Drug News
藥 物 情 報

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This is a monthly digest of local and overseas drug safety news released by the Drug Office of the Department of Health in February 2023 with relevant information update before publish. For the latest news and information, please refer to public announcements or the website of the Drug Office of the Department of Health (http://www.drugoffice.gov.hk).

Safety Update

Australia: Avoid prescribing pregabalin in pregnancy if possible

On 8 February 2023, the Therapeutic Goods Administration (TGA) announced that the Product Information (PI) for pregabalin has been updated to strengthen the warning to avoid prescribing in pregnancy. The change was made after a study showed an increased risk of major congenital malformations associated with the medicine.

Women should use effective contraception if they are taking pregabalin and treatment should not be prescribed to pregnant women unless the benefits to the mother clearly outweigh the potential risks to their unborn child.

The strengthened warning follows recent data from a Nordic observational study of more than 2,700 pregnant women exposed to pregabalin in the first trimester. The study used data from national registries in Denmark, Finland, Norway and Sweden and compared babies born to mothers who took pregabalin, lamotrigine, duloxetine or none of these medicines. The study found a higher prevalence of major congenital malformations among babies exposed to pregabalin in utero compared to babies who were not exposed (5.9% vs. 4.1%).

In response to these findings, the pregnancy category for pregabalin has been changed from B3 to D in Australia. The PI for the innovator pregabalin product, Lyrica, has been updated to include additional warnings and a summary of the results from the Nordic study. Generic sponsors of pregabalin will update their PIs to align with this safety information.

Health professionals should inform women using pregabalin about the potential risks to an unborn baby and advise them to use effective contraception during treatment. Pregabalin should only be prescribed during pregnancy if the benefit to the patient clearly outweighs the potential risk to the fetus. The patient should understand the benefits and risks of pregabalin and be aware of alternatives, and be part of the decision-making process.

PI changes for Lyrica:

- The pregnancy category for pregabalin has been changed from B3 to D.
- Section 4.4 now includes a special warning for women of childbearing age which states:
  'Lyrica use in the first trimester of pregnancy may cause major birth defects in the unborn child. Pregabalin should not be used during pregnancy unless the benefit to the mother clearly outweighs the potential risk to the fetus. Women of childbearing potential have to use effective contraception during treatment.'
- Section 4.6 now includes a summary of the Nordic observational study:
  'Data from a Nordic observational study of more than 2,700 pregnancies exposed to pregabalin in the first trimester showed a higher prevalence of major congenital malformations (MCM) among the paediatric population (live or stillborn) exposed to pregabalin compared to the unexposed population (5.9% vs. 4.1%). The risk of MCM among the paediatric population exposed to pregabalin in the first trimester was slightly higher compared to unexposed population (adjusted prevalence ratio and 95% confidence interval: 1.14 (0.96-1.35)), and compared to population exposed to lamotrigine (1.29 (1.01–1.65)) or to duloxetine (1.39 (1.07–1.82)). The analyses on specific malformations showed higher risks for malformations of the nervous system, the eye, orofacial clefts, urinary malformations and

genital malformations, but numbers were small and estimates imprecise.'

In Hong Kong, there are 51 registered pharmaceutical products containing pregabalin. All products are prescription-only medicines. As of the end of February 2023, the Department of Health (DH) had received 19 cases of adverse drug reaction related to pregabalin, but these cases were not related to congenital malformations. Related news was previously issued by the United Kingdom Medicines and Healthcare products Regulatory Agency, and was reported in Drug News Issue No. 150. The DH issued letters to inform local healthcare professionals to draw their attention on 20 April 2022.

In February 2023, the Registration Committee of the Pharmacy and Poisons Board discussed the matter and decided that the sales pack label and/or package insert of pregabalin-containing products should include relevant safety information related to pregnancy.

Canada: Summary Safety Review: Rocuronium: Assessing the potential risk of mydriasis

On 9 February 2023, Health Canada announced that it reviewed the potential risk of mydriasis with the use of rocuronium. The safety review was triggered by international case reports published in the literature concerning this risk.

