PLEASE READ

IMPORTANT MEDICINE SAFETY INFORMATION

APPROVED BY THE HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

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16 June 2023

Pholcodine-containing medicinal products no longer available on the Irish market

Dear Healthcare Professional,

Haleon Ireland Ltd. in agreement with the European Medicines Agency and the HPRA would like to inform you of the following new safety information which resulted in a precautionary withdrawal from the Irish market and a recall of all batches for the following product:

Day Nurse Capsules Paracetamol 500mg, Pseudoephedrine Hydrochloride 30mg, Pholcodine 5mg	**PA 678/100/1**

Summary

- **Use of pholcodine within 12 months preceding anaesthesia with neuromuscular blocking agents (NMBAs) has been linked to a slightly increased risk of peri anaesthetic anaphylactic reaction to NMBAs.**
- **No effective measures have been identified to minimise this risk to an acceptable level in patients exposed to pholcodine-containing medicinal products.**
- **As a precaution, a decision was made in December 2022 to voluntarily recall all pholcodine-containing medicinal products from Pharmacy sale in Ireland to reduce this risk.**
- **Doctors should re-evaluate their patients, consider other treatment alternatives, and advise patients to stop using pholcodine-containing medicinal products.**
- **In case of anaesthesia requiring administration of NMBAs, healthcare professionals should check whether patients think they have used pholcodine-containing medicinal products especially in the past 12 months and if so, maintain awareness about the potential for peri anaesthetic anaphylactic reactions to NMBAs.**
- **HPRA published a Notice to Healthcare Professionals on 06 December 2022: available here. The European Commission adopted the decision on 06 March 2023.**

Background on the safety concern

Pholcodine is an opioid medicine that is used for the treatment of non-productive (dry) cough in adults and children over 6 years of age and, in combination with other active substances, for the treatment of symptoms of cold and influenza.

Pholcodine-containing medicinal products have been the subject of safety reviews by the EU in 2011 and in 2022 regarding the potential risk that pholcodine may lead to IgE-sensitisation to NMBAs and consequently to an increased risk of anaphylactic reactions.

The 2011 review concluded that the benefit-risk balance of pholcodine-containing medicinal products in the treatment of non-productive cough was positive under normal conditions of use. However, it was concluded that the possibility of an association between pholcodine use and a peri anaesthetic anaphylactic reaction to NMBAs should be further investigated. Therefore, a post-authorisation safety study (PASS) was imposed.

In 2022, the final results of the PASS, called ALPHO, became available showing a link between use of pholcodine within 12 months preceding anaesthesia with NMBAs and an increased risk of peri anaesthetic

anaphylactic reactions related to NMBAs (odds ratio [OR] adjusted=4.2 95% CI [2.5 to 6.9]). Data on the risk related to the use of pholcodine beyond the period of 12 months was not available from this study, although data from an earlier study in Norway[1] suggest that the increased risk may persist for up to 3 years. In December 2022, EMA's Pharmacovigilance Risk Assessment Committee (PRAC) assessed the final results of the ALPHO study, together with additional data from available medical literature and post-marketing experience.

PRAC concluded that, as it is not possible to identify who may be affected, the risk cannot be effectively mitigated and pholcodine products have therefore been withdrawn from the market as a precaution. The MAHs for pholcodine-containing medicinal products voluntarily recalled all stock in pharmacies of the above products as a risk mitigation measure in December 2022.

Advice for healthcare professionals

In case of anaesthesia requiring administration of NMBAs, anaesthetists are advised to check whether patients have used or think they may have used a pholcodine-containing medicinal products in the past, and particularly in the previous 12 months.

Patients should be screened on prior use of pholcodine and increased vigilance should be maintained in cases of confirmed exposure, particularly in the 12 months preceding surgery. Consider:

- **that it is not always possible to positively confirm past use of pholcodine (possibly due to difficulty recalling what type of medicine a patient has taken).**
- **pholcodine is not the only risk factor for NMBA anaphylaxis and anaesthetists/other relevant healthcare professionals should maintain awareness of potential peri anaesthetic anaphylactic reactions to NMBAs.**

Further Information

Recipients of this communication should bring it to the attention of relevant contacts by copy of this notice. Hospital pharmacists are asked to forward this to hospital anaesthetists.

The Pharmacovigilance Risk Assessment Committee (PRAC) has ruled that pholcodine-containing medicinal products should no longer be available on the European Union market:
Pholcodine-containing medicinal products | European Medicines Agency (europa.eu).

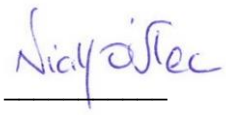
Reporting of suspected side effects

You can report side effects directly via HPRA Pharmacovigilance, Website: www.hpra.ie
When reporting please provide as much information as possible. By reporting side effects, you can help provide more information on the safety of this medicine.

Company Contact Point

Haleon Ireland Ltd. on 1800 441 442 or email mystory.ie@haleon.com.

Yours sincerely,



Niall O'Shea
Quality Lead
Haleon Ireland Ltd.

[1] IgE-sensitization to the cough suppressant pholcodine and the effects of its withdrawal from the Norwegian market IgE-sensitization to the cough suppressant pholcodine and the effects of its withdrawal from the Norwegian market