Drug News
藥 物 情 報

Issue Number 191

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

Singapore: Lipidem® 200mg/ml Emulsion for Infusion (10 x 500 ml): Important information on subvisual agglomerates and the need to use an infusion filter for fat emulsions

On 1 September 2025, Health Sciences Authority (HSA) announced that a Dear Healthcare Professional Letter has been issued by B. Braun Singapore Pte Ltd to inform healthcare professionals that subvisual droplet-like structures of emulsion components were detected in Lipidem® 200mg/ml Emulsion for Infusion (10 x 500 ml). The earliest time of the subvisual droplet-like structures of emulsion components detection was 18 months. At higher temperatures, this effect may occur earlier. Intravenous administration of the droplet-like structures can lead to adverse events such as embolism in the capillary tissue of the lungs. Healthcare professionals are advised to use the lipid emulsion filter with a pore size of 1.2 µm (Intrapur® Lipid 1.2µm infusion filter) with Lipidem® 200mg/ml Emulsion for Infusion until further notice.

In Hong Kong, Lipidem Emulsion For Infusion (HK-58945) is a pharmaceutical product registered by B. Braun Medical (HK) Ltd. It is a prescription-only medicine indicated for supply of energy, including a readily utilisable lipid component (medium-chain triglycerides) and essential omega-6 fatty acids and omega-3 fatty acids, as part of parenteral nutrition when oral or enteral nutrition is impossible, insufficient or contraindicated. As of the end of September 2025, the Department of Health (DH) had not received any case of adverse drug reaction with regard to Lipidem. In light of the above HSA's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 4 September 2025. The DH will remain vigilant on safety update of the drug issued by other overseas drug regulatory authorities.

Singapore: Polivy (polatuzumab vedotin): New identified risk of severe infusion site extravasation events

On 5 September 2025, Health Sciences Authority (HSA) announced that a Dear Healthcare Professional Letter has been issued by Roche Singapore Pte Ltd to update healthcare professionals on the new identified risk of infusion site extravasation with polatuzumab vedotin. Analysis of data from post marketing and clinical settings have provided sufficient evidence of a causal association of the events with polatuzumab vedotin.

Healthcare professionals are advised to ensure adequate venous access before initiating infusion and maintain close monitoring throughout administration for signs of extravasation. If extravasation is suspected, the infusion should be stopped immediately. The needle should be withdrawn following a brief aspiration and the affected limb elevated. Appropriate symptomatic management may be initiated as required. Roche will be updating the product label to reflect this risk.

Polivy in combination with rituximab, cyclophosphamide, doxorubicin, and prednisone (R-CHP) is indicated for the treatment of adult patients with previously untreated diffuse large B-cell lymphoma (DLBCL). Polivy in combination with bendamustine and MabThera is indicated for the treatment of adult patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) who are not eligible for haematopoietic cell transplant.

In Hong Kong, Polivy Powder For Concentrate For Solution For Infusion 140mg (HK-66664) and

Polivy Powder For Concentrate For Solution For Infusion 30mg (HK-67107) are pharmaceutical products registered by Roche Hong Kong Limited. They are prescription-only medicines. As of the end of September 2025, with regard to polatuzumab vedotin, the Department of Health (DH) had received 29 cases of adverse drug reaction, but these cases were not reported as infusion site extravasation. In light of the above HSA's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 5 September 2025. The DH will remain vigilant on safety update of the drug issued by other overseas drug regulatory authorities.

European Union: Caspofungin: new warning against use of polyacrylonitrile-based membranes during continuous renal replacement therapy

On 5 September 2025, the European Medicines Agency (EMA) announced that its safety committee, Pharmacovigilance Risk Assessment Committee (PRAC), has endorsed a direct healthcare professional communication (DHPC) warning about the use of polyacrylonitrile (PAN)-based membranes during continuous renal replacement therapy (CRRT) in critically ill patients receiving caspofungin. CRRT involves non-stop dialysis in patients with acute kidney injury and fluid overload.

Caspofungin is an antifungal medicine, given by intravenous infusion for the treatment of fungal infections in adults and children.

Laboratory data suggest that the PAN-based membranes used to filter the blood in CRRT can bind caspofungin and decrease its effectiveness. In addition, lack of caspofungin effectiveness has been reported in patients undergoing CRRT with these membranes.

Antifungal treatment failure may lead to worsening of the systemic fungal infection, which may be fatal in these critically ill patients.

Healthcare professionals should verify the type of haemofiltration membrane used before initiating and during treatment with caspofungin. If PAN-derived membranes are being used, healthcare professionals should either switch to an alternative membrane or consider an alternative antifungal medicine.

The DHPC for caspofungin will be disseminated to healthcare professionals by the marketing authorisation holder, according to an agreed communication plan, and published on the direct healthcare professional communications page and/or in national registers in EU Member States.

In Hong Kong, there are 4 registered pharmaceutical products containing caspofungin. All products are prescription-only medicines. As of the end of September 2025, the Department of Health (DH) had not received any case of adverse drug reaction with regard to caspofungin. In light of the above EMA's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 8 September 2025, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board of Hong Kong .

European Union: Tegretol (carbamazepine): use restricted in neonates as concentration of one excipient, propylene glycol, exceeds recommended threshold

On 5 September 2025, the European Medicines Agency (EMA) announced that its safety committee, Pharmacovigilance Risk Assessment Committee (PRAC), discussed a direct healthcare professional communication (DHPC) to inform healthcare professionals that the use of Tegretol 100 mg/5 mL oral suspension is restricted in neonates.