Mydriasis is a condition in which the pupil is not responsive to external light stimulation and remains large (dilated) for a prolonged period. Rocuronium is a prescription drug that belongs to a group of drugs referred to as muscle relaxants. Rocuronium is authorized for sale in Canada to relax muscles during an operation as part of the general anesthesia and to facilitate mechanical ventilation in patients requiring intensive care.

Health Canada reviewed information provided by manufacturers, from foreign regulatory agencies, and from searches of the Canada Vigilance database and published literature. At the time of the review, Health Canada had not received any Canadian reports of mydriasis related to the use of rocuronium. Health Canada reviewed 9 international cases of mydriasis in patients administered rocuronium. Of the 9 cases assessed, 3 were found to be probably linked to the use of rocuronium, 2 were found to be possibly linked, 1 was unlikely to be linked and 3 could not be assessed.

Three cases (2 probable and 1 possible) involved adult patients with serious infection requiring mechanical ventilation. All 3 cases resolved following discontinuation of rocuronium. Two cases (1 probable and 1 possible) involved newborn infants undergoing surgery. One newborn infant experiencing prolonged general muscle relaxation received medication to reverse the mydriasis. The remaining case resolved following discontinuation of rocuronium.

Health Canada's review of the available information found a link between the use of rocuronium and the risk of mydriasis in mechanically ventilated adult patients with systemic infection, and in newborn infants undergoing surgery. Mydriasis is expected to reverse when rocuronium is discontinued. Health Canada will work with the manufacturers to update the Canadian product monograph for rocuronium-containing products to include the risk of mydriasis.

In Hong Kong, there are 7 registered pharmaceutical products containing rocuronium. All products are prescription-only medicines. As of the end of February 2023, the Department of Health (DH) had not received any case of adverse drug reaction related to rocuronium. In light of the above Health Canada's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 10 February 2023, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

European Union: PRAC starts safety review of pseudoephedrine-containing medicines

On 10 February 2023, the European Medicines Agency (EMA) announced that its safety committee, Pharmacovigilance Risk Assessment Committee (PRAC), has started a review of medicines containing pseudoephedrine following concerns about the risk of posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS), conditions affecting blood vessels in the brain. Pseudoephedrine is taken by mouth and is used alone or in combination with other medicines to treat nasal congestion (a blocked nose) resulting from a cold, flu or allergy.

PRES and RCVS can involve reduced blood supply (ischaemia) to the brain and may cause major and life-threatening complications in some cases. Common symptoms associated with PRES and RCVS include headache, nausea and seizures.

The review follows new data from a small number of cases of PRES and RCVS in people using pseudoephedrine-containing medicines which were reported in pharmacovigilance databases and the medical literature.

Pseudoephedrine-containing medicines have a known risk of cardiovascular and cerebrovascular ischaemic events (side effects involving ischaemia in the heart and brain), including stroke and heart attack. Restrictions and warnings are already included in the medicines' product information to reduce these risks.

Considering the seriousness of PRES and RCVS, the overall safety profile of pseudoephedrine and the indications for which the medicines are approved, the PRAC will review available evidence and decide whether the marketing authorisations for pseudoephedrine-containing medicines should be maintained, varied, suspended or withdrawn across the European Union.

In Hong Kong, there are 105 registered pharmaceutical products containing pseudoephedrine. All products are pharmacy only medicines. As of the end of February 2023, the Department of Health (DH) had received 2 cases of adverse drug reaction related to pseudoephedrine, but these cases were not related to PRES or RCVS. Related news was also issued by the Medicines and Healthcare products Regulatory Agency (MHRA). The DH will remain vigilant on the conclusion of the review and any safety update of the drug issued by EMA and other overseas drug regulatory authorities for consideration of any action deemed necessary.

Singapore: SIMPONI (golimumab) 50 mg and 100 mg: Important changes to the patient information leaflet for the SmartJect pre-filled pen

On 23 February 2023, the Health Sciences Authority (HSA) announced that a Dear Healthcare Professional Letter has been issued by Johnson & Johnson International (Singapore) Pte. Ltd. to inform healthcare professionals of the important changes to the patient information leaflet (PIL) for the SIMPONI SmartJect pre-filled pen.

