Drug News
藥 物 情 報

Issue Number 181

This is a monthly digest of local and overseas drug safety news released by the Drug Office of the Department of Health in November 2024 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

Singapore: TOPAMAX (topiramate): Safety measures to prevent exposure during pregnancy

On 7 November 2024, 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 safety measures developed for TOPAMAX (topiramate) to prevent its exposure during pregnancy. The product is indicated for adjunctive and monotherapy of epilepsy and for prophylaxis of migraine.

Topiramate can cause major congenital malformations and foetal growth restriction when used during pregnancy, and recent data also suggests a possible increased risk of neurodevelopmental disorders in children of mothers exposed to topiramate during pregnancy. Topiramate for prophylaxis of migraine is already contraindicated in pregnancy and in women of childbearing potential who do not use a highly effective method of contraception. Safety measures include performing pregnancy testing and use of a highly effective contraceptive method prior to initiating topiramate in women of childbearing potential, and informing patients of the risk of topiramate use during pregnancy. Treatment with topiramate should also be reassessed periodically to confirm if the pregnancy prevention measures are adhered to. Healthcare professionals are advised to weigh the benefits of topiramate therapy against the risks and consider alternative therapeutic options when treating women of childbearing potential.

In Hong Kong, there are 29 registered pharmaceutical products containing topiramate. All products are prescription-only medicines. As of the end of November 2024, the Department of Health (DH) had received 5 cases of adverse drug reaction related to topiramate, but these cases were not related to birth defects.

Currently, the package insert and/or sales pack label of locally registered topiramate-containing products should include safety information on fetal harm and the increased risk of cleft lip and/or cleft palate (oral clefts) in infants exposed to topiramate in utero.

Related news on the risk of birth defects associated with the use of topiramate during pregnancy was previously issued by various overseas drug regulatory authorities, and was reported in the Drug News since Issue No. 153, with the latest update reported in Drug News Issue No. 176. The DH issued letters to inform local healthcare professionals to draw their attention on 4 September 2023. As previously reported, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Singapore: Tegretol (carbamazepine) Oral Suspension 2%: Update to the posology, method of administration, and limitation of use in neonates

On 12 November 2024, Health Sciences Authority (HSA) announced that a Dear Healthcare Professional Letter has been issued by Novartis (Singapore) Pte Ltd to inform healthcare professionals of updates to the posology, method of administration, and limitation of use in neonates with Tegretol Oral Suspension 2% (OS) (carbamazepine). The product is indicated for epilepsy including complex or simple partial seizures (with or without loss of consciousness) with or without secondary generalization, generalized tonic-clonic seizures and mixed forms of seizures.

The revised maximum daily dose for Tegretol OS is recommended to be limited to 1200 mg/day. This

recommendation is initiated to limit the amount of sorbitol intake given current constraints in sourcing sorbitol batches compliant with appropriate specifications. In addition, Tegretol OS is no longer recommended for neonates (below 4 weeks of age for term babies or 44 weeks post-menstrual age for pre-term babies) due to the amount of propylene glycol in this formulation.

In Hong Kong, Tegretol Syrup 2% (HK-35117) is a pharmaceutical product registered by Novartis Pharmaceuticals (HK) Limited (Novartis), and is a prescription-only medicine. As of the end of November 2024, the Department of Health (DH) had received 10 cases of adverse events related to carbamazepine, but these cases were not related to neonates. In light of the above HSA's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 13 November 2024. Novartis was contacted and confirmed that they will apply for change of package insert of their product. The DH will remain vigilant on safety update of the drug issued by other overseas drug regulatory authorities.

European Union: EMA updated advice to minimise risks of interaction between weight loss medicine Mysimba and opioids

On 15 November 2024, the European Medicines Agency (EMA) announced after re-examining its initial opinion, EMA recommended updating the advice aimed at minimising the risks of interaction between the weight loss medicine Mysimba (naltrexone/bupropion) and opioid-containing medicines (including painkillers such as morphine and codeine, other opioids used during surgery and certain medicines for cough, cold or diarrhoea).

Opioid medicines may not work effectively in patients taking Mysimba, because one of the active substances in Mysimba, naltrexone, blocks the effects of opioids. There is also a risk of rare but serious and potentially life-threatening reactions, such as seizures and serotonin syndrome (a potentially life-threatening condition that results from having too much serotonin in the body), in people taking Mysimba together with medicines for treating depression and opioids.