Tegretol 100 mg/5 mL oral suspension should not be used in neonates below 4 weeks of age for term babies, or 44 weeks post-menstrual age for pre-term babies, unless there is no other treatment option available and the expected benefit outweighs the risks. This is because this formulation of Tegretol contains 25 mg of the excipient (ingredient) propylene glycol per 1 mL, which exceeds the recommended threshold for neonates of 1 mg/kg/day. At doses of 1 mg/kg/day or higher, propylene glycol accumulates in neonates as their liver and kidneys are not mature enough to fully process and remove it from the body. This increases the risk of serious adverse reactions such as metabolic acidosis (a condition in which the blood is too acidic), renal (kidney) dysfunction including acute tubular necrosis (damage to the structures in the kidneys that filter blood), acute renal failure and liver dysfunction.

Neonates treated with Tegretol 100 mg/5 mL

should be monitored by healthcare professionals, including measurements of osmolarity and/or anion gap (tests to assess the body's fluid balance and detect abnormal levels of acids in the blood). Healthcare professionals should also be aware that if Tegretol 100 mg/5 mL is given with other medicines containing propylene glycol or with any substance that is broken down by the enzyme alcohol dehydrogenase, such as ethanol, the risk of propylene glycol accumulation and toxicity is increased.

The product information of Tegretol 100 mg/5 mL is being updated to reflect its restricted use in neonates and to inform about the risk of serious adverse reactions in these patients due to the concentration of this excipient. This restriction does not apply to other liquid formulations of carbamazepine that do not contain propylene glycol.

Tegretol 100 mg/5 mL oral suspension is a nationally authorised medicine that is used to treat various conditions including some forms of epilepsy.

The DHPC for Tegretol will be disseminated to healthcare professionals by the marketing authorisation holder, according to an agreed communication plan, and published on the direct healthcare professional communications page and/or in national registers in EU Member States.

In Hong Kong, Tegretol Syrup 2% (HK-35117) is a pharmaceutical product registered by Novartis Pharmaceuticals (HK) Limited (Novartis), and is a prescription-only medicine. As of the end of September 2025, the Department of Health (DH) had received 10 cases of adverse events with regard to carbamazepine, but these cases were not related to neonates. In light of the above EMA's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 8 September 2025, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board of Hong Kong .

European Union: Crysvita (burosumab): new recommendations for monitoring due to risk of severe hypercalcaemia

On 5 September 2025, the European Medicines Agency (EMA) announced that its safety committee, Pharmacovigilance Risk Assessment Committee (PRAC), discussed a direct healthcare professional communication (DHPC) to inform healthcare professionals about the risk of severe hypercalcaemia (high blood levels of calcium) in people treated with burosumab. Increases in serum calcium, including severe hypercalcaemia, and/or parathyroid hormone (a substance made by the parathyroid gland that helps the body store and use calcium) have been reported in patients treated with burosumab. In particular, severe hypercalcaemia has been reported in patients with tertiary hyperparathyroidism (overproduction of parathyroid hormone that leads to hypercalcaemia).

Patients with moderate to severe hypercalcaemia (> 3.0 mmol/L) should not be given burosumab until hypercalcaemia is adequately treated and resolved.

In patients treated with burosumab, blood calcium levels should be measured before treatment initiation, one to two weeks after initiation or dose adjustment, and every six months during the treatment (or every three months in one to two-year-old children). Parathyroid hormones should also be measured every six months (or every three months in one to two-year-olds).

Healthcare professionals should also be aware that factors such as hyperparathyroidism, prolonged lack of movement, dehydration, hypervitaminosis D (vitamin D toxicity) or renal impairment may increase the risk of hypercalcaemia.

The product information for Crysvita will be updated to include these monitoring recommendations and to add the following possible side effects: hyperparathyroidism, hypercalcaemia, hypercalciuria (increased levels of calcium in the urine) and increased blood parathyroid hormone levels.

Crysvita is used to treat X-linked hypophosphataemia, a hereditary disorder characterised by low levels of phosphate in the blood. It is also used to treat osteomalacia (softening and weakening of the bones) caused by phosphaturic mesenchymal tumours. This type of tumour produces hormones, particularly a substance called fibroblast growth factor 23 (FGF23), which cause the body to lose phosphate.

The DHPC for Crysvita will be disseminated to healthcare professionals by the marketing authorisation holder, according to an agreed communication plan, and published on the direct

healthcare professional communications page and/or in national registers in EU Member States.

In Hong Kong, Crysvita Solution For Injection 10 mg/1ml (HK-66641), Crysvita Solution For Injection 20 mg/1ml (HK-66642) and Crysvita Solution For Injection 30 mg/1ml (HK-66643) are pharmaceutical products containing burosumab registered by DKSH Hong Kong Limited. All products are prescription-only medicines. As of the end of September 2025, the Department of Health (DH) had not received any case of adverse drug reaction with regard to burosumab. Related news was previously issued by Health Canada, and was reported in the Drug News Issue No. 190. The DH issued letters to inform local healthcare professionals to draw their attention on 26 August 2025. As previously reported, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board of Hong Kong .

Singapore: Reminder on risk of extrapyramidal side effects with metoclopramide in paediatric patients aged 18 years and below

On 11 September 2025, the Health Sciences Authority (HSA) announced that metoclopramide has been registered in Singapore since 1989 for the prevention and treatment of nausea and vomiting due to various conditions. It inhibits dopamine receptors both centrally in the chemoreceptor trigger zone (CTZ) and peripherally in the upper gastrointestinal tract, blocks the action of serotonin at the 5-hydroxytryptamine (5-HT3) receptors in the CTZ and has prokinetic activity. Six registered products are available locally in various dosage forms (i.e., tablets, syrups and injections).

