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 March 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

Australia: Potential risk of neurodevelopmental disorders in children born to men taking sodium valproate

On 7 March 2025, the Therapeutic Goods Administration (TGA) announced that a retrospective observational study in Europe has suggested there may be an increased risk of neurodevelopmental disorders in children born to men who had been taking sodium valproate in the 3 months before conception compared to children born to men treated with lamotrigine or levetiracetam.

Sodium valproate belongs to a group of medicines called anticonvulsants. It is used to treat epilepsy and mania. Neurodevelopmental disorders studied included autism spectrum disorder, intellectual disability, communication disorder and attention deficit/hyperactivity disorder, and movement disorders.

Due to methodological limitations, the findings of this study should be interpreted with caution. As a precaution, Sanofi-Aventis, the sponsor of Epilim, which is the original brand of sodium valproate, have added new warnings about paternal exposure to the Product Information (PI) and Consumer Medicine Information (CMI). Sponsors of generic sodium valproate products will be required to align their safety information with Epilim.

The TGA reviewed the evidence provided by the sponsor and approved the sponsor's application to add warnings to the PI in April 2024. After reviewing further evidence, including careful consideration of the limitations of the European study, the TGA made the decision to retain the new warnings in the PI out of an abundance of caution, and to align with other regulators. No Australian adverse events relating to paternal exposure to sodium valproate have been reported to the TGA. For details of the additions of warnings to the PI, please refer to the website in TGA.

Sodium valproate is a known teratogen with a long-documented history of congenital malformations (including spina bifida) and neurodevelopmental disorders following maternal sodium valproate exposure. There are already recommendations in the Australian PI to avoid this medicine in pregnancy and advice about its use in people with childbearing potential.

Prescribing restrictions for sodium valproate for all patients under 55 years have been recently introduced in the UK. In response to this change, we conducted a review and requested expert advice from the Advisory Committee on Medicines (ACM) on whether Australia should follow the UK in imposing similar restrictions.

The ACM advised there has been no real change in the risk profile to children following maternal exposure since they last reviewed this issue in 2018, and that there was insufficient evidence to amend the indication or implement restrictions for sodium valproate to exclude particular patient groups. The TGA will continue to monitor this signal as part of its routine safety monitoring of medicines.

What health professionals should do:

- The new warnings instruct health professionals to inform their male patients about the potential risks of sodium valproate and discuss the need for effective contraception, for both the patient and their female partner.
- Male patients taking sodium valproate should be specifically advised to consult their doctor to discuss alternative treatment options if they are planning to father a child, and before discontinuing contraception; to consult their

doctor to discuss alternative treatment options if they are planning to father a child, and before discontinuing contraception; to consult their doctor to discuss alternative treatment options if they are planning to father a child, and before discontinuing contraception.

- Men taking sodium valproate should be reviewed regularly (at least annually) by a specialist experienced in the management of epilepsy or bipolar disorder to consider whether valproate-containing medicine remains the most suitable option, particularly when the patient is planning to conceive a child.
- Existing recommendations in the PI about maternal exposure to sodium valproate remain unchanged as we continue routine safety monitoring and surveillance of this medicine. Patients with childbearing potential and taking sodium valproate are encouraged to discuss any concerns with a health professional.

In Hong Kong, there are 10 registered pharmaceutical products containing valproate. All products are prescription-only medicines. As of the end of March 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 following maternal exposure to valproate during pregnancy, and these cases were not related to neurodevelopmental disorders in children after paternal exposure to valproate. Related news 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. 184. 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 minimization 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.

Australia: More prominent warnings about serious side effects for fluoroquinolone antibiotics

On 7 March 2025, the Therapeutic Goods Administration (TGA) announced that more prominent warnings are being added to the product information (PI) and consumer medicine information (CMI) for all oral and injectable (systemic) fluoroquinolones to strengthen existing warnings about serious side effects. These include central nervous system stimulation leading to transient tremor, restlessness, light-headedness, confusion, and very rarely to hallucinations or seizures; tendonitis and tendon ruptures; psychiatric reactions.

