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## ANNEX

### Groups of substances

#### I. Anaesthetics

Active substance <sup>1</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
Oxybuprocaine <sup>a</sup>	Local topical anaesthesia for use in eyes	None identified	Wide clinical experience
Prilocaine <sup>b</sup>	Local topical anaesthesia prior to intravenous injection or catheterisation	Lidocaine	In specific preparations (eutectic mixture of local anaesthetics), for topical application to skin; can be used to facilitate intravenous injection or catheterisation

#### II. Analgesics

Active substance <sup>1</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
Bromfenac <sup>b</sup>	Treatment of uveitis and ocular inflammation	Systemic nonsteroidal anti-inflammatory drugs (NSAIDs) (e.g. flunixin); topical (ocular) ketorolac	Topical NSAIDs may result in less patient discomfort, reduced postoperative inflammation, prevention of miosis, and improvements in visual acuity in the early postoperative period
Fentanyl <sup>b</sup>	Multimodal approach for moderate to severe acute painful conditions	Butorphanol, morphine	Produces better analgesia than certain other opioids and can be used for very painful conditions; recognized value for use in

<sup>1</sup> Active substances identified with an “a” are essential substances for which there is no satisfactory alternative treatment. Substances identified with a “b” are substances that bring added clinical benefit compared to other treatment options.

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Active substance <sup>1</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
			multi-modal approaches
Ketorolac <sup>b</sup>	Treatment of eye pain and inflammation	Systemic NSAID therapy (e.g. flunixin)	Formulated for local application
Methocarbamol <sup>b</sup>	As part of treatment protocols in severe painful muscle spasms/muscle inflammation conditions	Systemic NSAIDs (e.g. flunixin)	Potent skeletal muscle relaxation; specific action on the internuncial neurons of the spinal cord to reduce acute skeletal muscle spasms without a concomitant alteration in muscle tone
Morphine <sup>b</sup>	Analgesia	Butorphanol, fentanyl	More potent than other analgesics
Triamcinolone acetonide <sup>b</sup>	Treatment of joint inflammation	Methylprednisolone	Less harmful effects on cartilage metabolism

### III. Antimicrobials

Active substance <sup>1</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
<b>I. Antibiotics</b>			
Amikacin <sup>b</sup>	Treatment of septicemia in horses and foals	Gentamicin, ceftiofur	Better safety profile in the target animal
Azithromycin <sup>b</sup>	Treatment of <i>Rhodococcus equi</i> infections susceptible to azithromycin	Clarithromycin, erythromycin, gamithromycin, tulathromycin, doxycycline	Added clinical benefit in cases of <i>Rhodococcus equi</i> infections in foals that can be resolved as monotherapy or in combination with doxycycline only
Clarithromycin <sup>b</sup>	Treatment of <i>Rhodococcus equi</i> infections susceptible to clarithromycin	Azithromycin, erythromycin, gamithromycin, tulathromycin, doxycycline	More active against <i>Rhodococcus equi</i> in vitro than erythromycin or azithromycin; achieves greater concentrations in

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Active substance <sup>1</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
			pulmonary epithelial lining fluid and alveolar macrophages than either erythromycin or azithromycin, though the half-life is shorter
Fusidic acid <sup>b</sup>	Topical treatment of eye infections caused by gram-positive bacteria susceptible to fusidic acid	Ofloxacin, moxifloxacin	Broad spectrum for treatment of gram-positive infections; primary choice in superficial, uncomplicated corneal ulcers and acute conjunctivitis in horses
Moxifloxacin <sup>b</sup>	Topical treatment of external eye infections caused by gram-positive cocci, gram-negative, atypical and anaerobic bacteria such as <i>Pseudomonas aeruginosa</i> species susceptible to moxifloxacin	Ofloxacin	Advantageous pharmacokinetic profile; spectrum of activity includes gram-positive cocci and anaerobic bacteria that may be resistant to other quinolones
Ofloxacin <sup>b</sup>	Treatment of external eye infections caused by gram-positive and gram-negative micro-organisms susceptible to ofloxacin	Moxifloxacin	Clinical experience; penetrates the entire cornea up to the anterior chamber of the eye
Polymyxin B <sup>b</sup>	Treatment of bacterial keratitis, topical use	Ofloxacin, moxifloxacin	Effective alternative to systemic treatments; different mechanism of action to other topical alternatives
<b>II. Antifungals</b>			
Amphotericin B <sup>a</sup>	Treatment of	None identified	Treatment of choice

