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New recommendations for injectable veterinary medicines containing procaine benzylpenicillin

On 7 September 2023, the EMA's veterinary medicines committee, CVMP, completed a review concluding that the benefits of veterinary medicines containing procaine benzylpenicillin continue to outweigh their risks, provided some changes are made to their product information. Particularly, changes to the indications, dosage regimen (dose rate and duration of treatment), warnings on the effective use of these veterinary medicines, and the meat and offal withdrawal periods for food producing species. The withdrawal period is the minimum time that has to elapse before an animal treated with a medicine can be slaughtered so that its meat or other animal derived products may be used for human consumption.

The recommendations addressed concerns that the dosage regimen for some injectable veterinary medicines containing procaine benzylpenicillin might not be appropriate to ensure effective use of these veterinary medicines, which could also contribute to the development of antimicrobial resistance.

Injectable veterinary medicines containing procaine benzylpenicillin are marketed in many European Union (EU) Member States and have been widely used for decades in cattle, horses, sheep, goats, pigs, dogs and cats for the treatment of a variety of infections caused by bacteria susceptible to benzylpenicillin and affecting e.g., the urinary, respiratory or reproductive system.

The CVMP considered it important to provide practicing veterinarians with the necessary tools to correctly use procaine benzylpenicillin as a first-choice antimicrobial, in line with AMEG recommendations, guidelines and national policies (https://www.ema.europa.eu/system/files/documents/report/ameg_infographic_en.pdf).

The review of the CVMP was limited to the use of these veterinary medicines when administered via intramuscular and subcutaneous routes of administration only.

To ensure an effective use for the proposed indications whilst minimising the risk of antimicrobial resistance development, the Committee concluded that the dose rate and treatment duration for some of the concerned veterinary medicines should be increased. Consequently, for those medicines the meat and offal withdrawal periods in all target species should be increased to ensure consumer safety. The CVMP considered that the withdrawal periods for milk already provide sufficient assurance of consumer safety and do not need to be amended.

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The CVMP recommended not to use these veterinary medicines for the treatment of infections caused by certain pathogens, as they are not in line with current scientific knowledge. The CVMP considered it beneficial to include warnings on the mode of action of procaine benzylpenicillin in the package leaflet as well as to indicate resistance or decreased susceptibility in specific target pathogens to ensure efficacious use of these veterinary medicines.

It was also recommended to add a warning on potential side effects following the administration of these medicines in young piglets.

The recommendations follow a review by the CVMP of all available data for injectable veterinary medicines containing procaine benzylpenicillin to assess the risk identified indicating inappropriate dosage and treatment duration and the increased risk of antimicrobial resistance development. This data included scientific literature, studies covering pharmacology, target animal safety and residue depletion, clinical studies as well as data provided by stakeholders.

The CVMP recommendations were sent to the European Commission, which issued a final legally binding decision applicable in all EU Member States on 11 December 2023.

Information for veterinarians

- EMA recommended changes to the product information of some injectable veterinary medicines containing procaine benzylpenicillin, to ensure that advice regarding their administration (dose rate and duration of treatment) is consistent across the EU while guaranteeing their correct use as a first-choice antimicrobial. The recommended increase of the meat and offal withdrawal periods for some of these veterinary medicines ensures consumer safety.
- Current scientific knowledge has shown that these veterinary medicines should not be used for the treatment of infections caused by certain pathogens and the indications have been amended accordingly.
- Systemic toxic effects have been observed in young piglets, which are transitory but can be potentially lethal, especially at higher doses and a warning has been added to highlight this potential side effect.

More about the medicine

Benzylpenicillin is an antibiotic belonging to the AMEG category D that should be used as a first line treatment, whenever possible. Injectable veterinary medicines containing procaine benzylpenicillin within the scope of this referral have been used for decades against various diseases caused by bacteria, affecting different organ systems in the target species cattle, horses, sheep, goats, pigs, dogs and cats.

Injectable veterinary medicines containing procaine benzylpenicillin are marketed in many European Union (EU) Member States and as with any other antibiotic, benzylpenicillin should be used prudently and only when medically needed. Moreover, any unnecessary use, overly long treatment periods, and under-dosing should be avoided.

More about the procedure

The review of injectable veterinary medicines containing procaine benzylpenicillin was initiated on 16 February 2022 at the request of Germany under Article 82 of Regulation (EU) 2019/6.

The review was carried out by the Committee for Veterinary Medicinal Products (CVMP), the Committee responsible for the evaluation of veterinary medicines, which made a set of recommendations. The CVMP recommendations were sent to the European Commission, which issued an EU-wide legally binding decision on 11 December 2023.