This followed identified safety issues such as accidental needle stick injuries from skin pinching when administering the injection and failure of the device to actuate from prematurely pressing the button. Healthcare professionals are advised to inform all patients and caregivers on the proper use of the SmartJect pre-filled pen, in accordance with the revised PIL.

In Hong Kong, Simponi Pre-filled Smartject Autoinjector 50mg/0.5ml (HK-59900), Simponi Pre-filled Smartject Autoinjector 100mg/1ml (HK-64295) and Simponi Pre-filled Smartject Autoinjector 50mg/0.5ml (HK-66453) are pharmaceutical products registered by Johnson & Johnson (Hong Kong) Ltd. All products are prescription-only medicines. As of the end of February 2023, the Department of Health (DH) had received 5 cases of adverse drug reaction related to golimumab, but these cases were not related to accidental needle stick injuries or failure of the device to actuate. The DH will remain vigilant on any safety update of the drug issued by other overseas drug regulatory authorities for consideration of any action deemed necessary.

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

On 27 February 2023, the Therapeutic Goods Administration (TGA) announced 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)

Safety Update

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.

In Hong Kong, there are 28 registered pharmaceutical products containing pholcodine. All products are pharmacy only medicines. As of the end of February 2023, the Department of Health (DH) had 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 reported in the Drug News since Issue No. 17, with the latest update reported in Drug News Issue No.158. In light of the above TGA's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 1 March 2023, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Drug Recall

Further Batch Recall of Poliformin Tab 500mg

On 2 February 2023, the Department of Health (DH) endorsed a licensed drug wholesaler, Natural Health Resources Company Limited (Natural Health), to further recall one batch (batch number: 90881) of Poliformin Tab 500mg (HK-50589) from the market as a precautionary measure due to the presence of an impurity in the product.

On 2 February 2023, the DH received notification from Natural Health that the overseas manufacturer of the product is initiating a voluntary recall of the above batch due to the presence of a higher than accepted level of an impurity, N-nitrosodimethylamine (NDMA) in the affected batch. NDMA is classified as a probable human carcinogen based on results from laboratory tests. As a precautionary measure, Natural Health is voluntarily recalling the affected product from the market.

Drug Recall

The above product, containing metformin, is a prescription medicine used for the treatment of diabetes mellitus. According to Natural Health, the product has been imported into Hong Kong and supplied to local doctors.

As of the end of February 2023, the DH had not received any adverse drug reaction reports related to the affected batch of product. A notice was posted in the Drug Office website on 2 February 2023 to alert the public of the product recall. The DH noted that the recall was completed.

Batch recall of Apo-Amitriptyline Tablets 10 mg

On 3 February 2023, the Department of Health (DH) endorsed a licensed drug wholesaler, Hind Wing Co Ltd (Hind Wing), to recall one batch (batch number: PY1904) of Apo-Amitriptyline Tablets 10 mg (Hong Kong registration number: HK-09273) from the market as a precautionary measure due to the presence of an impurity in the product.

On 3 February 2023, the DH received notification from Hind Wing that the overseas manufacturer of the product is initiating a voluntary recall of the batch concerned due to the presence of a higher than accepted level of an impurity, N-nitrosodimethylamine (NDMA), in the affected batch. NDMA is classified as a probable human carcinogen based on results from laboratory tests. As a precautionary measure, Hind Wing is voluntarily recalling the affected product from the market.

The above product containing amitriptyline is a prescription medicine used for the treatment of depression. According to Hind Wing, the product has been supplied to DH clinics, private hospitals, local doctors and pharmacies as well as re-exported to Macau.

As of the end of February 2023, the DH had not received any adverse reaction reports in connection with the affected batch of product. A notice was posted in the Drug Office website on 3 February 2023 to alert the public of the product recall. The DH will closely monitor the recall.

