

## EMA/FVE webinar on veterinary prescription

Conditions for using certain  
antimicrobials under the 'cascade'

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# Structure of the presentation



The veterinary  
**prescription**  
**'cascade'**

The **use of**  
**antimicrobials** and  
**recommendations**

Key **takeaway**  
**messages** for  
veterinarians

**Q&A session**



# The veterinary prescription 'cascade'



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# Lack of (availability) of veterinary medicines

- Veterinarians can face difficulties when no veterinary medicinal product (VMP) is authorised for a particular animal or disease indication in their country.
- Limited markets and minor species are particularly impacted.
- [Regulation \(EU\) 2019/6](#) has a safety net commonly known as the **'cascade'** to exceptionally allow a veterinarian to treat the animals concerned.

**The 'cascade' is a set of rules to guide veterinarians on how to use medicines when no authorised veterinary medicinal product is available.**

# The veterinary 'cascade'

An EU-authorized VMP for use in the same or **another species**, for the same or **another indication**

An EU-authorized **human** medicinal product

An **extemporaneous** VMP

A VMP authorised in a **third country** for the same species and the same indication

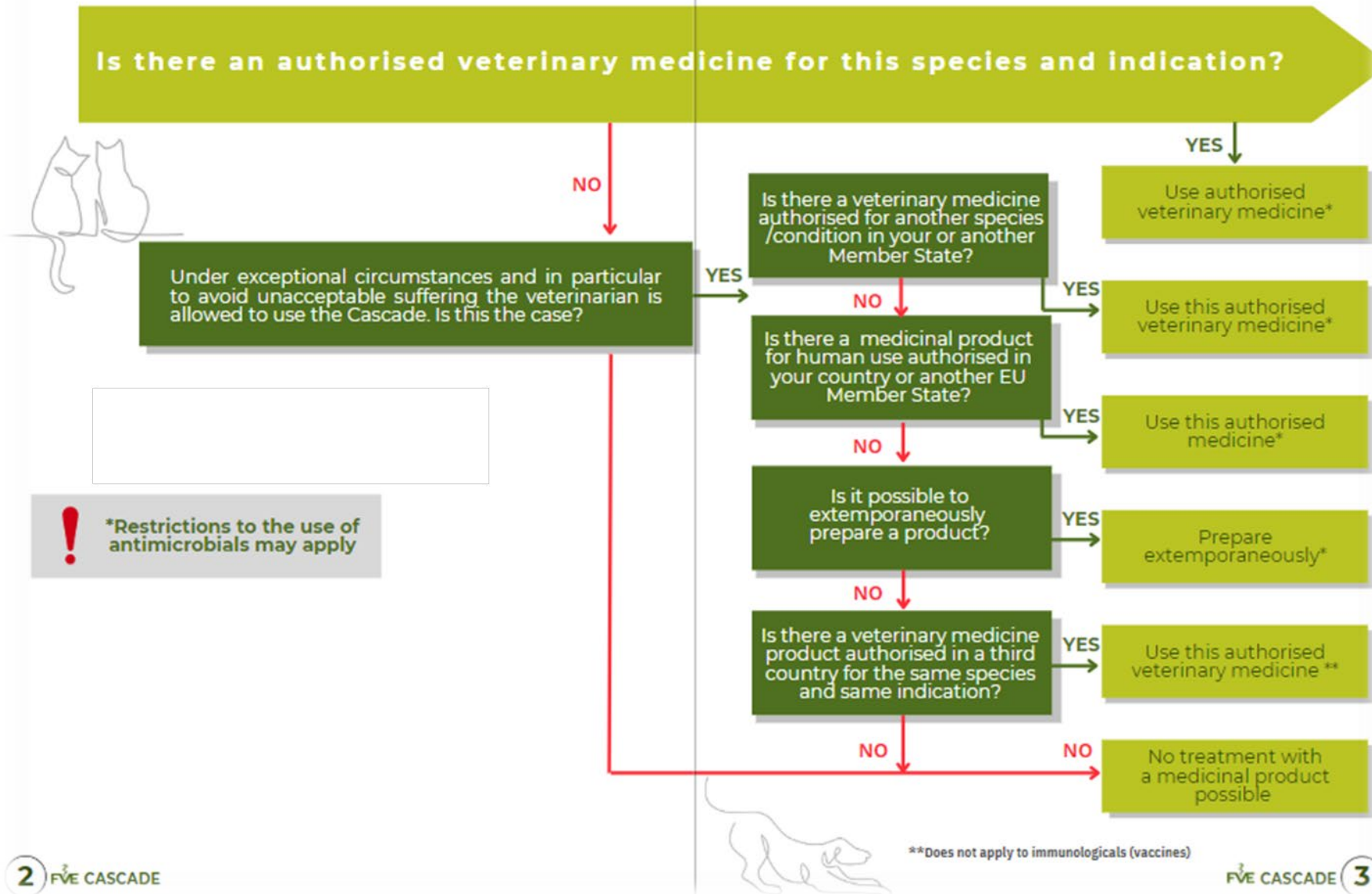
However, the 'cascade' has **limitations:**