Although rare, these side effects can be disabling and potentially irreversible. They can occur in patients of any age without pre-existing risk factors and have been reported simultaneously in the same patient. The nervous system and psychiatric reactions can occur after the first dose. These updated warnings do not apply to fluoroquinolone eye or ear drops.

Fluoroquinolones, including ciprofloxacin, norfloxacin and moxifloxacin, are broad-spectrum antibiotics used against susceptible infections and are usually reserved for patients who have no other treatment options. Fluoroquinolones are broad-spectrum antibiotics that are active against a wide range of bacteria, including gram-negative and some gram-positive organisms. Oral and intravenous fluoroquinolone antibiotics marketed in Australia include ciprofloxacin, norfloxacin, moxifloxacin.

A 2023 review by the UK's Medicines and Healthcare products Regulatory Agency (MHRA) into the serious side effects associated with fluoroquinolones found that regulatory changes taken by the MHRA to restrict use in 2019 had not appeared to reduce prescribing rates. These regulatory changes stated that fluoroquinolones should not be prescribed for non-severe or

self-limiting conditions, or non-bacterial conditions, for example non-bacterial prostatitis. As a result, the MHRA review recommended several updates to the safety information to highlight the risks of these side effects. They also recommended the updates should be communicated directly to health professionals.

After investigating this issue, the TGA is introducing 'boxed warnings' to the Australian PIs and CMIs to raise awareness of these serious side effects in line with warnings from other international regulators. Boxed warnings are included on the first page of PIs and CMIs to highlight significant medicine safety risks. The boxed warning will be included in the Australian PIs for oral and injectable ciprofloxacin, norfloxacin and moxifloxacin products and relates to existing information in Section 4.4 Special warnings and precautions. Health professionals should refer to the PI of the relevant product for more detailed information as the wording in section 4.4 differs between products.

The boxed warning text (ciprofloxacin is given as the example) is:
Serious disabling and potentially irreversible adverse reactions
Fluoroquinolones, including ciprofloxacin, have been associated with disabling and potentially irreversible serious adverse reactions involving different body systems that have occurred together in the same patient. Patients of any age or without pre-existing risk factors have experienced these adverse reactions. These include but are not limited to serious adverse reactions involving the nervous system (see section 4.4 Effects on the CNS), musculoskeletal system (see section 4.4 Tendonitis and tendon rupture) and psychiatric effects (see section 4.4 Psychiatric reactions).

Health professionals should:

- be aware of these potential serious side effects and are reminded to use fluoroquinolones judiciously in line with Australian antibiotic prescribing guidelines.
- warn patients to be alert to any unusual symptoms following treatment with fluoroquinolones and to seek health advice.
- promptly discontinue fluoroquinolones in the event of an adverse reaction and consider prescribing alternative treatment.

In Hong Kong, there are registered pharmaceutical products containing oral and injectable (systemic) fluoroquinolones for use in human, including ciprofloxacin (49 products), levofloxacin (42 products), moxifloxacin (6 products), norfloxacin (3 products), ofloxacin (12 products), prulifloxacin (one product) and delafloxacin (2 products). All products are prescription-only medicines.

As of the end of March 2025, the Department of Health (DH) had received adverse drug reaction with regard to levofloxacin (13 cases; of which 3 cases were reported as musculoskeletal, nervous and/or psychiatric reactions) and ofloxacin (4 cases; all of these cases were reported as attempted suicide/completed suicide). The DH had received adverse drug reaction related to ciprofloxacin (2 cases) and moxifloxacin (one case), but these cases were not related to the disabling side effects mentioned in the above TGA's announcement. The DH had not received any case of adverse drug reaction related to norfloxacin, prulifloxacin and delafloxacin.

Related news on the risk of musculoskeletal, nervous and psychiatric adverse reactions associated with the use of fluoroquinolones was previously issued by various overseas drug regulatory authorities, and was reported in the Drug News since Issue No. 25, with the latest update reported in the Drug News Issue No. 171. The DH issued letters to inform local healthcare professionals to draw their attention on 8 November 2011, 16 August 2013, 13 May 2016, 11 July 2018, 8 October 2018 and 23 January 2024.