Since 2023, HSA has observed more cases of metoclopramide-induced extrapyramidal side effects (EPSE) in paediatric patients aged 18 years and below. Most cases (82.6%) were prescribed oral metoclopramide in the primary care setting (i.e., General Practitioners (GPs), polyclinics) for off-label uses such as vomiting secondary to gastritis, gastroenteritis or other viral illnesses. Standard adult dosing (10 mg three times daily) was commonly prescribed regardless of patient weight.

Use of metoclopramide in paediatric patients

HSA would like to remind healthcare professionals about the approved indications of metoclopramide-containing products to reduce the risk of neurological and other dose-related adverse reactions. Metoclopramide is contraindicated in infants less than one year old. In patients aged one to 18 years, metoclopramide is approved as a second-line treatment of established post-operative nausea and vomiting, administered via the intravenous route. The approved dose for paediatric patients is 0.10 to 0.15 mg/kg body weight, up to three times daily. The recommended maximum dose in 24 hours is 0.5 mg/kg body weight, up to 30 mg daily.

As potentially serious neurological adverse events are dose-related, healthcare professionals are recommended to use the minimum effective dose of metoclopramide. Treatment should be kept as short as possible and treatment beyond 12 weeks should be avoided unless the therapeutic benefit outweighs the risk.

Local Situation

As at 1 August 2025, HSA has identified 84 cases of metoclopramide-induced EPSE (e.g., oculogyric crisis, dystonia, akathisia and tardive dyskinesia) in paediatric patients over the past five years, with increasing number of cases observed since 2023 (Figure 1). These included reports to HSA by healthcare professionals and cases detected from electronic medical records of patients who visited the emergency department or were admitted in public hospitals. There were more reports in females (n=52, 61.9%), and the affected patients ranged from 8–18 years old (median: 16 years). Majority of the patients were Chinese (n=57, 67.8%), followed by Indians (n=14, 16.7%), Malays (n=8, 9.5%) and patients of other ethnicities (n=5, 6.0%). None were reported to have irreversible tardive dyskinesia.

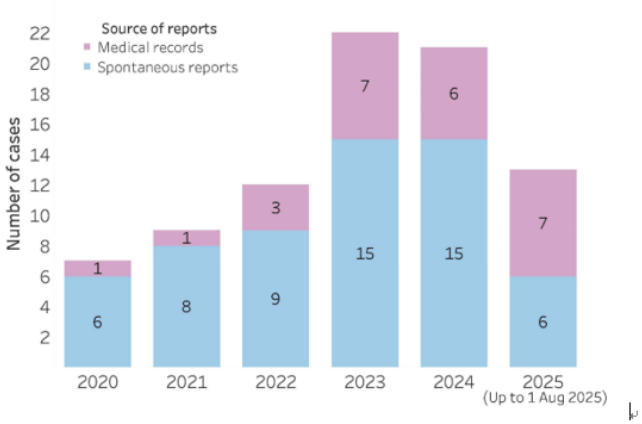

Figure 1. Local cases of metoclopramide-induced extrapyramidal side effects among paediatric patients aged 18 years and below in the past five years (January 2020 – August 2025)

Of the 69 cases with documented sources of metoclopramide, majority (n=57, 82.6%) were prescribed oral metoclopramide in the primary care setting (GPs 79.7%, polyclinics 2.9%). Seven (10.1%) patients received metoclopramide while admitted in public hospitals, with four administered intravenously and three orally. The remaining five patients self-medicated with oral metoclopramide. Majority of the patients (n=58/64, 90.6%) were prescribed metoclopramide for off-label indications such as vomiting secondary to gastritis, gastroenteritis or other viral illnesses. Patients were most frequently prescribed metoclopramide at a dose of 10 mg three times daily regardless of their weight, which ranged from 34 kg to 82 kg where documented. Notably, concurrent use of other drugs (e.g., fluoxetine, olanzapine, domperidone and prochlorperazine) in seven cases could have increased the risk of EPSE.

Choice of anti-emetics in paediatric patients

Where the use of anti-emetics is warranted, healthcare professionals could consider alternative anti-emetics for paediatric patients aged 18 years and below due to the risk of potentially serious neurological and cardiovascular adverse events with metoclopramide. The incidence of EPSE was found to be 9% (95% confidence interval 5–17%) in a meta-analysis of children administered metoclopramide although the dose of metoclopramide used in these studies varied widely. Risk factors for metoclopramide-induced EPSE include:

- Use in paediatric patients
- Females
- Doses exceeding recommended doses
- Extended duration of therapy (>12 weeks)
- Kidney impairment
- Concurrent use of drugs that can cause EPSE (e.g., anti- psychotics)
- Concurrent use of strong CYP2D6 inhibitors (e.g., fluoxetine, paroxetine, bupropion)

Domperidone, promethazine and ondansetron are among the anti-emetics recommended by PaedsENGAGE, a pilot programme led by KK Women's and Children's Hospital and National University Hospital to partner GPs across Singapore in determining the appropriate care setting for mild and moderate paediatric conditions. Recommended paediatric doses from the PaedsENGAGE drug reference guide are shown in Table 1.

