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 July 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

European Union: Global regulators confirm good safety profile of COVID-19 vaccines

On 5 July 2023, the European Medicines Agency (EMA) announced that it has just endorsed a joint statement on the safety of COVID-19 vaccines issued by the International Coalition of Medicines Regulatory Authorities (ICMRA).

Evidence from more than 13 billion doses of COVID-19 vaccines administered worldwide shows that these vaccines aimed at protecting people from severe outcomes of COVID-19 have a very good safety profile in all age groups, including children and people with underlying medical conditions, immunocompromised patients and pregnant women. The vaccines have saved millions of lives worldwide by significantly reducing the risk of severe disease, hospitalisation and death from infection with SARS-CoV-2.

The statement also highlighted that vaccines reduce the impact of long COVID based on several real-world data studies and that there is no safety signal from the very large data set held by international regulators suggesting that this condition is a possible side effect of COVID-19 vaccination.

While the vast majority of side effects of COVID-19 vaccines are mild and temporary, safety monitoring systems have identified some very rare (occurring in less than 1 in 10,000 people) but serious side effects. The statement emphasises that ICMRA countries have very solid safety monitoring systems that continuously collect and analyse reports of suspected side effects, and also robust measures in place to reduce the risk of harm from these side effects.

The statement draws attention to the devastating impact of false and misleading information about the safety of COVID-19 vaccines on public health, as it can result in deaths or severe disease if people avoid getting the vaccines they need. As there have been false claims on social media that COVID-19 vaccines are to blame for the excess deaths during the pandemic, the statement underlines the lack of any evidence to show that COVID-19 vaccines are causing excess mortality. Global regulators encourage people to get information from trusted sources, such as healthcare professionals, scientific sources and medicines regulators.

In Hong Kong, there are 9 registered pharmaceutical products which are COVID-19 vaccines, namely:

- Coronavac COVID-19 Vaccine (Vero Cell) Inactivated 0.5ml/dose 0.5ml Pre-filled Syringe (HK-67662), Coronavac COVID-19 Vaccine (Vero Cell) Inactivated 0.5ml/dose 0.5ml Vial (HK-67663) and Coronavac COVID-19 Vaccine (Vero Cell) Inactivated 0.5ml/dose 1ml Vial (HK-67664) which are registered by Sinovac Biotech (Hong Kong) Ltd;
- Comirnaty Dispersion For Injection COVID-19 mRNA Vaccine (Nucleoside Modified) 30 micrograms/dose (HK-67665) and Comirnaty Original/Omicron BA.4-5 Dispersion For Injection COVID-19 mRNA Vaccine (Nucleoside Modified) (15/15 micrograms)/dose (HK-67666) which are registered by Fosun Industrial Co Limited;
- Convidecia COVID-19 Vaccine (Ad5-nCoV-S) Recombinant 0.5ml/dose 0.5ml Vial (HK-67825) and Convidecia COVID-19 Vaccine (Ad5-nCoV-S) Recombinant 0.5ml/dose 1.5ml Vial (HK-67826) which are registered by Cansino Biologics (Hong Kong) Limited; and
- Spikevax Bivalent Original/Omicron BA.4-5

Dispersion For Injection COVID-19 mRNA Vaccine (Nucleoside Modified) (50 micrograms/50 micrograms)/ml (HK-67830) and Spikevax Bivalent Original/Omicron BA.4-5 Dispersion For Injection In Pre-filled Syringe COVID-19 mRNA Vaccine (Nucleoside Modified) (25 micrograms/25 micrograms) (HK-67831) which are registered by DKSH Hong Kong Limited.

All products are prescription-only medicines. Related news was also issued by Therapeutic Goods Administration (TGA) in July 2023.The Department of Health will remain vigilant on any safety update of the products issued by other overseas drug regulatory authorities.

European Union: EMA statement on ongoing review of GLP-1 receptor agonists

On 11 July 2023, the European Medicines Agency (EMA) announced that its safety committee, the Pharmacovigilance Risk Assessment Committee (PRAC), is reviewing data on the risk of suicidal thoughts and thoughts of self-harm with medicines known as glucagon-like peptide-1 (GLP-1) receptor agonists, including Ozempic (semaglutide), Saxenda (liraglutide) and Wegovy (semaglutide). These medicines are used for weight loss and for treating type 2 diabetes.