The Registration Committee of the Pharmacy and Poisons Board discussed the matter related to the above risks associated with the use of fluoroquinolones in September 2016, June 2019 and September 2024. Currently, the sales pack labels and/or package inserts of locally registered pharmaceutical products containing fluoroquinolones for systemic use should contain safety information about the risk of disabling and potentially irreversible serious adverse reactions, including tendinitis, tendon rupture and central nervous system effects (hallucinations, anxiety, depression, insomnia, severe headaches, and confusion). The DH will remain vigilant on safety update of the drug issued by other overseas drug regulatory authorities for consideration of any action deemed necessary.

The United Kingdom: Prolonged-release opioids: Removal of indication for relief of postoperative pain

On 12 March 2025, the Medicines and Healthcare products Regulatory Agency (MHRA) announced that the indication for the treatment of post-operative pain has been removed from the licenses of all prolonged-release opioids due to the increased risk of persistent post-operative opioid use (PPOU) and opioid-induced ventilatory impairment (OIVI). It is not recommended to use transdermal patches for the treatment of post-operative pain.

Prolonged-release (modified release) opioids are indicated for moderate or severe pain and cancer pain, although NICE guidance recommends that opioids are not used for chronic primary pain where there is no underlying condition accounting for the pain. A small number of prolonged-release opioids containing morphine or oxycodone were also authorized for the treatment of postoperative pain, however concerns were raised on the potential for harm and an increased risk of PPOU and OIVI.

PPOU is defined as continued opioid use beyond 90 days from the day of operation. Dependence is a well-known side effect of opioids and we continue to communicate to raise awareness on this issue. Evidence from across the EU including the UK has shown that the incidence of PPOU ranges from 2% - 44% in patients treated with prolonged-release opioids. Also PPOU is more prevalent (incidence up to 60%) in patients taking prolonged-release opioids pre-operatively.

Respiratory depression is also a well-known side effect of opioids, especially if taken in excess or in combination with other sedating medicines (for example benzodiazepines, pregabalin or gabapentin) which can lead to coma and potentially death. OIVI is a serious form of respiratory depression associated with depression of respiratory rate and/or depth of breathing – 'central respiratory depression', depression of consciousness – 'sedation', depression of supraglottic airway muscle tone – 'upper airway obstruction'. The reported incidence of OIVI is difficult to determine, although the international multidisciplinary consensus statement quotes an incidence of OIVI ranging from 0.4% to 41% depending on the identification measures used.

Following the conclusion of a safety review undertaken by the MHRA, and advice from the Commission on Human Medicines (CHM), the indication for the treatment of post-operative pain will be removed from the licenses of prolonged-release morphine and prolonged-release oxycodone. The remaining prolonged-release opioids are not recommended for acute post-operative pain relief and may already not be indicated for acute use or are contraindicated in acute pain relief. The information considered by the CHM and the advice issued is presented in a Public Assessment Report. For details, please refer to the website in MHRA.

Pain following surgery is usually short-lived, lasting between 5 – 7 days and therefore should only require short-term pain management best treated with immediate release opioids. However, many patients are discharged from hospitals with excessive amounts of opioids to meet their needs for acute post-operative pain management. This excess supply of opioids increases the risk of developing PPOU, dependence, addiction, or could lead to opioid diversion, and an increased risk of OIVI with unmanaged use. Therefore, patients should only be provided with a prescription for a sufficient amount of instant release opioids to manage their acute post-operative pain on discharge from hospital.

A Consensus Best Practice Guideline agreed between the Faculty of Pain Medicine, Royal College of Anaesthetists, Royal College of General Practitioners, Royal College of Surgeons of England, Royal College of Nursing, The British Pain Society, the Centre for Perioperative Care and endorsed by the Royal Pharmaceutical Society, recommend that pre-operative use of opioids should be reviewed prior to surgery.

