Prescriber Update

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MINISTRY OF HEALTH
MANATŪ HAUORA

Bowel-ed over by ACE inhibitors and angiotensin II receptor blockers: When angioedema hits the intestines

Key messages

- Angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) can cause angioedema in any mucosal surface, and typically affects the tongue, face and upper airway.
- Angioedema can also occur in the intestines. It is likely to be under-recognised and underreported as it is less obvious than when it occurs in other locations.
- Consider intestinal angioedema in patients taking an ACE inhibitor or ARB who present with non-specific symptoms such as abdominal pain, diarrhoea, nausea or vomiting.

At their September 2025 meeting, the Medicines Adverse Reactions Committee reviewed the risk of intestinal angioedema with angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs).

This article highlights the risk of angioedema with these medicines, with a focus on intestinal angioedema.

Angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers

ACE inhibitors and ARBs (Table 1) act on the renin-angiotensin-aldosterone system. This system regulates blood volume, electrolyte balance and systemic vascular resistance.[1]

Table 1: Approved angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARB) in New Zealand, 1 October 2025

ACE inhibitors	ARBs
Captopril	Candesartan
Enalapril	Irbesartan
Lisinopril	Losartan
Perindopril	Valsartan*
Quinapril	
Ramipril	

* Valsartan is only available as part of the combination product Entresto, which also contains the neprilysin inhibitor sacubitril. Neprilysin inhibitors prevent the degradation of vasoactive substances, including natriuretic peptides, bradykinin and angiotensin II.

Source: Medsafe Product/Application search, accessed 1 October 2025.

Angioedema with ACE inhibitors and ARBs

Angioedema is a localised subcutaneous or submucosal swelling caused by extravasation (leakage) of fluid into interstitial tissues.[2] Any mucosal tissue can be involved, although angioedema typically affects the tongue, face and upper airway.[3]

ACE inhibitors are thought to cause angioedema due to a build-up of bradykinin.[3] ACE inhibitor-induced angioedema is rare, occurring in around 0.1% to 0.7% of patients treated with this class of medicines.[3] ACE inhibitors are contraindicated in patients with a previous episode of angioedema from an ACE inhibitor.[4]

The risk of developing angioedema is lower with ARBs compared with ACE inhibitors.[5] Some studies suggest that the risk of angioedema with ARBs is similar to other antihypertensives (eg, beta-blockers) and placebo.[5] The mechanism of ARB-induced angioedema is unknown.[6]

Use of ARBs is not contraindicated in people who have experienced angioedema with an ACE inhibitor.[4] The reoccurrence of angioedema after switching to an ARB has been reported to occur in 1.5% of patients.[7]

Sacubitril + valsartan is contraindicated in patients with a known history of ACE inhibitor or ARB-induced angioedema.[8]

Intestinal angioedema – a presentation to keep in mind

Angioedema can also occur in the mucosal tissue of the intestines, with or without other sites being affected.[5] Intestinal angioedema is likely to be under-recognised and underreported as it is less obvious than when it occurs in the tongue, face and upper airway.[5]

Patients can also present with non-specific gastrointestinal symptoms, such as abdominal pain, diarrhoea, nausea or vomiting.[3] As many other conditions and diseases have these same symptoms, diagnosing intestinal angioedema can be challenging.[3]

There are reports of patients undergoing unnecessary procedures in attempts to exclude other possible causes.[9] Some patients also report their symptoms as self-limiting, resolving within 2 to 3 days even without discontinuing the suspected medicine.[10] Patients may have bouts of intestinal angioedema for many years before being diagnosed.[10]

Consider intestinal angioedema in patients who are using an ACE inhibitor or ARB, and:[9]

- have abdominal pain with or without other gastrointestinal symptoms
- computerised tomography or ultrasound of abdomen or pelvis showing bowel wall thickening with or without ascites
- have normal C1-esterase inhibitor levels
- symptoms resolve after stopping the ACE inhibitor or ARB.

If intestinal angioedema is diagnosed, discontinue the suspect medicine.[11]

New Zealand case reports

From 1 January 2010 to 30 September 2025, the New Zealand Pharmacovigilance database received:

- 278 case reports of angioedema where the suspect medicine was an ACE inhibitor
- 26 case reports of angioedema where the suspect medicine was an ARB.

To date, there have been no cases of intestinal angioedema reported in New Zealand with these medicines.