Table 1. Recommended anti-emetics in the PaedsENGAGE Drug Reference Guide (1st edition)

Drug (Route)	Paediatric dose	Usual adult dose	Remarks
Domperidone (Oral)	0.25 mg/kg three times daily	10 mg three times daily	Maximum one week duration
Promethazine (Oral)	0.25–0.5 mg/kg every 6 – 8 hours	12.5–25 mg every four to six hours	Contraindicated in children < two years old
Ondansetron (Oral / Sublingual)	0.1–0.2 mg/kg every 8 hours	4–8 mg every eight to 12 hours	For use in children > six months old. Only to be given in clinic setting

Some considerations with the use of anti-emetics in paediatric patients

Domperidone has a similar mechanism of action to metoclopramide, but it has a lower risk of EPSE as it penetrates poorly into the central nervous system. Promethazine, an antihistamine and dopamine antagonist, is contraindicated for use in children less than two years old due to the risk of sedation and respiratory depression. Studies have found ondansetron to be effective in cessation of vomiting, reducing the need for intravenous fluids and risk of hospitalisation, even when given as a single dose. In a meta-analysis, ondansetron was found to be more effective than domperidone in the cessation of vomiting in children with gastroenteritis. The use of ondansetron is generally well-tolerated, although there is mixed evidence on whether ondansetron increases the frequency of diarrhoea when used in children with gastroenteritis. It is recommended for use in the clinic setting to allow for close monitoring of the child's hydration status and to avoid masking surgical conditions which present with persistent vomiting. In addition, multiple doses of ondansetron have been associated with the risk of QT interval prolongation, which can lead to potentially fatal cardiac arrythmias, although this has been mainly observed in adults. This risk is increased when ondansetron is used in high doses and in patients with risk factors such as pre-existing cardiac disease or disorders associated with electrolyte abnormalities.

HSA's advisory

Although EPSE is generally reversible with drug discontinuation and treatment, its unexpected occurrence can be distressing for both patients and caregivers. Healthcare professionals are encouraged to consider alternatives to metoclopramide when use of anti-emetics is required in paediatric patients, and to adopt weight-based dosing of metoclopramide for patients up to 18 years of age. Treatment duration should be limited, and both patients and caregivers should be counselled on the risk of EPSE.

In Hong Kong, there are 19 registered pharmaceutical products containing metoclopramide. They are prescription-only medicines. As of the end of September 2025, with regard to metoclopramide, the Department of Health (DH) had received 5 cases of adverse drug reaction, but these cases were not related to extrapyramidal side effects. Related news was previously issued by various overseas drug regulatory authorities, and was reported in the Drug News since Issue No. 45, with the latest update reported in the Drug News Issue No. 69. The DH issued letters to inform local healthcare professionals to draw their attention on 29 July 2013. In September 2014, the Registration Committee of the Pharmacy and Poisons Board Hong Kong discussed the matter and decided that the sales pack labels and/or package inserts of locally registered metoclopramide-containing pharamaceutical products should include the appropriate use of metoclopramide in paediatric patients. The risk of extrapyramidal side effects associated with metoclopramide in paediatric patients is also documented in overseas reputable drug references such as the "Martindale: The Complete Drug Reference", "American Hospital Formulary Service Drug Information" and "British National Formulary for Children". The DH will remain vigilant on safety update of the drug issued by other overseas drug regulatory authorities.

The United States: FDA Responds to Evidence of Possible Association Between Autism and Acetaminophen (Paracetamol) Use During Pregnancy

On 22 September 2025, the United States Food and Drug Administration (FDA) announced that the process for a label change for acetaminophen (paracetamol) to reflect evidence suggesting that the use of acetaminophen by pregnant women may be associated with an increased risk of neurological conditions such as autism and attention deficit hyperactivity disorder (ADHD) in children is initiated. The agency also issued a related letter alerting physicians nationwide.

"The FDA is taking action to make parents and doctors aware of a considerable body of evidence about potential risks associated with acetaminophen," said FDA Commissioner Marty Makary, M.D., M.P.H. "Even with this body of evidence, the choice still belongs with parents. The precautionary principle may lead many to avoid using acetaminophen during pregnancy, especially since most low-grade fevers don't require treatment. It remains reasonable, however, for pregnant women to use acetaminophen in certain scenarios."

Evidence in recent years has suggested a correlation between acetaminophen use during pregnancy and subsequent diagnosis of conditions like autism and ADHD. Multiple large-scale cohort studies, including the Nurses' Health Study II and the Boston Birth Cohort, find this association. Some studies have described that the risk may be most pronounced when acetaminophen is taken chronically throughout pregnancy.

It is important to note that while an association between acetaminophen and neurological conditions has been described in many studies, a causal relationship has not been established and there are contrary studies in the scientific literature. It is also noted that acetaminophen is the only over-the-counter drug approved for use to treat fevers during pregnancy, and high fevers in pregnant women can pose a risk to their children. Additionally, aspirin and ibuprofen have well-documented adverse impacts on the fetus.

In Hong Kong, there are 707 registered pharmaceutical products containing paracetamol (acetaminophen). As of the end of September 2025, with regard to paracetamol, the Department of Health (DH) had received 59 cases of adverse drug reaction, but these cases were not related to autism and ADHD in children associated with pregnancy use. In light of the above FDA's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 23 September 2025, and the DH will remain vigilant on any safety update of the drug issued by other overseas drug regulatory authorities.

Announcements on the use of Paracetamol (also known as Acetaminophen) during pregnancy released by the World Health Organization and overseas drug regulatory authorities

The Department of Health ("DH") noted that the World Health Organization ("WHO") had issued a statement on 24 September 2025 indicating that there is currently insufficient scientific evidence to conclude that paracetamol (also known as acetaminophen) use during pregnancy causes autism or other neurodevelopmental disorders in children, or that there is any association between the two. Furthermore, several drug regulatory

authorities, including those in the European Union, the United Kingdom, Australia, and Canada, had also made announcements and emphasised that, based on rigorous assessments of existing scientific data, paracetamol remains an important option for pregnant women to relieve pain or fever when clinically indicated and under medical advice. Some authorities specifically noted that studies suggesting a potential link between the two exhibit significant limitations and in fact failed to establish a causal relationship. Conversely, the medical community has long confirmed through more rigorous large-scale studies that there is no association between paracetamol use during pregnancy and autism or attention deficit/hyperactivity disorder (ADHD).

Based on current scientific evidence, claims that taking paracetamol during pregnancy causes autism or other neurodevelopmental disorders in children lack sufficient supporting evidence.

