Divergent position to CHMP Opinion

Article 31 of Directive 2001/83/EC resulting from pharmacovigilance data

Procedure No: EMEA/H/A-31/1526

Procedure No: Aerinaze EMEA/H/A-31/1526/ C/000772/0047

Pseudoephedrine-containing medicinal products

Divergent statement

The following CHMP Member considers that the benefit-risk balance of pseudoephedrine-containing products is not favourable based on the following grounds:

Pseudoephedrine, as single active substance or in fixed dose combinations, is used as short-term symptomatic relief of nasal or sinus congestion caused by the common cold, sinusitis, allergic rhinosinusitis or aerotitis. These medicines are only available in oral forms and are authorised for more than 35 years in Europe.

In February 2023, France triggered a referral procedure under Article 31 of Directive 2001/83/CE in view of new serious risks pointed out with the use of pseudoephedrine, i.e. Posterior Reversible Encephalopathy Syndrome (PRES) and Reversible Cerebral Vasoconstriction Syndrome (RCVS). The PRAC was especially asked to assess the overall benefit-risk balance of pseudoephedrine-containing medicinal products taking into consideration the overall safety profile of pseudoephedrine, including the risks of PRES/RCVS and all other known risks.

The PRAC concluded that a causal relationship between pseudoephedrine and the risks of PRES/RCVS is established. Some risk factors of PRES and RCVS have been identified and the PRAC recommended an update of the product information with additional contraindications (i.e. severe or uncontrolled hypertension, acute or chronic kidney disease) and a warning to further describe these adverse drug reactions and their clinical management in order to mitigate these risks. However, these risk minimisation measures are deemed insufficient since cases of PRES/RCVS have been reported without any risk factors or notable medical history and numerous contraindications are already in place nationally for some pseudoephedrine containing products. The compliance towards all these measures cannot be guaranteed in clinical practice in view of the approved therapeutic indications and the context of use of these medicines.

These newly identified risks of PRES and RCVS add to the already numerous serious ischaemic risks associated to pseudoephedrine use (cardiovascular events such as haemorrhagic or ischaemic strokes, myocardial infarction, ischaemic cardiomyopathies, ischemic colitis, etc.) which are still reported in France despite risk minimisation measures in place (such as contraindications and warnings in the product information).

The current indications of pseudoephedrine containing products in symptomatic relief of nasal or sinus congestion are benign, non-life threatening and self-resolving conditions. Pseudoephedrine is thus only a symptomatic treatment. In France, the ANSM with the support from several learned societies including ENTs (otolaryngologists), general practitioners, and pharmacists encourages the use of simple hygienic measures that are considered sufficient in the relief of common cold symptoms, and advises not to use vasoconstrictors as nasal decongestant considering the risk of serious adverse drug reactions. The identified vascular and ischaemic events associated to pseudoephedrine use can lead to death or life-threatening conditions with sequels in some cases. This accumulation of identified vascular and ischaemic risks considerably weighs down the safety profile of pseudoephedrine.

Moreover, the proposed risk minimisation measures (product information updates with contraindications and warnings) are not expected to prevent any of these risks.

The time is coming to stop to collect the already considerable list of very serious adverse drugs reactions without reconsidering the very limited benefits of this symptomatic medicine.

Therefore, the benefit-risk balance of pseudoephedrine containing products is considered as negative.

CHMP Member expressing a divergent opinion:

- Alexandre Moreau (France)