- it can only be applicable under veterinarians' own responsibility.

**and**

- only to avoid unacceptable suffering and exceptional circumstances.

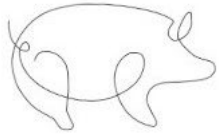
## COMPANION ANIMALS



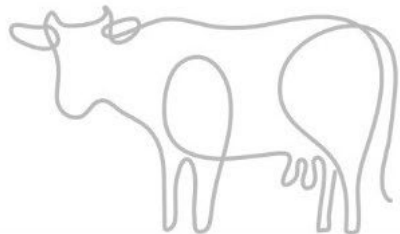
**Article 112 for non-food-producing animal species (companion animals)**

Is there an authorised veterinary medicine for this species and indication?

Under exceptional circumstances and in particular to avoid unacceptable suffering the veterinarian is allowed to use the Cascade. Is this the case?



! \*Restrictions to the use of antimicrobials may apply



Is there a veterinary medicine for another **food-producing** species/condition in your or in another Member State?

Use this authorised veterinary medicine\*

Is there a veterinary medicine authorised in your Member State for use in a **non-food-producing** animal species for the same indication?

Use this authorised veterinary medicine\*

Is there a medicinal product for human use authorised in your country or another EU Member State?

Use this authorised product\*

Is it possible to extemporaneously prepare a product?

Prepare extemporaneously\*

Is there a veterinary medicine product authorised in a third country for the same species and same indication?

Use this authorised veterinary medicine \*\*

No treatment with a medicinal product possible

\*\*Does not apply to immunologicals (vaccines)