The review was triggered by the Icelandic medicines agency following reports of suicidal thoughts and self-injury in people using liraglutide and semaglutide medicines. So far authorities have retrieved and are analysing about 150 reports of possible cases of self-injury and suicidal thoughts.

Liraglutide and semaglutide medicines are widely used, with an exposure of over 20 million patient- years to date (one patient-year is the equivalent of one patient taking a medicine for one year). It is not yet clear whether the reported cases are linked to the medicines themselves or to the patients' underlying conditions or other factors.

The review is being carried out in the context of a signal procedure. A signal is information on a new adverse event that is potentially caused by a medicine or a new aspect of a known adverse event that warrants further investigation. The presence of a signal does not necessarily mean that a medicine caused the adverse event in question.

Suicidal behaviour is not currently listed as a side effect in the European Union product information for any GLP-1 receptor agonists.

The review of Ozempic, Saxenda and Wegovy started on 3 July 2023 and has now been extended to include other GLP-1 receptor agonists (dulaglutide, exenatide and lixisenatide). This review is expected to conclude in November 2023.

As with all medicines, patients and healthcare professionals are advised to use GLP-1 receptor agonists in accordance with the approved product information. Patients and healthcare professionals should also report suspected side effects to authorities.

In Hong Kong, there are registered pharmaceutical products containing dulaglutide (4 products), exenatide (1 product), liraglutide (3 products), lixisenatide (2 products) and semaglutide (6 products). All products are prescription-only medicines. As of the end of July 2023, the Department of Health (DH) had received adverse drug reaction related to dulaglutide (5 cases), exenatide (2 cases), liraglutide (1 case), lixisenatide (1 case) and semaglutide (2 cases), but these cases were not related to suicidal thoughts or self-injury. As the EMA's review is ongoing, the DH will remain vigilant on the conclusion of the review and any safety update of the drugs issued by other overseas drug regulatory authorities.

European Union: Start of a review concerning the conduct of studies at Synapse Labs Pvt. Ltd, India

On 21 July 2023, the European Medicines Agency (EMA) announced that it has started a review of medicines for which studies have been conducted by Synapse Labs Pvt. Ltd, a contract research organisation (CRO) located in Kharadi, India. This follows a good clinical practice (GCP) inspection carried out by the Spanish Agency of Medicines and Medical Devices (AEMPS) which raised serious concerns about the validity and reliability of study data generated at the CRO.

Having considered the findings of the GCP inspection, the Spanish medicines agency requested EMA's human medicines committee, Committee for Medicinal Products for Human Use (CHMP), to assess the impact on the benefits and risks of medicines that were authorised on the basis of studies performed at Synapse Labs' facilities. EMA has also been requested to look at the impact on medicines currently being evaluated for

authorisation that use study data generated at the CRO.

EMA will now review the available data to determine if any action is necessary to protect public health.

The review covers generic medicines authorised or currently being evaluated via national, decentralised or mutual recognition procedures on the basis of studies conducted by Synapse Labs Pvt. Ltd, India, on behalf of marketing authorisation holders and applicants.

In view of EMA is starting a review to determine which medicines are affected by Synapse Labs Pvt. Ltd, the Department of Health will remain vigilant on the conclusion of the review and safety update issued by other overseas drug regulatory authorities for consideration of any action deemed necessary.

The United Kingdom: Hyoscine hydrobromide patches (Scopoderm 1.5mg Patch or Scopoderm TTS Patch): risk of anticholinergic side effects, including hyperthermia

On 24 July 2023, the Medicines and Healthcare products Regulatory Agency (MHRA) announced that there have been a small number of reports of serious and life-threatening anticholinergic side effects associated with hyoscine hydrobromide patches, particularly when used outside the licence.

In the United Kingdom, the licensed indication of a hyoscine hydrobromide patch (Scopoderm 1.5mg Patch or Scopoderm TTS Patch) is for the prevention of motion or travel sickness symptoms (for example nausea, vomiting and vertigo) in adults and children aged 10 years of age or older. Each patch should be used for 72 hours. There is widespread use of hyoscine hydrobromide patches outside the licence. Hyoscine hydrobromide patches are often recommended in clinical guidance for indications other than motion or travel sickness.

