Drug News
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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 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 Kingdom: Abrysvo (Pfizer RSV vaccine) and Arexvy (GSK RSV vaccine): be alert to a small risk of Guillain-Barré syndrome following vaccination in older adults

On 7 July 2025, the Medicines and Healthcare products Regulatory Agency (MHRA) announced that there is a small increase in the risk of Guillain-Barré syndrome following vaccination with Abrysvo (Pfizer respiratory syncytial virus (RSV) vaccine) and Arexvy (GSK RSV vaccine) in adults aged 60 years and older. Healthcare professionals should advise all recipients of Abrysvo and Arexvy that they should be alert to signs and symptoms of Guillain-Barré syndrome and, if they occur, to seek immediate medical attention as it requires urgent treatment in hospital.

There is currently no evidence of an increased risk of Guillain-Barré syndrome in pregnant women following vaccination with Abrysvo, the only RSV vaccine approved for use during pregnancy. The Commission on Human Medicines (CHM) advise that the benefits of vaccination against RSV outweigh the small risk of developing Guillain-Barré syndrome in older adults.

Advice for Healthcare Professionals:

- there is a small increase in the risk of Guillain-Barré syndrome following vaccination with Abrysvo and Arexvy in adults (aged 60 years and older). Currently, there is no evidence of an increased risk of Guillain-Barré syndrome in pregnant women following vaccination with Abrysvo, the only RSV vaccine approved for use during pregnancy.
- be attentive to signs and symptoms of Guillain-Barré syndrome in all recipients of Abrysvo and Arexvy to ensure early and correct diagnosis, initiate adequate supportive care and treatment, and rule out other causes.
- early medical care can reduce severity and improve outcomes.

Advice for Healthcare Professionals to Provide to Patients:

- the RSV vaccine helps protect against respiratory syncytial virus (RSV), a virus which can make older adults and babies seriously ill. RSV can cause a type of chest infection called bronchiolitis in babies which can cause breathing problems and may need to be treated in hospital. RSV can also cause a serious lung infection (pneumonia) in and older adults requiring hospital care in some cases.
- the Pfizer RSV vaccine Abrysvo is currently offered in NHS vaccination programmes against RSV to adults aged 75-79 years old and to pregnant women to help protect babies after they are born.
- the GSK RSV vaccine Arexvy is not currently available on the NHS but may be available privately for use in individuals aged 60 years and older, or those aged 50–59 years who are at increased risk of RSV disease; Arexvy should not be given to pregnant individuals.
- rare or very rare cases of Guillain-Barré syndrome have been reported in older adults who have received the Abrysvo or Arexvy RSV vaccines respectively. Currently, there is no evidence that the Abrysvo RSV vaccine increases the risk of Guillain-Barré syndrome in pregnant women.
- Guillain-Barré syndrome is a serious nerve condition. It usually affects your arms and legs first before you get symptoms in other parts of your body.
- you might feel tingling, numbness or pins and needles in your feet and hands first. This is usually followed by muscle weakness and difficulty moving your joints.

- other symptoms can include:
  - tingling, numbness or pins and needles in your feet and hands
  - muscle weakness and difficulty moving your joints
  - sharp, shooting pain (nerve pain), often in your legs or back
  - problems breathing
  - problems with your face, such as drooping face muscles or trouble swallowing or speaking
  - problems with your eyes, such as double vision
- some people's symptoms become so severe that they are not able to move their legs, arms and face (paralysis)
- urgent hospital treatment is required to help prevent the symptoms progressing and improve recovery, however the effects of Guillain-Barré syndrome may sometimes be long-lasting
- seek immediate medical attention if you notice signs of Guillain-Barré syndrome

Background

NHS vaccination programmes against RSV
Respiratory syncytial virus (RSV) is an infectious disease of the airways and lungs. RSV infection is common in young children but is most serious for small babies and for older people. Abrysvo (Pfizer RSV vaccine) is currently being used in NHS vaccination programmes against RSV in older adults aged 75 to 79 years old and in pregnant women to protect their infants.

Risk of Guillain-Barré syndrome in older adults following RSV vaccine
An increase in the risk of Guillain-Barré syndrome has been observed following vaccination with Abrysvo and Arexvy in adults aged 60 years and older.

Up to 2 June 2025, the MHRA received 21 Yellow Card reports of suspected Guillain-Barré syndrome in older adults (75-79 years, where known) following Abrysvo. This is in the context of over 1.9 million doses of Abrysvo administered in the older adult RSV vaccination programme up to 26 May 2025. Over the same time period, the MHRA has not received any Yellow Card reports of suspected Guillain-Barré syndrome following Arexvy however there has been very limited use of this vaccine in the UK to date as Arexvy (GSK RSV vaccine) is not currently deployed by the NHS.

A post-marketing observational study in the United States in individuals aged 65 years and older estimated that Abrysvo and Arexvy were associated with 9 and 7 excess Guillain-Barré syndrome cases per million vaccine doses administered, respectively. Preliminary unpublished post-marketing study data from the UK Health Security Agency and Public Health Scotland studies in adults aged 75-79 years estimate a combined excess of 15-25 Guillain-Barré syndrome cases per million vaccine doses of Abrysvo administered across England and Scotland. The risk of experiencing Guillain-Barré syndrome following Abrysvo in older adults remains rare. No UK post-marketing study data for Arexvy are available.

The new UK data regarding Abrysvo were reviewed by the Commission on Human Medicines (CHM) who advised that the benefits of the vaccine outweighed the risk of developing Guillain-Barré syndrome in older adults.