Drug Incident

Public urged not to buy or consume product containing undeclared controlled ingredient

On 27 February 2023, the Department of Health (DH) urged the public not to buy or consume a product named Soloco as it was found to contain an undeclared controlled ingredient.

Acting upon intelligence, a sample of the above product was purchased from a retail shop in Mong Kok earlier for analysis. A test result from the Government Laboratory revealed that the product sample contained tadalafil, which is a Part 1 poison under the Pharmacy and Poisons Ordinance (Cap. 138). The product is also suspected to be an unregistered pharmaceutical product.

The DH and the Police conducted an operation against the above premises on 27 February 2023. During the operation, a 35-year-old man and a 34-year-old woman were arrested by the Police for suspected illegal sale and possession of a Part 1 poison and an unregistered pharmaceutical product. The DH's investigation is continuing.

Tadalafil is used for treatment of erectile dysfunction and should only be used under the advice of a doctor. Side effects of tadalafil include low blood pressure, headache, vomiting, dizziness and transient vision disturbances. It may interact with some drugs (such as nitroglycerin for treatment of angina) and cause a decrease in blood pressure to dangerous levels. Improper use of tadalafil may pose serious health risks, especially for patients with heart problems.

A press release was posted in the Drug Office website on 27 February 2023 to alert the public of the drug incident.

A product containing any western drug ingredient must be registered under the Pharmacy and Poisons Ordinance before it can be sold in Hong Kong. Part 1 poisons should be sold at registered pharmacies under the supervision of registered pharmacists. Illegal sale or possession of Part 1 poisons and unregistered pharmaceutical products are offences under the Pharmacy and Poisons Ordinance (Cap. 138). The maximum penalty is a fine of $100,000 and two years' imprisonment for each offence. Antibiotics can only be supplied at registered pharmacies by registered pharmacists or under their supervision and upon a doctor's prescription. They should only be used under the advice of a doctor. Illegal sale or possession of antibiotics are offences under the Antibiotics Ordinance (Cap. 137) and the maximum penalty is a $50,000 fine and one year's imprisonment for each offence.

Under the Import and Export Ordinance (Cap. 60), pharmaceutical products must be imported or exported under and in accordance with an import or export licence issued under the Import and Export Ordinance. Illegal import or export of pharmaceutical products are offences under the Import and Export Ordinance (Cap. 60) and the maximum penalty is a fine of $500,000 and 2 years' imprisonment.

All registered pharmaceutical products should carry a Hong Kong registration number on the package in the format of "HK-XXXXX". The products mentioned in the above incidents were not registered pharmaceutical products under the Ordinance in Hong Kong. Their safety, quality and efficacy cannot be guaranteed. Members of the public were exhorted not to use products of unknown or doubtful composition. They should stop using the aforementioned products immediately if they had them in their possession and to consult healthcare professionals if they felt unwell after taking the products. The products should be destroyed or disposed properly, or submitted to the Department's Drug Office during office hours.

Update on Drug Office's website: You can now search the newly registered medicines in the past year at http://www.drugoffice.gov.hk/eps/drug/newsNRM60/en/healthcare_providers?pageNoRequested=1.

Details of ALL registered pharmaceutical products can still be found in the Drug Office website at http://www.drugoffice.gov.hk/eps/do/en/healthcare_providers/news_informations/

Useful Contact

Drug Complaint:

Tel: 2572 2068

Fax: 3904 1224

E-mail: pharmgeneral@dh.gov.hk

Adverse Drug Reaction (ADR) Reporting:

Tel: 2319 2920

Fax: 2319 6319

E-mail: adr@dh.gov.hk

Link: http://www.drugoffice.gov.hk/adr.html

Post: Adverse Drug Reaction and Adverse Event Following Immunization Unit,
Drug Office, Department of Health,
Room 1856, 18/F, Wu Chung House,
213 Queen's Road East,
Wanchai, Hong Kong

The purpose of Drug News is to provide healthcare professionals with a summary of local and overseas drug safety news released. Healthcare professionals are advised to keep update with the information and provide corresponding advice or therapeutic measure to patients and public.