



COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

Position Paper on Availability of Veterinary Medicines agreed on 17 March 1999

Background

An issue of importance in the Veterinary Sector relates to an emerging crisis resulting from the loss of certain medicines for which a Maximum Residue Limit cannot be established for the active substances contained in them by the deadline of 1 January 2000 as laid down in Council Regulation (EEC) 2377/90 as amended. This inability to set MRLs is due to a number of reasons. In the first place, many companies did not defend certain substances contained in certain niche products that were indicated for minor uses in major species or in minor species e.g. sheep, goats, rabbits, laying hens etc. for which there was little commercial return.

In addition many applications were withdrawn by companies when they received the list of questions from CVMP after the Committee's first assessment of the application, because it was considered uneconomical to invest necessary funds to generate the requisite data for what were small volume, low sale products. The CVMP has also, regrettably, been unable to reach opinions on some substances because of the inadequacy of data provided by the applicant. Finally some substances considered unsafe to the consumer have been placed in Annex IV of Council Regulation (EEC) 2377/90.

The net result of all these developments is the loss already of some substances considered essential to the practising veterinary surgeon in the treatment of animals, or the impending loss of further medicines after the deadline for setting MRLs for old substances expires after 1 January 2000.

The problem is most acute as mentioned above for minor species. In some Member States what may be a minor species in one country may be a major species in another e.g. milk producing sheep and goats in southern European countries. It is now a reality that for certain of these species there are indications for which no medicinal product is legally available leading to illegal use of other medicines with likely consequences of concern for the human consumer.

The situation regarding the horse is also the subject of much debate. The horse is classed as a food animal in the Community but many products used in equine medicine prior to the entry into force of Regulation 2377/90 were not authorised for equine medicines or contained substances not defended to establish MRLs. Therefore, many of these products are being withdrawn from the market with, according to the Federation of Veterinarians in Europe, serious consequences for health and welfare in this species.

The CVMP in April 1998 became sufficiently concerned at the seriousness of the problem that it created an ad-hoc group under the chairmanship of Professor C. Friis, Member for Denmark, to examine ways of identifying possible solutions. One of the main problems has been to accurately identify which indications in which species will not be treatable with legally available products.

The working group in collaboration with the Veterinary Mutual Recognition Facilitation group has worked hard over the last 9 months to achieve a list of these therapeutic gaps for which substances are already unavailable or are unlikely to be available after 1 January 2000. As part of this exercise it has also become apparent that in certain Member States, some indications in minor species as well as minor indications in major species can be identified for which medicines have never been available.

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The EMEA Management Board has also been made aware of the problem due in part to some intense lobbying of certain of its members by a wide range of interested parties. At its June 1998 meeting it held a brainstorming session (rapporteur Dr Kothmann – member from Germany) and called upon the CVMP to advance its efforts as quickly as possible to find ways of addressing the problem within current legislation. In addition the Commission was requested to investigate possible measures to find solutions at a political and legal level.

The Commission representative present at the Management Board meeting agreed to consider further measures the Commission might take and some suggestions submitted by CVMP through contacts with DG III have included the following:

- Creation of an European orphan drug fund in the veterinary sector financed by the Community budget to be administered by the EMEA to support provision of additional data to enable MRLs to be established for these products which have been or might otherwise be lost. Funds are also required to fund developments of products *de novo* for minor species since the pharmaceutical industry will never invest in these types of products. The amounts involved will have to be estimated once the extent of the problem is finalised.
- Relaxation of the ‘cascade’ system under measures listed in Article 4.4 of Council Directive 81/851 (EEC) by an amendment to the Directive so that any products licensed in one Member State for any species, with an MRL established for the active ingredient in that species can be used in any other species within the same class (i.e. mammalian, piscine, avian) without an MRL being required in the new species. This could only be allowed where no other medicinal product is legally authorised.
- With the co-ordinated effort of colleagues from the EMEA/CVMP, DG VI and DG III to define means of identifying horses so that those used only in sporting and performance activities and not destined for the human food chain can be treated with products containing substances not having an MRL.
- Modification of Council Regulation (EEC) 2377/90 to grant protection to those companies which sponsored the residue evaluation of a substance, and limited in time.