Risk of Guillain-Barré syndrome in pregnancy following Abrysvo
Abrysvo is the only RSV vaccine indicated for use during pregnancy to protect infants. Up to 2 June 2025, the MHRA has not received any Yellow Card reports of suspected Guillain-Barré syndrome in pregnant individuals following Abrysvo. This is in the context of over a quarter of million doses of Abrysvo administered in the pregnancy RSV vaccination programme up to 26 May 2025.

Currently, there is no evidence of an increase in the risk of Guillain-Barré syndrome following Abrysvo in pregnant individuals from either UK or world-wide data.

Product information for patients and healthcare professionals
The Summary of Product Characteristics (SmPC) and the Patient Information Leaflet (PIL) for Abrysvo and Arexvy contain warnings about the risk of Guillain-Barré syndrome. Guillain-Barré syndrome is also listed as possible side effect in older adults in the product information for these vaccines.

In Hong Kong, Abrysvo Vaccine Powder And Solvent For Solution For Injection (HK-68213) and Arexvy Vaccine Powder And Suspension For Suspension For Injection (HK-67997) are pharmaceutical products registered by Pfizer

Corporation Hong Kong Limited and GlaxoSmithKline Limited, respectively. Both are prescription-only medicines. As of the end of July 2025, the Department of Health (DH) had received one case of adverse event following immunisation with Arexvy, but this case was not reported as GBS. The DH had not received any case of adverse event following immunisation with Abrysvo.

Related news was previously issued by the US Food and Drug Administration and Australia Therapeutic Goods Administration, and was reported in the Drug News Issue No. 183 and 187. The DH issued letters to inform local healthcare professionals to draw their attention on 8 January 2025. As previously reported, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board of Hong Kong.

European Union: Review of risk of encephalitis with varicella vaccines concluded

On 11 July 2025, the European Medicines Agency (EMA) announced that its Pharmacovigilance Risk Assessment Committee (PRAC) has concluded its review of the known risk of encephalitis (inflammation of the brain) with the varicella (chickenpox) vaccines Varilrix and Varivax. The review was triggered by a case of encephalitis with fatal outcome after vaccination with Varilrix.

After carefully evaluating the available evidence from clinical trials, the scientific literature and post-marketing exposure, the committee has recommended an update to the product information of Varilrix and Varivax to further describe the severity of the risk of encephalitis. The two vaccines remain contraindicated in immunocompromised people and no additional risk minimisation measures are required.

Varicella vaccines are also authorised as part of measles, mumps, rubella, and varicella (MMRV) vaccines, namely Priorix Tetra and Proquad. PRAC considered that the product information of MMRV vaccines should also be updated in line with varicella vaccines.

The amended product information will give further detail on the known side effect encephalitis which has been observed with live attenuated varicella vaccines, including in a few cases with fatal outcome.

People who receive the vaccine should seek immediate medical attention if they develop signs of infection or inflammation of the brain.

In Hong Kong, Varilrix Vaccine For Inj (HK-41798) and Priorix-Tetra Vaccine (HK-57798) are pharmaceutical products registered by GlaxoSmithKline Limited, and Varivax Vaccine (HK-39958) and Proquad Vaccine (HK-54831) are pharmaceutical products registered by Merck Sharp & Dohme (Asia) Ltd. All products are prescription-only medicines. As of the end of July 2025, the Department of Health (DH) had received 1 case of adverse event following immunisation with Priorix-Tetra, 1 case of adverse event following immunisation with Varilrix and 4 cases of adverse event following immunisation with Proquad, but these cases were not related to encephalitis. The DH had not received any cases of adverse event following immunisation with Varivax.

The current product inserts of locally registered products Varilrix, Varivax, Priorix-Tetra and Proquad include safety information about encephalitis. Related news was previously issued by EMA, and was reported in the Drug News Issue No. 188. The DH will remain vigilant on safety update of the drug issued by other overseas drug regulatory authorities.

European Union: PRAC assessing new data on potential risk of neurodevelopmental disorders in children born to men treated with valproate

On 11 July 2025, the European Medicines Agency (EMA) announced that its Pharmacovigilance Risk Assessment Committee (PRAC) is assessing new data from a recent study which used multiple databases in Denmark to investigate the potential risk of neurodevelopmental disorders (NDD) in children born to men treated with valproate, levetiracetam or lamotrigine before conception.

Valproate is a medicine used to treat epilepsy, bipolar disorders and in some countries for migraine.

Neurodevelopmental disorders are problems with development that begin in early childhood, such as autism spectrum disorders, intellectual disability, communication disorders, attention deficit/hyperactivity disorders and movement disorders.

In January 2024, the assessment of the findings of a

post authorisation safety study (PASS) carried out by companies that market valproate, which used data from multiple registry databases in Denmark, Norway and Sweden, together with other available information, led the PRAC to recommend precautionary measures for the treatment of male patients with valproate medicines. At that time, while the committee acknowledged that the PASS data had limitations, PRAC concluded that NDD are a potential risk in children born to men treated with valproate during the three months before conception, and therefore information to patients and health care professionals were warranted.

The aim of this new study using Danish data sources was to replicate the results from the PASS. However, results from this new study did not suggest an association between valproate use by the father and an increased risk of NDD in the child.

PRAC has initiated a signal procedure to understand the difference in the findings across the studies and requested further information and analysis from the marketing authorisation holders for valproate.

EMA will communicate further when more information becomes available.

In Hong Kong, there are 10 registered pharmaceutical products containing valproate. All products are prescription-only medicines. As of the end of July 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 valproate exposure in utero, 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. 188. 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, 22 March 2023 and 11 June 2025.

