Drug News
藥 物 情 報

Issue Number 177

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

European Union: New recommendations for GLP-1 receptor agonists to minimise risk of aspiration and pneumonia aspiration during general anaesthesia or deep sedation

On 12 July 2024, the European Medicines Agency (EMA) announced that its Pharmacovigilance Risk Assessment Committee (PRAC) recommended new measures to minimise the risk of aspiration and pneumonia aspiration reported in patients taking glucagon-like peptide-1 receptor agonists (GLP-1 RAs) who undergo surgery with general anaesthesia or deep sedation. GLP-1 RAs are medicines used for treatment of type 2 diabetes and obesity.

Aspiration and pneumonia aspiration can be caused by accidentally inhaling food or liquid into an airway instead of swallowing it through the oesophagus (the tube that connects the throat to the stomach). It can also occur when stomach content goes back into the throat. Aspiration and pneumonia aspiration complicate between one in 900 to one in 10,000 general anaesthesia procedures, depending on risk factors.

As part of their action, GLP-1 RAs slow down gastric emptying (emptying of the stomach) and there is a biologically plausible increased risk for aspiration in association with anaesthesia and deep sedation when taking these medicines. Delayed gastric emptying is already listed in the product information for the different GLP-1 RAs: dulaglutide, exenatide, liraglutide, lixisenatide, semaglutide and tirzepatide.

The PRAC reviewed available data including case reports in EudraVigilance, scientific literature and clinical and non-clinical data submitted by the marketing authorisation holders for these medicines.

The committee could not establish a causal association between GLP-1 analogues and aspiration, but because of the known action of delayed gastric emptying and the presence of clinical trial cases and post marketing cases, the PRAC considered that healthcare professionals and patients should be informed on this potential consequence of delayed gastric emptying.

Therefore, the PRAC has recommended that the risk of residual gastric content being present because of delayed gastric emptying should be considered before performing procedures with general anaesthesia or deep sedation. The product information of GLP-1 RAs will be updated accordingly, including a warning to patients that they should inform the doctor involved if they take these medicines and are scheduled to undergo surgery under anaesthesia or deep sedation.

In Hong Kong, there are registered pharmaceutical products containing dulaglutide (4 products), exenatide (1 product), liraglutide (5 products), lixisenatide (2 products), semaglutide (11 products), and tirzepatide (6 products). All products are prescription-only medicines. As of the end of July 2024, the Department of Health (DH) had received adverse drug reactions with semaglutide (9 cases; of which 3 were related to aspiration pneumonia). The DH had also received adverse drug reactions with dulaglutide (5 cases), exenatide (2 cases), liraglutide (1 case) and lixisenatide (1 case), but these cases were not related to aspiration and pneumonia aspiration. The DH had not received any case of adverse drug reaction related to tirzepatide. In light of the above EMA's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 15 July 2024, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board .

Canada: Summary Safety Review: Isotretinoin: Assessing the potential risk of sexual dysfunction, including persistent sexual dysfunction after drug discontinuation

On 25 July 2024, Health Canada announced that it completed a safety review on oral retinoids and erectile dysfunction in 2016. The review found that there may be a link between the use of oral isotretinoin products and the risk of erectile dysfunction. At the time of the review, the Canadian product monograph (CPM) for Epuris already included this risk. The CPMs for the other isotretinoin-containing products that were on the market were subsequently updated to include erectile dysfunction, thereby aligning the product safety information for all isotretinoin products.

In 2023, following the publication of a report by the United Kingdom Medicines and Healthcare products Regulatory Agency (MHRA) on the risk of sexual dysfunction with the use of isotretinoin, Health Canada reviewed the potential risk of additional sexual dysfunction-related events, including persistent sexual dysfunction after drug discontinuation. At the time of this review, the CPMs for isotretinoin-containing products were not consistently labelled for these additional events.

Sexual dysfunctions are a group of disorders that can affect a person's ability to engage in sexual activity. Sexual dysfunction-related events include, but are not limited to, erectile dysfunction, vulvovaginal dryness, and reduced libido.