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Active substance <sup>1</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
	fungal pneumonia, systemic use		
Miconazole <sup>b</sup>	Treatment of fungal infection of the eye	Natamycin, nystatin, voriconazole	Broad spectrum of activity; less irritant compared to other topical antifungals
Nystatin <sup>b</sup>	Treatment of fungal and yeast infections of the eye and genital tract	Miconazole	Treatment of choice for yeast infections
Voriconazole <sup>b</sup>	Treatment of fungal keratitis, topical use	Miconazole	Broad spectrum of activity
<b>III. Antivirals</b>			
Aciclovir <sup>b</sup>	Treatment of cases of equine herpes virus infection associated with complications, topical use only	Ganciclovir	Treatment of choice for ocular ulcers when the implication of a viral pathogen is suspected
Ganciclovir <sup>b</sup>	Treatment of cases of equine herpes virus infection associated with complications, topical use	Aciclovir, valaciclovir	Wealth of evidence for the treatment of different virus-types causing herpetic infections
Valaciclovir <sup>b</sup>	Treatment of cases of equine herpes virus infections, oral use	Aciclovir	Better pharmacokinetic profile and a different route of administration

#### IV. Substances for respiratory disorders

Active substance <sup>1</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
Ambroxol <sup>b</sup>	Stimulation of surfactant in	Steroids, bromhexine,	Preferred clinical choice for premature foal

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Active substance <sup>1</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
	premature foals	dembrexine, surfactant transfer from healthy donor	
Fluticasone <sup>b</sup>	Control of allergic pulmonary disease including mild to moderate cases of equine asthma and subtypes via inhalation	Beclomethasone	Inhalation leads to less adreno-cortical suppression, quicker rebound after therapy ends and fewer systemic side effects than systemic corticosteroid therapy because of its limited systemic absorption; especially indicated for control of mild-moderate and refractory severe asthma as well as long-term maintenance therapy
Ipratropium bromide <sup>b</sup>	As a bronchodilator in horses with mild-moderate asthma	Clenbuterol	Anticholinergic action, as an alternative to beta-agonists
Oxymetazoline <sup>b</sup>	Treatment of nasal oedema	Phenylephrine	Alpha-adrenoceptor agonist with strong vasoconstrictive properties and longer acting effect
Phenylephrine <sup>b</sup>	Treatment of nasal oedema	Oxymetazoline	Reduces the need for insertion of nasal tubes during recovery

#### V. Substances for cardiology

Active substance <sup>1</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
Amiodarone <sup>b</sup>	Systemic and oral treatment of atrial fibrillation, supraventricular and ventricular tachycardias	Quinidine sulphate/gluconate, sotalol, verapamil	Different mode of action: class III anti-dysrhythmic

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Active substance <sup>1</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
Propafenone <sup>b</sup>	Treatment of ventricular tachycardia and tachyarrhythmia	Quinidine sulphate/gluconate	Different mode of action: sodium channel antagonist that decreases heart excitability
Quinapril <sup>b</sup>	Treatment of heart failure; cardiovascular protection in horses with atrial fibrillation (AF) or mitral regurgitation (MR)	None identified	Different mode of action: angiotensin-converting-enzyme (ACE) inhibitor
Quinidine sulphate/gluconate <sup>b</sup>	Treatment of cardiac arrhythmias	Amiodarone, sotalol, verapamil	Treatment of choice for atrial fibrillation
Sotalol <sup>b</sup>	Long-term treatment of cardiac arrhythmias	Amiodarone, quinidine sulphate/gluconate	More suitable in horses requiring long-term anti-arrhythmic therapy; less adverse events than amiodarone
Verapamil <sup>b</sup>	Treatment of supraventricular arrhythmias	Amiodarone, quinidine sulphate/gluconate, sotalol	Different mode of action: calcium channel blocker