With this in mind the EMEA is anxious to make progress to find ways of resolving the current difficulties but recognises that results can only be achieved if efforts are jointly undertaken with Commission services.

The Commission wishes to point out however, that solutions such as provision of an orphan drug fund, and relaxation of the ‘cascade’ would require modification of the legislation based on Article 100a of the Treaty and can therefore only be considered a solution after 31 December 1999. Therefore any solution to mitigate the situation before 1 January 2000 would have to use the tools provided by the current legislation. Any immediate action to salvage substances can only then be considered if the substances in question are used in treatments where no alternative is available.

Recommendations

The CVMP reiterates the recommendations presented at the meeting of the Management Board as outlined above.

Furthermore, the Committee has now identified the substances listed below as being indispensable to the practice of veterinary medicine as no alternatives are, or will be available for the indications concerned. The original objective was to establish what substances were considered essential from those for which MRL applications had been submitted (‘defended substances’), *inter alia* as for these some data are already available.

However, in the co-operation undertaken with Member States, it became apparent that a number of substances whilst not defended, were on the market prior to the entry into of Council Regulation (EEC) No 2377/90 and once lost due to the absence of MRLs would add to the list of therapeutic gaps in some Member States. These substances are also therefore being considered by CVMP and it is hoped that some of these may also be supported notwithstanding that any data available to set an MRL may be difficult to come by. The legal provisions to be considered to enable a reassessment of this latter group have to be further examined.

The substances and indication identified are:

1. Indication: general anaesthesia by injection
Substances:
 - Narcobarbital (pigs), Thiamylal (cattle, sheep, goats, horses, pigs), Thiopental sodium (cattle, goats, horses, pigs, rabbits, birds), Pentobarbital sodium (horses)¹;
 - Etorphine/Diprenophine (cattle)¹
2. Indication: sedation and premedication of narcosis
Substances: Propionylpromazine (cattle, horses, pigs), Acepromazine (cattle, sheep, goats, horses, pigs)
3. Indication: sedation
Substances: Metomidate (pigs)¹
4. Indication: anxiolysis, tranquilisation
Substance: Diazepam (cattle, sheep, goats, horses, donkeys, pigs, poultry and game birds)¹
5. Indication: Antagonism of α_2 -adrenergic effects
Substance: Yohimbine (cattle, deer)¹

It should be noted that this list is considered as a draft and can possibly only be finalised once the procedure of all MRL applications for old substances have been closed, i.e. the responses to the lists of questions have been submitted by the applicants and were assessed by the CVMP.

It is intended that during the remaining months in 1999 every effort will be made by the CVMP to obtain further data possibly available in the public domain or within institutions outside the EU, which have not been included in the dossier or the assessment in order to set MRLs. If such efforts are unsuccessful it is proposed that these substances be considered as orphan substances and consideration given to seeking available funds to undertake the outstanding studies so that MRLs can be established.

The CVMP also identified a therapeutic gap in respect to trichomoniasis in cattle and birds, as well as histomoniasis in turkeys, for which the nitroimidazoles Dimetridazole, Ronidazole and Metronidazole were previously used. However, due to safety concerns, these substances have been included in Annex IV of Regulation 2377/90.

Enclosed are the lists of substances which served as working documents for the CVMP in its attempts to identify those products which are indispensable in veterinary medicine today (Annexes 1 to 2 to this document).

The CVMP also noted particular the issue of availability of veterinary medicines in a wider context considering those indications in certain species, notably minor ones, where a therapeutic gap exists, irrespective of their MRL or authorisation status. Among the issues to be considered are:

¹ Not defended

- a) Problems of emerging resistance to antibacterials and anti-parasitic substances where there are few authorised medicines available.
- b) Problems of new diseases or diseases which may re-emerge due to changes in animal husbandry, welfare needs and the recent ban on feed-additives.
- c) Problems of small market size in some member states even where MRL issues are not of concern.
- d) Article 4 of Council Directive 81/851/EEC refers to the exceptional application of the 'cascade' principle in one animal or in a small number of animals only. The provision should not routinely be given as the solution to the availability of authorised medicines for the minor species, where large numbers of animals/birds or fish may need treatment and where the stated minimum withdrawal period is not adequate or appropriate.