More information

- Reminder: ACE inhibitor-induced angioedema can be fatal – *Prescriber Update* June 2023
- Prescribing ACE inhibitors: time to reconsider old habits – bpac^{nz} updated May 2023
- Vildagliptin and ACE inhibitors – increased risk of angioedema – *Prescriber Update* March 2021

References

1. Fountain JH, Kaur J and Lappin SL. 2023. Physiology, renin angiotensin system. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing 12 March 2023. URL: www.ncbi.nlm.nih.gov/books/NBK470410/ (accessed 6 October 2025).
2. Zuraw B, Saini S, Li H, et al. 2025. An overview of angioedema: Clinical features, diagnosis, and management. In: *UpToDate* 4 September 2025. URL: www.uptodate.com/contents/an-overview-of-angioedema-clinical-features-diagnosis-and-management (accessed 22 September 2025).
3. Guyer A, Banerji A, Saini S, et al. 2025. ACE inhibitor-induced angioedema. In: *UpToDate* 16 April 2025. URL: www.uptodate.com/contents/ace-inhibitor-induced-angioedema (accessed 22 September 2025).
4. bpac^{nz}. 2021. *Prescribing ACE inhibitors: time to reconsider old habits* updated 12 May 2023. URL: bpac.org.nz/2021/ace.aspx (accessed 6 October 2025).
5. Rosas S, Fowler A, Stodgill E, et al. 2023. A rare case of losartan-induced visceral angioedema. *Journal of Primary Care & Community Health* 14: 1–3. DOI: 10.1177/21501319231213744 (accessed 6 October 2025).
6. Sharma P and Nagarajan V. 2013. Q: Can an ARB be given to patients who have had angioedema on an ACE inhibitor? *Cleveland Clinical Journal of Medicine* 80(12): 755-7. DOI: 10.3949/ccjm.80a.13041 (accessed 6 October 2025).
7. Inayat F and Hurairah A. 2016. Small bowel angioedema secondary to angiotensin-converting enzyme inhibitors. *Cureus* 8(12): e943. DOI: 10.7759/cureus.943 (accessed 6 October 2025).
8. Novartis New Zealand Limited. 2022. *New Zealand Entresto Data Sheet* 7 December 2022. URL: www.medsafe.govt.nz/profs/datasheet/e/entrestotab.pdf (accessed 6 October 2025).
9. Korniyenko A, Alviar CL, Cordova JP, et al. 2011. Visceral angioedema due to angiotensin-converting enzyme inhibitor therapy. *Cleveland Clinical Journal of Medicine* 78(5): 297-304. DOI: 10.3949/ccjm.78a.10102 (accessed 6 October 2025).
10. Pirzada S, Raza B, Mankani AA, et al. 2023. A case of angiotensin-converting enzyme (ACE) Inhibitor-induced small bowel angioedema. *Cureus* 15(10): e47739. DOI: 10.7759/cureus.47739 (accessed 6 October 2025).
11. Teva Pharma (New Zealand) Limited. 2025. *New Zealand Losartan Actavis Data Sheet* 31 January 2025. URL: www.medsafe.govt.nz/profs/datasheet/l/losartanactavistab.pdf (accessed 6 October 2025).

Quarterly summary of recent safety communications

The table below is a summary of recent safety communications for healthcare professionals and consumers. Click on a specific topic to go to the communication.

Date	Communication	Topic
11/11/2025	Monitoring	Further Update - Estradot (estradiol) transdermal patches: reports of quality and efficacy
04/11/2025	Monitoring	Update - Estradot (estradiol) transdermal patches: reports of quality and efficacy
22/10/2025	Dear Healthcare Professional Letter	Recent complaints for Estradot transdermal patches (25, 50, 75 and 100 mcg/24 hrs) (PDF, 3 pages, 451 KB)
22/10/2025	Monitoring	Estradot (estradiol) transdermal patches: reports of quality and efficacy
13/10/2025	Dear Healthcare Professional Letter	Paxlovid (nirmatrelvir/ritonavir) treatment in patients with severe renal impairment (PDF, 5 pages, 322 KB)
26/09/2025	News article	Ministry of Health: Paracetamol use in pregnancy
24/09/2025	Dear Healthcare Professional Letter	Risperdal: Discontinuation of Risperdal (risperidone) tablets across all strengths as of 15 December 2025 (PDF, 3 pages, 213 KB)
23/09/2025	Alert	Topiramate: New measures and advice to prevent exposure during pregnancy
22/09/2025	Dear Healthcare Professional Letter	Ribomustin: Discontinuation of Ribomustin (bendamustine hydrochloride) 25mg & 100mg powder for infusion as of 30 November 2025 (PDF, 2 pages, 216 KB)
17/09/2025	Dear Healthcare Professional Letter	Epilim: Updated safety information for valproate: Risk in pregnancy and women of childbearing potential – lower birth weight following in utero exposure to valproate (PDF, 2 pages, 167 KB)
15/09/2025	Dear Healthcare Professional Letter	Lenalidomide Viatris (lenalidomide) capsules: NZ-specific cartons (PDF, 2 pages, 379 KB)
12/09/2025	Dear Healthcare Professional Letter	Polivy: Infusion site extravasation is a new identified risk for Polivy (polatuzumab vedotin) (PDF, 3 pages, 169 KB)
08/09/2025	Dear Healthcare Professional Letter	Tegretol (carbamazepine) liquid: limitation of use in neonates (PDF, 1 page, 156 KB)

Note that sponsors write Dear Healthcare Professional Letters and distribute them to relevant healthcare professionals. Medsafe publishes copies of these letters on the Medsafe website.