4 FVE CASCADE

FVE CASCADE 5

Article 113 for food-producing terrestrial animal species



# The use of antimicrobials in animals

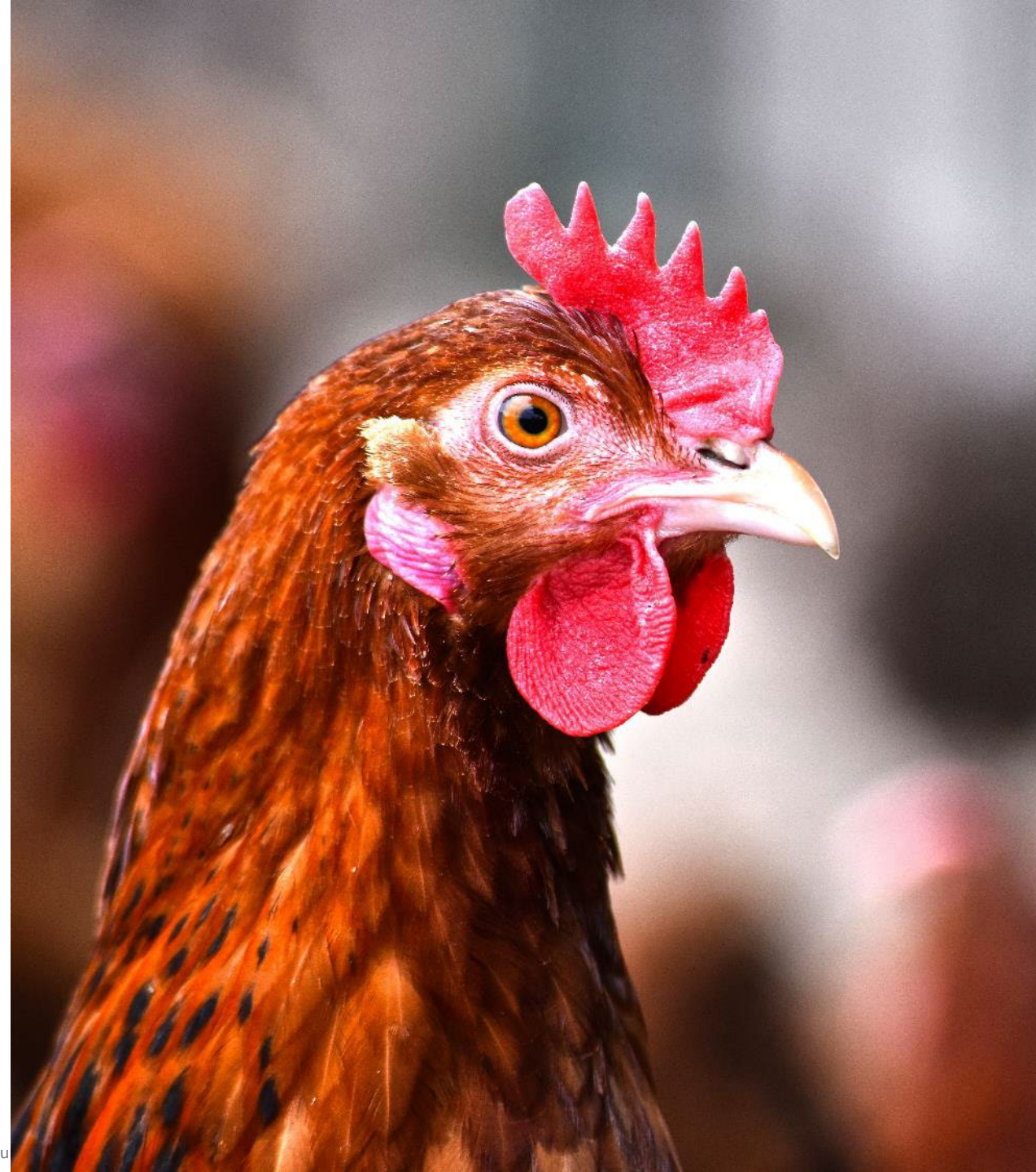


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# The 'cascade' and the use of antimicrobials

- Restrictions to the use of antimicrobials may apply.
  1. [Regulation \(EU\) 2022/1255](#): human-reserved antimicrobials, substances designated under Article 37(5) are **not allowed** to be used.
  2. [Regulation \(EU\) 2024/1973](#): antimicrobials, substances not be used under Articles 112, 113 or shall be used **under certain conditions**. This list is complementary to the list of antimicrobials reserved for humans.



# Human-reserved antimicrobials



## Antibiotics

- Carboxypenicillins
- Ureidopenicillins
- Ceftobiprole
- Ceftaroline
- Cephalosporins with beta-lactamase inhibitors
- Siderophore cephalosporins
- Carbapenems
- Penems
- Monobactams
- Phosphonic acid derivatives
- Glycopeptides
- Lipopeptides
- Oxazolidinones
- Fidaxomicin
- Plazomicin
- Glycylcyclines
- Eravacycline
- Omadacycline



## Antivirals

- Amantadine
- Baloxavir marboxil
- Celgosivir
- Favipiravir
- Galidesivir
- Lactimidomycin
- Laninamivir
- Methisazone/  
metisazone
- Molnupiravir
- Nitazoxanide\*
- Oseltamivir
- Peramivir
- Ribavirin
- Rimantadine
- Tizoxanide
- Triazavirin
- Umifenovir
- Zanamivir

\*Nitazoxanide is also an antiprotozoal and included in the list due to antiviral properties

### Banned use in animals

- 11 antibiotic classes
- 6 antibiotic substances
- 18 antiviral substances

# Scientific advice relating to Article 107(6)

To “help preserve their efficacy for humans and/or animals”, European Commission requested EMA for scientific advice to establish a list of antimicrobials with the purpose in which:

- shall **not be used under Articles 112 and 113**,
- or
- shall only be used under **certain conditions**.

The screenshot shows an email from the European Commission, Directorate-General for Health and Food Safety, to Prof. Guido Rasi, Executive Director of the European Medicines Agency. The email is dated 7 January 2019 and is titled "Implementing measures under Article 107(6) of Regulation (EU) 2019/6 on veterinary medicinal products". The subject line is "Implementing measures under Article 107(6) of Regulation (EU) 2019/6 on veterinary medicinal products", regarding the establishment of a list of antimicrobials, which shall not be used in accordance with Articles 112, 113 and 114 or which may be used in accordance with these articles subject to certain conditions.