Adjustments in dose or dosing regimen might be necessary in patients at increased risk of experiencing these severe adverse reactions, including patients with compromised respiratory function or respiratory disease, with neurological disease, with renal impairment, with cardiovascular disorders, using concomitant central nervous system (CNS) depressants, older than 65 years, with opioid tolerance, using opioids pre-operatively. Patients and healthcare professionals are encouraged to discuss treatment regimens and agree a post-operative pain management plan prior to the proposed surgical procedure.

Advice for healthcare professionals:

- prolonged-release opioids provide relief from chronic severe pain, however, they should not be used for the treatment of acute pain following surgery.
- prolonged-release opioids are associated with an increased risk of PPOU characterized as continued opioid use beyond 90 days following the operation, and an increased risk of OIVI causing serious respiratory depression, sedation, and depression of upper airway muscle tone.
- before surgery, discuss with the patient the followings:
  - explain the risks of PPOU, dependence and potential risk of addiction and withdrawal reactions.
  - explain the risk of OIVI especially for patients with underlying respiratory conditions.
  - immediate-release opioids are used for short-term treatment of pain.
  - discuss with the patient pain management strategies involving the use of immediate-release opioids and multimodal analgesia and plan for end of treatment.
- patients whose pain is managed with opioids pre-operatively should have their treatment reviewed before and after surgery in line with Consensus Best Practice Guidelines.
- at discharge from hospital:
  - only prescribe and supply a sufficient amount of immediate-release opioids to treat acute post-operative pain to minimise the risk of PPOU, dependence, stock piling of unused opioids and potential for diversion.
  - communicate the pain management plan with the primary care practice taking over care in the community and document in patient clinical notes.

In Hong Kong, there are 14 pharmaceutical products which belong to prolonged-release opioids, including the ingredients codeine, morphine, oxycodone and tramadol. There are 3 registered pharmaceutical products which is transdermal patch containing fentanyl. These products are prescription-only medicines. As of the end of March 2025, the Department of Health (DH) had received adverse drug reaction with regard to morphine (11 cases), tramadol (9 cases), fentanyl (6 cases), codeine (4 cases) and oxycodone (2 cases), of which 5 cases were related to ventilatory impairment and none of these cases were related to persistent post-operative opioid use.

Related news on the safe and appropriate use of opioid analgesics including prolonged-release opioids was previously issued by various overseas drug regulatory authorities, and was reported in the Drug News since Issue No. 47, with the latest update reported in the Drug News Issue No. 170. The DH issued letters to inform local healthcare professionals to draw their attention on 11 September 2013 and 14 April 2023. In February 2015, the Registration Committee of the Pharmacy and Poisons Board discussed the matter, and decided that pharmaceutical products which are controlled-release, extended-release or long-acting opioid analgesics (containing hydromorphone, morphine, oxycodone, oxymorphone, tapentadol, fentanyl, buprenorphine and methadone) should include safety information about the risks of addiction, abuse, misuse, overdose and death, and limitations of use in patients with severe pain for which alternative treatment options are inadequate.

In light of the above MHRA's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 13 March 2025, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Canada: Summary Safety Review: Glucagon-like Peptide 1 Receptor Agonists (GLP-1 RAs) (dulaglutide, exenatide, liraglutide, lixisenatide and semaglutide) - Assessing the potential risks of suicide, self-harm and suicidal/self-harm ideation

On 27 March 2025, Health Canada announced that it reviewed the potential risks of suicide, self-harm and suicidal/self-harm ideation with the use of GLP-1 RAs. The safety review was triggered by case reports of suicidal thoughts and self-harm submitted to the European Medicines Agency (EMA).

Glucagon-like peptide 1 receptor agonists are a class of prescription drugs authorized for sale in Canada for adults with type 2 diabetes [Ozempic/Rybelsus (semaglutide), Victoza (liraglutide), Trulicity (dulaglutide), Xultophy (insulin degludec and liraglutide) and Soliqua (insulin glargine and lixisenatide)], or for chronic weight management in adults and adolescents who are obese or overweight [Wegovy (semaglutide)

and Saxenda (liraglutide)].