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 of Hong Kong.

Singapore: Cellcept (Mycophenolate mofetil): New risk of anaphylactic reaction identified from post-marketing data

On 11 July 2025, the Health Sciences Authority (HSA) announced that a Dear Healthcare Professional Letter has been issued by Roche Singapore Pte Ltd to update healthcare professionals that cases of anaphylaxis, anaphylactic reaction, anaphylactic shock and anaphylactoid reaction were identified from the post-marketing data for Cellcept (mycophenolate mofetil).

Mycophenolate mofetil is an immunosuppressant for the prophylaxis of acute transplant rejection in patients receiving various transplants.

Healthcare professionals are advised to be aware of the full range of signs and symptoms of anaphylactic reaction and the appropriate medical treatment. It is recommended to advise patients to seek immediate medical attention at the first signs of an anaphylactic reaction and discontinue Cellcept permanently. Roche will be updating the product label of Cellcept to reflect this newly identified risk.

In Hong Kong, there are 23 registered pharmaceutical products containing mycophenolate mofetil, including 5 registered pharmaceutical products under the brand name Cellcept that are registered by Roche Hong Kong Limited. All products are prescription-only medicines. As of the end of July 2025, the Department of Health (DH) had received 82 cases of adverse drug reactions with regard to mycophenolate mofetil, these cases were not related to anaphylactic reaction.

The risk of anaphylactic reaction associated with the use of mycophenolate mofetil is documented in overseas reputable drug references such as the "Martindale: The Complete Drug Reference". 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.

Singapore: Liver injury with Ocrevus® (ocrelizumab)

On 28 July 2025, the Health Sciences Authority (HSA) announced that a Dear Healthcare Professional Letter has been issued by Roche Singapore Pte Ltd to inform healthcare professionals that following a recent data review, clinically significant liver injury without findings of viral hepatitis has been classified as an identified risk for Ocrevus® (ocrelizumab), with reasonable evidence showing a temporal association with the first administration of ocrelizumab.

Healthcare professionals are advised to counsel patients on the risks and benefits of ocrelizumab, conduct liver function tests prior to initiating treatment with ocrelizumab and monitor patients for signs and symptoms of any hepatic injury during treatment. Liver function tests should be performed promptly in patients who report symptoms that may indicate liver injury and if liver injury is present, ocrelizumab should be discontinued. In the event that an alternative etiology is identified, treatment with ocrelizumab can be resumed only when the liver injury has fully resolved. The local product information will be updated accordingly.

Ocrevus® is indicated for the treatment of adult patients with relapsing forms of multiple sclerosis with active disease defined by clinical or imaging features, to reduce the frequency of clinical relapses and delay the progression of physical disability. It is also indicated for the treatment of adult patients with early primary progressive multiple sclerosis with imaging features characteristic of inflammatory activity to delay progression of physical disability.

In Hong Kong, Ocrevus Concentrate For Solution For Infusion 300mg/10ml (HK-67765) is a pharmaceutical product registered by Roche Hong Kong Limited (Roche). The product is a prescription-only medicine. As of the end of July 2025, the Department of Health (DH) had not received any case of adverse drug reaction with regard to ocrelizumab. The DH noted Roche has already disseminated a Dear Healthcare Professional Letter to healthcare professionals in Hong Kong regarding the issue. 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 States: FDA is requiring opioid pain medicine manufacturers to update prescribing information regarding long-term use

On 31 July 2025, the United States Food and Drug Administration (FDA) announced that class-wide action will further emphasize and characterize risks of long-term use to help patients, healthcare professionals make informed treatment decisions.

What Safety Concern Is FDA Announcing?
In May 2025, the FDA convened a joint meeting of the Drug Safety and Risk Management Advisory Committee and the Anesthetic and Analgesic Drug Products Advisory Committee to discuss two recently completed observational studies examining the risks of misuse, abuse, addiction, and fatal and non-fatal overdose in patients on long-term opioid analgesic (also referred to as opioid pain medicine) therapy. These studies (postmarketing requirements [PMR] 3033-1 and 3033-2) provided new, quantitative data on risks of these serious adverse outcomes in patients prescribed opioid pain medicines long term. After reviewing the study findings and the medical literature, as well as considering the committees' and public input, FDA has determined that this new information should be included in drug labeling to help healthcare professionals and patients better understand the benefit-risk profile of opioid pain medicines when prescribed long term and to make more informed decisions. Separately, a prospective, randomized, controlled clinical trial will address a different PMR to examine the risks relative to the efficacy of long-term opioid use.

What Is FDA Doing?
The Agency is requiring safety labeling changes for opioid pain medicines to further emphasize and characterize the risks associated with long-term use. Specifically, FDA is notifying application holders the following labeling changes are needed:

- Remove the phrase "extended treatment period" in the Indications and Usage section to avoid misinterpretation that there are data to support safety and efficacy of opioid

analgesics over an indefinitely long duration
- Further emphasize that higher doses are associated with increased risk of serious harm, and that the risks of serious harms persist over the course of therapy
- Provide a brief description of the results of studies conducted to fulfill postmarketing requirements 3033-1 and 3033-2, including new quantitative estimates of the risks of addiction, abuse, misuse, and fatal and non-fatal overdose in patients taking opioid analgesics long-term

FDA is also requiring labeling updates to further clarify that extended-release/long-acting opioid pain medicines should only be used when alternative therapies, including immediate-release opioid pain medicines, are inadequate to manage severe and persistent pain, and to emphasize the importance of avoiding rapid dose reduction or abrupt discontinuation in patients who may be physically dependent on opioid pain medicines.

