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Committee for Medicinal Products for Veterinary Use

Questions and answers on how to express the frequency of adverse reactions within the product information

These questions and answers were developed to aid the writing or update of section 4.6 of the summary of product characteristics (SPC) (and consequently section 6 of the package leaflet) in line with the convention of frequency groupings for adverse reactions that is included in the veterinary Quality of Review Document (QRD) template. These principles, agreed by the Committee for Medicinal Products for Veterinary Use (CVMP) at their meeting in March 2016, are applicable to authorised veterinary medicinal products for which the product information is undergoing an update to bring it in line with the latest QRD template.

1. How should the frequency of adverse reactions (ARs) be expressed?

a. The frequency of adverse reactions (ARs) should be described using the frequency terms described in the guidelines on preparation of summary of product characteristics (for immunologicals and pharmaceuticals), which are also included at the end of section 4.6 of the QRD template.

b. The most frequently occurring ARs should be listed first. In cases where ARs have not yet been expressed according to this frequency classification, the marketing authorisation holder (MAH) will be asked to update section 4.6 to include information on frequency.

c. The adverse reaction should appear at the start of the sentence in the product information (see example below).

d. The origin of the information on which the AR frequency is based should be stated i.e. whether the ARs have been observed during studies, from spontaneous (pharmacovigilance) reports or other sources (N.B. the source should be specified). The origin of the ARs should be put at the end of the sentence so that it does not detract from their description.

   For example, ‘Swelling at the injection site was commonly observed during safety and clinical studies’ instead of ‘During safety and clinical studies, swelling at the injection site was commonly observed’.

e. Statements relating to different data sources should be presented in separate sub-sections e.g.

   Application site reactions characterised by hair loss and erythema occurred rarely in field studies.

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Vomiting and diarrhoea have been reported very commonly based on post marketing safety experience.

f. For ARs that are observed both pre-authorisation (in the context of safety and/or efficacy studies) and post-authorisation (reported through the pharmacovigilance system), the source of the ARs that results in the highest frequency should be retained on the product information. In support of any application to vary the frequently information in section 4.6 of the SPC, it should be made clear (within the application) on what basis the frequency of ARs has been updated (i.e. which data source was used).

2. Can I update the SPC to change the frequency of adverse reactions?

Yes, the frequency of ARs may be updated in the SPC. However, in general, frequency information originating from controlled studies takes precedence over that originating from spontaneous (pharmacovigilance) reporting (it is generally accepted that frequency information originating from pharmacovigilance may not reflect the 'true' incidence of adverse reactions due to under-reporting). Therefore, the frequency of ARs observed in controlled safety/efficacy studies should not be replaced by frequency information originating from pharmacovigilance data. However, if post-authorisation experience indicates reporting of an AR at a higher frequency compared with that observed in pre-authorisation safety/efficacy studies, consideration should be given to revising upwards the frequency of that AR in the product information.

References

- European Commission (2006) Guideline on preparation of summary of product characteristics – Immunologicals for veterinary medicinal products
- European Commission (2006) Guideline on preparation of summary of product characteristics – Pharmaceuticals for veterinary medicinal products
- European Medicines Agency (2016) Quality Review of Documents veterinary product-information annotated template (English) version 9