Health Canada reviewed the available information provided by manufacturers, and from searches of the Canada Vigilance database, the World Health Organization's adverse drug reaction database and the scientific literature. Health Canada reviewed 15 cases (3 Canadian and 12 international) of suicide, self-harm and suicidal/self-harm ideation in patients using GLP-1 RAs, including 2 from the published literature. Of the 15 cases, 12 (3 Canadian) were found to be possibly linked to the use of GLP-1 RAs and 3 could not be assessed due to missing clinical information.

A definitive link could not be confirmed due to insufficient information about possible confounders (other factors that may have contributed to the occurrence of suicide, self-harm and suicidal/self-harm ideation), such as pre-existing mental health problems, family history, life stressors, social and environmental factors, and use of other medications that has labelling related to suicidality.

Health Canada also reviewed clinical trial data from the manufacturers, and real-world data from published and unpublished sources. Overall, the evidence from these studies does not support a link between GLP-1 RAs and the risks of suicide, self-harm and suicide/self-harm ideation in patients with type 2 diabetes. However, in the subgroup of patients with obesity (with or without type 2 diabetes), the evidence was not as clear. Additional information is needed to determine if there is a link between GLP-1 RAs and suicide, self-harm, and suicide/self-harm ideation in patients with obesity (with or without type 2 diabetes).

Health Canada's review did not find evidence to support a link between GLP-1 RAs and the risks of suicide, self-harm and suicidal/self-harm ideation in patients with type 2 diabetes. There was not enough information to determine if there is a link in patients with obesity. Health Canada published a Health Product InfoWatch communication in December 2024 to share information about the review with healthcare professionals. Health Canada will continue to monitor the safety of GLP-1 RAs.

In Hong Kong, there are registered pharmaceutical products containing exenatide (1 product), lixisenatide (2 products), liraglutide (5 products), dulaglutide (4 products), and semaglutide (11 products). All products are prescription-only medicines. As of the end of March 2025, the Department of Health (DH) had received adverse drug reactions with regard to exenatide (2 cases), lixisenatide (1 case), liraglutide (1 case), dulaglutide (5 cases), and semaglutide (10 cases), but these cases were not related to suicide or self-harm ideation. Related news was previously issued by various overseas drug regulatory authorities, and was reported in the Drug News since Issue No. 165, with the latest update reported in the Drug News Issue No. 179. The DH will remain vigilant on safety update of the drugs issued by other overseas drug regulatory authorities.

Canada: Summary Safety Review: Isotretinoin: Assessing the potential risk of sacroiliitis

On 27 March 2025, Health Canada announced that it reviewed the potential risk of sacroiliitis associated with the use of isotretinoin. The safety review was triggered by a labelling update by the European Medicines Agency.

Isotretinoin is a prescription drug authorized for sale in Canada for the treatment of severe forms of acne in patients 12 years of age and older that should be used when the acne fails to respond to other treatments.

Health Canada reviewed the available information provided by manufacturers, as well as from searches of the Canada Vigilance database, international databases and the scientific literature. Health Canada reviewed 24 international cases of sacroiliitis in patients taking isotretinoin. Of those 24 cases, 23 were found to be possibly linked to the use of isotretinoin and 1 was unlikely to be linked. The average age was 20 years in cases where the age was provided. No deaths were reported among the 24 cases reviewed.

Health Canada also reviewed 18 articles published in the scientific literature. While the studies supported a link between the risk of sacroiliitis and the use of isotretinoin, they did not identify a clear biological mechanism to explain how isotretinoin use could lead to sacroiliitis. In both the cases reviewed and the scientific literature, sacroiliitis improved after discontinuation of isotretinoin and appropriate treatment.

Health Canada's review of the available information found a possible link between isotretinoin and the risk of sacroiliitis. Health

Canada is working with the manufacturers to update the Canadian product monograph for isotretinoin-containing products to include the risk of sacroiliitis. Health Canada will also 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 March 2025, with regard to isotretinoin, the Department of Health (DH) had received 2 cases of adverse drug reaction, but these cases were not related to sacroiliitis. In light of the above Health Canada's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 28 March 2025, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Canada: Summary Safety Review: Oral anticoagulants (apixaban, dabigatran, edoxaban, rivaroxaban and warfarin): Assessing the potential risk of splenic rupture

On 27 March 2025, Health Canada announced that it reviewed the potential risk of splenic rupture with the use of oral anticoagulants. The safety review was triggered by international reports concerning this risk in patients taking rivaroxaban where no trauma or other risk factor was identified.