Additionally, FDA is requiring labeling updates regarding the availability of opioid overdose reversal agents; revising drug-drug interactions with central nervous system depressants to include gabapentinoids; adding information about toxic leukoencephalopathy (a neurological disorder due to a variety of causes, including exposure to toxic substances) in the opioid overdose setting; and modifying warnings about gastrointestinal effects to include opioid-induced esophageal dysfunction.

What Is an Opioid Pain Medicine and How Can It Help Me?
Opioid pain medicines are a class of powerful pain medicines prescribed to treat pain that does not respond well to other treatments, including non-opioid pain medicines. They activate an area of nerve cells in the brain and body that block pain signals. These medicines have benefits when used appropriately, but they also have serious risks, including misuse, abuse, addiction, overdose, and death. Examples of common opioid pain medicines include codeine, hydrocodone, hydromorphone, morphine, oxycodone, oxymorphone, fentanyl, buprenorphine, methadone, and tramadol.

What Should I Do as a Healthcare Professional?
In assessing the severity of pain, discuss with the patient the source of the pain and the impact of the pain on their ability to function and their quality of life. Pain assessment should consider the cause of pain and individual patient factors and include non-pharmaceutical, non-interventional targeted treatments that address the root cause of the underlying pain, when possible. Use a multimodal approach to pain management when initiating treatment, throughout the course of therapy, and if you decide to taper or discontinue the opioid pain medicine.

If the patient's pain is severe enough to require an opioid pain medicine and alternative treatment options are insufficient, prescribe the lowest effective dose of an immediate-release (IR) opioid pain medicine for the shortest duration of time needed to reduce the risks associated with these products. Discuss what is known about the risks and benefits of using the medication. Reserve increasing to higher doses only when lower doses are inadequate and the benefits of using a higher dose outweigh the substantial risks. Many acute pain conditions, such as pain occurring with surgical procedures or musculoskeletal injuries, require no more than a few days of an IR opioid pain medicine. Remind the patient that opioid use can paradoxically increase pain (i.e., opioid-induced hyperalgesia).

Reserve extended-release/long-acting opioid pain medicines only for severe and persistent pain that cannot be adequately treated with alternative options, including IR opioid pain medicines. Regularly re-evaluate and discuss with your patients the optimum management of pain that seeks to address the root cause and appropriately balances the known benefits and risks, and frequently assess for development of addiction, abuse, or misuse. Inform patients and caregivers of the added risks of using opioid pain medicines with benzodiazepines and other central nervous system depressants, including gabapentinoids, and educate them on the signs and symptoms of respiratory depression.

For all patients prescribed opioid pain medicines, discuss opioid overdose reversal agents, such as naloxone and nalmefene. In March 2023, FDA approved the first nasal spray version of naloxone to be sold over-the-counter. There are now several versions of naloxone nasal sprays available over-the-counter, including generics, as well as versions available by prescription. In addition, in August 2024, FDA approved the first nalmefene hydrochloride auto-injector as a prescription drug to treat opioid overdose in adults and pediatric patients aged 12 years and older.

Regularly re-evaluate the benefit-risk profile for any individual taking opioid pain medicines for more than a few days. Be aware that overdose risk is increased with higher opioid pain medicine doses, and risks of serious harms persist over the course of therapy. If you determine opioid pain medicines are indicated, consider an IR opioid pain medicine as an as-needed, first-line treatment. Avoid rapidly reducing or abruptly discontinuing opioid pain medicines in patients who may be physically dependent on the medication because such changes have resulted in serious withdrawal symptoms, uncontrolled pain, and suicide.

What Should I Do as a Patient or Parent/Caregiver?
Always take your opioid pain medicine exactly as prescribed. Do not take more of the medicine or take it more often than prescribed without first talking to your healthcare professional. Talk with them if your pain increases, you feel more sensitive to pain, or if you have new pain, especially from touch or other things that are not usually painful such as combing your hair.

Store your opioid pain medicines securely, out of sight and reach of children and pets, and in a location not accessible by others, including home visitors. Do not share these medicines with anyone else, and immediately dispose of unused or expired opioid pain medicines or take them to a drug take-back site, location, or program. If provided, use the prepaid mail-back envelopes included with the prescription.

Seek emergency medical help or call 911 immediately if you or someone you are caring for experiences symptoms of respiratory problems, which can be life-threatening. Signs and symptoms include slowed, shallow, or difficult breathing, severe sleepiness, or not being able to respond or wake up.

Talk to your healthcare professionals about the benefits of naloxone and nalmefene, which can reverse an opioid overdose, and how to obtain these drugs. There are several versions of naloxone, some of which are available without a prescription. Nalmefene hydrochloride is available with a prescription from your healthcare professional.

Be aware that overdose risks are increased with higher opioid pain medicine doses and that the risks of serious harms persist over the course of therapy. Regularly visit your healthcare professional to ensure you are on the most appropriate treatment plan. Avoid rapidly reducing or abruptly discontinuing opioid pain medicine treatment without consulting a healthcare professional.

What Did FDA Find?
The labeling changes being announced today are based on the findings from observational studies conducted to fulfill two postmarketing requirements ([PMRs] 3033-1 and 3033-2) and the ensuing discussion at the May 2025 Advisory Committee meeting, alongside other data published in medical literature. The PMR studies — which were completed by the Opioid Postmarketing Consortium, a collaboration of all new drug application holders of extended-release/long-acting (ER/LA) opioid pain medicines — provided new, quantitative data on the risks of misuse, abuse, addiction, and fatal and non-fatal overdose for patients on long-term opioid pain medicine therapy.

