Drug News
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Issue Number 184

This is a monthly digest of local and overseas drug safety news released by the Drug Office of the Department of Health in February 2025 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

The United States: FDA alerts healthcare professionals about the risk of medication errors with tranexamic acid injection resulting in inadvertent intrathecal (spinal) injection: Update

On 10 February 2025, the United States Food and Drug Administration (FDA) announced that it continues to receive reports of tranexamic acid injection being erroneously administered intrathecally instead of the intended intrathecal (spinal) anesthetic (e.g., bupivacaine injection) for neuraxial anesthesia.

These medication errors have resulted in severe outcomes, including death, disability, and prolonged hospitalization. FDA is conducting a safety evaluation and is investigating the issue. After the evaluation is complete, FDA will communicate any findings or additional actions that will help mitigate these medication errors.

In Hong Kong, there are 7 registered pharmaceutical products which are tranexamic acid injectables. All products are prescription-only medicines. As of the end of February 2025, with regard to tranexamic acid, the Department of Health (DH) had received 6 cases of adverse drug reaction, but these cases were not related to medication errors. Related news was previously issued by FDA, and was reported in the Drug News Issue No. 134. As the safety evaluation is ongoing, the DH will remain vigilant on its conclusion and any safety update of the drug issued by other overseas drug regulatory authorities for consideration of any actions deemed necessary.

The United Kingdom: Valproate (Belvo, Convulex, Depakote, Dyzantil, Epilim, Epilim Chrono or Chronosphere, Episenta, Epival, and Syonell): review by two specialists is required for initiating valproate but not for male patients already taking valproate

On 13 February 2025, the Medicines and Healthcare products Regulatory Agency (MHRA) announced that review by two specialists remains in place for patients initiating valproate under 55 years of age but the Commission on Human Medicines (CHM) has advised that it will not be required for men (or males) currently taking valproate. Three infographics have been developed to provide clarity regarding valproate prescribing.

Valproate (as sodium valproate, valproic acid or valproate semisodium) is authorised for the treatment of epilepsy and bipolar disorder. Valproate is known to have potential risks of major congenital malformations or neurodevelopmental disorders in children when mothers take valproate during pregnancy. More recently, the risk of a range of neurodevelopmental disorders in children born to fathers taking valproate compared to other antiseizures medicines has been described.

Studies have shown that the use of valproate during pregnancy is associated with risks of physical defects, in around 1 in 9 babies exposed, and neurodevelopmental disorders, in around 3-4 in 10 babies when mothers use valproate in pregnancy. There is a much lower potential risk of neurodevelopmental disorders, in around 5 in 100 babies when fathers take valproate in the 3 months before conception. Additional reproductive risks of valproate in male patients include infertility in humans and evidence of testicular toxicity in animals.

In 2022, the CHM reviewed the latest data on the reproductive risks with valproate. Their advice was communicated in Drug Safety Update December 2022. The CHM formed an implementation group

to advise on the safe introduction of the new measures into clinical practice. The measures were applied first to all new patients under 55 years old and women of childbearing potential already under specialist review. The National Patient Safety Alert on 28 November 2023 and Drug Safety Update January 2024 provided further advice on the implementation of these requirements.

No requirement for specialist review of men currently taking valproate was introduced at this time unless the male patient was planning to father a child. The CHM recommended that any further measures should consider advice from healthcare professionals and patients developed in light of experience with the initial phase.

Advice for Healthcare Professionals:

- Review by two specialists remains in place for all patients initiating valproate under 55 years of age but the CHM has advised that it will not be required for men (or males) currently taking valproate. Given the recent recommendations in Drug Safety Update September 2024, the CHM advised that there is already sufficient risk minimisation in place for this patient group but that this position should be kept under review. In addition to the Drug Safety Update September 2024, further information on the reproductive risks for males can be found in a Public Assessment Report published in November 2023. Any patient wishing to change their medication should be referred to a specialist. The information considered by CHM and the advice issued is presented in a Public Assessment Report.
- Three infographics have been produced to clarify in which situations review by two specialists may be required:
  (i) for female patients under 55 years old
  (ii) for male patients under 55 years old
  (iii) for male and female patients 55 years and older
- A list of who might qualify as a specialist can be found at Valproate safety measures

  For details of the above advice, please refer to the website in MHRA.