Oral anticoagulants are prescription drugs, also known as blood thinners, authorized for sale in Canada to prevent blood clots from forming after knee or hip replacement surgery; reduce the risk of stroke (damage to part of the brain caused by an interruption of its blood supply) or systemic embolism (the sudden blocking of a blood vessel by a blood clot) in people who have a heart condition called atrial fibrillation (irregular heart beat); treat deep vein thrombosis (blood clots in the veins of the legs) and pulmonary embolism (blood clots in the blood vessels of the lungs), and reduce the risk of them occurring again.

Health Canada reviewed the available information from searches of the Canada Vigilance database and the scientific literature. Health Canada reviewed 42 cases (3 Canadian and 39 international) of splenic rupture in patients taking oral anticoagulants, including 39 from the published literature. Of the 42 cases, 1 was found to be probably linked to the use of oral anticoagulants, 21 (1 Canadian) were found to be possibly linked, 16 were unlikely to be linked, and 4 (2 Canadian) could not be assessed due to missing information.

Besides having taken oral anticoagulants, in 9 of the 21 possible cases, there was no other possible explanation (for example, trauma or existing medical condition) reported for the splenic rupture. However, atraumatic rupture of the spleen is known to occasionally occur. Given the known increased risk of bleeding associated with anticoagulants, patients taking these drugs are at an increased risk of bleeding within their spleen, which can lead to a rupture of its capsule (the outer layer surrounding the spleen).

Health Canada also reviewed the findings from a study that examined over 27,000 international reports of suspected adverse drug reactions associated with oral anticoagulants. The findings showed that events of splenic rupture were more frequently reported than expected with these drugs, thereby supporting a link.

Health Canada's review of the available information found a possible link between oral anticoagulants and the risk of atraumatic splenic rupture. Health Canada is working with the manufacturers to update the Canadian product monograph for all oral anticoagulants to include the risk of atraumatic splenic rupture.

In Hong Kong, there are registered pharmaceutical products containing apixaban (6 products), dabigatran (6 products), edoxaban (3 products), rivaroxaban (20 products) and warfarin (4 products). All products are prescription-only medicines.

As of the end of March 2025, the Department of Health (DH) had received adverse drug reaction with regard to apixaban (66 cases), dabigatran (22 cases), edoxaban (29 cases) and rivaroxaban (26 cases), but these cases were not related to splenic rupture. With regard to warfarin, the DH had received 15 cases of adverse drug reaction, of which one case was reported as splenic rupture.

In light of the above Health Canada's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 28 March 2025, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

European Union: EMA concludes review of weight management medicine Mysimba (naltrexone/bupropion) - Benefits continue to outweigh risks, with new risk minimization measures and more information to be provided about long-term effect on the heart

On 28 March 2025, the European Medicines Agency (EMA) announced that the EMA's Committee for Medicinal Products for Human Use (CHMP) has finalized its review of Mysimba (naltrexone/bupropion), a medicine used for weight management in adults with obesity or overweight. The review was prompted by concerns about a potential long-term cardiovascular risk (risk affecting the heart and blood circulation) with the medicine.

The CHMP has concluded that the benefits of Mysimba continue to outweigh its risks. However, the company must provide more information from an ongoing study on the medicine's cardiovascular effects in patients treated for longer than one year. New measures are also being implemented to minimize potential cardiovascular risks with long-term use.

At the time of Mysimba's authorization, the CHMP noted uncertainties regarding the long-term effects of Mysimba on the cardiovascular system. To date, studies have shown that there is no cardiovascular safety concern when Mysimba is used for up to 12 months. However, the data available are not sufficient to fully determine the cardiovascular safety beyond this time.