To minimise these risks, patients and healthcare professionals are reminded that Mysimba must not be used in people who are dependent on opioids, people receiving treatment with opioid agonists such as methadone or buprenorphine and people going through acute opioid withdrawal.

People using Mysimba will be given a patient card to be carried with them at all times. The card will remind them to inform their doctor, in case of surgery, that they are using Mysimba. This is because Mysimba should be stopped for a minimum of three days before starting treatment with opioids, which are often used to prevent pain and discomfort during surgery and medical procedures.

The product information for Mysimba is being updated to reflect these changes.
Advice for healthcare professionals:

- Insufficient intra- and post-operative opioid analgesia has been described in case reports and the literature in patients treated with Mysimba.
- Rare but serious and potentially life-threatening reactions such as seizures and serotonin syndrome have been observed after co-administration of Mysimba with a serotonergic agent (such as selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine re-uptake inhibitors (SNRIs)) and opioids.
- Mysimba must not be used in patients dependent on opioids, patients treated with opioid agonists used in opioid dependence (e.g. methadone, buprenorphine) or patients in acute opioid withdrawal. If opioid use is suspected, a test may be performed to ensure clearance of opioid medication before starting treatment with Mysimba.
- Patients must be warned against the concomitant use of opioids during treatment with Mysimba. If opioid use is required (e.g. due to a planned surgery), Mysimba should be stopped for a minimum of three days before starting opioid treatment.
- In case of emergency surgery in patients potentially treated with Mysimba, there is a risk that the effects of opioids may be reduced.

In Hong Kong, Mysimba is a registered pharmaceutical product under the name Contrave Prolonged-release Tablets 8mg/90mg (HK-66934), a prescription-only medicine and is the only registered pharmaceutical product containing naltrexone and bupropion. As of the end of November 2024, the Department of Health (DH) had not received any case of adverse drug reaction related to naltrexone and combination product of

naltrexone with bupropion. The DH had received 5 cases of adverse drug reactions related to bupropion, but these cases were not related to concomitant use of bupropion with opioids.

Related news previously issued by EMA was reported in Drug News Issue No. 177. The DH issued letters to inform local healthcare professionals to draw their attention on 29 July 2024. As previously reported, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Australia: Promethazine hydrochloride (Phenergan) not to be used in children under 6

On 19 November 2024, the Therapeutic Goods Administration (TGA) announced that health professionals and consumers are advised that the oral antihistamine promethazine hydrochloride, sold as Phenergan and other generic brands, should not be used in children under 6 years of age.

This updated advice follows a TGA investigation and advice from the Advisory Committee on Medicines (ACM) in 2022, with warnings published in a previous Medicines Safety Update: first-generation oral sedating antihistamines - do not use in children.

The pharmaceutical company Sanofi-Aventis Healthcare requested the latest updates to its Product Information (PI), Consumer Medicine Information (CMI) and product label for its product Phenergan, following an internal investigation prompted by the ACM advice.

The PI and CMI documents have been updated to include the risks of psychiatric and central nervous system side effects in children under 6, including hyperactivity, aggression and hallucination. When high doses are given, these children may also experience difficulties in learning and understanding, including reversible cognitive deficit and intellectual disability.

Sanofi-Aventis Healthcare's benefit-risk review of the cumulative safety data in children between 2 to 5 years of age (inclusive) found that the cumulative weight of evidence was sufficient to support a causal association between promethazine (and combinations) and safety concerns relating to psychiatric and central nervous system events.

Phenergan is used to treat a range of conditions including allergies, hayfever and nausea, as well as for short-term sedation.

There are almost 50 other brands of oral promethazine hydrochloride on the Australian market and the sponsors of these products will also be required to update their PI and CMI documents, and product labelling. Oral promethazine products are currently scheduled S3, which means they can be sold over-the-counter with advice from a pharmacist.

Health professionals should be alert to the updated advice and appropriately counsel parents and carers who may intend to use Phenergan or another oral promethazine product in a child under 6 years old. These parents and carers should be directed to alternative products.

The TGA expects there will be a time lag before all products available in pharmacies will have updated package labelling. In the interim, the updated advice to not use oral promethazine medicines in children under the age of 6 years applies across all products.

At this stage, the updated advice does not apply to the single intravenous form of promethazine hydrochloride on the Australian market, noting that this product is only available with a prescription from a doctor.

In Hong Kong, there are 236 registered oral pharmaceutical products containing promethazine. As of the end of November 2024, the Department of Health (DH) had received 5 cases of adverse drug reaction related to promethazine, but these cases were not related to psychiatric and central nervous system event in children under the age of 6.