The email text includes the following key points:

- On 7 January 2019, the new Regulation on Veterinary Medicinal Products (VMP Regulation) was published.
- In accordance with its Article 160, it will start applying 3 years from its entry into force, i.e. on 28 January 2022.
- The Commission strongly supports the fight against antimicrobial resistance (AMR) in the EU and at global level. The misuse or overuse of antimicrobials in veterinary settings can create an important source of antimicrobial resistant microorganisms that can spread across animal species, as well as between animals, humans and the environment in various ways. For this reason, improving the management of the use of antimicrobials in animals is paramount.
- To ensure a well-rounded approach to fighting AMR, the new Regulation lays down that certain antimicrobials may be reserved for treatment of certain infections in humans (Article 37(5)). In addition, it envisages that the use of certain antimicrobials under Articles 112, 113 and 114 ("cascade use") may not be allowed or be subject to certain restrictions in order to help preserve their efficacy for humans and/or animals.

The email also includes a list of criteria for the selection of antimicrobials to be included in the list, such as:

- (a) risks to animal or public health if the antimicrobial is used under the "cascade";
- (b) risks for animal or public health in case of development of AMR;
- (c) availability of other treatments for animals;
- (d) availability of other antimicrobial treatments for humans;
- (e) impact on aquaculture and farming if the animal affected by the condition receives no treatment.

The email concludes with a request for scientific advice from the Agency and provides contact information for Prof. Guido Rasi.

EC request for scientific advice

# Behind the development of the advice

## Criterion A

Risks to animal or public health if the antimicrobial is used in accordance with Art. 112 and 113.

## Criterion B

Risk for animal or public health in case of development of antimicrobial resistance.

## Criterion C

Availability of other treatments for animals.

## Criterion D

Availability of other antimicrobial treatments for humans.

## Criterion E

Impact on aquaculture and farming if the animal affected by the condition receives no treatment.



Conditions to be considered for certain antimicrobial classes according to the circumstances of cascade use

