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

Procedure No: EMEA/H/A-31/1501

Amfepramone-containing medicinal products

(INN: Amfepramone)

Divergent statement :

We undersigned do not find that sufficient documentation is available to support a significant change in the benefit/risk balance for amfepramone, that would justify revocation of the marketing authorisations.

Superiority over placebo has been proved in accordance with standards at the time of approval, although the efficacy is modest. No new efficacy data are available. Although amfepramone is today not recommended as an obesity treatment option in any EU or national clinical guideline, some participants at the ad hoc expert meeting expressed that there may be a patient population where this treatment may be useful.

There are concerns about known serious risks, as already listed in the product information (mainly cardiac, pulmonary, neuropsychiatric, use in pregnancy, drug abuse). However, no significant new scientific data or information with regards to these known risks for amfepramone was identified during the current referral procedure.

A Danish registry study revealed off-label use (longer than 3 months, use of higher doses and use in pregnancy, in the period from 1997-2022) which could lead to an increased risk of adverse reactions including drug abuse and dependence, as well as adverse birth outcomes. Although the study could not identify serious adverse consequences linked to the off-label use, due to methodological limitations, it is not possible to refute these risks based on these data.

Based on these considerations, a package of further Risk Minimisation Measures (including Product Information update, limited package size, a DHPC, Physician´s Checklist, Patient Card) have been proposed, to reduce off-label use and to warn about serious risks. Furthermore, 2 PASS to assess the effectiveness of these RMMs have been proposed. Since currently only routine risk minimisation measures (product information) are in place, implementing additional measures as proposed are considered proportionate at the present time. There is no evidence that these measures together would not be effective in enhancing adherence to the current product information. Nevertheless, evaluation of effectiveness is critical.

Taken together, we consider that in case these measures are implemented, and that adherence is further evaluated within a Drug utilisation study, the benefit/risk balance of amfepramone remains unchanged.

To conclude, after reviewing all the data presented as part of this procedure, including the re-examination, no significant new data and information was identified that would alter the benefit/risk balance of amfepramone, and justify a revocation of the marketing authorisations. We consider that

the observed non-adherence to the current risk minimisation measures of amfepramone can be sufficiently mitigated by implementing new, both routine and additional, risk minimisation measures.

CMDh Members expressing a divergent opinion:

- Jitka Vokrouhlická (CZ)
- Katrine Damkjær Madsen (DK)
- Christin Olofsson (SE)