A draft list of such substances in relation to minor species and minor indications for major species, which were identified by the VMRFG, containing substances which had never been authorised as veterinary medicines is attached to illustrate the additional shortage of medicines which have become apparent in Member States (Annex 3). However, no recommendations in respect of whether alternatives exist or how therapeutic gaps in certain Member States could be addressed, can be presented currently. The review of this list will be undertaken at a later stage.



Substances, which are no longer available as veterinary medicines

Substances considered under Article 7 of Regulation 2377/90 (defended substances)

(MRL applications withdrawn, no recommendation for inclusion in Annex I, II or III possible, included in Annex IV)

Substances	Indication	Species ²	MRL Status	Examples for alternatives	MRL Status for these alternatives ³
Antibacterials and antiprotozoals					
Chloramphenicol	Treatment of bacterial infections (against broad-spectrum of bacteria)	Cattle (calves), pigs, poultry	Annex IV	Thiamphenicol Florfenicol Amoxicillin	Annex I bovine, chicken Annex I bovine Annex I all food producing species
Dapsone	Coccidiosis Treatment of mastitis and endometritis	Cattle	Annex IV	Sulfonamides There are several drugs available against mastitis and endometritis	Annex I all food producing species
Spiramycin	Treatment of mycoplasmal infections Treatment of bacterial infections	Pigs	No rec.	Tylosin Tiamulin Valnemulin Lincomycin Josamycin Erythromycin Tetracycline There are several antibiotics available against bacterial infections in pigs	Annex I porcine <i>List of questions</i> Annex I porcine <i>Annex III porcine</i> <i>Annex III porcine</i> Annex III porcine Annex I all food producing species
Furazolidone	Coccidiosis	Cattle Poultry	Annex IV	(see Dapsone) Amprolium Toltrazuril Sulfonamides	<i>List of questions (chicken, turkey)</i> Annex I chicken, turkey Annex I all food producing species

² Species, for which MRL application was made; also species for which products are authorised in the EU, as far as information available and included in Summary Report

³ CVMP recommendations not yet published in the OJ are written in *italics*

Substances	Indication	Species ²	MRL Status	Examples for alternatives	MRL Status for these alternatives ³
Furazolidone (cont.)	Treatment of bacterial infections (against Gram positive and Gram negative bacteria)	Pigs Rabbits Fish		Sulfonamides (sulphaquinoxaline) Sulfonamides (sulphaquinoxaline) Sarafloxacin Flumequine	Annex I all food producing species Annex I all food producing species Annex I salmonidae Annex I salmonidae
Nitrofurans (except Furazolidone)	Treatment of bacterial infections (against Gram positive and Gram negative bacteria) Treatment of protozoal diseases	All food producing species	Annex IV	There are several drugs available against infection of Gram positive and Gram negative bacteria Imidocarb Toltrazuril	<i>Annex III ovine, bovine</i> Annex I chicken, turkey
Dimetridazole	Histomoniasis Trichomoniasis Genital trichomoniasis Haemorrhagic enteritis	Turkeys Pigeons Cattle Pigs	Annex IV	No alternatives	
Metronidazole	Dysentery (<i>Serpulina hyodysenteriae</i>), Retentio secundarium (in combination with neomycin)	Pigs Cattle	Annex IV	Tiamulin Lincomycin Valnemulin No alternatives	<i>List of questions (porcine)</i> <i>Annex III porcine</i> Annex III porcine
Ronidazole	Histomoniasis, Trichomoniasis, Genital trichomoniasis, Dysentery	Turkeys Pigeons Cattle Pigs	Annex IV	No alternatives (see Metronidazole)	

