



**Veterinary Medicines  
Guidance Note**

**Guidance on the use of  
the  
Cascade**

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**ASSURING THE SAFETY, QUALITY AND EFFICACY  
OF VETERINARY MEDICINES**



**THESE NOTES ARE ONLY A GENERAL GUIDE AND MUST NOT BE TREATED AS A COMPLETE OR AUTHORITATIVE STATEMENT OF THE LAW ON ANY PARTICULAR CASE**

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**INVESTOR IN PEOPLE**

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## INTRODUCTION

1. This is one of a series of Veterinary Medicines Guidance (VMG) Notes explaining the requirements under the Veterinary Medicines Regulations ('the Regulations'). The Regulations are revoked and replaced every year, so the references to them should be read as referring to the ones that are currently in force. Therefore, the date and number of the Statutory Instrument are not shown in this VMG Note. The VMG Notes will be updated as necessary and the date of the most recent update is shown on the front cover.
2. The Regulations set out the UK controls on veterinary medicines, including their manufacture, advertising, marketing, supply and administration. VMG Note 1: *An Introduction to Marketing Controls on Veterinary Medicines* gives basic information about the scope of the Regulations and the requirement for Marketing Authorisations (MAs). This VMG Note describes the provisions controlling the administration of veterinary medicines in the UK.

## THE AUTHORISATION PROCESS

3. Under the authorisation process veterinary medicines are scientifically assessed against statutory criteria of safety, quality and efficacy **when used in accordance with the manufacturer's recommendations for use**. This takes account of potential risks to animals, people who administer the medicine and those who may consume produce from treated animals, and the environment. It also forms the basis of a risk/benefit evaluation on which the decision to grant an authorisation is based.
4. The use of medicines in ways that have not been authorised may pose potential risks that the authorisation process seeks to minimise. The law therefore requires that, wherever possible, only medicines authorised for the condition and species being treated are used. However, the legislation recognises that there will be conditions affecting species for which no medicine is authorised and provides exemptions in certain circumstances and subject to specified conditions. These are explained below.

## PROHIBITION ON ADMINISTRATION

5. The controls on the administration of veterinary medicines are set out in the Regulations. Subject to the exemptions provided in the Regulations, these prohibit the administration of a veterinary medicine unless it is authorised and the administration is in accordance with the applicable MA. In the case of food-producing animals, the Regulations also prohibit the administration of medicines unless they have been prescribed by an appropriate person in accordance with controls on distribution. Non-compliance with the provisions is an offence and may result in prosecution.

## EXEMPTIONS FROM PROHIBITION

### PRODUCTS ADMINISTERED FOR RESEARCH

6. The above prohibitions do not apply in the case of medicines administered for research purposes in accordance with an animal test certificate (ATC) or a licence issued under the Animals (Scientific Procedures) Act 1986.

### EXCEPTIONAL CIRCUMSTANCES

7. In the event of serious epizootic diseases the VMD, acting on behalf of the Secretary of State, may permit in writing the marketing and use of immunological products without an MA. Also, the VMD may grant a certificate to a veterinarian permitting the import and use of a medicine authorised outside the UK, subject to any conditions specified in the certificate. However, this may only happen where the health situation merits such action and no suitable product is available. In either case, the prohibition on administration will not apply.

### IMMUNOLOGICAL PRODUCTS FOR IMPORTED/EXPORTED ANIMALS

8. Where an animal is being imported from, or exported to, a country that is not on the European Economic Area, the VMD may permit the use of an immunological product that is not authorised in the UK but is authorised in the exporting/importing country. The European Economic Area comprises the EU plus Iceland, Liechtenstein and Norway.

### THE PRESCRIBING CASCADE – NON-FOOD ANIMALS

9. The prescribing cascade provisions are set out in the Regulations. They are available only to veterinarians that have responsibility for the treatment of the animals concerned.
10. If there is no medicine authorised in the UK for a condition affecting a non food-producing species, the veterinary surgeon responsible for treating the animal(s) may, in particular to avoid unacceptable suffering, treat the animal(s) in accordance with the following sequence:
  - (a) a veterinary medicine authorised in the UK for use in another animal species or for a different condition in the same species; or, if there is no such product:
  - (b) either:
    - (i) a medicine authorised in the UK for human use; or
    - (ii) in accordance with an import certificate (see VMG Note 7: *Import Certificate Schemes*), a medicine authorised for veterinary use in

accordance with Directive 2001/82 (as amended) in another Member State; or, if there is no such product:

(c) a medicine prepared extemporaneously, by a veterinary surgeon, a pharmacist or a person holding an appropriate manufacturer's authorisation, as prescribed by the veterinary surgeon responsible for treating the animal.

