MADRAC Bulletin

For healthcare professionals only
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The MADRAC Bulletin is a bi-monthly publication that provides a selection of local safety signals and articles discussing local individual case safety reports (ICSRs) meant to raise awareness among health care professionals. Information contained in this publication is not comprehensive but rather represents a selection of clinically relevant items warranting enhanced dissemination.

The MADRAC Bulletin also features pharmacovigilance-related activities conducted by the National Pharmaceutical Regulatory Agency (NPRA) and contains a list of directives based on safety issues advised by the Malaysian Adverse Drug Reactions Advisory Committee (MADRAC) and endorsed by the Drug Control Authority (DCA) as well as safety alerts that have been published on the NPRA website.

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Article Based on Case Reports

Features

What's New

We would like to thank the Director General of Health, Malaysia for his permission to publish the case report articles.

Article Based on Case Reports

This section discusses local individual case safety reports of suspected adverse events recorded in the Malaysian Pharmacovigilance Database (QUEST).[1] The case reports presented in this section are intended to serve as a reminder of potential adverse events that healthcare providers should be aware of in day-to-day clinical practice, take account of, and report to the NPRA if any relevant events occur. Information contained in these articles is not exhaustive but rather represents a selection of clinically relevant items that warrants dissemination..

Risperidone-Induced Hyponatraemia

By Foo Wei Fuen

Case Report 1[1]

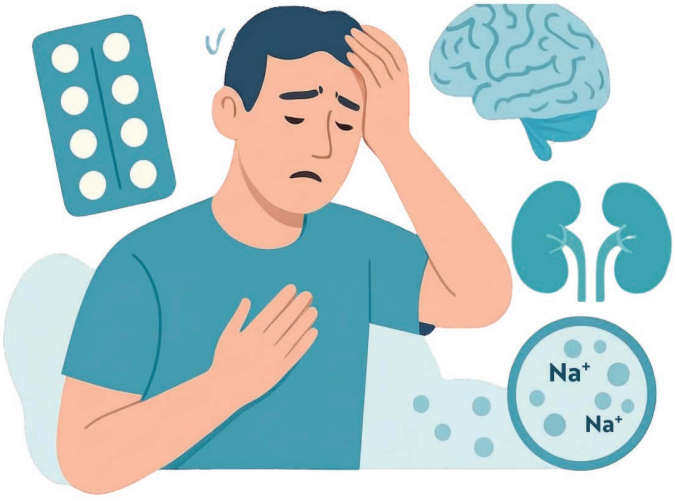
An 80-year-old female with underlying type 2 diabetes mellitus, hypertension, ischaemic heart disease, and newly diagnosed dementia was prescribed oral risperidone 0.5 mg as needed for delirium. Approximately 14 days after initiation of risperidone, she was admitted with reduced responsiveness. Laboratory investigations revealed severe hyponatraemia with a serum sodium level of <100 mmol/L, and she was diagnosed with **risperidone-induced hyponatraemia**. Risperidone was discontinued, and she was treated with intravenous 0.9% sodium chloride infusion with a sodium correction rate of 6–8 mmol/L per day. The patient subsequently recovered. Given the presence of underlying medical conditions and concomitant medications, the adverse event was assessed as possibly related to risperidone use.

Case Report 2[1]

A 59-year-old male with underlying benign prostatic hyperplasia and schizophrenia was receiving oral risperidone at a dose of 2 mg in the morning and 3 mg at night. The risperidone dose was subsequently increased to 3 mg twice daily. Approximately one month after the dose escalation, laboratory investigations revealed hyponatraemia with a serum sodium level of 112 mmol/L. The patient was diagnosed with **risperidone-induced hyponatraemia**, and the dose was reduced to 2 mg twice daily. Following dose reduction, his serum sodium level returned to the normal range. He was subsequently discharged on risperidone 2 mg twice daily. Considering the presence of underlying medical conditions and concomitant medications, the adverse event was given a causality possibly related to risperidone use.