Test your knowledge: the *Prescriber Update* quiz 2025

Have you been reading *Prescriber Update* in 2025?

Have you kept up to date with emerging safety signals?

Test your knowledge with the end-of-year *Prescriber Update* quiz.

Answers to the quiz are on page 72 and the Medsafe website.

1. The use of Contrave (naltrexone + bupropion) is **contraindicated** in which of the following patients?
   a. A patient with controlled hypertension and a BMI of 32
   b. A patient receiving opioid substitution therapy
   c. A patient with a history of smoking and mild depression
   d. A patient with well-managed type 2 diabetes and no psychiatric history

2. True or false: Fluoroquinolone-induced tendon rupture can occur months after stopping treatment.

3. How long after starting immunotherapy does immune effector cell-associated neurotoxicity syndrome (ICANS) usually occur?

4. A patient on long-term systemic retinoid therapy starts to experience musculoskeletal problems, including back pain, morning stiffness and reduced range of motion. What condition may have developed?

5. What advice should be given to patients starting on GLP-1 receptor agonists to reduce the risk of acute renal injury?

6. Which of the following statements about colchicine is false?
   a. Reduce the colchicine dose by half if the patient's creatinine clearance is ≤10 mL/min
   b. Itraconazole, clarithromycin, verapamil and amiodarone can interact with colchicine
   c. Colchicine may increase the risk of bleeding in patients taking anticoagulants
   d. The first signs of colchicine toxicity may be a feeling of burning and rawness in the mouth and throat and difficulty in swallowing

7. What is the mechanism for paracetamol-induced high anion gap metabolic acidosis (HAGMA)?
   a. 5-oxoproline depletion due to low glutathione levels
   b. 5-oxoproline accumulation due to high glutathione levels
   c. Pyroglutamate accumulation due to low glutathione levels
   d. Pyroglutamate depletion due to high glutathione levels

8. Is cholestatic jaundice typically associated with short or long term use of nitrofurantoin?

9. A 45-year-old woman presents with intermittent abdominal pain, nausea and vomiting. Imaging shows bowel wall thickening and mild ascites. Of the medicines listed below that she is taking, which is the most likely to have caused this?
    a. Paracetamol
    b. Levonorgestrel
    c. Perindopril
    d. Gabapentin

10. A couple is considering starting a family but one of them is taking methotrexate. How long after stopping methotrexate should they continue to use contraception for?
    a. At least 3 months after stopping for males and at least 3 months for females
    b. At least 6 months after stopping for males and at least 6 months for females
    c. At least 6 months after stopping for males and at least 3 months for females
    d. At least 3 months after stopping for males and at least 6 months for females

MARC's remarks: September 2025 meeting

The Medicines Adverse Reaction Committee (MARC) convened for their 203rd meeting on 11 September 2025.

The Committee reviewed the potential interaction between glucagon-like peptide-1 (GLP-1) receptor agonists, such as **dulaglutide**, **liraglutide** and **semaglutide,** with **oral contraceptives**. The Committee considered that there was insufficient evidence at this time to support updates to the data sheets.

The risk of intestinal angioedema with **angiotensin converting enzyme (ACE) inhibitors** and **angiotensin II receptor blockers (ARBs)** was discussed. The Committee considered that intestinal angioedema may be a less well recognised manifestation of angioedema due to its non-specific presentation. They recommended data sheet updates to include information about intestinal angioedema. See also the article about intestinal angioedema in this edition of *Prescriber Update*.

The Committee reviewed the risk of seizures in patients with convulsive disorders using **beta-2 agonists**. They determined there was insufficient evidence to support a causal association. The Committee noted that the data sheets of specific beta-2 agonist containing medicines currently containing seizure-related information. The Committee asked Medsafe to review this data to ensure there is consistent information across the beta-2 agonist data sheets.

See the Medsafe website for the MARC meeting minutes and the reports presented to the MARC.

Paracetamol can cause high anion gap metabolic acidosis (HAGMA)

Key messages

- Paracetamol can cause pyroglutamic acidosis, a form of high anion gap metabolic acidosis (HAGMA).
- HAGMA has been reported in patients taking paracetamol long term at therapeutic doses, and who have the additional risk factors of severe illness, malnutrition or alcoholism. The risk is higher with concomitant flucloxacillin.
- If HAGMA is suspected, promptly discontinue paracetamol treatment. Follow local clinical treatment guidelines.