The CHMP has agreed that an ongoing safety study with Mysimba in patients with obesity or overweight carried out by the company is appropriate to generate evidence about this risk in the long term. The results are expected in 2028, and the company must provide annual reports on the progress of the study. The CHMP has imposed this study as a condition to the marketing authorization.

In addition, further measures will be implemented to minimize potential cardiovascular risks with long-term use. Treatment with Mysimba should be stopped after one year if weight loss of at least 5% of the initial body weight is not maintained. In addition, healthcare professionals should carry out a yearly assessment and discuss with their patients whether Mysimba remains beneficial for them, taking into account any changes to their cardiovascular risk and whether weight loss has been maintained.

During the review, the CHMP considered all available data in relation to the cardiovascular safety of Mysimba, including data from clinical studies and from clinical practice, as well as data from spontaneous reports of side effects and from the literature. Clinical and literature data in relation to the effectiveness of the medicine were also considered.

The product information for Mysimba as well as a checklist for healthcare professionals will be updated to reflect the outcome of this review. A letter including the above recommendations will be sent in due course to healthcare professionals prescribing, dispensing or administering the medicine.

Advice for healthcare professionals:

- A review of available data has concluded that the benefits of Mysimba in its authorized indication continue to outweigh its risks. However, the cardiovascular safety of Mysimba in patients treated for longer than 12 months has not been fully determined and remains uncertain.
- An ongoing study (INFORMUS) proposed by the company will provide further information about this risk in the long term.
- The INFORMUS cardiovascular outcomes trial (NB-CVOT-3; a prospective, pragmatic randomized placebo-controlled study) is evaluating the long-term cardiovascular safety of Mysimba beyond the 12-months period; results are expected in 2028.
- Currently, treatment with Mysimba should be discontinued if there are concerns with the safety or tolerability of ongoing treatment, including concerns about increased blood pressure, or if patients have lost less than 5% of their initial body weight after 16 weeks. The need for continued treatment should be re-evaluated annually.
- To minimize potential cardiovascular risks with long-term use of Mysimba, the existing recommendations have now been clarified and reinforced by the EMA:
    - treatment with Mysimba should be discontinued after one year if weight loss of at least 5% of the initial body weight is not maintained;
    - healthcare professionals should carry out an annual assessment and discuss with their patients whether Mysimba

remains beneficial for them, taking into account any changes to the patient's cardiovascular risk and whether weight loss has been maintained.

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 March 2025, the Department of Health (DH) had not received any case of adverse drug reaction related to naltrexone alone and naltrexone/bupropion combination. The DH had received 5 cases of adverse drug reactions with bupropion alone, of which 2 cases were reported as increased blood pressure and heart rate; but none of these cases were related to the combination use of naltrexone/bupropion.

Related news of Mysimba was previously issued by EMA, and was reported in the Drug News since Issue No. 177, with the latest update reported in the Drug News Issue No. 181. The DH issued letters to inform local healthcare professionals to draw their attention on 29 July 2024. In light of the above EMA's latest announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 31 March 2025, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

European Union: Pemazyre (pemigatinib) - opinion on variation to marketing authorization

On 28 March 2025, the European Medicines Agency (EMA) announced that it has recommended the refusal of a change to the marketing authorization for Pemazyre to extend its use to the treatment of myeloid/lymphoid neoplasms with fibroblast growth factor receptor 1 (FGFR1) rearrangement (changes in the FGFR1 gene that produce an abnormal form of a protein called FGFR1). Myeloid/lymphoid neoplasms are very rare cancers that affect the bone marrow and white blood cells.

The active substance in Pemazyre, pemigatinib, belongs to a group of medicines called protein kinase inhibitors. It works by blocking the activity of tyrosine kinase receptors, such as FGFR receptors. Abnormal FGFR receptors are found on the surface of cancer cells and are involved in the growth and spread of the cancer. By blocking their activity, Pemazyre slows the progression of the cancer.

EMA considered that the data were not sufficiently comprehensive, meaning that there were remaining uncertainties about the benefits and risks of the medicine. The study did not compare Pemazyre with another treatment or placebo and included a small number of patients, reflecting a limited range of the different forms of the disease. This, in addition to changes that were made in the design of study while it was carried out could have affected the validity of the results.