Discussion

Risperidone is a second-generation antipsychotic that acts as a selective monoaminergic antagonist with high affinity for serotonin (5-HT2) and dopamine (D2) receptors. It also binds to alpha1-adrenergic receptors and with lower affinity for histamine (H1) and alpha2-adrenergic receptors.[2] Its balanced central serotonin-dopamine antagonism improves both positive and negative symptoms of schizophrenia while reducing the risk of extrapyramidal side effects compared with first-generation antipsychotics. Risperidone is indicated for the treatment of schizophrenia and related psychotic conditions, the management of moderate to severe manic episodes associated with bipolar disorders, and the short-term symptomatic treatment of persistent aggression in conduct disorder in children from the age of five and in adolescents with subaverage intellectual functioning. There are currently 25 registered products containing risperidone in Malaysia, available in the form of tablets (19), syrups (3), and injections (3).[3]



**AI-generated image*

Hyponatraemia is a common electrolyte disorder, generally defined as a serum sodium level below 135 mmol/L, and is considered severe when the serum level falls below 125 mmol/L.[4-7] Symptoms of drug-induced hyponatraemia can range from asymptomatic to life-threatening, depending on the severity of sodium deficit. In mild to moderate cases, symptoms may include headache, nausea, vomiting, fatigue, confusion, sedation and muscle cramps. These symptoms are often overlooked, as they mimic typical medication side-effects or worsening of the underlying psychiatric illness.[5,6] If serum sodium falls below 125 mmol/L, serious complications such as seizures, delirium, coma, and death may occur.[4-7]

Clinical manifestations of hyponatraemia[5]:

Mild (130-134 mmol/L): Initially asymptomatic, later patients present with headache, nausea, muscle cramps, vomiting, fatigue, anorexia, confusion

Moderate (125-129 mmol/L): Disturbances in gait, headache, vomiting, fatigue, confusion, muscle weakness, spasms and cramps, depressed deep tendon reflexes

Severe (Less than 125 mmol/L): Restlessness, agitation or lethargy, delirium, seizures, brainstem herniation, respiratory arrest, coma, death

The risk of hyponatraemia is known to be associated with the use of antipsychotic medications, although risperidone carries a lower overall risk compared with first-generation antipsychotics.[4-7] The exact mechanism of risperidone-induced hyponatraemia is not fully understood, but it is thought to involve the syndrome of inappropriate antidiuretic hormone secretion (SIADH).[4-6] This may occur through serotonin-mediated activation of central 5-HT receptors, leading to excessive release of antidiuretic hormone (ADH). Furthermore, this serotonergic activity resets the brain's osmostat, thereby lowering the threshold for ADH secretion.[5,6] In local risperidone product information, inappropriate ADH secretion and water intoxication are documented as very rare adverse reactions.[2]

Primary risk factors for risperidone-induced hyponatraemia include older age, female gender and low body weight.[5-7] Additional risk factors include low baseline sodium, comorbidities affecting fluid balance, and concomitant medications known to cause SIADH. Rapid dose escalation and excessive fluid intake may further increase the risk.

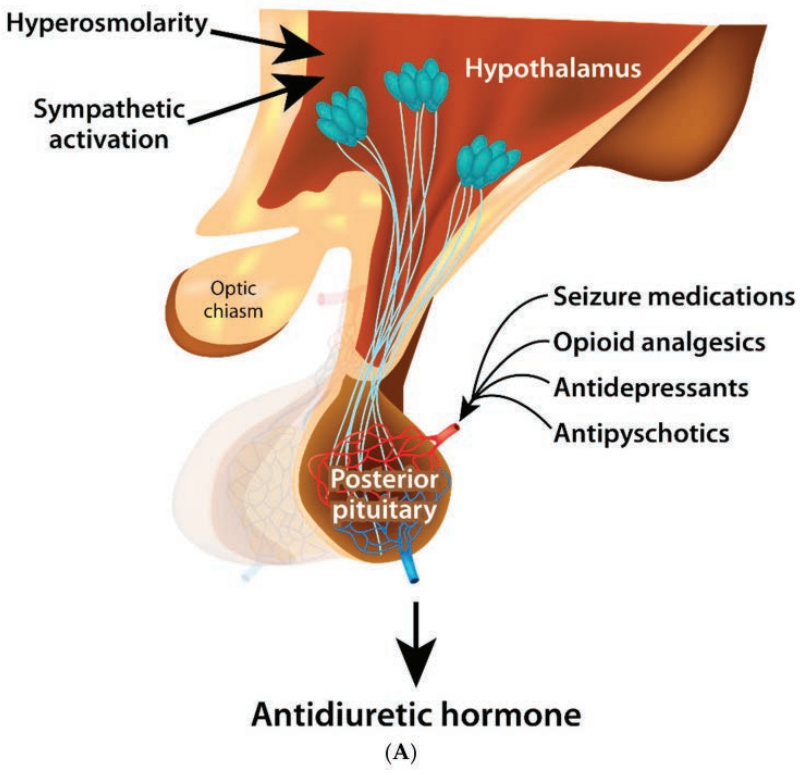


Figure 1. Syndrome of inappropriate antidiuretic hormone secretion (SIADH) as an adverse drug reaction.[9]