In this connection, the DH issued a press statement (https://www.info.gov.hk/gia/general/202509/25/P2025092501333.htm) on 25 September 2025 to emphasise that all public health policies and medical advice must be based on scientific evidence.

Below please find the announcements on the use of paracetamol during pregnancy issued by the WHO and overseas drug regulatory authorities:

i) World Health Organization (WHO) statement on autism-related issues

The World Health Organization (WHO) announces the following related to autism-related issues:

The World Health Organization emphasizes that there is currently no conclusive scientific evidence confirming a possible link between autism and use of acetaminophen (also known as paracetamol) during pregnancy.

Globally, nearly 62 million people (1 in 127) have autism spectrum disorder, a diverse group of conditions related to development of the brain. Although awareness and diagnosis have improved in recent years, the exact causes of autism have not been established, and it is understood there are multiple factors that can be involved.

Extensive research has been undertaken over the past decade, including large-scale studies, looking into links between acetaminophen use during pregnancy and autism. At this time, no consistent association has been established.

WHO recommends that all women continue to follow advice of their doctors or health workers, who can help assess individual circumstances and recommend necessary medicines. Any medicine should be used with caution during pregnancy, especially in the first three months, and in line with advice from health professionals.

ii) European Union: Use of paracetamol during pregnancy unchanged in the European Union

European Medicines Agency (EMA) announces that in the European Union (EU), paracetamol (also known as acetaminophen) can be used for reducing pain or fever during pregnancy if clinically needed. Paracetamol medicines can be used in pregnancy, in accordance with official recommendations. There is currently no new evidence that would require changes to the current EU recommendations for use.

"Paracetamol remains an important option to treat pain or fever in pregnant women. Our advice is based on a rigorous assessment of the available scientific data and we have found no evidence that taking paracetamol during pregnancy causes autism in children." - EMA's Chief Medical Officer, Steffen Thirstrup

As included in the product information for paracetamol in the EU, a large amount of data from pregnant women who used paracetamol during pregnancy indicates no risk of malformations in the developing foetus or in newborns.

In 2019, EMA reviewed available studies that investigated the neurodevelopment of children exposed to paracetamol in utero and found that the results were inconclusive and that no link with neurodevelopmental disorders could be established.

When needed, paracetamol can be used during pregnancy. As with any medicine for acute treatment, it should be used at the lowest effective dose, for the shortest possible time and as infrequently as possible.

Pregnant women should speak to their healthcare professional if they have questions about any medication during pregnancy.

As for all medicines, EMA and the national competent authorities in the EU will continue to monitor the safety of medicines containing paracetamol and promptly evaluate any new data as they emerge. Regulatory actions will be taken as necessary to protect public health.

iii) The United Kingdom: Paracetamol and pregnancy - reminder that taking paracetamol during pregnancy remains safe

The Medicines and Healthcare products Regulatory Agency (MHRA) announces that patients should be reminded and reassured that there is no evidence that taking paracetamol during pregnancy causes autism in children. Paracetamol is recommended as the first-choice pain reliever for pregnant women, used at the lowest dose and for the shortest duration. It also acts as an antipyretic and is therefore used to treat fever. Patients should not stop taking their pain medicines as untreated pain and fever can pose risks to the unborn child.

Advice for Healthcare Professionals:

- there is no evidence that taking paracetamol during pregnancy causes autism in children
- pregnant women should be advised to continue to follow existing NHS guidance and speak to their healthcare professional if they have questions about any medication during pregnancy
- untreated pain and fever can pose risks to the unborn baby, so it is important that patients continue to manage these symptoms with the recommended treatment. If pain or fever does not resolve, patients are advised to seek advice from their healthcare professional
- patients should not swap to alternatives such as ibuprofen. Non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, are generally not recommended during pregnancy
- the MHRA regularly reviews the safety of paracetamol including during pregnancy to ensure that the benefits to the patient and unborn baby outweigh any risks
- recent existing studies do not show a causal association between paracetamol use during pregnancy and autism. There are many potential contributing factors in the development of autism, including but not limited to concomitant diseases and family inheritance

Advice for Healthcare Professionals to Provide to Patients:

- paracetamol is recommended as the first-choice pain reliever for pregnant women, used at the lowest dose and for the shortest duration. It can also be used to treat fever
- pregnant women should be advised to continue to follow existing NHS guidance and speak to their healthcare professional if they have questions about any medication during pregnancy
- untreated pain and fever can pose risks to the unborn baby, so it is important that patients continue to manage these symptoms with the recommended treatment
- patients should not swap to alternatives such as ibuprofen, as non-steroidal anti-inflammatory drugs (NSAIDs) are generally not recommended during pregnancy

Background

Recent announcement

A recent US announcement suggested a link between paracetamol use in pregnancy and autism. However, there is no robust evidence to support this claim. The current evidence is outlined below.

The US announcement included a literature review published in Environmental Health (August 2025) looking at studies on paracetamol use in pregnancy and children later diagnosed with autism or attention deficit hyperactivity disorder (ADHD). The review considered a potential association between the use of paracetamol and the risk of autism; however, explicitly acknowledged that the evidence did not support that paracetamol caused autism. There were significant limitations to this review:

- Observational studies: these studies could not rule out alternative explanations for an association, such as confounding factors.
- Confounding factors: women taking paracetamol for fever, infection or pain, which themselves are risk factors for adverse pregnancy outcomes and risks to the child (this is known as confounding by indication).
- Self-reported use of paracetamol by mothers: many studies relied on mothers remembering if they took paracetamol years earlier, which is unreliable and prone to error (this is known as recall bias).
- Inconsistent methods: studies measured exposure and outcomes differently, making results hard to compare (misclassification bias).