Antimycotics					
Nystatin	Treatment of ringworm	Cattle, horses	Withdrawn	Natamycin (for topical use only) Enilconazole (for topical use only)	Annex II bovine, equidae <i>Annex II bovine, equidae</i>
	Treatment of candidiasis	Poultry		Not of importance	
Anthelmintics					
Thiophanate	Treatment of helminthoses	Cattle, sheep, goats, pigs	Withdrawn	Febantel Fenbendazole Albendazole Levamisole	Annex I bovine, equidae, ovine, porcine Annex I bovine, equidae, ovine, porcine Annex I bovine, ovine Annex I bovine, ovine, porcine, poultry
Bithionol sulfoxide	Treatment of helminthoses (against adult <i>Fasciola hepatica</i> and <i>Paramphistomum spp</i>)	Cattle, sheep	Withdrawn	Closantel Oxyclosanide + levamisole Triclabendazole Nitroxinil	Annex I bovine, ovine Annex III bovine, ovine; Annex I bovine, ovine, porcine, poultry Annex I bovine, ovine <i>Annex I bovine, ovine</i>
Niclosamide	Treatment of helminthoses	Sheep	Withdrawn	Praziquantel (as niclosamide also praziquantel is effective against <i>Taenia</i> and <i>Echinococcus</i>)	Annex II equidae, ovine
		Chicken		Not relevant for chicken; due to modern husbandry practice disease very rare	
Antiparasitics					
Bromopropylate	Diagnosis and treatment of acariasis (<i>Varroa jacobsoni</i> , <i>Acarapis woodi</i>)	Honey bees	Withdrawn	Flumethrin Tau fluvalinate Amitraz Cymiazole Coumaphos	Annex II honey bees Annex II honey bees Annex III bees Annex III honey bees Annex III honey bees
Heptenophos	Treatment of infestations by mange mites	Cattle, horses, pigs, laying hens	Withdrawn	Flumethrin Cyfluthrin Phoxim Moxidectin Ivermectin	Annex I bovine Annex III bovine <i>Annex III porcine</i> Annex I bovine, Annex III equidae Annex I bovine, porcine, equidae

Heptenophos (cont.)				Abamectin Doramectin Eprinomectin Amitraz Metrifonate Cypermethrin	Annex I bovine Annex I bovine, porcine Annex I bovine Annex I bovine, porcine <i>List of questions (cattle, horses)</i> Annex III bovine, ovine, caprine, chicken <i>List of questions (eggs)</i>
2-Ethyl-1,3-hexanediol	Mastitis prevention	Cattle	No rec.	There are several disinfectants available	
	Insect repellent	Cattle, horses		Polyethylene glycol-7-glyceryl cocoate	Annex II all food producing species
Agents acting on the autonomic nervous system					
Ephedrine	Treatment of respiratory and cardiac disorders	Cattle, sheep, goats, horses, pigs	No rec.	Epinephrine (as cardiac analeptic) Doxapram (as respiratory analeptic)	Annex II all food producing species <i>Annex II all mammalian food producing species</i>
Camylofine	Treatment of visceral spasms	Cattle, sheep, horses, pigs	Withdrawn	Atropine	<i>Annex II all food producing species</i>
Agents acting on the central nervous system					
Chloral hydrate	General anaesthesia	Cattle, horses, pigs	Withdrawn	Ketamine in combination with Xylazine	Annex II all food producing mammalian species; <i>List of questions</i>
Narcobarbital	General anaesthesia	Pigs	Withdrawn	No alternatives	
Thiopental sodium	General anaesthesia	Cattle, pigs, horses, goats, rabbits, birds	Withdrawn	No alternatives	
Thiamylal	General anaesthesia	Horses, cattle, pigs, sheep, goats	No rec.	No alternatives	
Chloroform	General anaesthesia	No information	Annex IV	Not of importance Isoflurane	Annex II equidae
Pentoxyverine	Treatment of cough	Horse	No rec.	Butorphanol (different mode of action)	Annex II Equidae
Propionylpromazine	Sedation and premedication of narcosis	Cattle, horses, pigs	Withdrawn	No alternatives	
Chlorpromazine	Sedation	Cattle, sheep, goats, horses, pigs	Annex IV	No alternatives	