The company was requested to generate additional data after authorization on the benefits and risks of Pemazyre in myeloid/lymphoid neoplasms with FGFR1 rearrangement to address the remaining uncertainties.

In Hong Kong, Pemazyre Tablets 13.5mg (HK-67328), Pemazyre Tablets 4.5mg (HK-67329) and Pemazyre Tablets 9mg (HK-67330) are pharmaceutical products registered by Innovent Biologics (HK) Limited. All products are prescription-only medicines. As of the end of March 2025, the Department of Health (DH) had not received any case of adverse drug reaction related to pemigatinib. The indication of Pemazyre approved in Hong Kong included locally advanced or metastatic cholangiocarcinoma but not the myeloid/lymphoid neoplasms. The DH will remain vigilant on safety update of the drug issued by other overseas drug regulatory authorities.

Drug Incident

Man arrested on suspicion of illegally selling topical eczema product with undeclared controlled drug ingredients

On 26 March 2025, the Department of Health (DH) carried out an enforcement operation with the Police against the suspected illegal sale of a topical product containing undeclared controlled medicines on the Internet, claiming that the product could be used to treat eczema. During the operation, a 42-year-old man was arrested on suspicion of the illegal sale of Part 1 poison and an unregistered pharmaceutical product.

Acting upon a complaint, a sample of the product was purchased from an eczema group on a social media platform for analysis. Test results from the Government Laboratory revealed that the sample contained clobetasol propionate, ketoconazole and miconazole, which are Part 1 poisons under the Pharmacy and Poisons Ordinance (Cap. 138). The product, unlabeled, is also suspected to be an unregistered pharmaceutical product. The DH's investigation is still in progress.

Clobetasol propionate is a steroid substance for treating inflammation. Inappropriate application of steroids could cause skin problems and systemic side effects such as moon face, high blood pressure, high blood sugar, adrenal insufficiency and osteoporosis. Ketoconazole and miconazole are antifungal substance used to treat fungal infections with side effects including local irritation and sensitivity reactions.

Topical products containing ketoconazole and miconazole should be supplied in the premises of an Authorized Seller of Poisons (i.e. a pharmacy) under the supervision of a registered pharmacist, while products containing clobetasol propionate are prescription medicines that should be used under a doctor's directions and be supplied in a pharmacy under the supervision of a registered pharmacist upon a doctor's prescription.

A press release was posted in the Drug Office website on 26 March 2025 to alert the public of the drug incident.

Department of Health investigates illegal online sale of slimming products containing controlled drug ingredients

On 27 March 2025, the Department of Health (DH) announced that it is investigating a case of illegal sale of slimming products containing undeclared controlled drug ingredients on the Internet and urged the public not to buy or consume the products concerned.

Acting upon intelligence, the DH purchased on a social media platform some slimming products, reportedly obtained from overseas, for analysis. The laboratory test results revealed that the samples of some products contained frusemide, metformin and thyroxine. All of them are Part 1 poisons under the Pharmacy and Poisons Ordinance (Cap. 138) (PPO).

The packages of the products concerned have Thai, Chinese and English characters, and are suspected to be unregistered pharmaceutical products. The DH will continue to follow up and investigate the case.

Frusemide is used for the treatment of heart diseases and its side effects include low blood pressure and electrolyte imbalance. Metformin is used for the treatment of diabetes mellitus and its side effects include nausea and diarrhoea. Thyroxine is used for the treatment of hypothyroidism and its side effects include arrhythmia and hypertension. Medicines containing these ingredients should be used under a doctor's directions and be supplied on the premises of an Authorized Seller of Poisons (i.e. pharmacy) under the supervision of a registered pharmacist upon a doctor's prescription.

A press release was posted in the Drug Office website on 27 March 2025 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: Clinical Trials and Pharmacovigilance Unit,
Drug Office, Department of Health,
Suite 2002-05, 20/F, AIA Kowloon Tower, Landmark East,
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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.