- Small effect sizes: even where associations are seen, they were small and could easily be explained by other factors.

Other studies and reviews
There are other more rigorous systematic reviews and studies using national population-based registries which have found no association between paracetamol and autism.

One of the largest studies on this topic, published in 2024, used registry data for 2.4 million children born in Sweden, and compared 185,909 children exposed to paracetamol during pregnancy with their own brothers and sisters in cases where the mother had not taken paracetamol when she was pregnant with them. It showed no evidence that paracetamol used during pregnancy causes autism, nor that taking more paracetamol increases risk. Similarly, there was no evidence of a dose-response pattern. The authors highlighted that associations observed in other studies may have been confounded.

A world-wide review of the scientific literature published February 2025, of patients with well documented diagnosis of ADHD or autism, indicated that there was no evidence to support a link between the use of paracetamol during pregnancy and autism.

Review by the Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency
Regulators have also repeatedly assessed evidence. In 2019, the Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency's (EMA) reviewed studies on paracetamol and possible effects on both the urinary and reproductive systems, as well as on brain development. It concluded that the evidence was inconclusive (not strong enough to prove or disprove a risk) but recommended that product information should be updated to reflect the state of knowledge. These updates were also adopted in the United Kingdom.

Review by the UK Commission on Human Medicines (CHM)
In 2022, the UK Commission for Human Medicines (CHM) reviewed the use of non-prescription pain medicines during pregnancy. The CHM advised that there was no need to change the advice on paracetamol. However, an update to warnings for ibuprofen were included to advise mothers not to use ibuprofen during pregnancy due the risk of heart and kidney disorders in the unborn child.

Paracetamol therefore remains the preferred pain and fever medicine in pregnancy, when used at the lowest effective dose for the shortest necessary time.

iv) Canada: Acetaminophen (paracetamol) is a recommended treatment for fever and pain during pregnancy

Affected products
Acetaminophen (also known as paracetamol)

Issue
Health Canada currently maintains that there is no conclusive evidence that using acetaminophen as directed during pregnancy causes autism or other neurodevelopmental disorders.

Acetaminophen is commonly used to relieve pain and reduce fever. It has been used safely by millions of Canadians for decades, including during pregnancy and while breastfeeding.

Acetaminophen is a recommended treatment of pain or fever in pregnancy when used as directed. It should be used at the lowest effective dose for the shortest duration needed. Untreated fever and pain in pregnant women can pose risks to the unborn child.

What you should do
- Continue to use acetaminophen for pain and/or fever during pregnancy, as directed. Always follow the directions on the label.
- Do not take more than the recommended dose. Taking too much acetaminophen can cause harms including serious harm to your liver.
- If you are pregnant or breastfeeding, talk to your health care provider if you have questions about the use of any medications.
- Contact a health care provider if:
  - pain lasts more than 5 days; or
  - fever lasts more than 3 days.

What Health Canada is doing
- Health Canada's advice is based on robust, rigorous assessments of the available scientific evidence. Any new evidence that could affect our recommendations will be carefully evaluated.
- Health Canada monitors the safety of all

medicines authorized for use in Canada, including acetaminophen. All Canadian non-prescription acetaminophen products already carry clear warnings about safe use during pregnancy and breastfeeding, as well as the risk of serious liver injury if too much is taken.
- If new scientific evidence demonstrates a risk, Health Canada would take action to update labels, inform health care professionals, and provide advice to Canadians.

v) Australia: Paracetamol use in pregnancy

The Therapeutic Goods Administration (TGA) announces the following in relation to use of paracetamol in pregnancy:

- Australia's Chief Medical Officer and the TGA join with other global medicines regulators, leading clinicians and scientists worldwide in rejecting claims regarding the use of paracetamol in pregnancy, and the subsequent risk of development of ADHD or autism in children.
- Robust scientific evidence shows no causal link between the use of paracetamol in pregnancy and autism or ADHD, with several large and reliable studies directly contradicting these claims.
- Paracetamol remains the recommended treatment option for pain or fever in pregnant women when used as directed. Importantly, untreated fever and pain can pose risks to the unborn baby, highlighting the importance of managing these symptoms with recommended treatment. Pregnant women should speak to their healthcare professionals if they have questions about any medication during pregnancy.
- Paracetamol remains pregnancy category A in Australia, meaning that it is considered safe for use in pregnancy when used according to directions in TGA-approved Product Information (PI) and Consumer Medicines Information (CMI) documents.
- This means that a medicine has been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other harmful effects on the fetus having been observed. As with the use of any medicine during pregnancy, people who are pregnant should seek medical advice tailored to their specific circumstances before taking paracetamol.
- The TGA is responsible for ensuring the safety, quality and efficacy of medicines on the Australian Register of Therapeutic Goods (ARTG), with safety in pregnancy a key consideration for all products on the ARTG.
- The TGA undertakes evaluation of clinical, scientific and toxicological data prior to registration of a medicine, and this information is summarised in TGA-approved PI and CMI documents, targeted at healthcare professionals and consumers respectively, to help support safe use of a medicine in the community. These documents include information relating to use of a medicine in pregnancy.
- The TGA is aware of announcements by the US Food and Drug Administration that use of paracetamol in pregnancy may be associated with an increased risk of autism and ADHD in children, though a causal association has not been established.
- TGA advice on medicines in pregnancy is based on rigorous assessment of the best available scientific evidence. Any new evidence that could affect our recommendations would be carefully evaluated by our independent scientific experts.
- Whilst there are published articles suggesting an association between maternal paracetamol use and childhood autism, they had methodological limitations. More recent and robust studies have refuted these claims, supporting the weight of other scientific evidence that does not support a causal link between paracetamol and autism or ADHD.
- The TGA maintains robust post-market safety surveillance and pharmacovigilance processes for all medicines registered in Australia, including paracetamol. This includes detailed analysis of adverse event reports made by medicine consumers, clinicians and pharmaceutical companies, review of published medical literature, and close liaison with international medicines regulators. If a safety issue is confirmed prompt regulatory action is taken to mitigate risks.
- International peer regulators including the Medicine and Healthcare products Regulatory Agency (MHRA) in the United Kingdom have reiterated that paracetamol should continue to be used in line with product information documents. Following evaluation in 2019, the European Medicines Agency (EMA) found

that scientific evidence regarding effects of paracetamol on childhood neurodevelopment was inconclusive.
- People who have concerns and are pregnant, or considering pregnancy, are advised to consult their healthcare professionals in the first instance to discuss this issue.