Hyponatraemia associated with antipsychotics typically develops within two to four weeks after treatment initiation or after a significant dose increase.[4,6] A systematic review reported a median onset of 14 days in case reports involving risperidone.[7] The primary management is immediate discontinuation of risperidone, which generally leads to full recovery of serum sodium levels.[4-7] If discontinuation is not feasible, switching to an alternative antipsychotic with a lower risk of hyponatraemia should be considered.[4-6]

To date, NPRA has received 922 adverse drug reaction (ADR) reports involving 1,664 adverse events suspected to be associated with risperidone.[1] The most commonly reported adverse events include stiffness (98 reports), akathisia (97), and tremor (80). Thirteen cases of hyponatraemia involving risperidone have been reported in Malaysia, including the two cases discussed in this article. As of December 2025, the World Health Organisation (WHO) global ADR database recorded a total of 683 cases of hyponatraemia suspected to be associated with risperidone.[8*]

*DISCLAIMER

VigiBase is the WHO global database of reported potential adverse effects of medicinal products, developed and maintained by Uppsala Monitoring Centre (UMC). This information comes from a variety of sources, and the likelihood that the suspected adverse effect is drug-related is not the same in all cases. This information does not represent the opinion of the UMC or the WHO.

*AI-generated image

Advice for Health Care Professionals

• Be **aware** of the risk of hyponatraemia associated with risperidone particularly in high risk patients such as the elderly, females, and those with low body weight or underlying comorbidities.

• **Obtain** baseline serum sodium levels before initiating risperidone and **monitor** levels 1-2 weeks after initiation, and following any dose increase.

• **Educate** patients or caregivers to recognise early symptoms of hyponatraemia (e.g., headache, nausea, fatigue, confusion, muscle cramps) and **advise** patients to avoid excessive fluid intake.

• If hyponatraemia occurs, **consider** dose reduction or discontinuation of risperidone. In cases of severe hyponatraemia, **correct** serum sodium levels cautiously to avoid osmotic demyelination syndrome.

• **Report** any adverse drug reactions suspected to be related to risperidone use to the NPRA.

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Features

Collaboration #MedSafetyWeek 2026 Kicks Off with Global Welcome Event

On 6 May 2026, the Uppsala Monitoring Centre (UMC) organised a global welcome event to kick-start the #MedSafetyWeek 2026 campaign. This virtual session provided an official introduction to the upcoming campaign, along with guidance on campaign planning, implementation, and evaluation strategies. The welcome event was attended by representatives from almost 20 countries, including members of the #MedSafetyWeek Malaysia task force and representatives from academic institutions, namely Universiti Teknologi MARA and Universiti Malaya.

#MedSafetyWeek 2026, now in its 11th year, will be held from 2 to 8 November 2026 with the theme "Side effects- don't ignore them, report them". The campaign continues its global mission to raise awareness on adverse drug reaction (ADR) reporting and strengthen pharmacovigilance activities worldwide. This year marks a new milestone, with 130 countries registered to participate, including 20 new countries, making it the largest participation to date. UMC presented the campaign essentials, including key messages, communication strategies, and available campaign materials. Participants were also provided with practical implementation guidance, including securing early management support, engaging communications teams and stakeholders at an early stage, and adapting materials to local contexts and resources.

Malaysia's #MedSafetyWeek achievements were featured as one of the campaign success stories during the welcome event. Representing Malaysia from the NPRA, Dr. Rema Panickar shared the country's journey since joining the campaign in 2021. Beginning with social media postings, Malaysia progressively expanded its activities through stakeholder collaboration and nationwide outreach. Key achievements included growth in social media reach from approximately 35,000 views in 2024 to over 83,000 in 2025, the "Info on Wheels" programme reaching more than 46,000 people across 808 locations, and expanded outreach through health carnivals, roadshows, broadcast media, and public transport visibility. Key lessons learned include the importance of collaboration, early stakeholder engagement, simple and flexible communication approaches, and effective use of existing campaign materials. Plans for 2026 include expanding outreach to educational institutions, strengthening in-house pharmacovigilance awareness within NPRA, and increasing engagement with community pharmacies.