PMR 3033-1 was a prospective, observational cohort study that estimated the risks of addiction, misuse, and abuse in patients initiating long-term use of Schedule II opioid analgesics (pain medicines). Patients were recruited and data collected from 2017 through 2021. Study participants had been enrolled in selected insurance plans or health systems for at least one year, were free of at least one outcome at baseline, and either 1) filled multiple ER/LA opioid analgesic prescriptions during a 90-day period; or 2) filled any Schedule II opioid analgesic prescriptions covering at least 70 of 90 days. Patients who received any of the qualifying opioid analgesics in the previous six months were excluded. Over 12 months, approximately 1-6% of included patients across the two cohorts newly met criteria for opioid addiction, as assessed with two validated interview-based measures of moderate-to-severe opioid use disorder based on Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition criteria. Over 12 months, across the two cohorts, approximately 9% of included patients newly met criteria for prescription opioid abuse (i.e., the intentional use of a drug for a nontherapeutic purpose, repeatedly or sporadically, for the purpose of achieving a positive psychological or physical effect) and approximately 22% newly met criteria for prescription opioid misuse (i.e., the intentional use of a drug for a therapeutic purpose inappropriately outside labeling directions or in a way other than prescribed or directed by a healthcare professional). Incidence of these outcomes varied according to patient- and drug-related factors, with the strongest

and most consistent risk factor being a personal history of a substance use disorder.

PMR 3033-2 was a retrospective, observational cohort study that estimated the risk of opioid-involved overdose or opioid overdose-related death (together, abbreviated as OOD) in patients with new long-term use of Schedule II opioid analgesics between 2006 and 2016. Included patients had been enrolled in either one of two commercial insurance programs, one managed care program, or one Medicaid program for at least nine months. New long-term use was defined as having Schedule II opioid analgesic prescriptions covering at least 70-days' supply over the three months before study entry and none during the preceding six months. Patients were excluded if they had an opioid-involved overdose in the nine months before cohort entry. The outcome was the first OOD during the follow-up period, as measured using a validated medical code -based algorithm with linkage to the National Death Index database. The five-year cumulative incidence estimates for OOD ranged from approximately 1.5-4% across study sites. Approximately 17% of first opioid overdoses observed over the entire study period (5-11 years, depending on the study site) were fatal. Again, incidence varied according to patient- and drug-related factors, with higher baseline opioid dose being a strong and consistent risk factor for OOD. Study exclusion criteria may have selected patients at lower risk of overdose, and substantial loss to follow-up (approximately 80%) also may have biased estimates.

The risk estimates from the studies described above may not be generalizable to all patients receiving opioid analgesics, such as those with exposures shorter or longer than the duration evaluated in the studies. Nonetheless, these new data may help inform the benefit-risk assessment in patients for whom long-term use of opioid analgesics is being considered. Additional details about PMRs 3033-1 and 3033-2 can be found in the "Background and Data Summary" section.

What Is My Risk?

Like all medicines, opioid pain medicines can have side effects, even when used correctly as prescribed. It is important to know that people respond differently to medicines depending on their health, the diseases they have, genetic factors, other medicines they are taking, and many other factors. As a result, we cannot determine how likely it is that someone will experience these side effects when taking opioid pain medicines. Talk to your healthcare professional if you have questions or concerns about the risks.

Table of Key Opioid Label Updates

For details of "Key Opioid Label Updates", please refer to the website in FDA.

Facts About Opioid Pain Medicines

- Opioid pain medicines are powerful prescription medicines that can help manage pain when other treatments and medicines are not able to provide enough relief. However, opioid pain medicines also carry serious risks, including misuse and abuse, addiction, overdose, and death.
- There are two main categories of prescription opioid pain medicines. Immediate-release (IR) products are usually intended for use every four to six hours as needed for acute pain. Extended-release/long-acting opioid pain medicines are intended to be taken only once or twice a day for severe and persistent pain that cannot be adequately treated with alternative options, including IR opioid pain medicines.
- Opioid pain medicines are available in many different forms, including tablets, capsules, lozenges, sublingual tablets, transdermal patches, nasal sprays, and injections.
- Common side effects include drowsiness, dizziness, nausea, vomiting, constipation, physical dependence, and slowed or difficult breathing.
- The risk of opioid addiction, misuse, or abuse is increased in patients with a personal or family history of substance use disorder or mental illness.
- Naloxone and nalmefene are opioid reversal medicines used to treat an opioid overdose or possible overdose and can help prevent death. Naloxone is available over-the-counter and by prescription; nalmefene hydrochloride is available by prescription only.

Additional Information for Healthcare Professionals

- As part of its ongoing efforts to address the nation's opioid crisis and based, in part, on results of postmarketing requirement studies, FDA is requiring safety labeling changes to provide more information on the risks of opioid pain medicines.
- Healthcare professionals are reminded to regularly re-evaluate the benefit-risk profile

for any individual taking opioid pain medication.