Dextrometorphan hydrobromide	Treatment of cough	Cattle, sheep, goats, horses, pigs	Withdrawn	Not of importance	
Ammonium phthalamate	Treatment of acute respiratory disorders of new-born calves	Calves	Withdrawn	Doxapram Prethcamide	<i>Annex II all mammalian food producing species</i> Annex II all food producing mammalian species
Pentetrazol	Treatment of acute respiratory disorders of new-born animals	Cattle, horses, pigs sheep	Withdrawn	Doxapram Prethcamide	<i>Annex II all mammalian food producing species</i> Annex II all food producing mammalian species
Opium tincture	Treatment of diarrhoea	Cattle	No rec.	Bismuth compounds	Annex II all food producing species
Agents acting on the reproductive system					
Testosterone	Androgen therapy	Cattle, horses, pigs	Withdrawn	Not of importance	
Fenprostalene (prostaglandin and analogues)	Synchronisation of oestrus, reproductive disorders associated with persistent corpus luteum, termination of unwanted pregnancies (cattle), induction of parturition (cattle, pigs)	Cattle, pigs	Withdrawn	Dinoprost Dinoprost tromethamine Cloprostenol R-Cloprostenol Tiaprost Etiproston tromethamine Luprostiol	Annex II all mammalian species Annex II all mammalian species Annex II bovine, porcine, equidae Annex II bovine, porcine, equidae <i>Annex II bovine, porcine, ovine, equidae</i> Annex II bovine, porcine Annex II all mammalian species
Aristolochia spp. and preparations thereof	Regulation of sexual functions, immunostimulation, antiphlogistic effects and other indications.	Cattle, sheep, goats, horses, pigs	Annex IV	Alternatives are available	

Antiinflammatory agents					
Methylprednisolone	Treatment of inflammations of the musculo-skeletal system, in combination with antibiotics: respiratory diseases, urogenital infections	Cattle, horses, pigs	Withdrawn	Prednisolone Dexamethasone Betamethasone Flumethasone	List of questions (cattle, pigs, horses, goats and sheep) Annex I bovine, porcine, equidae <i>List of questions</i> (horses, cattle, sheep, goats, pigs and turkeys) <i>List of questions</i> (cattle, horses, pigs, sheep and goats)
Phenylbutazone	Treatment of inflammatory conditions of the musculoskeletal/ locomotor system	Cattle, horses, pigs	No rec.	Vedaprofen Flunixin Meclofenamic acid Tolfenamic acid Acetylsalicylic acid Ketoprofen Meloxicam Diclofenac	Annex I equidae <i>List of questions</i> (horses, cattle, pigs) <i>List of questions</i> (horses, cattle) Annex I bovine, porcine <i>List of questions</i> (horses, cattle, pigs, poultry) Annex II bovine, equidae, porcine Annex III bovine <i>List of questions</i> (horses, cattle, pigs)
Suxibuzone	Treatment of inflammatory conditions of the musculoskeletal/ locomotor system	Cattle, sheep, pigs, horses	No rec.	See phenylbutazone	
Ramifenazone	Treatment of inflammatory conditions of the musculoskeletal/ locomotor system	Horses, cattle, pigs	No rec.	See phenylbutazone	
Phenazone	Excipient in a product against trypanosomiasis and babesiosis Treatment of inflammatory conditions	Cattle, sheep Cattle, sheep, horses, pigs	No rec.	Not relevant See phenylbutazone	
Populeum ointment	Local treatment of inflammations	Cattle, sheep, goats, horses, pigs	No rec.	Several parenteral drugs and herbal remedies for topical application are available	