## VI. Substances for diagnostic procedures

Active substance <sup>1</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
Barium sulfate <sup>a</sup>	Enhanced gastrointestinal tract visualization during radiographic examinations	None identified	No satisfactory alternative treatment for enhanced gastrointestinal tract visualisation during radiographic examinations
Fluorescein <sup>b</sup>	Diagnosing corneal keratitis or ulceration, topical	Rose bengal	Diagnostic tool of choice when a viral culture is needed afterwards

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Active substance <sup>1</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
	use		
Iohexol <sup>a</sup>	Contrast agent for lower urinary tract radiography, arthrography, myelography, sino- or fistulography and dacryocystography	None identified	Non-ionic, water-soluble contrast agent
Phenylephrine <sup>a</sup>	Diagnosing grass sickness	None identified	Ancillary diagnostic approach to equine grass sickness polyneuropathy
Rose bengal <sup>b</sup>	Diagnosing corneal keratitis or ulceration, topical use	Fluorescein	Diagnostic tool of choice for diagnosing eye keratitis/ulcers
Thyrotropin releasing hormone <sup>a</sup>	Diagnosing pituitary pars intermedia dysfunction	None identified	No satisfactory alternatives for diagnosing pituitary pars intermedia dysfunction

## VII. Substances for gastrointestinal disorders

Active substance <sup>1</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
Metoclopramide <sup>b</sup>	Treatment of post-operative ileus	Intravenous fluid substitution, painkillers (e.g. flunixin), lidocaine	Prokinetic drug
Misoprostol <sup>b</sup>	Treatment of gastric glandular disease and colitis	Omeprazole, sucralfate	Superior to omeprazole for the treatment of equine gastric glandular disease
Phenylephrine <sup>b</sup>	Treatment of splenic entrapment	Atropine	Clinical value in the resolution of splenic entrapment; causes a dose-dependent splenic contraction

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Active substance <sup>1</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
Ranitidine <sup>b</sup>	Treatment of gastric ulcers in critically ill neonates, intravenous use	Omeprazole	The intravenous route of administration brings added clinical benefit over other oral antiulcer medications
Sucralfate <sup>b</sup>	Treatment and prevention of gastric ulcers in horses	Omeprazole	Different mode of action than omeprazole (mucosal adherent), which provides physical lesion stabilisation

#### VIII. Substances for metabolic disorders

Active substance <sup>1</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
Insulin <sup>b</sup>	As an aid in the treatment of hyperlipidaemia unresponsive to glucose therapy or severe hyperlipidaemia, used in combination with glucose and other therapies  Diagnosing metabolic disorders (e.g. insulin resistance associated with equine metabolic syndrome or pituitary pars intermedia dysfunction)	Low-molecular weight heparin can be used for cases of hyperlipidaemia	Insulin is the preferred clinical choice

#### IX. Substances for musculoskeletal disorders

Active substance <sup>1</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
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<b>Active substance<sup>1</sup></b>	<b>Indication(s):</b>	<b>Identification of alternatives:</b>	<b>Explanation of use / specific advantages:</b>
Atracurium <sup>b</sup>	Inducing muscle paralysis under general anaesthesia	Cisatracurium, guaifenesin	Brings added clinical benefit in horses under general anaesthesia in cases where increased muscle relaxation is necessary such as ophthalmic surgeries, certain orthopaedic repairs and when deep access to the abdominal cavity is needed.
Cisatracurium <sup>b</sup>	Inducing muscle paralysis under general anaesthesia	Atracurium, guaifenesin	Brings added clinical benefit in horses under general anaesthesia in cases where increased muscle relaxation is necessary such as ophthalmic surgeries, certain orthopaedic repairs and when deep access to the abdominal cavity is needed.
Dantrolene sodium <sup>b</sup>	Prevention of rhabdomyolysis Prevention of malignant hyperthermia during anaesthesia	NSAIDs, intravenous fluids, vitamin E/selenium	Efficacious as preventative, inhibiting the release of calcium from the sarcoplasmic reticulum and thus causing dissociation of excitation-contraction coupling
Edrophonium <sup>a</sup>	Reversing the effects of atracurium muscle paralysis	None identified	Cholinesterase inhibitor, essential for reversal of neuromuscular blockade; least side effects of the cholinesterase inhibitors in horses
Guaifenesin <sup>b</sup>	Induction and maintenance of general anaesthesia in field conditions	Atracurium, cisatracurium	Particularly indicated in field (non-hospital) conditions where anaesthesia may be necessary; the reduced cardiopulmonary depressive effects facilitate safe anaesthesia without advanced monitoring