- Be aware that overdose risks are increased with higher opioid doses, and that the risks of serious harms persist throughout the course of therapy.
- If an opioid pain medicine is necessary, consider immediate-release opioid pain medicine as an as-needed, first-line treatment.
- Avoid rapidly reducing or abruptly discontinuing opioids in patients who may be physically dependent on the medication because such changes have resulted in serious withdrawal symptoms, uncontrolled pain, and suicide.
- For all opioid pain medicines, prescribe the lowest effective dose for the shortest duration consistent with a patient's individual treatment goals. Because the risk of overdose increases as opioid pain medicine dose increases, reserve titrating to higher doses for patients who have an inadequate response to lower doses and when the benefits of a higher dose clearly outweigh the substantial risks.
- Regularly reassess the continued need for opioid pain medicine use regardless of the dose and for signs of addiction, misuse, or abuse.
- Educate patients and caregivers that taking an opioid pain medicine other than how it is prescribed or with alcohol, benzodiazepines, or other central nervous system depressants (including gabapentinoids) could increase the risk of overdose, and how to recognize the signs and symptoms of respiratory depression.
- Naloxone and nalmefene are opioid reversal medicines used to treat an opioid overdose or possible overdose and can help prevent death. Naloxone is available over-the-counter and by prescription; nalmefene hydrochloride is available by prescription only.
- Encourage patients to read the patient Medication Guide they receive with their filled prescription(s). Important, new information may be included. The Medication Guide explains the important things they need to know about the medicine. These include the side effects, what the medicine is used for, how to take and store it properly, and other things to watch out for when they are taking the medicine.

Additional Information for Patients/Caregivers

- Be aware of the risks of opioid pain medicine use, including misuse, abuse, addiction, overdose, and death.
- Regularly visit your healthcare professional to ensure you are on the most appropriate treatment plan for opioid pain medicines.
- Be aware that overdose risks are increased with higher opioid pain medicine doses, and that the risk of serious harm persists throughout the course of therapy.
- Avoid rapidly reducing your dose or abruptly discontinuing opioid pain medicines without consulting a healthcare professional.
- Always take opioid pain medicines as prescribed. Do not take more doses or take them more often than prescribed.
- For many acute pain conditions such as pain occurring with a number of surgical procedures or musculoskeletal injuries, you may only need to take opioid pain medicine for a few days. You may have some medicine left over that you did not use. Never give anyone else your opioid pain medicine. They could die from taking it. Selling or giving away your opioid pain medicine is against the law. Immediately dispose of unused or expired opioid pain medicines or take them to a drug take-back site, location, or program. See disposal information in the Medication Guide on how to safely dispose of your opioid pain medicine. If provided, use the prepaid mail-back envelopes included with the prescription. Unused medicines must be disposed of properly to avoid harm. Visit the website in FDA to learn about how to properly dispose of unused medicine.
- Store your opioid pain medicines securely, out of sight and reach of children, and in a location not accessible by others, including visitors. Every year thousands of children are hospitalized, and some die, after taking medicine not meant for them. Millions of people misuse prescription opioid pain medicines each year, and thousands die from overdoses involving prescription opioid pain medicines.
- Signs of an opioid overdose include breathing problems, severe sleepiness, or not being able to respond or wake up. Seek medical attention immediately if you or someone you are caring for experiences these life-threatening symptoms.
- Naloxone and nalmefene are opioid reversal medicines used to treat an opioid overdose or possible overdose and can help prevent death. Naloxone is available over-the-counter and by prescription; nalmefene is available by

prescription only. Talk to your healthcare professional about how to use these products.

Background and Data Summary
Using its authority under Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act, FDA required extended-release/long-acting (ER/LA) opioid analgesic (OA) new drug application holders to conduct epidemiologic studies to 1) quantify the serious risks of misuse, abuse, addiction, and fatal and non-fatal overdose in patients using OAs long term and 2) assess potential risk factors for these outcomes. The studies were conducted using prespecified protocols and statistical analysis plans that were reviewed by FDA and discussed in a public scientific workshop. Studies conducted under postmarket requirements (PMRs) 3033-1 and 3033-2 were large, multisite investigations that included patients enrolled in various health insurance plans and health systems across the United States. These studies were, by design, restricted to the relatively small proportion of patients receiving OAs who go on to use them long term and therefore do not inform quantitative questions of risk related to shorter-term use of OAs.

PMR 3033-1 was a prospective, observational cohort study that estimated the risks of addiction, abuse, and misuse in adult patients initiating long-term use of Schedule II OAs. Patients were recruited and data were collected from 2017 through 2021. Study participants had been enrolled in selected health insurance plans or health systems for at least one year, and either 1) filled multiple ER/LA OA prescriptions during a 90-day period ("ER/LA cohort"); or 2) filled any Schedule II OA prescriptions covering at least 70 of 90 days ("long-term opioid therapy [LtOT] cohort"). Patients who received any of the qualifying opioid analgesics (i.e., ER/LA OAs or Schedule II OAs, depending on the study cohort) in the previous six months were excluded; however, patients were not excluded for use of other prescription OA therapy. In addition, patients with an existing diagnosis of a terminal illness or opioid use disorder (OUD) in the previous 12 months, receiving methadone or buprenorphine for the treatment of OUD, or receiving hospice care were excluded. Continued OA use was not required during follow-up. After meeting the study eligibility criteria, patients were required to be free of at least one outcome at baseline and to have completed a minimum number of follow-up assessments (at least two of the three-, six-, nine-, and 12-month assessments for misuse and abuse; the 12-month assessment for OUD) to be included in one or more analyses. This resulted in 978 and 1,244 patients being included in one or more analyses for the ER/LA and LtOT cohorts, respectively.

Opioid misuse was defined as the intentional use of a drug for a therapeutic purpose inappropriately outside labeling directions or in a way other than prescribed or directed by a healthcare professional. Opioid abuse was defined as the intentional use of a drug for a nontherapeutic purpose, repeatedly or sporadically, or for the purpose of achieving a positive psychological or physical effect. Misuse and abuse were measured using the Prescription Opioid Misuse and Abuse Questionnaire, a self-reported questionnaire validated for use in this population, which asks about symptoms in the past three months. Over 12 months, across the two cohorts, approximately 22% of included patients newly met criteria for prescription opioid misuse and approximately 9% of included patients newly met criteria for prescription opioid abuse, based on information reported at three-, six-, nine-, and 12-month assessments (Table 1).