Agents acting on the gastrointestinal system					
Benzonaphthol	Treatment of diarrhoea	Cattle, sheep, goats, horses, pigs	Withdrawn	Not relevant (not used)	
Clanobutin	Indigestion, atony, insufficient food consumption, obstipation and protective therapy for the liver	Cattle, sheep, goats, pigs	Withdrawn	Menbutone (different mode of action)	Annex II bovine, ovine, caprine, porcine, equidae
Chelidonii herba	Treatment of digestive disorders, disturbances of intestinal microflora, chronic gastritis, enteritis, coprophagy, metabolic disorders, lack of appetite	Cattle (except lactating cows), horses, pigs	No rec.	Lini oleum Quercus cortex Sodium 2-methyl-2-phenoxy-propanoate Tanninum	Annex II all food producing species Annex II all food producing species Annex II bovine, porcine, caprine, equidae Annex II all food producing species
Halquinol	Treatment of diarrhoea (microbial origin)	Pigs, poultry	Withdrawn	Flumequine	Annex III bovine, ovine, porcine, chicken
Topical agents					
Benzyl nicotinate	Local treatment of inflammatory conditions (rubifacient)	No information	Withdrawn	Not of importance	
Benzylideneacetone	Treatment of respiratory, vascular and rheumatoid disorders	Cattle, horses	No rec.	Not of importance	
Colchicine	Treatment of papillomas and warts	Cattle, horses	Annex IV	Concentrated lactic acid Other alternative therapies are auto-vaccination and cryosurgery	Annex II all food producing species
Copper naphthenate	Treatment of foot rot Treatment of ringworm	Cattle, sheep	Withdrawn	Copper sulphate Peracetic acid Natamycin (for topical use only) Enilconazole (for topical use only)	Annex II all food producing species Annex II all food producing species Annex II bovine, equidae Annex II bovine, equidae
Polyhexanide	Disinfectant for prevention of teats infection	Cattle	Withdrawn	Sodium chlorite Sodium dichloroisocyanurate Chlorhexidine Iodophors	Annex II bovine Annex II bovine, ovine, caprine Annex II all food producing species Annex II all food producing species

Miscellaneous					
Diethylamine copper oxyquinolone sulphate (cuproxoline)	Treatment of copper insufficiency	Cattle, sheep	Withdrawn	Copper sulphate Copper oxide Copper heptonate	Annex II all food producing species Annex II all food producing species Annex II all food producing species
Metesculetol sodium (Permethol)	Vascular diseases	Horses	No Rec.	Hesperidin Hesperidin methyl chalcone	Annex II equidae Annex II equidae
Extraxtum pini	Secretolytic for treatment of bronchitis	Cattle, sheep, horses, pigs,		Bromhexine Dembrexine	<i>Annex II bovine, porcine, poultry</i> Annex II equidae

Excipients					
Glycofurol	Excipient used in injectable solutions	Cattle, pigs	Withdrawn	Excipients not considered at present	
Polyethylene terephthalates	Excipient	No information	Withdrawn	Excipients not considered at present	



**Substances, which are not available as veterinary medicines,
 and where no MRL application has been made (non-defended substances)**

Substances previously authorised as veterinary medicines in at least one EU Member State

Substances	Indication	Species ⁴	Examples for alternatives	MRL Status for these alternatives ⁵
Anti-infectious agents				
Nalidixic acid	Treatment of urinary tract infections and septicaemia.	Cattle, pig, chicken, turkey, rabbit,	Enrofloxacin Danofloxacin Broad spectrum penicillins: Amoxicillin	Annex I bovine, porcine, poultry, rabbits <i>Annex III porcine</i> Annex I all food producing species
2-Hydroxy-propyl-tri-ammonium iodide	Treatment of actinomycosis	Cattle, sheep	Penicillins	Annex I All food producing species
Antimycotics				
Griseofulvin	Treatment of fungal diseases, treatment of dermatophytoses	Cattle, horse	Natamycin (for topical use only) Enilconazole (for topical use only)	Annex II bovine, equidae Annex II bovine, equidae
Antiparasitic agents				
Pyrimethamine	Treatment of coccidiosis and bacterial infections.	Rabbit	Sulfonamides (sulphaquinoxaline)	Annex I all food producing species, but only used in combination products with Diaminopyrimidines/Trimethoprim
Agents acting on the central nervous system				
Diazepam	Anxiety related behavioural problems and animal aggressiveness. Treatment of convulsions in hypoxic neonatal animals.	Cattle, sheep, goat, horse, donkey, pig, poultry	No alternatives (Alternatives with other mode of action, e.g. barbiturates, but no MRL)	