**Unauthorised indications**

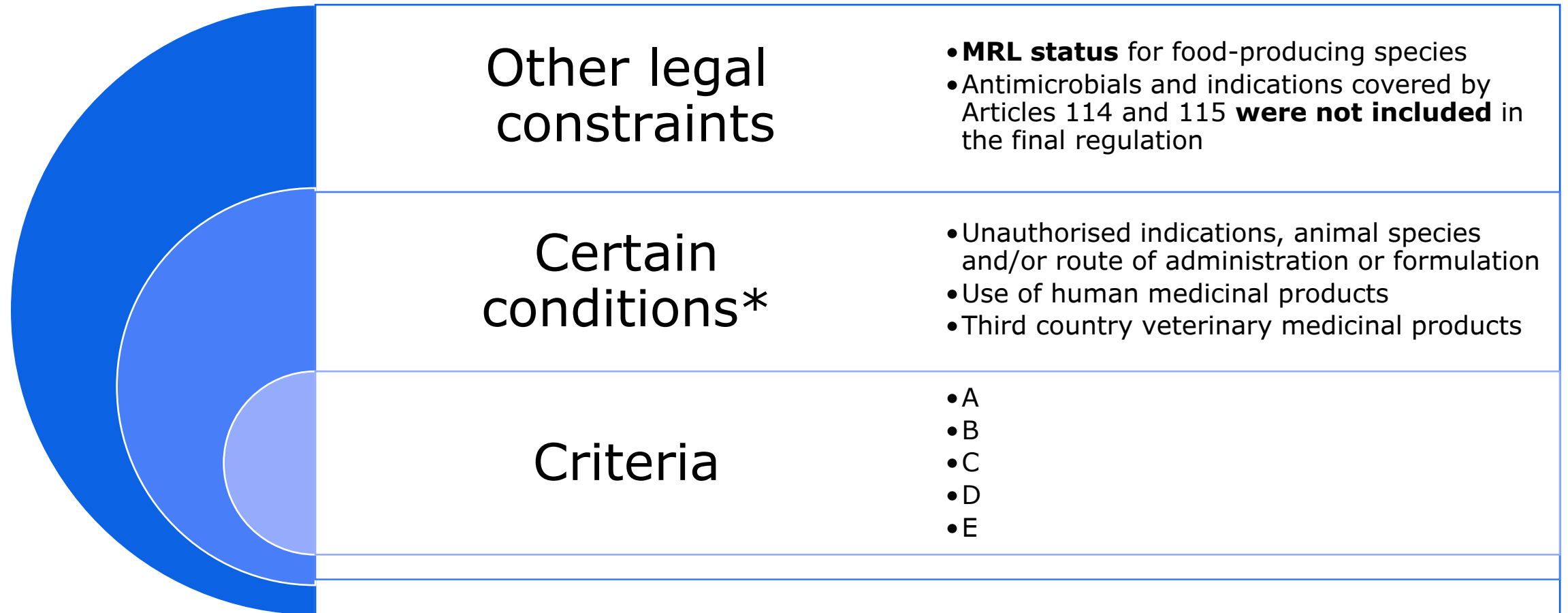
**Unauthorised animal species**

**Unauthorised route of administration or formulation**

**Use of human medicinal products**

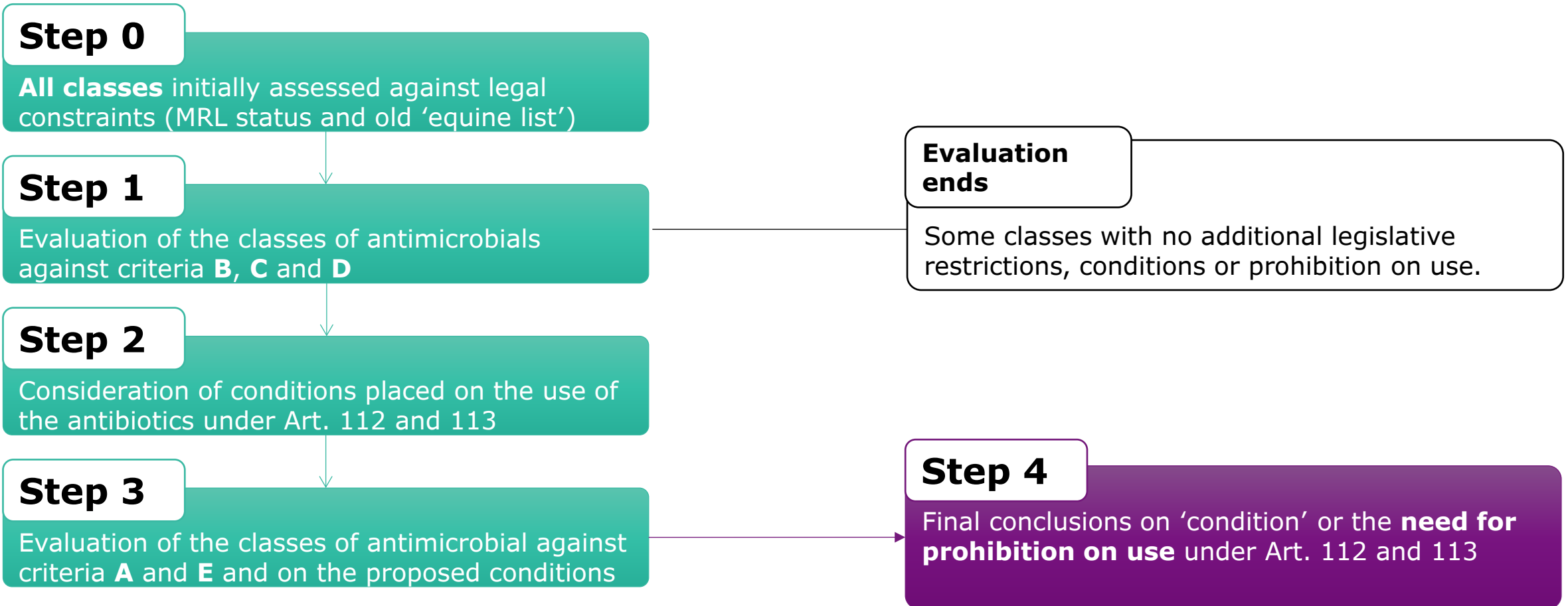
**Third country veterinary medicinal products**

# Criteria behind the development of the advice



\* Check summary table 1 in the annex

# Summary of the evaluation process



# Challenges

## Data gap

Lack of research and official data on the types and extent of use of antimicrobials outside the marketing authorisation.