11. When it is necessary to have a product prepared as an extemporaneous preparation, in the first instance it is recommended that the veterinary surgeon contacts a manufacturer holding an authorisation that permits them to manufacture such products (commonly referred to as Specials Manufacturers (ManSA)). A list of Specials Manufacturers can be found at <http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/ManufacturersandWholesaleDealerslicences/index.htm>. Specials Manufacturers may already have experience of preparing the product in question and will have the necessary equipment to prepare and check the quality of the product.
12. A medicine prescribed in accordance with the cascade may be administered by the prescribing veterinary surgeon or by a person acting under their direction. Responsibility for the prescription and use of the medicine remains with the prescribing veterinary surgeon.
13. Horses declared 'not for human consumption' under the horse passport scheme are regarded as non-food producing animals for the purposes of these provisions.

### **THE PRESCRIBING CASCADE – FOOD PRODUCING ANIMALS**

14. If there is no medicine authorised in the UK for a condition affecting a food-producing species, the veterinary surgeon responsible for treating the animal(s) may use the cascade options as set out in paragraphs 10 and 11 above except that the following additional conditions apply:
  - the treatment in any particular case is restricted to animals on a single holding;
  - any medicine imported from another Member State (option b(ii)) must be authorised for use in a food-producing species in the other Member State;
  - the pharmacologically active substances contained in the medicine must be listed in Annex I, II or III to Regulation (EEC) No. 2377/90;
  - the veterinary surgeon responsible for prescribing the medicine must specify an appropriate withdrawal period as set out in paragraph 16;
  - the veterinary surgeon responsible for prescribing the medicine must keep specified records.
15. These additional provisions are to ensure that the need for, and propensity to benefit from, the proposed treatment is assessed in each case and to safeguard

consumers of produce from treated animals against risk from any potentially harmful residues of the medicines administered.

16. In line with the Directive, the Regulations permit only medicines whose pharmacologically active substances (i.e. those which must appear on product labels) are listed in Annex I to III of Regulation 2377/90 to be used under the cascade in food-producing animals. This is to ensure that only substances whose residues implications have been evaluated and, that, where appropriate, a maximum residue limit (MRL) has been established. Details of the Annexes to Regulation 2377/90 and a consolidated list, which is updated periodically, are available on the European Commission website (<http://pharmacos.eudra.org/F2/mrl/index.htm>).
17. A veterinary surgeon prescribing for, or administering a medicine to, food-producing animals under the cascade is required to specify an appropriate withdrawal period. When setting the withdrawal period, a veterinary surgeon must take into account known information about the use of the product on the authorised species when prescribing to an authorised species under the cascade. Unless the medicine indicates a withdrawal period for the species concerned, **this should not be less than:**
  - 7 days for eggs and milk;
  - 28 days for meat from poultry and mammals;
  - 500 degree days for meat from fish.
18. As there is no minimum withdrawal period set for honey, it is up to the prescribing veterinarian to set a suitable withdrawal period that will ensure no risk to consumer health. Further guidance on setting a suitable withdrawal period is available from the National Bee Unit (telephone: 01904 462 510).
19. For products imported under a Special Import Certificate (SIC), provided that the product is used strictly according to the terms of its EU authorisation i.e. no "off label" use, the withdrawal period applied in UK should be the period stated on the EU product literature. For products imported under an SIC and used "off label" the UK minimum statutory withdrawal periods will apply.
20. Should there be a change to the terms of the authorisation or the product is not being used within the terms of its authorisation, then the minimum standard withdrawal periods for cascade products above continue to apply.
21. Where a homoeopathic veterinary medicinal product whose active principles are in Annex II to Regulation 2377/90 is used, a zero withdrawal period applies.