The paracetamol data sheets were recently updated with information about the risk of HAGMA associated with paracetamol use. We are including this article to provide more information about this condition.

What is HAGMA?

Metabolic acidosis is an acid-base disturbance characterised by a low blood pH with low bicarbonate.[1] It can be life-threatening, particularly in patients with comorbidities such as chronic kidney disease or advanced liver disease.[1]

Various measures are used to try and identify the cause of the metabolic acidosis, with the anion gap being the most popular.[2] The anion gap is a mathematical equation based on the balance of specific cations (sodium, and sometimes potassium) and anions (chloride, bicarbonate) measured in the blood.[3] A high anion gap indicates the presence of unmeasured anions in the blood.[1]

High anion gap metabolic acidosis (HAGMA) is a type of metabolic acidosis associated with acid accumulation and characterised by a high anion gap.[1] Causes include lactic acidosis, ketoacidosis, renal failure and poisoning.[1]

Pyroglutamate (5-oxoproline) is metabolite that can contribute to a high anion gap and is another cause of HAGMA.[1] The metabolism of paracetamol can cause pyroglutamate to accumulate (pyroglutamic acidosis), particularly when glutathione levels are low.[4,5]

Paracetamol-induced HAGMA

Cases of paracetamol-induced HAGMA, due to pyroglutamic acidosis, have been reported in patients with severe illness (renal impairment, sepsis), malnutrition or alcoholism, and who are taking paracetamol long term at therapeutic doses. The risk is higher if the patient is also taking flucloxacillin.[5–7]

Measuring urinary 5-oxoproline may be a useful way to identify pyroglutamic acidosis as the underlying cause of HAGMA in patients with multiple risk factors.[6,7]

If HAGMA due to pyroglutamic acidosis is suspected, promptly discontinue paracetamol and closely monitor the patient.[6,7] Follow local clinical guidelines for treatment.

New Zealand case reports

As of 30 September 2025, there were four case reports of metabolic acidosis associated with paracetamol (report IDs: 053710, 127319, 146042, NZ-Medsafe-163566). Flucloxacillin was a co-suspect medicine in three of the four reports. Reported terms included acidosis, anion gap abnormal, metabolic acidosis and/or pyroglutamic acidosis.

References

1. Kharsa A, Vashist R, Rout P, et al. 2025. Anion gap and non-anion gap metabolic acidosis (updated 6 August 2025). In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing. URL: www.ncbi.nlm.nih.gov/books/NBK448090/ (accessed 2 Octocber 2025).
2. Forni LG, McKinnon W, Hilton PH. 2006. Unmeasured anions in metabolic acidosis: unravelling the mystery. *Critical Care* 10(4): 220. DOI: 10.1186/cc4954 (accessed 7 November 2025).
3. Pandey DG and Sharma S. 2023. Biochemistry, anion gap. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing. URL: www.ncbi.nlm.nih.gov/books/NBK539757/ (accessed 12 November 2025).
4. Crisp T, Sizeland P, Du Toit S, et al. 2021. Pyroglutamic acidosis: an under-recognised cause of high anion gap metabolic acidosis. *New Zealand Medical Journal* 134 (1546): 117–21. URL: nzmj.org.nz/media/pages/journal/vol-134-no-1546/pyroglutamic-acidosis-an-under-recognised-cause-of-high-anion-gap-metabolic-acidosis/c74b54851f-1696476732/pyroglutamic-acidosis-an-under-recognised-cause-of-high-anion-gap-metabolic-acidosis.pdf (accessed 29 October 2025).
5. Scafetta T, Kovacs O, Milani GP, et al. 2024. Drug-related pyroglutamic acidosis: Systematic literature review. *Journal of Clinical Medicine* 13(19): 5781. DOI: 10.3390/jcm13195781 (accessed 1 October 2025).
6. Stewart GW. 2024. Pyroglutamate acidosis 2023. A review of 100 Cases. *Clinical Medicine* 24: 100030. DOI: 10.1016/j.clinme.2024.100030 (accessed 29 September 2025).
7. Ipca Pharma (NZ) Pty Limited. 2025. *Pacimol New Zealand Data Sheet* October 2025. URL: www.medsafe.govt.nz/profs/Datasheet/p/pacimoltab.pdf (accessed 12 November 2025).

Reminder: Allergic reactions with *Andrographis paniculata*

Key messages

- Andrographis-containing products may cause allergic reactions, including anaphylaxis.
- Be aware that patients presenting with hypersensitivity symptoms could be taking natural health products that may contain andrographis.
- Patients who experience allergic reactions with an andrographis-containing product should stop taking it and avoid these products in future.

We are reminding prescribers that allergic reactions can occur in patients taking andrographis-containing products. These reactions can be serious and include rash, urticaria (hives), pruritus (itchy skin), throat tightness or swelling, and anaphylaxis. Respiratory symptoms (eg, wheeze, stridor) and gastrointestinal symptoms (eg, diarrhoea, vomiting) may also be observed.