## Study gap

Lack of reliable published studies on the efficacy or safety of antimicrobials when used outside the marketing authorisation.

## Information gap

Limited information on prevalence of resistance in target animal pathogens, and the impact of cascade use, specifically, on development of antimicrobial resistance.

## Evidence gap

Very little evidence relating to the burden of animal diseases in the EU (criterion e).

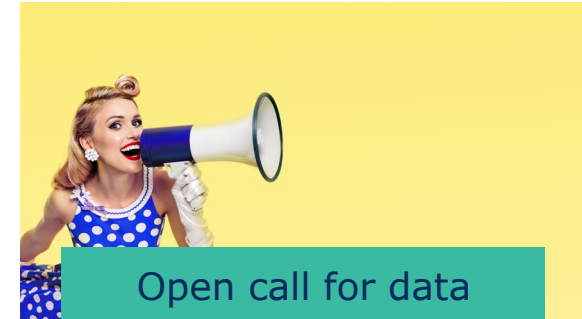
# Sources of evidence



Existing categorisations and recommendations



Peer-reviewed studies, textbooks, treatment guidelines



Open call for data



Official reports and surveillance data



More than 700 supporting references



13 experts, including veterinary sector-specific



# Recommendations



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# Examples of antimicrobials not been recommended for inclusion on the Art.107(6) list(s)

## Antibiotics

Narrow spectrum penicillins, antistaphylococcal penicillins, aminopenicillins, **amdinopenicillins\***, 1<sup>st</sup>/2<sup>nd</sup> G cephalosporins, cyclic polypeptides, pleuromutilins, macrolides, ketolides, lincosamides, **streptogramins\***, aminoglycosides, aminocyclitols, tetracyclines, sulfonamides, trimethoprim, nitrofurans, nitroimidazoles, rifaximin, steroid antibacterials + 6 classes not currently authorised as medicinal products (H&V) in the EU.

\*not currently authorised in VMPs in the EU

## Antivirals

Other than remdesivir, no antivirals are recommended for Article 107(6).



## Antifungals

Azoles, polyenes, flucytosine, griseofulvin, allylamines.

## Antiprotozoals

Nitroimidazoles, triazines (diclazuril, etc), benzimidazoles, pyrimethamine, halofuginone, decoquinat, meglumine, miltefosine, imidocarb, pentamidine, atovaquone, nitrofurans, and others.

# Commission Implementing Regulation (EU) 2024/1973

Conditions on the use of antimicrobials	Target pathogen identification and AST	Restricted around certain indications	Restricted to use for certain indications only	Restricted from use in certain species	Use in individual animals only	Restriction on route of administration	HMPs only for use in individual animals
Aminopenicillin- BLI combinations	✓						
3rd & 4th gen. cephalosporins	✓	Salmonella			✓		
Polymyxins	✓	Salmonella				✓	✓
Amphenicols	✓						
(Fluoro)quinolones	✓	Salmonella				✓	✓
Rifamycins (excl. EU-VMPs)	✓	Prophylaxis R. equi	Mycobacteria MDR Staph		✓		
TB drugs	✓				✓		
Riminofenazines	✓				✓		
Pseudemonic acids	✓	Not for decolonisation	MRSA/P		✓	Topical only	
Remdesivir			FIP only				
Echinocandins	✓	Last resort			✓		
Amphotericin B		Last resort					

- No antimicrobials have been recommended as **'not to be used'** under Articles 112-113.
- Applicable from **8 August 2026**.
- Full recommendations on pages 7-10 the [summary of advice](#).

# Take away messages



This advise is based on **current** knowledge and recommendations **could be reviewed** in the light of new scientific evidence or emerging information.

Regulation (EU) 2024/1973 is **applicable from 8 August 2026.**

Regulation (EU) [2024/1973](#) **will be reviewed** based on the new legal acts on horses and aquatic species.

Consult the [UPD public portal](#) to compare VMPs, check authorisation and availability status and search for potential alternatives.