⁴ Species, indicated by Member States

⁵ CVMP recommendations not yet published in the OJ are written in *italics*

Substances	Indication	Species ⁴	Examples for alternatives	MRL Status for these alternatives ⁵
Fluanisone + fentanyl	Neuroleptanalgesia	Rabbit	Only used for pets and laboratory animals, i.e. not relevant for food producing animals	
Halothane	Inhalation anaesthetic for general anaesthesia	Cattle, sheep, goat, horse, donkey, pig,	Isoflurane Xylazine (different application route) Comment: as far as known halothane is used only for horses, companion animals and laboratory animals. Not used as anaesthesia for pigs.	Annex II equidae <i>list of questions</i>
Metomidate	Sedation	Pig	No alternatives (Alternatives with other mode of action, e.g. barbiturates, but no MRL)	
Nikethamide	Respiratory stimulant for treatment of acute respiratory disorders	Cattle, horse, donkey, pig	Doxapram Prethcamide	<i>Annex II all mammalian food producing species</i> Annex II all food producing mammalian species
Pentobarbital sodium	General anaesthesia	Horse	No alternatives	
Pethidine	Analgesia	Horse, donkey	Butorphanol	<i>Annex II equidae</i>
Agents acting on the autonomic nervous system				
Adiphenine hydrochloride	Parasympatholytic for treatment of colics and spasmodic syndromes	Cattle, sheep, goat, horse, donkey, pig	Atropine Atropa belladonna Butylscopolaminium bromide	<i>Annex II all food producing species</i> <i>Annex II all food producing species</i> Annex II all food producing species
Carbachol	Parasympathomimetic for treatment of atony of gastrointestinal tract, urinary bladder and uterus. Treatment of ruminal atony and impaction.	Cattle, horse, donkey, pig	Neostigmine	Annex II All food producing species
Prifinium bromide	Parasympatholytic for treatment of gastro-intestinal and urinal tract spasms.	Cattle, horse, donkey	Atropine Atropa belladonna Butylscopolaminium bromide	<i>Annex II all food producing species</i> <i>Annex II all food producing species</i> Annex II all food producing species

Substances	Indication	Species ⁶	Examples for alternatives	MRL Status for these alternatives ⁷
Sinefrene	Treatment of shock, cardiac syncope and anaphylactic emergencies.	Cattle, pig	Epinephrine Ergometrine maleate Extractum secalis cornuti fluidem	Annex II all food producing species <i>List of questions</i> <i>List of questions (horses, cattle, pigs, sheep and goats)</i>
Yohimbine	Reversal of effects of α_2 - antagonist, e.g. Xylazine	Cattle, deer	No alternatives	
Etorphine	Neuroleptanalgesia	Cattle	No alternatives	
Miscellaneous				
Aminopromazine	Spasmolytic for treatment of gastro-intestinal, bronchial and genito-urinary tract spasms.	Cattle, sheep, horse, donkey, pig	Isoxsuprine Butylscopolaminium bromide Clenbuterol According to the indications there are several drugs available	Annex II bovine, equidae Annex II all food producing species Annex III bovine, equidae

⁶ Species, indicated by Member States

⁷ CVMP recommendations not yet published in the OJ are written in *italics*



**Substances, which are not available as veterinary medicines,
and where no MRL application has been made (non-defended substances)**

