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(IN REPLY PLEASE QUOTE THIS FILE REF.)

1 Mar 2023

Dear Healthcare Professionals,

TGA is cancelling the registration of all pholcodine-containing medicines in Australia

Your attention is drawn to the Australia Therapeutic Goods Administration's (TGA) announcement that, following an investigation into the safety of pholcodine-containing medicines, the TGA has decided to cancel the registration of these medicines in Australia and is recalling them from pharmacies.

Pholcodine has been used in adults and children to treat non-productive (dry) cough and is most commonly used in cough syrups and lozenge products. It has also been used in combination with other active substances in products that treat the symptoms of cold and flu.

The TGA investigation follows a review by the European Medicines Agency (EMA) recommending the withdrawal of marketing authorisations for these products. The EMA review supports a previously suspected link between pholcodine-containing medicines and a risk of anaphylactic reactions (a sudden, severe and life-threatening allergic reaction) to medicines called neuromuscular blocking agents (NMBAs) which are used as muscle relaxants during general anaesthesia. The EMA review was carried out by the Pharmacovigilance Risk Assessment Committee. During the review, the Committee evaluated all available evidence including the final results of the ALPHO study, post-marketing safety data and information submitted by third parties such as health professionals. The data showed that use of pholcodine in the 12 months before general anaesthesia with NMBAs puts people at risk of developing an anaphylactic reaction to these agents.

The TGA considers that the recommendations by the EMA and the results of the ALPHO study are applicable to the Australian population. This is supported by a Western Australian study which showed that previous pholcodine consumption was a statistically significant risk factor for NMBA anaphylaxis. A search of the TGA's Database of Adverse Event Notifications (DAEN) on 9 Feb 2023 identified 50 Australian cases of suspected pholcodine-related anaphylactic reactions to NMBAs. This included one

fatality. These reports of NMBA anaphylaxis documented either previous pholcodine use or test results indicating increased hypersensitivity to pholcodine. Sixteen of these cases have been published in the medical literature.

Anaphylactic reactions are serious and potentially life-threatening. However, while patients undergoing surgery are typically asked about the prescription medicines they may currently being treated with in preparation for the procedure, hospitals and surgery facilities do not consistently ask about over-the-counter medicine use such as cough lozenges and syrups, especially if such use was some months earlier.

Given it is difficult to reliably predict who may be at risk of anaphylaxis to NMBAs, and the seriousness of the safety risk for pholcodine-containing medicines, the TGA is cancelling the registration of all pholcodine-containing medicines in Australia and is recalling products from pharmacies.

Consumers should check if any of their over-the-counter cold and flu medicines contain pholcodine. Pholcodine is particularly used in cough lozenge or syrup products, but can be found in other medicines. If they do, ask their doctor or pharmacist to suggest an alternative treatment. If they need general anaesthesia and have taken pholcodine in the past 12 months, tell their health professional prior to the procedure.

Health professionals should advise patients to stop taking pholcodine-containing medicines and consider appropriate alternatives to treat their symptoms. Health professionals should also check whether patients scheduled to undergo general anaesthesia with NMBAs have used pholcodine in the previous 12 months and should remain aware of the risk of anaphylactic reactions in these patients.

Please refer to the following website in TGA for details:
https://www.tga.gov.au/news/safety-alerts/pholcodine

In Hong Kong, there are 28 registered pharmaceutical products containing pholcodine. All products are pharmacy only medicines. So far, the Department of Health (DH) has received one case of adverse drug reaction related to pholcodine, but this case was not related to anaphylaxis. Related news was previously issued by EMA, and was posted on the Drug Office website since 19 Feb 2011, with the latest update posted on 3 Dec 2022. In light of the above TGA's announcement, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Please note that this letter serves as a means for the DH to communicate important new safety information about registered pharmaceutical products with healthcare professionals in Hong Kong and is not intended to serve as guidelines or to replace professional clinical judgement. Healthcare professionals

are advised to balance the risk of possible adverse effects against the benefit of treatment.

Please report any adverse events caused by drugs to the Adverse Drug Reaction Unit of the DH (tel. no.: 2319 2920, fax: 2319 6319 or email: adr@dh.gov.hk). For details, please refer to the website at Drug Office under "ADR Reporting": http://www.drugoffice.gov.hk/adr.html. You may wish to visit the Drug Office's website for subscription and browsing of "Drug News" which is a monthly digest of drug safety news and information issued by Drug Office.

Yours faithfully,

(Terence MAN)
for Assistant Director (Drug)