Local Situation in Hong Kong

In Hong Kong, there are 707 registered pharmaceutical products containing paracetamol (acetaminophen). As of the end of September 2025, with regard to paracetamol, the Department of Health (DH) had received 59 cases of adverse drug reaction, but these cases were not related to autism and ADHD in children associated with pregnancy use.

In light of the above announcements issued by the overseas drug regulatory authorities and the World Health Organization (WHO), the DH issued letters to inform local healthcare professionals to draw their attention on 26 September 2025, and the DH will continue to closely monitor safety recommendations and research findings from other international health authorities and drug regulatory authorities regarding the use of paracetamol containing products, and to take appropriate follow-up actions as necessary.

Singapore: No Established Link Between Paracetamol Use During Pregnancy And Autism In Children

On 26 September 2025, Health Science Authority (HSA) announced it is aware of the recent US announcements suggesting a potential association between paracetamol use during pregnancy and autism in children. HSA would like to advise that there is currently no robust scientific evidence to support this claimed connection.

Paracetamol has been used worldwide for decades to manage pain and fever, including in pregnant women. It remains the recommended treatment for pain or fever in pregnant women when used as directed.

There is no conclusive scientific evidence that taking paracetamol during pregnancy causes autism in children. While some studies describe an association between paracetamol and neurological conditions such as autism, a causal relationship has not been established. Many other studies also found no such association.

HSA has a post-market surveillance programme to continually monitor the safety of medicines used in Singapore. To date, HSA has not detected any safety concerns of paracetamol use during pregnancy causing autism or other neurological issues in children.

Patients are advised of the following:
- Paracetamol can be used for reducing pain or fever during pregnancy if clinically needed. It should be used according to labelled instructions or as prescribed by healthcare professionals. Generally, it should be used at the lowest effective dose for the shortest duration needed.
- Untreated fever or pain during pregnancy can pose risks to the unborn child. Pregnant women should discuss with their healthcare professionals if they have questions or concerns about medications used during pregnancy.

HSA will continue to monitor relevant scientific evidence, safety signals and international developments in paracetamol use. We will inform healthcare professionals and members of the public if any significant safety risks are detected with medicines.

The Department of Health ("DH") noted that the World Health Organization ("WHO") had issued a statement on 24 September 2025 indicating that there is currently insufficient scientific evidence to conclude that paracetamol (also known as acetaminophen) use during pregnancy causes autism or other neurodevelopmental disorders in children, or that there is any association between the two. Furthermore, several drug regulatory authorities, including those in the European Union, the United Kingdom, Australia, and Canada, had also made announcements and emphasised that, based on rigorous assessments of existing scientific data, paracetamol remains an important option for pregnant women to relieve pain or fever when clinically indicated and under medical advice. Some authorities specifically noted that studies suggesting a potential link between the two exhibit significant limitations and in fact failed to establish a causal relationship. Conversely, the medical community has long confirmed through more rigorous large-scale studies that there is no association between paracetamol use during pregnancy and autism or attention deficit/hyperactivity disorder (ADHD).

Based on current scientific evidence, claims that taking paracetamol during pregnancy causes autism or other neurodevelopmental disorders in children lack sufficient supporting evidence.

In this connection, the DH issued a press statement (http://www.info.gov.hk/gia/general/202509/25/P2025092501333.htm) on 25 September 2025 to emphasise that all public health policies and medical advice must be based on scientific evidence.

Local Situation in Hong Kong

In Hong Kong, there are 707 registered pharmaceutical products containing paracetamol (acetaminophen). As of the end of September 2025, with regard to paracetamol, the DH had received 59 cases of adverse drug reaction, but these cases were not related to autism and ADHD in children associated with pregnancy use. Related news was previously issued by the WHO and various overseas drug regulatory authorities, and was posted on the Drug Office website on 23 September 2025 and 26 September 2025.

As previously reported, the DH issued letters to inform local healthcare professionals to draw their attention on 23 September 2025 and 26 September 2025, and the DH will maintain vigilant oversight of the matter, taking appropriate actions as necessary.

Canada: Summary Safety Review: Prescription Opioids (buprenorphine, butorphanol, codeine, diamorphine, fentanyl, hydrocodone, hydromorphone, meperidine, methadone, morphine, nalbuphine, normethadone, oxycodone, tapentadol and tramadol): Assessing the potential risk of esophageal dysfunction with long-term use

On 25 September 2025, Health Canada announced a summary safety review for assessing the potential risk of esophageal dysfunction with long-term use of prescription opioids, details as follows:

Product

Prescription opioids (buprenorphine-, butorphanol-, codeine-, diamorphine-, fentanyl-, hydrocodone-, hydromorphone-, meperidine-, methadone-, morphine-, nalbuphine-, normethadone-, oxycodone-, tapentadol- and tramadol-containing products)

Potential Safety Issue

Esophageal dysfunction (impaired function of the esophagus) with long-term use (daily for a few weeks) of prescription opioids

Key Messages

- Health Canada's review found a possible link between the long-term use of prescription opioids and the risk of esophageal dysfunction.
- Health Canada will work with the manufacturers to update the product safety information in the Canadian product monograph (CPM) for prescription opioids to include the risk of esophageal dysfunction with long-term use.