In Hong Kong, there are 10 registered pharmaceutical products containing valproate. All products are prescription-only medicines. As of the end of February 2025, the Department of Health (DH) had received 17 cases of adverse drug reaction with regard to valproate, of which 2 cases were reported as congenital malformations in neonates exposed to valproate during pregnancy. Related news on potential risks to children when mothers taking valproate during pregnancy or children born to fathers taking valproate, and measures to reduce the reproductive risks of valproate was previously issued by various overseas drug regulatory authorities, and was reported in the Drug News since Issue No. 21, with the latest update reported in the Drug News Issue No. 179. The DH issued letters to inform local healthcare professionals to draw their attention on 4 July 2011, 7 May 2013, 13 October 2014, 12 February 2018, 13 December 2022 and 22 March 2023.

The Registration Committee of the Pharmacy and Poisons Board discussed the matter related to the risks in pregnancy associated with the use of valproate in September 2011, December 2014, December 2018 and June 2019. Currently, the package insert or sales pack label of locally registered valproate-containing products should include safety information on the risk of malformations and impaired cognitive development in children exposed to valproate during pregnancy, and contraindications, e.g. in women of childbearing potential unless pregnancy preventive measures have been implemented, etc. The certificate holders of locally registered valproate-containing products are also required to implement risk minimisation measures, e.g. patient information leaflet should be provided, etc.

As previously reported, the matter will be further discussed by the Registration Committee of the Pharmacy and Poisons Board.

The United States: FDA issues class-wide labeling changes for testosterone products

On 28 February 2025, the United States Food and Drug Administration (FDA) announced that FDA informed sponsors of testosterone products about new labeling changes following the agency's review of the findings from the Testosterone Replacement Therapy for Assessment of Long-term Vascular Events and Efficacy Response in Hypogonadal Men (TRAVERSE) clinical trial and the results from required postmarket ambulatory blood pressure (ABPM) studies.

Led by the TRAVERSE trial's results, FDA is recommending changes to current labeling language, to include:

- adding the results of the TRAVERSE trial to all testosterone products;
- retaining "Limitation of Use" language for age-related hypogonadism; and
- removing language from the Boxed Warning related to an increased risk of adverse cardiovascular outcomes for all testosterone products.

Led by results of the ABPM studies, FDA is also requiring changes to current labeling language, to include:

- adding product-specific information on increased blood pressure for testosterone products with completed ABPM studies;
- adding a new warning about increased blood pressure for testosterone products which currently do not have such a warning in their labeling.

Testosterone, a hormone essential to the development of male growth and masculine characteristics, is used in men who lack or have low testosterone levels in conjunction with an associated medical condition. Current FDA-approved testosterone formulations include oral, topical gel, transdermal patch, buccal system (applied to upper gum or inner cheek), and injection.

FDA first convened a Joint Meeting of the Bone, Reproductive and Urologic Drugs and the Drug Safety and Risk Management Advisory Committee in September 2014 following increased reports of stroke, heart attack, and death in men taking FDA-approved testosterone products. This meeting resulted in the agency's recommendation for an industry-wide clinical trial to assess the safety of use in men with age-related hypogonadism (insufficient sex hormone production). Results from the TRAVERSE trial were submitted in 2023, concluding that there was no increase in the risk of adverse cardiovascular outcomes in men using testosterone for hypogonadism.

Additionally, in 2016 and 2017, FDA recommended ABPM studies as part of the premarket development of two different testosterone products, administered by two different routes (subcutaneous injection and oral). Consistent results from the premarket ABPM studies of the two products raised concerns that use of testosterone products could lead to increased blood pressure. In March 2018, FDA also issued a postmarket requirement that individual ABPM studies be conducted for all testosterone products. Results from the completed ABPM studies confirmed an increase in blood pressure with use of all testosterone products, class-wide.

The action in this announcement follows several prior FDA actions regarding the safety of testosterone products, including a January 2014 Drug Safety Communication (DSC) warning of reported risks of stroke, heart attack, and death in men taking FDA-approved testosterone products; and a March 2015 DSC informing of required labeling changes and urging caution when using testosterone products for low testosterone due to aging.