Addiction was defined in this study as moderate-to-severe OUD, as assessed using a validated, semi-structured interview tool, the Psychiatric Research Interview for Substance and Mental Disorders, DSM-5, Opioid Version (PRISM-5-Op), which asks about symptoms in the past 12 months. OUD was based on a count of symptoms reported in the interview and defined in two ways: 1) using standard DSM-5 criteria, and 2) using modified criteria in which most DSM-5 symptoms were counted toward an OUD designation only when the patient indicated a non-pain reason for opioid use associated with that symptom, and the "persistent desire or attempts to quit or cut down on opioid use" criterion was counted only if multiple unsuccessful attempts were made. Over 12 months, across the two cohorts, the percentage of included patients who newly met criteria for moderate-to-severe OUD was approximately 3-6% using the standard DSM-5 criteria and approximately 1-2% using the modified DSM-5 criteria, based on information reported at the 12-month assessment (Table 1). Several factors (e.g., potential volunteer bias, predominance of managed care and integrated healthcare systems) may have limited the generalizability and interpretability of findings.

PMR 3033-2 was a retrospective, observational cohort study that estimated the risk of

opioid-involved overdose or opioid overdose-related death (together, abbreviated as OOD) in adult patients with new long-term use of Schedule II OAs between 2006 and 2016 (n=220,249). The study included patients enrolled in either one of two commercial insurance programs, one managed care program, or one Medicaid program for at least nine months. New long-term use was defined as having Schedule II OA prescriptions[1] covering at least a 70-days' supply over the three months before cohort entry and none during the preceding six months. Patients were excluded if they had an opioid-involved overdose in the nine months prior to cohort entry. The outcome was the first OOD event during the follow-up period, as measured using a validated medical-code-based algorithm with linkage to the National Death Index database. The cumulative incidence of OOD increased steadily throughout the five-year follow up period, resulting in a five-year cumulative incidence ranging from approximately 1.5% to approximately 4% (Table 2). Over the entire study period (5-11 years, depending on study site), approximately 17% of first OOD events were fatal.

There are a number of considerations when interpreting the findings from PMR 3033-2. OOD events may not have involved the prescribed OAs; rather, they could have occurred after a patient discontinued prescribed OA use and could have involved illicit opioids like heroin or fentanyl. Since the outcome for this study included only the first OOD event, a patient could have experienced subsequent events, including fatal overdose, that would not have been included in the OOD incidence estimates. Additionally, the intentionality of the OOD event (i.e., suicide vs. accidental) could not be adequately confirmed. Several factors could have contributed to bias. There was substantial attrition over the first five years of follow-up, and although this study used an incidence measure designed to account for loss to follow-up, if those who left the cohort (e.g., due to insurance disenrollment) systematically had a different risk of OOD than those remaining in the study, incidence estimates could have been biased. In addition, limiting the cohort to patients with no recent documented opioid-involved overdose likely selected patients at lower risk of OOD during follow-up. Finally, opioid overdoses that were reversed by a bystander or that otherwise did not result in either a medical claim or death were not captured.

Both studies collected patient- and drug-related characteristics at baseline and conducted exploratory analyses of potential risk factors for misuse, abuse, addiction, and overdose. Many factors were associated with one or more outcomes, with one of the strongest and most consistent risk factors being a personal history of a substance use disorder.[2] In addition, higher OA dose during the three months before cohort entry was a strong and consistent risk factor for OOD. Neither study was designed to assess associations between changes in OA dose or discontinuation of opioids and adverse opioid-related outcomes.

[1] Hydrocodone fixed combinations were reclassified from Schedule III to Schedule II in October 2014. Products containing hydrocodone were treated as a Schedule II opioid throughout PMR 3033-2.

[2] A notable proportion of patients starting long-term OA therapy in these studies had a personal history of SUD, whether in the past year (in PMR 3033-1, 6.5% to 8% had a past-year non-opioid, non-nicotine substance use disorder, based on interview measures; in PMR 3033-2, approximately 4-6% each had OUD, alcohol use disorder, or another substance use disorder, based on diagnostic codes). PMR 3033-1 also assessed SUDs prior to the past year (29% to 34.1% had a prior-to-past-year non-opioid, non-nicotine substance use disorder, based on interview measures).

Table 1. Incidence of Prescription Opioid Misuse, Prescription Opioid Abuse, and OUD in Prospective PMR 3033-1

			Moderate-to-Severe OUD	
	Prescription Opioid Misuse	Prescription Opioid Abuse	Pain-Adjusted DSM-5-OUD[1]	DSM-5-OUD[2]
ER/LA cohort[3]				
N	804	911	850	850
12-month incidence proportion (%, 95% CI)	22.8 (21.6, 24.0)	9.4 (7.7, 11.6)	1.4 (0.9, 2.3)	5.8 (4.5, 7.3)
LtOT cohort[4]				
N	1,003	1,151	1,102	1,102
12-month incidence proportion (%, 95% CI)	21.6 (18.3, 25.5)	8.6 (7.4, 10.0)	1.6 (0.9, 2.9)	3.4 (2.5, 3.1)

Source: Adapted from Final Study Report for Prospective PMR 3033-1.

