019/6) on 28 January 2022, SPC section numbers have changed as a new format has been introduced for new products and will be applied to existing products before January 2027. Consequently, the SPCs of existing veterinary medicines will be updated to reflect the new format in due course.

- Section 3.6 (or 4.6 under the previous legislation) contains information on possible adverse reactions in the intended target species.
- Section 3.3 (or 4.3) contains contraindications and warnings to ensure safe use of the product.
- Section 3.5 (or 4.5) contains special precautions for use in animals and special precautions to be taken by the person administering the product to animals.
- Section 3.7 (or 4.7) contains information for use during pregnancy, lactation or lay.

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The information included in the SPC of a veterinary medicinal product is also included on the package leaflet of the product.

Due to space limitations and restrictions set in legislation, complete information is not normally included on the product's packaging and instead the prescriber/user is referred to the package leaflet before use of the product.

It is vitally important that users and prescribers of veterinary medicines take the necessary time to read the information included in the package leaflet - otherwise important information on the safe and effective use of the product may be overlooked.

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It is important to note that updates can made to SPCs at any time after a medicine is first authorised. This can include a change to the product's indication(s) or the withdrawal period(s), so it is important to make sure you are familiar with the most recently approved version that is available online.

SPC changes are updated normally within 24 hours on the HPRA website. However, it may take some months for the package leaflet and labelling to be updated by the marketing authorisation holder and introduced onto the market.

When significant changes to the SPC of a product are made, the HPRA normally publishes a safety advisory notice on the HPRA website. You can sign up to receive notification of when such notices are published. The following two slides provide more information on how to do this.

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This slide shows you where to find recently published safety notices. Under the 'VETERINARY' tab at the top, on the left hand side click the dropdown arrow beside 'Safety information' and then click on 'Safety Notices'. On the right hand side of the screen a list will appear and you can click on the title to see more information about that notice.

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There is an option to register for all safety alerts published by the HPRA. Click on Register in the 'My HPRA' box on the top right hand corner of the homepage which is shown in this slide. The alerts include updates on human as well as veterinary medicines.

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You can then enter your details, choose a password and click 'Register'. You will be emailed a link to confirm registration to the email address nominated and once registration is confirmed you can log in using your email address and password. You will be brought to the 'My HPRA' page to manage your preferences. Under 'My preferences', tick the stakeholder group, topics of interest and products of interest that you wish to receive updates about. You can refine your preferences to veterinary related alerts only. Please note that at any time you, can log into 'My HPRA' to update your preferences.

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We will now discuss why veterinary pharmacovigilance is important. When a product is first authorised the information available to regulatory authorities is based on the studies carried out. These studies are conducted in a limited population of animals. Once marketed, the product will be used in a much larger population of animals so adverse events that occur with a low frequency may come to light that were not observed in the controlled studies e.g. drug interactions.

Prescribers and users of veterinary medicines have an important role to play in terms of reporting adverse reactions so that the safety and efficacy of each product can be monitored once marketed and the product labelling and SPC can be updated as necessary.

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So, who should report an adverse event? It is recommended that adverse events are reported by those involved with the supply and/or use of veterinary medicines i.e., veterinary healthcare professionals. These include:

- registered veterinary practitioners,
- registered veterinary nurses,
- pharmacists,
- the holders of an animal remedies merchant's licence.

Reports can be sent to the company responsible for the marketing of the product, or directly to the HPRA. Animal owners may also report adverse events.

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There are some minimum criteria which must be included in an adverse event report for it to be considered valid. This includes:

- an identifiable reporter e.g., a vet, a veterinary nurse, pharmacist, animal owner,
- animal or human details e.g., species, breed, age,
- name of product and its marketing authorisation number,
- details and description of the adverse event.

Laboratory reports or necropsy findings can be provided where relevant.
New/additional information can be sent as a follow-up report e.g., if a cow aborted you could send the report and if you get necropsy results a few days later you can send this as new information in a follow-up report.

Just to reassure you that all adverse event reports and personal information are handled in full compliance with GDPR requirements and are treated confidentially.

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We will now look at how to report an adverse event.

The preferred method of report submission is via an online reporting form. This is available on the HPRA website.