Andrographis paniculata is a herb contained in some natural health products. Andrographis is often combined with other ingredients and these products are typically marketed for "immune support" or to aid recovery from cold and flu symptoms.

We previously issued an alert about the potential risk for allergic reactions with andrographis in 2017. We continue to receive reports of hypersensitivity reactions, with three cases received each year since 2023.

Ask patients presenting with hypersensitivity symptoms if they are taking any natural health products, as well as prescribed or over-the-counter medicines.

Advise patients who experience an allergic reaction with andrographis-containing products to stop taking it and to avoid these products in future. This may require carefully checking the ingredients listed on natural health product labels.

Please continue to report adverse reactions to natural health products. Reporting is easiest online.

Consider Triple M overlap syndrome (Myocarditis, Myositis and Myasthenia gravis) with immune checkpoint inhibitors

Key messages

- Immune checkpoint inhibitors (ICIs) can cause immune-mediated adverse reactions in multiple organ systems.
- ICIs have also been associated with the triad of myocarditis, myositis and myasthenia gravis, known as Triple M overlap syndrome (or myocarditis-myositis-myasthenia gravis overlap syndrome).
- Triple M overlap syndrome causes significant morbidity and has a high mortality rate.
- If any one of myasthenia gravis, myositis or myocarditis is suspected in a patient receiving an ICI, check for other autoimmune conditions.

There is increasing awareness of Triple M overlap syndrome, and cases have been reported in New Zealand in association with immune checkpoint inhibitors (ICIs).

Immune checkpoint inhibitors

ICIs are monoclonal antibodies that improve the immune response to tumour cells by increasing T-cell activity.[1] As a result, T-cell mediated attack can also occur on healthy cells, causing immune-mediated adverse reactions in multiple organ systems.[1]

ICIs approved in New Zealand include atezolizumab (Tecentriq), durvalumab (Imfinzi), ipilimumab (Yervoy), nivolumab (Opdivo) and pembrolizumab (Keytruda). ICIs are indicated for the treatment of several cancers.

Triple M overlap syndrome

Myocarditis, myositis and myasthenia gravis are immune-mediated adverse reactions known to occur with ICIs.[2-6] These reactions can occur separately, or sometimes together as a triad, known as Triple M overlap syndrome (or myocarditis-myositis-myasthenia gravis overlap syndrome).[7,8]

Triple M overlap syndrome varies in presentation and severity. Although rare, it can be life-threatening,[7,8] with in-hospital mortality rates approaching 40%.[8]

Prompt recognition and early treatment of Triple M overlap syndrome is vital. If any one of myocarditis, myositis or myasthenia gravis is suspected in a patient receiving an ICI, check for other autoimmune conditions.[7]

New Zealand case reports

As of 30 September 2025, there were three case reports of patients experiencing concurrent myasthenia gravis, myositis and myocarditis associated with an ICI.

Of these three cases:

- ipilimumab and nivolumab were the suspect medicines in one case (report ID: NZ-Medsafe-162153)
- pembrolizumab was the suspect medicine in two cases (NZ-Medsafe-156395, NZ-Medsafe-161059).

Further information

See the following for more information on ICIs and immune-mediated adverse reactions:

- Autoimmune complications of immunotherapy – *Prescriber Update* June 2023
- Medicine data sheets

References

1. New Zealand Formulary (NZF). 2025. *NZF v160: Immune checkpoint inhibitor*s 1 October 2025. URL: nzf.org.nz/nzf_70778 (accessed 30 October 2025).
2. Roche Products (New Zealand) Limited. 2025. *Tecentriq New Zealand Data Sheet* 29 July 2025. URL: www.medsafe.govt.nz/profs/Datasheet/t/Tecentriqinf.pdf (accessed 30 October 2025).
3. AstraZeneca Limited. 2025. *Imfinzi New Zealand Data Sheet* 17 July 2025. URL: www.medsafe.govt.nz/profs/Datasheet/i/imfinziinf.pdf (accessed 30 October 2025).
4. Bristol-Myers Squibb (NZ) Limited. 2024. *Yervoy New Zealand Data Sheet* 25 July 2024. URL: www.medsafe.govt.nz/profs/Datasheet/y/yervoyinj.pdf (accessed 30 October 2025).
5. Bristol-Myers Squibb (NZ) Limited. 2025. *Opdivo New Zealand Data Sheet* 18 September 2025. URL: www.medsafe.govt.nz/profs/Datasheet/o/opdivoinf.pdf (accessed 30 October 2025).
6. Merck Sharp & Dohme (New Zealand) Limited. 2025. *Keytruda New Zealand Data Sheet* 11 August 2025. URL: www.medsafe.govt.nz/profs/Datasheet/k/Keytruda.pdf (accessed 30 October 2025).
7. Aggarwal N, Bianchini D, Parkar R, et al. 2024. Immunotherapy-induced overlap syndrome: Myositis, myasthenia gravis, and myocarditis – A case series. *Case Reports in Medicine* 2024: 5399073. DOI: 10.1155/2024/5399073 (accessed 1 October 2025).
8. Furlepa M, Watts I, Carr A. 2025. Management of Triple M syndrome: A narrative review of immune checkpoint inhibitor-induced myasthenia gravis, myositis and myocarditis. *Cancers* 17(13): 2063. DOI: 10.3390/cancers17132063 (accessed 1 October 2025).