Hyoscine hydrobromide is a muscarinic acetylcholine receptor antagonist. Since it crosses the blood-brain barrier it has both central and peripheral actions, causing a range of anticholinergic side effects including hyperthermia, urinary retention, dry mouth, disturbances of visual accommodation (blurred vision), mydriasis, skin irritation, generalised rash, somnolence, dizziness, memory impairment, disturbances in attention, restlessness, disorientation, confusion, hallucinations, delirium, seizures, coma, and respiratory paralysis.

After removal of the patch, hyoscine in the skin continues to enter the blood stream. Side effects may therefore persist for up to 24 hours or longer after patch removal. Children and elderly people are more susceptible to anticholinergic toxicity. Other specific risk factors for developing side effects have not been identified and there is no robust data available to give an estimate of frequency.

Hyoscine hydrobromide patches are used widely, however there have been a small number of serious and life-threatening anticholinergic side effects reported, particularly in use outside the licence. This includes the unexpected death of a child from hyperthermia caused by the hyoscine hydrobromide patch.

Following advice from the Paediatric Medicines Expert Advisory Group (PMEAG) of the Commission on Human Medicines, MHRA has requested that Marketing Authorisation Holders (MAHs) for hyoscine hydrobromide patches add hyperthermia to both the list of side effects in section 4.8 (undesirable effects) of the Summary of Product Characteristic (SmPC) and to the Patient Information Leaflet (PIL). This is consistent with current warnings in the tablet formulation. MHRA has also requested that the MAHs include information in the PIL regarding actions to take if hyperthermia occurs. This is consistent with information in Section 4.9 (overdose) of the SmPC. The PMEAG also noted that underreporting of anticholinergic side effects is likely and encouraged the reporting of adverse reactions through the Yellow Card scheme.

Advice for healthcare professionals:

- Be alert to the potential for anticholinergic side effects in patients who are prescribed hyoscine hydrobromide patches, particularly if used outside the licence.
- Usage outside the licence includes: use for indications other than motion or travel sickness, use in children younger than 10 years of age, cutting patches, application of more than one patch at a time, continuous use of patches without a break, and long-term use.
- Children and elderly patients are more susceptible to anticholinergic toxicity.
- Serious anticholinergic side effects can include hyperthermia, urinary retention,

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delirium, hallucinations, seizures, coma, and respiratory paralysis.

- If used in hospital or residential care settings, monitor patients for signs and symptoms of anticholinergic side effects and manage these promptly if they occur.
- If used at home, counsel patients, parents and carers on side effects to be aware of and what to do if they occur.

In Hong Kong, there are 2 registered pharmaceutical products which are transdermal patches containing hyoscine. These products are pharmacy only medicines. As of the end of July 2023, the Department of Health (DH) had received 2 cases of adverse drug reactions related to hyoscine, but these cases were not related to anticholinergic side effects including hyperthermia. In light of the above MHRA's announcement, letters to inform local healthcare professionals will be issued, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board .

Drug Recall

Batch recall of Sabril Tablets 500mg

On 13 July 2023, the Department of Health (DH) endorsed a licensed drug wholesaler, Sanofi Hong Kong Limited (Sanofi), to recall one batch (batch number: 2991A) of Sabril Tablets 500mg (Hong Kong registration number: HK-35365) from the market due to potential quality issue.

The DH received notification from Sanofi that the overseas manufacturer of the product reported that trace amount of an impurity identified as tiapride was detected in the product. The most probable cause was due to carryover of tiapride on the same equipment during production of active ingredient vigabatrin. The level of tiapride detected was below the permitted daily exposure. As a precautionary measure, Sanofi is voluntarily recalling the affected product from the market.

The above product, containing vigabatrin, is a prescription medicine indicated for the treatment of epilepsy. According to Sanofi, the affected batch has been supplied to the Hospital Authority, local pharmacies and re-exported to Macau.

As of the end of July 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 13 July 2023 to alert the public of the product recall. The DH will closely monitor the recall.

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.

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,
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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.