In Hong Kong, there are 7 registered pharmaceutical products containing testosterone. All products are prescription-only medicines. As of the end of February 2025, with regard to testosterone, the Department of Health (DH) had received 1 case of adverse drug reaction which was not related to increased blood pressure. Related news on cardiovascular risk was previously issued by various overseas drug regulatory authorities, and was reported in the Drug News since Issue No. 52, with the latest update reported in the Drug News Issue No. 72. The DH issued letters to inform local healthcare professionals to draw their attention on 16 July 2014 and 13 October 2014.

In February 2015, the Registration Committee of the Pharmacy and Poisons Board discussed the matter, and decided that the package insert of products containing testosterone should include safety information on the cardiovascular risk, including the risk of increased blood pressure. The DH will remain vigilant on safety update of the drug issued by other overseas drug regulatory authorities.

Batch recall of Akynzeo Concentrate for Solution for Infusion 235mg/0.25mg in 20ml

On 6 February 2025, the Department of Health (DH) endorsed a licensed drug wholesaler, namely Pharmason Company Limited (Pharmason), distributor appointed by the holder of certificate of drug registration, Fosun Industrial Co., Limited (Fosun Industrial), to recall one batch (batch number: 43001977) of Akynzeo Concentrate for Solution for Infusion 235mg/0.25mg in 20ml (Hong Kong Registration number: HK- 67828), from the market as a precautionary measure due to potential quality issue.

The DH received notification from Fosun Industrial that the overseas manufacturer of the product is recalling the above batch due to stability test of retained sample showing out of specification assay result. As a precautionary measure, Fosun Industrial voluntarily recalls the above batch from the market.

The above product, containing fosnetupitant and palonosetron, is a prescription medicine indicated for the prevention of nausea and vomiting associated with chemotherapy. According to Fosun Industrial, the above batch of product was imported into Hong Kong and distributed by Pharmason and has been supplied to the Hospital Authority, local private hospitals and private doctors.

As of the end of February 2025, 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 6 February 2025 to alert the public of the product recall. The DH will closely monitor the recall.

Batch recall of Regpara Tablets 25mg due to presence of impurity

On 12 February 2025, the Department of Health (DH) endorsed a licensed drug wholesaler, DKSH Hong Kong Limited (DKSH), to recall a total of 10 batches (batch number: DES169675, DHS171505, DMS173037, DBS176064, DBS176065, EES176886, EES177675, EHS178805, EHS179575 and ENS181132) of Regpara Tablets 25mg (Hong Kong registration number: HK-58066) from the market as a precautionary measure due to the presence of impurity in the product.

The DH received notification from DKSH that the overseas manufacturer of the product is recalling the above batches of Regpara Tablets 25mg as they may exceed the acceptable daily intake limit of an impurity, N-nitroso-cinacalcet. N-nitroso-cinacalcet is classified as a probable human carcinogen based on results from laboratory tests. As a precautionary measure, DKSH is voluntarily recalling the affected batches of product from the market.

The above product, containing cinacalcet, is a prescription medicine primarily used for the treatment of secondary hyperparathyroidism in patients undergoing maintenance dialysis. According to DKSH, the affected batches of product have been imported into Hong Kong and supplied to the Hospital Authority, local private hospitals, private doctors and pharmacies, and re-exported to Macao.

As of the end of February 2025, the DH had not received any adverse reaction reports in connection with the product. A notice was posted in the Drug Office website on 12 February 2025 to alert the public of the product recall. The DH noted that the recall was completed.

Batch recall of Zovirax IV for Intravenous Infusion 250mg

On 28 February 2025, the Department of Health (DH) endorsed a licensed drug wholesaler, namely GlaxoSmithKline Limited (GSK), to recall one batch (batch number: RN3T) of Zovirax IV for Intravenous Infusion 250mg (Hong Kong Registration number: HK- 18688), from the market as a precautionary measure due to potential quality issue.

The DH received notification from GSK that the overseas manufacturer of the product is initiating a voluntary recall following a complaint reporting glass-like particles in a batch of the above product that was not supplied to Hong Kong. Upon the company's ongoing investigation, the above batch is considered to have the same potential quality issue. As a precautionary measure, GSK is voluntarily recalling the affected batch of product from the market

The above product, containing aciclovir, is a prescription medicine used for the treatment of Herpes simplex infections and Varicella zoster infections. According to GSK, the above batch of product has been imported into Hong Kong and supplied to the Hospital Authority, local private hospitals and private doctors, and re-exported to

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Macau.

As of the end of February 2025, 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 28 February 2025 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.

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.

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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.