Health Canada reviewed the available information from searches of the Canada Vigilance database and the scientific literature. Health Canada identified 111 cases (11 Canadian and 100 international) reporting 1 or more events of sexual dysfunction, including persistent sexual dysfunction after drug discontinuation, related to the use of isotretinoin. In just over half of the events, the sexual dysfunction was reported as persisting for months to years following drug discontinuation. The average age was 23 years in cases where age was provided. These cases overall did not include sufficient clinical information, including details on mental health at the time of sexual dysfunction, to definitively determine a link between isotretinoin use and sexual dysfunction. However, given the timing of the events, a link could not be ruled out.

Health Canada also reviewed 6 articles published in the scientific literature. The level of evidence in these articles was considered limited, but some reported sexual dysfunction with isotretinoin use, including those which continued after drug discontinuation.

Based on the totality of the evidence reviewed, a link between isotretinoin and sexual dysfunction, including persistent sexual dysfunction after drug discontinuation, could not be ruled out. The evidence reported was primarily for erectile dysfunction, reduced libido, and vulvovaginal dryness. Despite the limited available evidence, the young age of the intended population, the number of reported cases, and the significant impact of the adverse events are factors that warrant a precautionary approach for this risk.

Health Canada's review of the available information concluded that a link between isotretinoin and the risk of sexual dysfunction, including persistent sexual dysfunction after drug discontinuation, could not be ruled out.

Health Canada will work with the manufacturers to update and align the CPM for all isotretinoin-containing products to include this potential risk. Health Canada will also work with the manufacturers to implement additional measures to inform patients of this potential risk. Health Canada will inform healthcare professionals about this update through a Health Product InfoWatch communication.

In Hong Kong, there are 13 registered pharmaceutical products containing isotretinoin. All products are prescription-only medicines. As of the end of July 2024, with regard to isotretinoin, the Department of Health (DH) had received 2 cases of adverse drug reactions, but these cases were not related to sexual dysfunction.

Related news was previously issued by MHRA and Health Sciences Authority, and was reported in the Drug News since Issue No. 96, with the latest update reported in Drug News Issue No. 170. The DH issued letters to inform local healthcare professionals to draw their attention on 27 October 2017 and 27 April 2023. Currently, the sales pack or package insert of locally registered isotretinoin-containing products should include warnings on sexual dysfunction including erectile dysfunction and decreased libido. As previously reported, the matter will be discussed by the Registration Committee of the Pharmacy and

Poisons Board.

European Union: EMA advises about risks of using weight loss medicine Mysimba with opioids

On 26 July 2024, European Medicines Agency (EMA) announced that following a routine review of the safety of the weight loss medicine Mysimba (naltrexone/bupropion), EMA recommends strengthening existing advice to minimise the risks from interactions between Mysimba and opioid-containing medicines (including painkillers such as morphine and codeine, other opioids used during surgery, and certain medicines for cough, cold or diarrhoea).

In particular, EMA is advising that opioid painkillers may not work effectively in patients taking Mysimba, because one of the active substances in Mysimba, naltrexone, blocks the effects of opioids. If a patient requires opioid treatment while taking Mysimba, for example due to a planned surgery, they should therefore stop taking Mysimba for at least three days before treatment with opioid medicines starts.

Furthermore, EMA is informing patients and healthcare professionals about the 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 with opioids.

To minimise these risks, EMA recommends that Mysimba must not be used in people receiving treatment with opioid medicines. This is in addition to the existing contraindications stating that Mysimba must not be used in people who are dependent on long-term opioids, people receiving treatment with opioid agonist such as methadone, and people going through opioid withdrawal.

Advice for healthcare professionals:

- Insufficient effects of opioids as part of anaesthesia and intra- or post-operative analgesia have been described in case reports and the literature in patients treated with Mysimba.
- Furthermore, rare but serious and potentially life-threatening reactions such as seizures and serotonin syndrome have been observed after co-administration of Mysimba and opioids.
- Mysimba must not be used in patients receiving opioid-containing medicines, patients currently dependent on opioids, patients treated with opioid agonists used in opioid dependence (e.g. methadone) or in patients in acute opioid withdrawal. If opioid use is suspected, a test should be performed to ensure clearance of opioid medication before starting treatment with Mysimba.
- Patients should 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 July 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 with bupropion, but these cases were not related to concomitant use of bupropion with opioids. In light of the above EMA's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 29 July 2024, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