Gathering knowledge from adverse reaction reports: December 2025

Adverse drug reaction (ADR) reporting is an important component of medicine safety monitoring. Case reports can highlight significant safety issues with medicines and how they are used.

The table below presents a selection of recent informative cases reported to the New Zealand Pharmacovigilance Database.

Case details[a,b]	Reaction description and data sheet information[b,c]
Report ID: 163131 **Age:** 85 years **Gender:** Male **Medicine(s):** Goserelin **Reaction(s):** Cardiac failure	Approximately three weeks after receiving the goserelin injection, the patient developed cardiac failure. Symptoms included leg oedema and shortness of breath. Finasteride (an anti-androgen) was reported as a concomitant medicine.
	The Zoladex 10.8mg data sheet lists cardiac failure as a common ADR in males. The risk is increased when used in combination with anti-androgens.
Report ID: 163317 **Age:** 68 years **Gender:** Male **Medicine(s):** Fusidic acid, atorvastatin **Reaction(s):** Drug interaction, rhabdomyolysis	A patient taking atorvastatin was started on fusidic acid and developed rhabdomyolysis.
	As stated in the Lorstat and Fucidin data sheets, concomitant treatment with statins and systemic fusidic acid is contraindicated. There have been reports of rhabdomyolysis (including some fatalities) in patients receiving this combination. Discontinue treatment with statins throughout the duration of treatment with systemic fusidic acid. Statins may be reintroduced 7 days after the last dose of fusidic acid.
Report ID: 163403 **Age:** 40 years **Gender:** Female **Medicine(s):** Botulinum toxin type A **Reaction(s):** Tinnitus, hyperacusis, facial paralysis, neurosensory deafness, dermatochalasis, myalgia, pyrexia, headache	Just over a week after the Botox injection into the forehead, the patient developed tinnitus, increased sensitivity to sound, frontal muscle paralysis, sudden hearing loss, hooding of both eyes, muscle aches, fever and headache.
	The Botox data sheet lists tinnitus, facial palsy, facial paresis, eyelid oedema, blepharoptosis (drooping of upper eyelid that can affect one or both eyes), myalgia, pyrexia and headache as possible ADRs.
Report ID: 163473 **Age:** Not reported **Gender:** Female **Medicine(s):** Semaglutide **Reaction(s):** Small intestinal obstruction	During semaglutide treatment, the patient developed a small bowel obstruction.
	Intestinal obstruction, including ileus and small intestinal obstruction, are listed in the Wegovy data sheet.

Continues

Case details[a,b]	Reaction description and data sheet information[b,c]
Report ID: 163573 **Age:** 49 years **Gender:** Female **Medicine(s):** Terbinafine, fluoxetine **Reaction(s):** Delusions of grandeur, suicidal ideation, withdrawal syndrome, drug interaction, euphoric mood	A patient taking fluoxetine started treatment with terbinafine and experienced elevated mood and grandiose feelings. After stopping terbinafine, her mood suddenly dropped, and she reported having suicidal thoughts.
	The Deolate data sheet states that terbinafine may increase the effect or plasma concentrations of medicines that are metabolised by CYP2D6, including selective serotonin reuptake inhibitors (SSRIs).

Notes:

a. Only the medicines suspected to have caused the reaction are listed in the table.
b. The reactions listed in the 'Case details' column are coded according to the Medical Dictionary for Regulatory Activities (MedDRA), an internationally used set of standardised terms relating to medical conditions, medicines and medical devices. The reactions listed in the 'Reaction description' column are based on what was reported, and do not always match the MedDRA term exactly.
c. If the suspect medicine's brand name is not described in the ADR report, only the data sheet for the funded medicine is included in the table.

Information about reported suspected adverse reactions is available on the Medsafe website using the Suspected Medicines Adverse Reaction Search (SMARS).

By selecting the ingredient of a medicine or vaccine, you can find out:

- the number of reports and suspected adverse reactions for that ingredient. The suspected reactions are grouped by body system or organs (Summary report)
- single case reports, listing the medicines and/or vaccines involved that contain the ingredient and the suspected adverse reactions (Detail report).