The welcome event concluded with a group photo session involving participants from across the globe, reflecting the strong international commitment towards improving medicine safety and promoting ADR reporting globally. The event successfully set the stage for another impactful #MedSafetyWeek campaign and reinforced the importance of global collaboration in strengthening pharmacovigilance systems.

Training

Pharmacovigilance Seminar - Back to Basics: Strengthening Medicine Safety in Malaysia

The NPRA Pharmacovigilance Section organised an online seminar titled "Back to Basics: Strengthening Medicine Safety in Malaysia" on 22 April 2026, with the participation of over 800 pharmacists and assistant pharmacists from public health facilities nationwide. The seminar aimed to enhance awareness and understanding among healthcare providers on the importance of medicine safety, including the identification and reporting of adverse drug reactions (ADR), adverse events following immunisation (AEFI), drug allergies, and medication errors, while strengthening reporting practices and the management of medicine safety issues in Malaysia.

The seminar began with speakers from the Pharmacovigilance Section providing a comprehensive overview of pharmacovigilance practices in Malaysia. The session highlighted the role of NPRA in ensuring the safety, quality, and efficacy of medicines through continuous post-market surveillance, signal detection, and risk communication. Participants were guided on the importance of high-quality ADR and AEFI reporting, including complete documentation, clear case narratives, and accurate clinical details to support effective causality assessment and regulatory decision-making. Proper reporting channels and key elements of good reports were also emphasised.

This was followed by a session delivered by invited speakers from the Pharmacy Practice and Development Division, Ministry of Health, who shared valuable insights on the issuance of medicine allergy cards and medication error reporting, both of which are key components in improving patient safety. This session emphasised on physician confirmation of clinically significant allergies, pharmacists' roles in verification and patient counselling, and the need for accurate documentation. In addition, practical insights on medication error reporting were shared, highlighting that both errors and near misses are valuable for identifying system gaps and improving patient safety, supported by national reporting systems and safety frameworks. The seminar concluded with a brief segment on handling Special Approval Products (UKK), with emphasis on accurate product identification and reporting.

The seminar showed strong engagement from participants, who actively posed questions and shared experiences throughout the sessions. Discussions were focused on ADR reporting and drug allergy management, reflecting a keen interest in improving reporting quality. This interactive exchange further enhanced participants' understanding and supported their practical application of pharmacovigilance principles in daily practice. Overall, the seminar reinforced the importance of continuous vigilance and collaborative efforts in strengthening medicine safety practices in Malaysia.

What's New

List of Safety Alerts/Directives Related to Drug Safety Issues

NPRA reviews and presents drug safety issues at meetings of the Malaysian Adverse Drug Reactions Advisory Committee (MADRAC) to determine the appropriate risk minimisation measures. Regulatory actions are proposed to the Drug Control Authority (DCA), resulting in DCA directives issued to ensure local package inserts and consumer medication information leaflets (RiMUP) for all products containing the affected active ingredients are updated with the required safety information. The table below shows the safety alerts/DCA directives that were recently issued, which are available on the NPRA website.

	Active Ingredients	Safety Alerts (SA)	SA Date	Directive Ref. No. [Date]
1	Sunitinib	Risk of Hyperammonaemic Encephalopathy	30-April-2026	NPRA.600-1/9/13(5) Jld.2 [14-Apr-2026]
2	Lamotrigine	Risk of Photosensitivity		NPRA.600-1/9/13(6) Jld.2 [14-Apr-2026]
3	Moxifloxacin	Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), Fixed-Drug Eruption (FDE), and Photosensitivity Associated with Systemic Use	30-April-2026	-
4	Mesalazine	Risk of Idiopathic Intracranial Hypertension (IIH)	7-May-2026	-
5	Clindamycin (Oral Capsules)	Risk of Oesophagitis and Oesophageal Ulcer	13-May-2026	NPRA.600-1/9/13(75) Jld. 1 [15-Jan-2026]

How to report adverse events?

NPRA encourages all healthcare professionals to report all suspected adverse drug reactions (ADR) to medicines, including pharmaceutical products, over-the-counter medicines, traditional medicines, and health supplements, as well as adverse events following immunisation (AEFI) with vaccines.

To report ADR/AEFI:

1. Visit **www.npra.gov.my**
2. Report ADR **as Healthcare Professional**
   a) Choose **ADR/AEFI Google Form**; or
   b) Download the **ADR manual form** and submit the completed form via email or post:

fv@npra.gov.my

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NPRA Safety Information Mailing List

To join the mailing list:

a) scan the QR code to complete the **subscription form**, or

b) send an email with your details to **fv@npra.gov.my**