The United States: FDA alerts healthcare providers, compounders and patients of dosing errors associated with compounded injectable semaglutide products

On 26 July 2024, the US Food and Drug Administration (FDA) announced that FDA has received reports of adverse events, some requiring hospitalization, that may be related to overdoses due to dosing errors associated with compounded semaglutide injectable products. Dosing errors have resulted from patients measuring and self-administering incorrect doses of the drug and healthcare providers miscalculating doses of the drug. Adverse events included gastrointestinal effects (e.g., nausea, vomiting, abdominal pain), fainting, headache, migraine, dehydration, acute pancreatitis and gallstones.

Safety Update

The majority of the reports described patients mistakenly drawing up more than the prescribed dose from a multiple-dose vial during self-administration. In these instances, patients administered five to 20 times more than the intended dose of semaglutide. Most of the reports indicated that patients were unfamiliar with how to measure the intended dose using a syringe.

In several reports, patients were instructed to use a U-100 (1 milliliter) insulin syringe to draw small doses, such as a 5-unit (0.05 milliliter) dose, from a multiple-dose vial. These patients were directed to administer 5 units from a vial. However, these patients mistakenly administered 50 units instead. In one reported case, it was difficult for the patient to obtain clarity on dosing instructions from the telemedicine provider, who prescribed the compounded semaglutide, leading the patient to conduct an online search for medical advice and resulting in the patient taking five times the intended dose.

Several reports describe healthcare providers incorrectly calculating the intended dose when converting from milligrams to units or milliliters, which resulted in patients administering five to 10 times more than the intended dose of semaglutide. One provider intended to dose 0.25 milligrams (5 units), but prescribed 25 units instead, leading to a patient receiving five times the intended dose and experiencing severe vomiting. Another provider prescribed 20 units instead of 2 units, affecting three patients who, after receiving 10 times the intended dose, experienced nausea and vomiting. Additionally, a patient, who is a healthcare provider, attempted to recalculate their own dose in units and inadvertently self-administered a dose 10 times higher than intended.

FDA encourages patients to talk with their healthcare provider or compounder about how to measure and administer the intended dose of compounded semaglutide. Many of the patients who received vials of compounded semaglutide lacked experience with self-injections, according to the adverse event reports. Unfamiliarity with withdrawing medication from a vial into a syringe and coupled with confusion between different units of measurement (e.g., milliliters, milligrams and "units") may have contributed to dosing errors. FDA encourages healthcare providers and compounders to provide patients with the appropriate syringe size for the intended dose and counsel patients on how to measure the intended dose using the syringe.

FDA further advises that there may be a risk of medication dosing errors due to conversion from milligrams to other units of measurement, availability of compounded semaglutide products in varying concentrations and use of multiple-dose vials. Healthcare providers should be vigilant when prescribing and administering compounded semaglutide, as there may be different concentrations available. If uncertain, healthcare providers should contact the compounder about calculating the correct dose of medication to prescribe or administer.

In Hong Kong, there are 8 registered pharmaceutical products which are semaglutide injectables. All products are prescription-only medicines. As of the end of July 2024, the Department of Health (DH) had received 9 cases of adverse drug reaction related to semaglutide, but these cases were not related to medication errors. Healthcare professionals should check the product label carefully and follow the product instructions accordingly.

Drug Recall

Batch recall of Atama Capsules 10mg

On 26 July 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: 1300360) of Atama Capsules 10mg (Hong Kong Registration number: HK-66751), 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 retained sample retesting showed out of specification result. As a precautionary measure, I & C is voluntarily recalling the above batch from the market.

The above product, containing atomoxetine hydrochloride, is a prescription medicine used for the treatment of attention deficit/hyperactivity disorder. According to I & C, the above batch of product has been imported into Hong Kong and supplied to Hospital Authority only.

Drug Recall

As of the end of July 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 July 2024 to alert the public of the product recall. The DH noted that the recall was completed.

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

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E-mail: pharmgeneral@dh.gov.hk

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.