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Active substance <sup>1</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
			equipment or mechanical ventilation

#### X. Substances for nervous system disorders

Active substance <sup>1</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
Diazepam <sup>b</sup>	Short-term anti-convulsant for treatment of seizures	None identified	Second-generation antiseizure

#### XI. Substances for ophthalmology

Active substance <sup>11</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
Acetazolamide <sup>b</sup>	Treatment of glaucoma, oral use	Phenylephrine	Its mechanism of action as carbonic anhydrase inhibitor
Cyclopentolate <sup>b</sup>	Mydriatic agent	Atropine, phenylephrine	Induces significant mydriasis without affecting tear production, intraocular pressure, digestive function (i.e. gut motility and faeces production), or heart rate
Cyclosporine A <sup>b</sup>	Treatment of autoimmune diseases of the eye	Topical steroids	Immunosuppressive effect by inhibiting T-lymphocyte proliferation and reducing cytokine gene expression
Phenylephrine <sup>b</sup>	Treatment of glaucoma and epiphora	Atropine and tropicamide	It does not (or only slightly) increase intra ocular pressure
Synephrine <sup>b</sup>	Treatment of the mucous membranes of the eye as a decongestant	Phenylephrine, tetrahydrozoline	Fast local effect; enhances penetration of local therapy, providing synergistic effects with e.g. local antimicrobial therapy

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Active substance <sup>11</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
Tetryzoline <sup>b</sup>	Treatment of the mucous membranes of the eye as a decongestant	Phenylephrine, synephrine	Fast local effect
Timolol maleate <sup>b</sup>	Treatment of glaucoma, topical use	Acetazolamide	Its specific mode of action as a non-selective beta-adrenergic receptor blocking agent, provides for an important therapeutic choice in the treatment of glaucoma
Triamcinolone acetonide <sup>b</sup>	Treatment of recurrent uveitis in cases that are refractory to other treatments	Atropine, tropicamide	Effective, low-morbidity treatment in cases that are refractory to other treatments
Tropicamide <sup>b</sup>	Treatment of recurrent uveitis	Atropine, cyclopentolate, triamcinolone acetonide	Rapid onset of action

## XII. Substances for sedation and premedication (and antagonism)

Active substance <sup>1</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
Acepromazine <sup>b</sup>	For a multimodal approach for tranquilisation and premedication in combination with other sedatives	Detomidine, romifidine, xylazine, diazepam	The mode of action of acepromazine and its unique quality of sedation cannot be produced by alpha-2 agonist sedatives or benzodiazepines
Atipamezole <sup>a</sup>	Reversing the effects of alpha-2 agonists	None identified	Reverses sedative and analgesic effects and adverse cardiovascular reactions
Dexmedetomidine <sup>b</sup>	Sedation or general anaesthesia as part of partial or total	Detomidine, romifidine,	The most selective alpha-2 agonist; short half-life and rapid redistribution, which