Alternatively, a reporting form may be downloaded from the HPRA website, printed, completed and posted to the HPRA by Freepost.

An adverse event can also be reported directly to the company responsible for marketing the product.

Please see our separate presentation under 'Adverse reaction/event reporting' which provides a step-by-step guide on how to complete the online form and submit it to the HPRA.

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On this slide we show a snapshot of the homepage of the HPRA website page where you will be able to download the form. Under the tab 'VETERINARY' at the top there is an option to 'Report an issue' as is marked in the red box here – then click on 'report an issue'.

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You will then be directed to another page that lists the available online report forms where you should click on 'Veterinary Medicines Adverse Reaction/Event'. As mentioned, a separate presentation is available under 'Adverse reaction/event reporting' which provides a step-by-step approach on how to complete and submit this online reporting form.

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We will now look at what happens to an adverse event report once it is received by the HPRA. Every report received is recorded in the HPRA national database and an email acknowledgement will be sent to the reporter to confirm receipt of the report. Every valid report is then uploaded to the Union Pharmacovigilance database. This database contains reports for all veterinary medicines authorised in the EU. This database is new since the end of 2021. Since 28th January 2022 companies now submit all adverse events reported to them directly to the Union Pharmacovigilance database.

A process known as 'signal management' is used to screen and identify any potential signals of importance. Should a trend of adverse events involving a specific product or group of products emerge, then regulatory action may be taken to protect human and/or animal health or safety for the environment.

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We will now look at some examples of regulatory action which might arise as a result of post-marketing pharmacovigilance information.

One example would be enhanced monitoring of the veterinary medicine in question. This could take the form of 'targeted signal management' which can be directed at one particular product or to a group of similar products.

Another action could be changes to the product information such as adding information about new adverse reactions, contraindications or user safety warnings to the relevant sections of the SPC and package leaflet.

Other more stringent regulatory actions include the recall of a particular batch of product or suspending the sale and supply of the product to the market. These actions are taken only where necessary to safeguard human or animal health.

Finally, the most severe action is to suspend or revoke the marketing authorisation for the product concerned. This is a last resort action and is not very common. It is important to remember that no product will ever be 100% safe and adverse reactions are possible after administration of any product and the overall benefit-risk balance of a product is always taken into account.

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Every year, the HPRA publishes an annual pharmacovigilance report with in-depth information on the adverse events received for the previous year. You can find these reports on the HPRA website under the 'VETERINARY' tab at the top, then on the left-hand side click the dropdown arrow beside safety information and then click on 'Annual Pharmacovigilance Reports'. This will open a brief introduction explaining the nature and purpose of the annual pharmacovigilance reports followed by a list of the reports published to date.

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The European Medicines Agency also publishes annual pharmacovigilance bulletins which provide an overview of pharmacovigilance in the European Union. As shown on this slide, these bulletins can be found on the EMA website under the 'Veterinary regulatory' tab, then by clicking on 'Post-authorisation', then on the left-hand side click on 'Pharmacovigilance' and then select 'Annual bulletins'.

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This brings us to the end of this presentation. In conclusion, I would like to reiterate the importance of vets, vet nurses and veterinary healthcare professionals reporting adverse events.

Adverse event reporting is important in order to ensure the safe and effective use of veterinary medicines for both the animal and the person administering the product. Unless information on adverse events is reported, the regulatory bodies (such as the HPRA) as well as companies that place veterinary medicines on the market will be unaware of such events following the placing of a product on the market.

The reporting of adverse events provides valuable information to allow ongoing assessment of the safety and effectiveness for each veterinary medicine and may aid in making decisions on any regulatory action that may be required e.g. including new or updating existing warnings in the package leaflet.

Reporting benefits both the animal receiving the product and future prescribers or users of the product.

So, the take home message is please do your part and report suspected adverse events as this will benefit animals receiving and those using veterinary medicines.

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And finally, please refer to other information sections and presentations available on our website for further guidance and instruction on adverse events, pharmacovigilance and the work of the HPRA. If you have any questions regarding the reporting of adverse events or product safety, please contact us here at the HPRA using this email address: **vetsafety@hpra.ie**.

Thank you for listening and we hope this presentation has been of interest. Goodbye.