Substances never authorised as veterinary medicines in the EU

Substances	Indication	Species
Anti-infectious agents		
Acyclovir	Antiviral agents	Horse, donkey
Gramicidine	Antibacterial	Cattle, sheep, goat, horse, donkey, pig
Olaquinox	Antibacterial	Rabbit
Rifampin (rifampicin)	Antibacterial	Horse, donkey
Antimycotic agents		
Itraconazole	Antifungal	Chicken, turkey, duck, geese, pigeon, rabbit
Antiparasitic agents		
Iprnidazole	Antiprotozoal, antimicrobial (dermatomycosis)	Rabbit
Malachitegreen	Antiparasitic, antifungal	Fish
Potassium permanganate	Antiseptic, antimycotic, antiparasitic	Fish
Quinuronium	Babesiosis (red water)	Cattle, sheep
Agents acting on the central nervous system		
Atipamezole	Sedative	Horse
Climazolam	Tranquilizer	Horse
Codeine phosphate	Narcotic analgesic; antitussive	Horse, donkey
Methocarbamol	Muscle relaxant, Ty-ing up syndrome	Horse, donkey
Morphine	Narcotic analgesic, preanaesthetic, antitussive, antiperistaltic	Horse, donkey
Nitrous oxide	Anaesthetic (inhalation); analgesic	Cattle, sheep, goat, horse, donkey, pig
Propofol	General anaesthetic	Horse, donkey
Sevoflurane	Anaesthetic	Horse
Tiletamine	General anaesthetic	Horse
Tiletamine + zolazepam	General anaesthetic	Pig
Agents acting on the autonomic nervous system		
Atracurium (Atracurium besylate)	Muscle relaxant	Horse
Dopamine	Cardiotonic; antihypotensive (arythmias cardiac, stimulant)	Horse, donkey
Edrophonium (edrophonium chloride)	Cholinergic; muscle relaxant	Horse

Glycopyrrolate	Anticholinergic (bronchodilator)	Cattle, horse, donkey
Idazoxan	Adrenergic α -antagonist	Cattle, sheep, goat
Pancuronium bromide	Muscle relaxant	Horse, donkey
Salbutamol	Sympathomimetic (for asthma)	Horse, donkey
Scopolamine	Parasympatholytic, spasmolytic	Horse, donkey
Tolazoline	Anti-adrenergic	Cattle, sheep, goat
Tropicamide	Anticholinergic (eye mydriasis)	Horse, donkey
Vecuronium bromide	Muscle relaxant	Horse
<u>Local anaesthetics</u>		
Bupivacaine (anecaine, marcaine)	Local anaesthetic	Horse, donkey
Oxybucaine (oxibucaina)	Local anaesthetic	Cattle, sheep, goat, horse, donkey, pig
<u>Antihistaminic agents</u>		
Tripelennamine hydrochloride	Antihistaminic, analeptic	Cattle
<u>Cardiotropic agents</u>		
Digitalis	Cardiotonic	Horse
Digoxin	Cardiotonic (neonatal dyspnea cardiac conditions)	Cattle, sheep, goat, horse, donkey
Dobutamine	Cardiotonic, β_2 -agonist (cardiac stimulant, arhythmias)	Horse, donkey
Quinidine sulphate	Cardiac depressant (anti-arrhythmic)	Horse, donkey
<u>Corticoids</u>		
Triamcinolone	Adrenocortical steroid; anti-inflammatory glyocorticoid (arthritis)	Horse, donkey
<i>Agents acting on the gastrointestinal system</i>		
Cimetidine	Antiulcerative (gastric ulcers)	Horse, donkey
Metoclopramide	Anti-emetic (narcotic antagonist)	Horse, donkey
Ranitidine	Antiulcerative	Horse, donkey
<u>Topical agents</u>		
Fluorescein	Diagnostic aid (diagnosis of corneal ulcers)	Horse, donkey
Phenoxyethanol (2-phenoxyethanol)	Topical antiseptic	Fish (salmon)
<i>Miscellaneous</i>		
Dantrolene	Muscle relaxant (myositis)	Horse, donkey
Iron cacodylate	Anemia	Horse, donkey