[1] Moderate-to-severe pain-adjusted DSM-5-OUD was defined as having four or more pain-adjusted DSM-5 criteria for OUD related to prescription opioid use or two or more DSM-5

criteria related to heroin use, as measured by the PRISM-5-Op.
[2] Moderate-to-severe DSM-5 OUD was defined as having four or more standard DSM-5 criteria for OUD related to prescription opioid use or two or more DSM-5 criteria related to heroin use, as measured by the PRISM-5-Op.
[3] Includes patients who initiated an ER/LA OA that included at least 28 days' supply of an ER/LA OA within a 60-day window followed by a subsequent ER/LA OA prescription within a 7-day period, all within a 90-day period prior to the patient's baseline interview. Patients could not have used an ER/LA OA in the 6 months before the initial 28 days' supply of an ER/LA OA, but patients on IR/SA OAs during the same 6 months were still eligible for this cohort.
[4] Includes patients who initiated either an ER/LA OA or a Schedule II IR/SA OA for at least 70 of the past 90 days. Patients could not have used an ER/LA OA or a Schedule II IR/SA OA in the 6 months before the initial ER/LA OA or Schedule II IR/SA OA prescription contributing to at least 70 days of use, but other prescription OA therapy would not exclude them (e.g., tramadol use).
Abbreviations: CI, confidence interval; DSM-5, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; ER/LA, extended-release/long-acting; LtOT, long-term opioid therapy; N, number; OA, opioid analgesic; OUD, opioid use disorder; PMR, postmarketing requirement; PRISM-5-Op, Psychiatric Research Interview for Substance and Mental Disorders, DMS-5, Opioid Version

Table 2. Cumulative Incidence of OOD in PMR 3033-2

	HealthCore	KPNW	Optum	VUMC
N	81,782	12,009	54,515	71,932
5-year cumulative incidence (%, 95% CI)[1]	1.5 (1.4, 1.6)	1.4 (1.2, 1.7)	1.5 (1.3, 1.8)	4.1 (3.9, 4.3)

Source: Adapted from the Final Study Report for PMR 3033-2.

[1] Five-year cumulative incidence is the complement of the Kaplan-Meier OOD-free survival preceding 5 years measured in percent (%) scale
Abbreviations: CI, confidence interval; KPNW, Kaiser Permanente Northwest; N, number; OOD, opioid-involved overdose or opioid overdose-related death; PMR, postmarketing requirement; VUMC, Vanderbilt University Medical Center (Medicaid)

In Hong Kong, there are registered pharmaceutical products containing buprenorphine (4 products), codeine (348 products), fentanyl (14 products), methadone (2 products), morphine (15 products), oxycodone (14 products), and tramadol (42 products). These products are pharmacy-only medicines or prescription-only medicines. There is no registered pharmaceutical product containing hydrocodone, hydromorphone, and oxymorphone. As of the end of 31 July 2025, the Department of Health (DH) had received adverse drug reaction related to codeine (4 cases), fentanyl (6 cases), methadone (5 cases), morphine (11 cases), oxycodone (2 cases), and tramadol (9 cases). The DH had not received any case of adverse drug reaction related to buprenorphine.

Related news on the safe and appropriate use of opioid analgesics 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. 185. The DH issued letters to inform local healthcare professionals to draw their attention on 11 September 2013, 14 April 2023 and 13 March 2025. In February 2015, the Registration Committee of the Pharmacy and Poisons Board of Hong Kong 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.

The risk of tolerance, dependence, withdrawal symptoms, respiratory depression associated with the use of opioid analgesics, and the risks associated with using opioid analgesics in conjunction with benzodiazepines or other medicines that depress the central nervous system (CNS) are documented in overseas reputable drug references such as the "Martindale: The Complete Drug Reference" and "AHFS Drug Information". The DH will remain vigilant on any safety update of the drugs issued by other overseas drug regulatory authorities for consideration of any action deemed necessary.

Drug Recall

Recall of four batches of Pms-Fluoxetine capsules 10mg due to presence of impurity

On 2 July 2025, the Department of Health (DH) endorsed a licensed drug wholesaler, Trenton-Boma Limited (Trenton-Boma), to recall a total of four batches (batch number: 651197, 658508, 660425 and 661412) of Pms-Fluoxetine capsules 10mg (Hong Kong Registration number: HK-61931), from the market as a precautionary measure due to the presence of impurity in the products.

The DH received notification from Trenton-Boma that the overseas manufacturer of the products is recalling the above batches of Pms-Fluoxetine capsules 10mg as they may exceed the accepted level of an impurity, N-nitroso-fluoxetine. N-nitroso-fluoxetine is classified as a probable human carcinogen based on results from laboratory tests. As a precautionary measure, Trenton-Boma is voluntarily recalling the affected batches of product from the market.

The above product, containing fluoxetine, is a prescription medicine used for the treatment of depression. According to Trenton-Boma, the affected batches of product have been imported into Hong Kong and supplied to the private doctors, veterinary surgeon, private hospitals and pharmacies.

As of the end of July 2025, the DH had not received any adverse reaction reports in connection with the products. A notice was posted in the Drug Office website on 2 July 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.

Update on Drug Office's website: You can now search the newly registered medicines in the past year at http://www.drugoffice.gov.hk/eps/drug/newsNRM60/en/healthcare_providers?pageNoRequested=1.
Details of ALL registered pharmaceutical products can still be found in the Drug Office website at http://www.drugoffice.gov.hk/eps/do/en/healthcare_providers/news_informations/reListRPP_index.html.

Useful Contact

Drug Complaint:

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,
100 How Ming Street,
Kwun Tong, Kowloon

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.