# When using the 'cascade'...

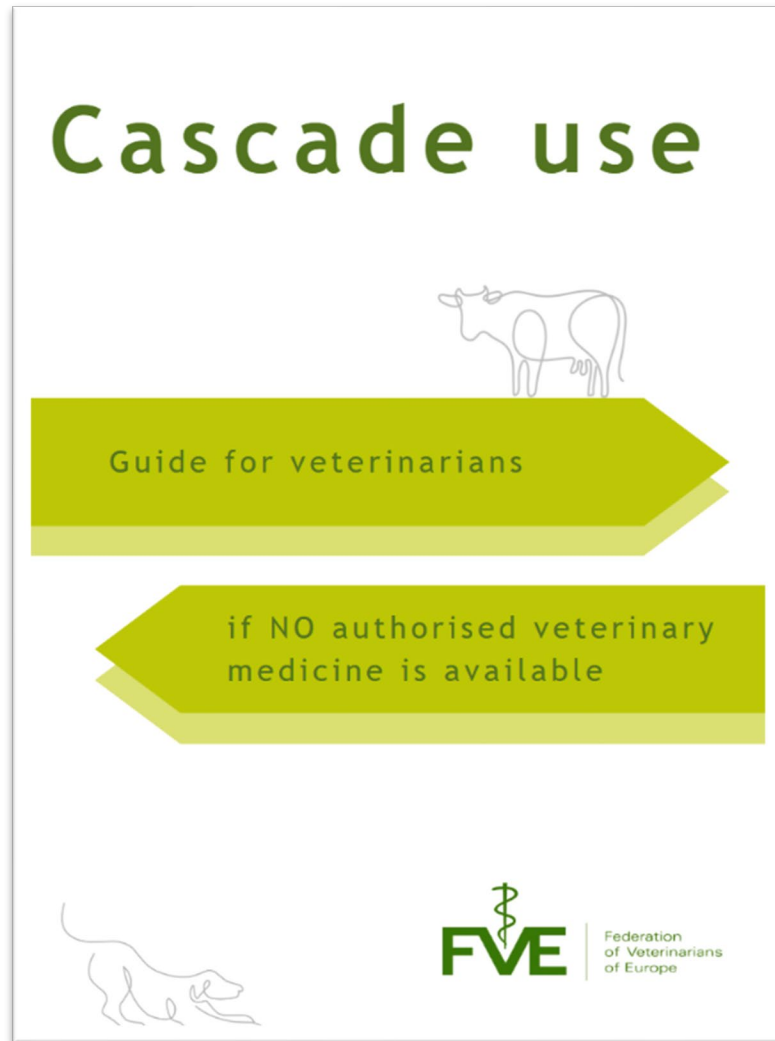


...**always check the MRL status** of the active substance when prescribing a VMP to a food-producing animal.

... to prescribe a VMP authorised in another Member State(s) for the same species, the **applicable withdrawal period is the one mentioned in package leaflet.**

... and in the absence of a withdrawal period in the package leaflet for the treating animal, the **withdrawal period shall be set up according to Art. 115(1).**

# FVE 'cascade' update announcement



- With the support of EMA, FVE is currently updating the Cascade leaflet to align with the new rules under Regulation (EU) 2019/6.
- **In the coming weeks**, we will release the revised version, which will include updates reflecting the latest guidelines.
- Further updates will follow to incorporate details on the **horse** and **aquatic species** lists, as they become available.

***Stay tuned for the launch of the updated 'cascade' leaflet!***



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# Annex



# Summary table 1 in the advice

<b>Type/Nature of use under Articles 112, 113 &amp; 114</b>	<b>Potential conditions to be considered</b>
Unauthorised indications	<ul style="list-style-type: none"> <li>• Target pathogen identification and susceptibility testing for indications not included in the SPC</li> <li>• Prohibit use for treatment of certain zoonotic pathogens associated with public health risk</li> </ul>
Unauthorised animal species	<ul style="list-style-type: none"> <li>• Prohibit use in major animal species (excluding sheep) for which the antimicrobial is not yet authorised</li> </ul>
Unauthorised route of administration or formulation	<ul style="list-style-type: none"> <li>• Restrict to certain routes of administration</li> <li>• Restrict use of extemporaneous formulations</li> <li>• Restrict use to individual animals only</li> <li>• Restrict from use in food-production aquaculture (i.e. administration into aquatic environment)</li> </ul>
Use of human medicinal products	<ul style="list-style-type: none"> <li>• Target pathogen identification and susceptibility testing</li> <li>• Restrict to named indications</li> <li>• Restrict to use in individual animals only</li> </ul>
Third country VMPs	<ul style="list-style-type: none"> <li>• Target pathogen identification and susceptibility testing</li> </ul>