Overview

Health Canada reviewed the potential risk of esophageal dysfunction with the long-term use of prescription opioids. The safety review was triggered by Health Canada's identification of several scientific studies reporting a possible association between the long-term use of opioids and esophageal dysfunction, confirmed by tests measuring how well the esophagus is working (esophageal pressure testing). Health Canada's review did not include non-prescription opioid-containing products since this risk has not been reported with these products.

Use in Canada

- Prescription opioids are authorized in Canada for the treatment of various conditions including certain types of pain, opioid use disorder and chronic non-productive cough.
- Prescription opioids are widely used and have been marketed in Canada for over 50 years. The prescription opioids included in this safety review are: buprenorphine, butorphanol, codeine, diamorphine, fentanyl, hydrocodone, hydromorphone, meperidine, methadone, morphine, nalbuphine, normethadone, oxycodone, tapentadol and tramadol. These opioids are available in various formulations and combinations under different brand names. Generic versions are also available.
- While the number of prescriptions dispensed for the majority of opioids has decreased from 2018 to 2023, the overall number of prescriptions remains high.

Safety Review Findings

- Health Canada reviewed the available information from searches of the Canada

Vigilance database and the scientific literature.
- At the time of the review, Health Canada had received 28 Canadian reports of esophageal dysfunction in patients taking prescription opioids. However, none of these cases met the criteria for further assessment to determine if there was a link due to several contributing factors, such as: incomplete information in the reports, lack of information about when or how long the opioid was taken relative to the esophageal dysfunction, or the reported diagnosis was not confirmed by esophageal pressure testing.
- Health Canada reviewed 14 international cases of esophageal dysfunction in patients taking prescription opioids. Of the 14 cases, 3 were found to be probably linked to the use of prescription opioids and 11 were found to be possibly linked. One death occurred among the 3 cases found to be probably linked, although the death was unlikely to be linked to the use of prescription opioids.
- The patients in the 14 cases were taking doses equivalent to between 30 and 300 mg of morphine per day, with a midrange daily dose of 67.5 mg. Esophageal dysfunction was more likely to occur in patients taking a higher daily opioid dose. The time to onset of symptoms ranged from several weeks to months, with the most common symptoms reported being difficulty swallowing, gastroesophageal reflux and chest pain.
- Health Canada also reviewed articles published in the scientific literature, which identified potential biological mechanisms that may explain how the long-term use of prescription opioids could lead to esophageal dysfunction.

Conclusions and Actions
- Health Canada's review found a possible link between the long-term use of prescription opioids and the risk of esophageal dysfunction.
- Health Canada will work with the manufacturers to update the CPM for prescription opioids to include the risk of esophageal dysfunction with long-term use.
- Health Canada will continue to monitor safety information for prescription opioids, as it does for all health products on the Canadian market, to identify and assess potential harms. Health Canada will take appropriate and timely action should new health risks be identified.

In Hong Kong, there are registered pharmaceutical products containing buprenorphine (4 products), codeine (346 products), fentanyl (14 products), meperidine (pethidine) (7 products), methadone (2 products), morphine (15 products), nalbuphine (1 product), oxycodone (14 products) and tramadol (42 products). These products are pharmacy-only medicines or prescription-only medicines. There is no registered pharmaceutical product containing butorphanol, diamorphine, hydrocodone, hydromorphone, normethadone and tapentadol. As of the end of September 2025, the Department of Health (DH) had received adverse drug reaction with regard to codeine (4 cases), fentanyl (6 cases), meperidine (pethidine) (5 cases), methadone (5 cases), morphine (11 cases), oxycodone (2 cases) and tramadol (9 cases) but these cases were not reported as esophageal dysfunction. The DH had not received any case of adverse drug reaction with regard to buprenorphine and nalbuphine.

Related news regarding the long-term use of opioids was previously issued by the United States Food and Drug Administration, and was reported in the Drug News Issue No. 189. The risk of inhibited gastrointestinal motility associated with the use of opioid analgesics is documented in overseas reputable drug references such as the "Martindale: The Complete Drug Reference". 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.

A product containing any western drug ingredient must be registered under the Pharmacy and Poisons Ordinance before it can be sold in Hong Kong. Part 1 poisons should be sold at registered pharmacies under the supervision of registered pharmacists. Illegal sale or possession of Part 1 poisons and unregistered pharmaceutical products are offences under the Pharmacy and Poisons Ordinance (Cap. 138). The maximum penalty is a fine of $100,000 and two years' imprisonment for each offence. Antibiotics can only be supplied at registered pharmacies by registered pharmacists or under their supervision and upon a doctor's prescription. They should only be used under the advice of a doctor. Illegal sale or possession of antibiotics are offences under the Antibiotics Ordinance (Cap. 137) and the maximum penalty is a $50,000 fine and one year's imprisonment for each offence.

Under the Import and Export Ordinance (Cap. 60), pharmaceutical products must be imported or exported under and in accordance with an import or export licence issued under the Import and Export Ordinance. Illegal import or export of pharmaceutical products are offences under the Import and Export Ordinance (Cap. 60) and the maximum penalty is a fine of $500,000 and 2 years' imprisonment.

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

Useful Contact

Drug Complaint:
Tel: 2572 2068
Fax: 3904 1224
E-mail: pharmgeneral@dh.gov.hk

Adverse Drug Reaction (ADR) Reporting:
Tel: 2319 2920
Fax: 2319 6319
E-mail: adr@dh.gov.hk
Link: http://www.drugoffice.gov.hk/adr.html
Post: 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.