Recent approvals: new active ingredients or new indications

New active ingredients

Table 1 shows recent approval of medicines with new active ingredients gazetted during the period 25 July 2025 to 23 October 2025.

Table 1: Recent approvals of medicines with new active ingredients

Medicine	New active ingredient(s)	Dose form: • strength(s)	Therapeutic area
Alyftrek*	Vanzacaftor, Deutivacaftor	Film coated tablet: • 4 mg + 20 mg* + 50 mg • 10 mg + 50 mg* + 125 mg	Cystic fibrosis
Berinert IV Berinert SC	Human C1-esterase inhibitor	Powder for injection with diluent: • 500 IU (IV) • 1500 IU (IV) • 2000 IU (SC) • 3000 IU (SC)	Hereditary angioedema
Camzyos	Mavacamten	Capsule: • 2.5 mg • 5 mg • 10 mg • 15 mg	Cardiomyopathy
Elahere	Mirvetuximab	Concentrate for injection: • 100 mg/20mL	Epithelial ovarian, fallopian tube, or primary peritoneal cancer
Saphnelo	Anifrolumab	Concentrate for infusion: • 150 mg/mL	Systemic lupus erythematosus

* Also contains tezacaftor

New indications

Table 2 shows approved medicines with new indications for additional therapeutic areas gazetted during the period 25 July 2025 to 23 October 2025.

Table 2: Approved medicines with new indications for additional therapeutic areas

Medicine (active ingredient)	Dose form: • strength(s)	New therapeutic area
Nicorette Quick Mist (nicotine)	Oral spray • 1 mg/spray	Nicotine vaping dependence

More information

See the Medsafe website for:

- more information about these medicines
- data sheets of currently marketed medicines
- Gazette notices for approved medicine applications.

Recent data sheet updates: important new safety information

Table 1 below provides a list of data sheets recently updated with important new safety information. Note that this is not a comprehensive list of all recently updated data sheets, nor does it describe all changes to a particular data sheet.

To find out if sponsors have made any changes to their data sheets, refer to:

- section 10 'Date of revision of the text' at the end of each data sheet. Search for a data sheet
- the New/updates to data sheets and CMIs page on the Medsafe website.

Table 1: Recently updated data sheets (by active ingredient): important new safety information

Click on the specific medicine to open the data sheet.

Active ingredient(s): Medicine(s)	Data sheet updates	
	Section*	Summary of new safety information
Abemaciclib: Verzenio	4.6	Lactation: Do not breastfeed during treatment or for 3 weeks after the last dose of abemaciclib.
	4.8	Erythema multiforme
Atezolizumab: Tecentriq	4.4	Other immune-mediated adverse reactions: uveitis
	4.8	Uveitis; Neutropenia; Sarcoidosis; Cytomegalovirus
Atomoxetine: Apo-Atomoxetine	4.4, 4.5, 4.9	Serotonin syndrome: reported with concomitant use of atomoxetine with other serotonergic medicines.
	4.4	Aggressive behaviour or Hostility or Emotional lability: warning expanded to include severe cases in paediatric patients
	4.8	Bruxism
Axitinib: Inlyta	4.8	Pancreatitis
Colchicine: Colgout	4.4	Toxicity and fatal overdose: narrow therapeutic index, keep out of sight and reach of children, counsel patients on when and how to take colchicine.
	4.7	Possible drowsiness and dizziness
	4.8	Amenorrhoea; Dysmenorrhoea
Cladribine: Leustatin	4.3, 4.6	Contraindicated during pregnancy and lactation and for 6 months after the last cladribine dose.
Dactinomycin: Cosmegen	4.6	Use effective contraception during treatment, and for at least 7 months after the last dose for female patients of childbearing potential and for at least 4 months after the last dose for male patients with female partners of childbearing potential.
Dolutegravir: Dovato Tivicay	4.8	Sideroblastic anaemia (reversible) reported with dolutegravir-containing regimens.
Estriol: Ovestin Pessary + Vaginal Cream	4.8	Dysuria; Genital burning sensation; Vulvovaginal burning sensation
Hyoscine: Scopolamine Transdermal System	4.4, 4.8	Hyperthermia, including fatal cases.
Lisdexamfetamine: Vyvanse	4.4	Can interfere with the test results from certain radioactive diagnostic agents and lead to false-positive diagnostic results.
	4.9	Posterior reversible encephalopathy syndrome (PRES) reported in association with amphetamine overdose.