Related news was previously issued by the TGA, and was reported in Drug News Issue No. 153. In light of the above TGA's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 20 November 2024, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Drug Recall

Batch recall of Evecet Prolonged-Release Tablets 8mg

On 18 November 2024, the Department of Health (DH) endorsed a licensed drug wholesaler, namely I & C (HONG KONG) LIMITED (I & C), to recall one batch (batch number: 1306311) of Evecet Prolonged-Release Tablets 8mg (Hong Kong Registration number: HK- 66674), from the market as a precautionary measure due to potential quality issue.

The DH received notification from I & C that the overseas manufacturer of the product is recalling the above batch due to retesting of retained sample showed out of specification assay result. As a precautionary measure, I & C is voluntarily recalling the above batch from the market.

The above product, containing ropinirole, is a prescription medicine used for the treatment of Parkinson's disease. According to I & C, the above batch of product has been imported into Hong Kong and supplied to Hospital Authority, private doctors and pharmacy.

As of the end of November 2024, the DH had not received any adverse reaction reports in connection with the above batch of product. A notice was posted in the Drug Office website on 18 November 2024 to alert the public of the product recall. The DH will closely monitor the recall.

Batch recall of Indapin SR Film-coated Tab 1.5mg

On 26 November 2024, the Department of Health (DH) endorsed a licensed drug wholesaler, namely Suntol Medical Limited (Suntol), to recall one batch (batch number: IDSA44A) of Indapin SR Film-coated Tab 1.5mg (Hong Kong Registration number: HK- 58173), from the market as a precautionary measure due to potential quality issue.

The DH received notification from Suntol that the overseas manufacturer of the product is recalling the above batch due to sample failed dissolution test during ongoing stability testing, which might affect the efficacy of the product. As a precautionary measure, Suntol is voluntarily recalling the above batch from the market.

The above product, containing indapamide, is a prescription medicine used for the treatment of hypertension. According to Suntol, the above batch of product has been imported into Hong Kong and supplied to private doctors and pharmacy.

As of the end of November 2024, the DH had not received any adverse reaction reports in connection with the above batch of product. A notice was posted in the Drug Office website on 26 November 2024 to alert the public of the product recall. The DH noted that the recall was completed.

Drug Incident

Public urged not to buy or consume oral product labelled "Tian Ma Tu Chung Seven Leave Ginseng"

On 29 November 2024, the Department of Health (DH) conducted a joint operation with the Police at a premises in Sai Ying Pun suspected of illegal sale of Part 1 Poison and unregistered pharmaceutical product, and arrested a man aged 66 years for suspected illegal sale of Part 1 poison and unregistered pharmaceutical product. The DH appealed to the public not to buy or consume an oral product labelled "TIAN MA TU CHUNG SEVEN LEAVE GINSENG" as shown in the photo, as it is suspected of containing undeclared controlled drug ingredients.

The DH received information that a premises of Listed Seller of Poisons (commonly known as medicine store) in Sai Ying Pun was suspected of selling the above product and immediately took follow-up action by purchasing a product sample from the premises concerned for analysis. The laboratory test results revealed that the product sample contained diclofenac, terbinafine and paracetamol. The first two substances are Part 1 poisons under the Pharmacy and Poisons Ordinance (Cap. 138) (PPO), while paracetamol, when contained in pharmaceutical products, is Part 2 poison under the PPO. The product is also suspected of being an unregistered pharmaceutical product. The DH will continue to follow up and investigate the incident.

Diclofenac is a non-steroidal anti-inflammatory drug for pain relieve. Its side effects include gastrointestinal discomfort, nausea and peptic ulcer. Terbinafine is an antifungal drug. Its side effects include nausea, diarrhoea and abdominal pain. Products containing diclofenac and

terbinafine for oral consumption are prescription medicines that should only be used under a doctor's directions and be supplied in the premises of an Authorized Seller of Poisons (i.e. pharmacy) under the supervision of a registered pharmacist upon a doctor's prescription. On the other hand, paracetamol is for pain relieve and an antipyretic. Overdose can result in severe liver damage. Pharmaceutical products containing paracetamol are Part 2 poisons that should only be supplied in a pharmacy or medicine store.

A press release was posted in the Drug Office website on 29 November 2024 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/reListRPP_index.html.

Useful Contact

Drug Complaint:

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Adverse Drug Reaction (ADR) Reporting:

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