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Active substance <sup>1</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
	intravenous anaesthesia protocols	xylazine, diazepam	particularly favour its use as a continuous-rate infusion
Diazepam <sup>b</sup>	Premedication and induction of anaesthesia, mild tranquilisation with minimal cardiovascular and respiratory side effects	Acepromazine, detomidine, romifidine, xylazine	The mode of action (at gamma-aminobutyric acid (GABA) receptor) provides unique tranquilisation without cardiorespiratory depression that cannot be produced by alpha-2 agonist sedatives (detomidine, romifidine and xylazine) or acepromazine
Flumazenil <sup>a</sup>	Intravenous reversal agent for benzodiazepine effect during recovery from Total Intravenous Anaesthesia (TIVA) techniques	None identified	Antagonist that competitively inhibits the benzodiazepine binding site at the GABA receptor
Naloxone <sup>a</sup>	Reversal of opioid effects during emergencies	None identified	No alternatives available
Propofol <sup>b</sup>	Induction of anaesthesia in foals via intravenous administration	Isoflurane	Improvement in cardiovascular stability and quality of recovery over inhalation anaesthesia in foals

### XIII. Substances for systemic disorders

Active substance <sup>1</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
Allopurinol <sup>b</sup>	Neonatal ischaemia reperfusion injury	Vitamin E	Different mode of action in inhibiting the formation of reactive oxygen species (ROS) than vitamin E

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Active substance <sup>1</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
Dalteparin <sup>b</sup>	Anticoagulant	Heparin	Reduction in molecular size is associated with a loss of thrombin inhibitory activity, but conversely an increase in factor Xa (FXa) inhibition compared to unfractionated heparin
Dobutamine <sup>b</sup>	Management of hypotension under general anaesthesia	Ephedrine	First-line medication for the treatment of hypotension in adult equines under general anaesthesia
Dopamine <sup>a</sup>	As part of a treatment protocol for acute kidney injury/renal failure only	None identified	Low doses have been shown to cause renal vasodilation, increased renal blood flow, and increased urine production without systemic cardiovascular effects in conscious healthy horses
Ephedrine <sup>b</sup>	Treatment of hypotension under general anaesthesia	Dobutamine	Used to treat hypotension in adult equines under general anaesthesia where dobutamine is ineffective. Different mode of action to dobutamine with a more direct effect on cardiac contractility
Gelatinpolysuccinate <sup>b</sup>	Addressing long-term hypovolaemia resulting from conditions like e.g. low albumin	Crystalloids	Colloids are larger molecules compared to crystalloids (smaller molecules that stay longer in the intravascular space), which is an advantage for correcting hypovolemia from e.g. hypoalbuminemia
Glycopyrrolate <sup>b</sup>	Treatment and prevention of bradycardia	Atropine	Minimal central effect; suitable in conscious horses, before and after

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Active substance <sup>1</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
			anaesthesia
Noradrenaline / norepinephrine <sup>b</sup>	Treatment of early septic shock Supporting cardiovascular function in critically ill foals	Dobutamine, dopamine	In compromised (sick) foals it is generally the only catecholamine effective in treatment of hypotension
Vasopressin <sup>b</sup>	Treatment of circulatory collapse in foals and adult horses	Epinephrine, dopamine, dobutamine	Alternative in cases where standard catecholamine therapies like dopamine, dobutamine, epinephrine are ineffective or require potentiation to restore vascular tone in refractory vasodilatory shock states

#### XIV. Substances for tumours

Active substance <sup>1</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
Imiquimod <sup>a</sup>	Treatment of sarcoids	None identified	Current research suggests that equine sarcoids likely result from a complex interaction including host immune system dysfunction

#### XV. Z. Miscellaneous

Active substance <sup>1</sup>	Indication(s):	Identification of alternatives:	Explanation of use / specific advantages:
Cetirizine <sup>b</sup>	Treatment of conditions where an antihistamine is deemed necessary	Chlorphenamine	Second-generation histamine-1 (H1) receptor inverse agonists are alternatives with fewer central nervous system (CNS) (sedative) side effects

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Domperidone <sup>b</sup>	Treatment of agalactia/dysgalactia in mares	Sulpiride	Its ability to stimulate prolactin secretion in situations of dopaminergic inhibition
Sulpiride <sup>b</sup>	Treatment of agalactia/dysgalactia in mares	Domperidone	Its ability to stimulate prolactin secretion in situations of dopaminergic inhibition