Continues

Active ingredient(s): Medicine(s)	Data sheet updates	
	Section*	Summary of new safety information
Measles + mumps + rubella vaccine: Priorix	4.3, 4.4	Contraindicated in patients on current or recent immunosuppressive therapy (includes high dose systemic corticosteroids).
Modafinil: Modavigil	4.3, 4.4, 4.6	Contraindicated during pregnancy; women of childbearing potential must use effective contraception during treatment
Morphine: DBL Morphine Sulfate Injection	4.8	Oesophageal disorder (eg, oesophageal motility disorder, lower oesophageal sphincter relaxation impaired, oesophageal peristalsis decreased) reported with opioid therapy.
Paclitaxel: Anzatax	4.6	Pregnancy: guidance for effective use of contraception increased to 7 months after the last dose for females and to 4 months for males (from 6 and 3 months, respectively). Breastfeeding: Do not breastfeed during treatment and for 2 weeks after the last dose.
Pegfilgrastim: Ziextenzo	4.4	Stevens-Johnson Syndrome (SJS)
Recombinant respiratory syncytial virus pre-fusion F protein: Arexvy	4.4, 4.8	Guillain-Barré Syndrome (GBS): reported very rarely following vaccination in individuals aged ≥60 years.
Pethidine: DBL Pethidine Hydrochloride Injection	4.8	Oesophageal disorder (eg, oesophageal motility disorder, lower oesophageal sphincter relaxation impaired, oesophageal peristalsis decreased) reported with opioid therapy.
Rifampicin + isoniazid: Rifinah	4.8	Hyperuricaemia
Semaglutide: Wegovy	4.8	Hypotension; Orthostatic hypotension
	6.6	Dispose of the pen after 4 doses, even if there is residual solution.
Teriparatide: Forteo	4.8	Anaemia; Renal impairment
Testosterone: Androfeme 1	4.3	Contraindicated in females with known or suspected androgen-dependent neoplasia, nephrotic syndrome, history of thromboembolism or hypercalcaemia.
	4.5	Concurrent use of testosterone with ACTH or corticosteroids may result in increased fluid retention and should be monitored, particularly in patients with cardiac, renal or hepatic disease.
Upadacitinib: Rinvoq	4.4	Hypoglycaemia in patients treated for diabetes – dose adjustments of diabetes medicines may be required if hypoglycaemia occurs.
Vaccinia vaccine: Jynneos	4.4	Myo-/pericarditis: Smallpox vaccines have been associated with myo-/pericarditis. Advise vaccinees of symptoms. Urgently refer patients with symptoms to specialists for diagnosis and treatment.
Valproic acid (sodium valproate): Epilim Epilim IV	4.4, 4.6	Risk of lower birth weight for the gestational age in children exposed to valproate *in utero.*
Vedolizumab: Entyvio	4.8	Tubulointerstitial nephritis
Warfarin: Marevan	4.8	Leukocytoclastic vasculitis

* Data sheet sections listed in the table are: 4.3: Contraindications; 4.4: Special warnings and precautions for use; 4.5: Interaction with other medicines and other forms of interaction; 4.6: Fertility, pregnancy and lactation; 4.7: Effects on ability to drive and use machines; 4.8: Undesirable effects; 4.9: Overdose; 6.6: Special precautions for disposal.

Quiz answers

1. **b**. Contrave is contraindicated in patients currently dependent on opioids, including those on opioid substitution therapy, due to the risk of serious life-threatening reactions. (June 2025)

2. **True**. Tendon rupture may occur months after stopping fluoroquinolone therapy, and reactions can affect patients of any age, even without pre-existing risk factors. (September 2025)

3. **4–5 days**. Immune effector cell-associated neurotoxicity syndrome (ICANS) occurs a median of 4–5 days following the use of any immunotherapy that activates or engages T-cells and/or other immune effector cells. (March 2025)

4. **Diffuse idiopathic skeletal hyperostosis (DISH)**. Cases of DISH have been reported following use of systemic retinoids, usually after prolonged use and/or at high doses. (September 2025)

5. To reduce the risk of renal injury in patients starting GLP-1 receptor agonists, advise them to stay well hydrated by drinking plenty of fluids (eg, water) and inform them of the potential risks associated with dehydration. Also advise them to seek medical attention if gastrointestinal symptoms are severe or persistent. (June 2025)

6. **a**. Colchicine is contraindicated if the patient's creatinine clearance is ≤10 mL/min. (March 2025)

7. **c**. Paracetamol can cause HAGMA due to pyroglutamic acidosis. It is associated with glutathione depletion, which causes 5-oxoproline/pyroglutamic acid to accumulate. (December 2025)

8. **Short-term use**. Cholestatic jaundice is typically associated with short-term nitrofurantoin use, while chronic active hepatitis, which can progress to hepatic necrosis, is generally linked to long-term use. (June 2025)

9. **c**. This patient may be experiencing intestinal angioedema due to perindopril (an ACE inhibitor). (December 2025)

10. **d**. If either partner is receiving methotrexate, pregnancy should be avoided and effective contraception used during treatment and after discontinuation for at least 3 months after treatment for males and at least 6 months for females. (March 2025)

Medsafe

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