### RECORD KEEPING

22. The records referred to in paragraph 13 should be retained for at least 5 years and be made available on request to a duly authorised person. The information recorded shall include the:

- date of examination;
  - owner's name and address;
  - the identification and number of animals treated;
  - result of the veterinary surgeons clinical assessment;
  - trade name of the product(s) prescribed, if applicable;
  - manufacturer's batch number;
  - name and quantity of the active substance;
  - doses administered;
  - duration of treatment;
  - withdrawal period.
23. Where client, or other records, contain this information, this will be acceptable. It is not necessary to maintain additional separate records as long as the information is accessible. Veterinary surgeons may also find it helpful to include information identifying treated animals among their records. Notwithstanding the legal requirements, it is good practice for veterinary surgeons to keep records of all unauthorised and off-label treatments. Wherever possible, veterinary surgeons should explain to clients what they are doing, and why, and secure their agreement to the treatment. VMG Note 16 contains further information on record-keeping requirements.

### **LABELLING**

24. The following information should be included on labels for products administered under the cascade. If it is not feasible to include all of the information on the label due to the size of the packaging it must be included on a separate sheet.
- a) the name and address of the pharmacy, veterinary surgery or approved premises supplying the veterinary medicinal product;
  - b) the name of the veterinary surgeon who has prescribed the product;
  - c) the name and address of the animal owner;
  - d) the identification (including the species) of the animal or group of animals;
  - e) the date of supply;
  - f) the expiry date of the product, if applicable;
  - g) the name or description of the product, which should include at least the name and quantity of active ingredients;
  - h) dosage and administration instructions;
  - i) any special storage precautions;
  - j) any necessary warnings for the user, target species, administration or disposal of the product;
  - k) the withdrawal period, if relevant; and

- i) the words “Keep out of reach of children” and “For animal treatment only.”

### **VETERINARY SURGEONS FROM OTHER MEMBER STATES**

25. Veterinary surgeons practising in another Member State of the EEA but providing services in the UK may bring with them and administer small quantities of non-immunological veterinary medicinal products (VMPs) that are not authorised in the UK. However, this is subject to the following conditions:
  - the overall range and quantities brought in must not exceed those generally required for daily needs of good veterinary practice;
  - the VMPs must be authorised in the Member State in which the veterinary surgeon is established;
  - the VMPs must be transported into the UK by the veterinary surgeon in the original manufacturer’s packaging;
  - VMPs for food-producing animals must have the same composition of active substances as a UK authorised product;
  - the veterinary surgeon must be familiar with good veterinary practices applied in the UK;
  - the veterinary surgeon must ensure that withdrawal periods specified on labels are complied with unless longer periods are appropriate;
  - only sufficient VMPs to complete the course of treatment may be supplied to animal owners/keepers;
  - the veterinary surgeon must keep records of animals treated, diagnosis, products administered, dosage, duration of treatment and withdrawal periods;
  - the veterinary surgeon must make such records available to a duly authorised person in the UK for at least three years.
26. Additionally a veterinary surgeon that practices in both the United Kingdom and another Member State may hold veterinary medicinal products authorised in the other Member State provided that the amount that he holds does not exceed the amount expected to be used.

### **POSSESSION AND STORAGE OF MEDICINES FOR USE IN ACCORDANCE WITH THE CASCADE**

27. i) A veterinary surgeon may have in his possession human medicinal products intended for administration to animals under the cascade. However, he commits an offence if he has in his possession more products than is proportionate to the amount expected to be used under the cascade. We would expect these quantities to correspond with the records of receipt or supply of these products prescribed under the cascade.

ii) In the interest of animal welfare, a vet can hold an extemporaneous preparation (also known as a 'special') in stock as long as the quantity held can be justified by the clinical need under the cascade rules and even if he hasn't yet a particular animal needing the treatment. Such a product is to be used in a particular animal in accordance with the cascade and it must not to be stored in the practice for routine use.

### **SUPPLY BY A SUITABLY QUALIFIED PERSON**

28. An SQP may supply an authorised veterinary medicinal product, which falls within the scope of the qualification they hold, for use under the cascade against a valid prescription from a veterinary surgeon. Where a product is supplied by an SQP under the cascade it must still be labelled in accordance with para 23 above.

## **FURTHER GUIDANCE ON THE PRESCRIBING CASCADE**

### **SMALL ANIMAL EXEMPTION SCHEME (SAES)**

29. A veterinary surgeon may choose to use an SAES product at any time in accordance with the product's recommended use. Should the veterinary surgeon wish to use the product in a different way because in his/her professional judgement such a product could provide a safer or better option for treatment, then this would be considered to fall under the last of the cascade options.
30. For more information on the Small Animal Exemption Scheme please see Veterinary Medicines Guidance Note 14: *Marketing Authorisation Exemption Scheme for Pet Animal Medicines* or our website ([www.vmd.gov.uk](http://www.vmd.gov.uk)) under "Industry Information", then "Small Animal Exemption Scheme".

### **SUBSTANCES CONSIDERED ESSENTIAL FOR THE TREATMENT OF HORSES**

31. European Regulation (EC) No 1950/2006 establishing a list of substances considered essential for the treatment of horses was published by the European Commission and came into force on 25 December 2006. It directly applies throughout the EU and therefore in the United Kingdom. The text of the Regulation is available on our website under Product Information - Authorised Medicines – Horse Medicines.
32. Substances included in the annex of this Regulation can be administered to horses under a prescription from a veterinary surgeon where there is no suitable treatment under the cascade.
33. The person administering the substance must comply with Article 3(2) of Commission Regulation (EC) No 1950/2006 and record the details of the treatment in the animal's passport.
34. For more information on the list of essential substances please see the VMD website ([www.vmd.gov.uk](http://www.vmd.gov.uk)) under Product Information / Authorised Medicines / Horse Medicines.

### INTERPRETATION OF THE CASCADE PROVISIONS

35. Definitive interpretation of legislation can only be given by the Courts. The aims of the administration provisions are to ensure that unauthorised medicines are used only when there is no authorised product for the condition and species concerned. In the case of food-producing animals, the aims are to ensure that potentially harmful residues of veterinary medicines do not enter the food chain. It is likely that they will be interpreted in the light of how a competent and professional veterinary surgeon would reasonably act in pursuance of the aims in a particular set of circumstances. The following notes are offered as illustrative examples of the VMD's view of how the cascade provisions may be applied.

### A CONDITION AFFECTING A PARTICULAR SPECIES

36. Where a product is authorised for the treatment of the condition in the species concerned, the veterinary surgeon's first port of call should be that product. The starting point for recourse to the cascade is where there is no such authorised product in the UK. In such an event, the veterinary surgeon, in exercising his or her professional expertise and judgment in the interests of the animals concerned, may prescribe another product in accordance with the cascade provisions.
37. One such event might be where microbiological tests show that a particular strain of an organism has developed resistance to all products whose labels contain indications against it. In this situation, a veterinarian may consider that no authorised treatment exists for that condition and would, of course, wish to prescribe a treatment that will be effective. If treating food animals, he or she should work down the cascade to identify a treatment whose ingredients are authorised for food animal use. However, this constraint does not apply when treating companion animals.
38. Further examples of possible circumstances where a veterinarian might have recourse to the cascade are set out below. The list is neither exhaustive nor definitive, and each case would need to be judged on its individual merits. Most of the examples given derive from companion animal practice, since the consumer protection considerations given at paragraph 13 above mean that less flexibility exists when treating food-producing animals.
- **Dosage considerations** - Sometimes a veterinarian may consider that the effective treatment of a particular condition in a particular animal requires a different dosage from one that appears on the label of a product. In such circumstances recourse to the cascade may be appropriate and the next option would be to consider the merits of using that product at an off-label dosage (another condition in the same species) or a different authorised veterinary medicine. If neither can safely be administered at the dosage required, the veterinary surgeon should consider further options under the cascade.

- **Individual Characteristics** - If a particular animal has characteristics, such as age, general condition or known sensitivity to a particular substance, which the veterinarian judged to present unacceptable risks and to contra-indicate the use of the authorised product, he or she could conclude that no authorised product existed for that condition in that animal and consider other treatments.
- **Chronic Infections** - If a condition persists following treatment with an authorised product, the veterinarian may consider in a particular case that there is no authorised treatment for that particular condition and that further use of medicines containing similar substances is contra-indicated. In such circumstances it would be legitimate to consider alternatives in accordance with the cascade.
- **Build-up of resistance** - In relation to anthelmintics, current advice is that resistance is likely to be encouraged by the repeated use of a single product. This can be avoided, with beneficial consequences for the health and welfare of the treated animals, by the use of two or more products in rotation. If there is only a single product authorised for anthelmintic use in a particular species, the veterinarian may consider that the condition cannot be controlled using only the authorised product and use it in rotation with another product selected according to the cascade.
- **Complex conditions** - Diagnosis is a matter for the veterinary surgeon under whose care an animal or animals have been placed. Some conditions can be viewed overall and treated accordingly. For instance, pneumonia may be regarded as a single condition. On the other hand, the diagnosis may be of more than one concurrent condition, such as pneumonia with fluid retention. In such circumstances the veterinarian would need to exercise his or her professional skills to reach a diagnosis and prescribe the most effective treatment.

If he or she considered that in the circumstances there were two or more concurrent conditions, the treatment of each would need to be considered in accordance with the Regulations. However, due account of the usual factors such as drug incompatibilities or side-effects must be considered.

- **Unavailability of Products** - If a product cannot be obtained despite diligent search and in a reasonable time, the veterinary surgeon may conclude that in the circumstances it does not exist. In such circumstances the cascade should be followed to identify a suitable alternative. However, it is appreciated that there may be cases where urgency dictates that a veterinary surgeon uses whatever is to hand, whether authorised or not.

### SUSPECTED ADVERSE REACTIONS

39. In some of the above examples, a veterinarian might conclude that an authorised product does not exist in a particular case because he or she suspects a lack of

efficacy or the likelihood of unacceptable side effects. All experiences of this kind involving veterinary medicines, whether authorised or unauthorised, should be reported as suspected adverse reactions to the VMD where they are recorded and monitored. Unless such reports are received the incidence and severity of side effects, and the ongoing efficacy of products, cannot be assessed, and consequential action taken as necessary, for example, to amend product literature.

### COMPANION ANIMALS – PARTICULAR POINTS

40. The following circumstances might arise in companion animal practice:

- **Animal Owner Considerations** - If a veterinary surgeon considers that, for example, an elderly or disabled pet owner would have difficulty in crushing and administering tablets which were the only form in which an authorised product was available, it would be unlikely that action would be taken if he or she concluded that medicine in tablet form were not appropriate in the circumstances, and alternatives in line with the cascade were considered.
- **Medicines Commonly Found Around the Home** - Sometimes a veterinarian may judge there is a need to alleviate a pet's discomfort until a home visit can be made or the animal brought to the surgery. It would be unlikely that action would be taken if in such circumstances a home remedy, e.g. aspirin, were to be recommended.

### GENERIC AND NOVEL DRUGS

41. Generic medicinal products authorised for veterinary use may, of course, be used in the same way as any other authorised veterinary medicine. However, medicinal products authorised for human use, whether generics or not, may only be used in accordance with the cascade when there is no authorised veterinary product.
42. Novel medicines are authorised only following scientific evaluation designed to assess and minimise any potential risks (see paragraph 3). If a veterinary surgeon considers that there is no authorised treatment for a particular condition or species then, in order to avoid unacceptable suffering, a novel drug may be prescribed in accordance with the cascade. Where food-producing animals are concerned, the use of novel medicines remains subject to compliance with the requirements set out in paragraph 13 above.

### COST OF MEDICINES

43. EU and UK legislation on the cascade does not allow the cost of the medicine to be taken into account when deciding which medicine to use. For example, it is not permissible to use a human medicine because it is cheaper. Any use of a human medicine instead of the authorised veterinary medicine has to be justified by the veterinary surgeon on clinical grounds alone.

### FURTHER INFORMATION

44. Further information is available from the Veterinary Medicines Directorate, Woodham Lane, New Haw, Addlestone, Surrey, KT15 3LS - Tel: +44 (0)1932 336911; Fax: +44 (0)1932 336618 or E-mail: [VMGNotes@vmd.defra.gsi.gov.uk](mailto:VMGNotes@vmd.defra.gsi.gov.uk). Veterinary Medicines Guidance Notes and other information, including details of VMD contacts, are available on the VMD website ([www.vmd.gov.uk](http://www.vmd.gov.uk)).

# VETERINARY MEDICINES GUIDANCE NOTE

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