KEMENTERIAN KESIHATAN MALAYSIA
BAHAGIAN REGULATORI FARMASI NEGARA
National Pharmaceutical Regulatory Agency
Ministry of Health, Malaysia
57

MADRAC Bulletin

For healthcare professionals only
Volume 57 | Issue 06/2025

In this issue

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 healthcare professionals.

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.

Highlights

Articles Based on Case Reports

What's New

To receive each new issue of this bulletin, complete the subscription form available on the NPRA website.

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

Highlights

10th Anniversary of #MedSafetyWeek Campaign

#MedSafetyWeek is an annual global campaign spearheaded by the World Health Organisation (WHO) Uppsala Monitoring Centre in Sweden, aimed at enhancing awareness on the safe use of medicines and the importance of reporting side effects. The campaign ran from 3 to 9 November 2025, involving around 130 organisations from almost 120 countries.

This year marked Malaysia's fifth consecutive year of participation in the #MedSafetyWeek campaign as well as the 10th anniversary of this global initiative. The theme this year: "We can all help make medicines safer" carried a simple yet meaningful message: everyone, be it pharmacists, doctors, other healthcare professionals, the pharmaceutical industry, or consumers, shares the responsibility of ensuring the safety of medicines.

In 2025, the #MedSafetyWeek Malaysia task force was expanded to include pharmacists from each state across Malaysia, in addition to the existing members from the National Pharmaceutical Regulatory Agency (NPRA) and Headquarters of Pharmacy Practice & Development Division. Collaboration with the private healthcare sector was also increased, through the Pharmaceutical Association of Malaysia (PhAMA) and Malaysian Pharmacists Society (MPS).

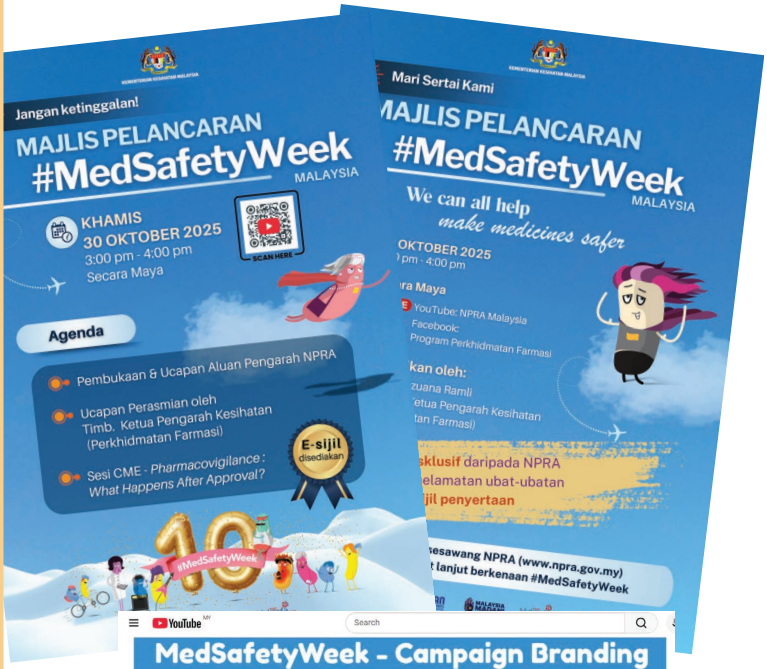
The impact of these collaborations was immediately evident! This year, the #MedSafetyWeek social media posts were shared by health facilities and individuals all across Malaysia — from Johor to Perlis, as well as in Sarawak — with various activities being carried out, including health awareness campaigns, talk shows, radio interviews, and live quizzes held nationwide.

We will let the photos speak for themselves...

Highlights

Soft launch of #MedSafetyWeek 2025

The soft launch event of #MedSafetyWeek 2025 was successfully held via live streaming through the National Pharmaceutical Regulatory Agency (NPRA) YouTube Channel and the Pharmaceutical Services Programme Facebook page on 30 October 2025, attracting over 2,000 participants from various backgrounds including doctors, dentists, nurses, pharmacists, pharmaceutical industry, other professional fields, and consumers. The ceremony commenced with an opening speech by Pn. Wan Noraimi Wan Ibrahim, Director of NPRA, followed by an address and officiation by Dr. Azuana Ramli, Deputy Director General of Health (Pharmaceutical Services), Ministry of Health. The event concluded with a Continuing Medical Education (CME) session titled "Pharmacovigilance: What Happens After Approval" by Pn. Nurul Aimi Mohd. Reduzan, a pharmacovigilance officer from NPRA. The launch aimed to raise public awareness on pharmacovigilance and the #MedSafetyWeek campaign.


Jangan ketinggalan!
MAJLIS PELANCARAN
#MedSafetyWeek
MALAYSIA
KHAMIS
30 OKTOBER 2025
3:00 pm - 4:00 pm
Secara Maya
Agenda
Pembukaan & Ucapan Aluan Pengarah NPRA
Ucapan Perasmian oleh Timb. Ketua Pengarah Kesihatan (Perkhidmatan Farmasi)
Sesi CME - Pharmacovigilance : What Happens After Approval?
E-sijil disediakan
Mari Sertai Kami
We can all help make medicines safer
OKTOBER 2025
4:00 pm
Facebook: Program Perkhidmatan Farmasi
eksklusif daripada NPRA
pelancaran ubat-ubatan
sijil penyertaan
#MedSafetyWeek

Press Release & Media Coverage

SIARAN MEDIA
KEMENTERIAN KESIHATAN MALAYSIA

PELANCARAN MINGGU KESELAMATAN UBAT
#MedSafetyWeek 2025

8 November 2025 - Kementerian Kesihatan Malaysia (KKM) melalui Bahagian Regulatori Farmasi Negara (NPRA) sedang mengambil bahagian dalam kempen tahunan Keselamatan Pengubatan, #MedSafetyWeek yang berlangsung dari 3 hingga 9 November 2025. Kempen *#MedSafetyWeek* merupakan inisiatif global yang diterajui oleh Pertubuhan Kesihatan Sedunia (WHO) dengan melibatkan 130 organisasi di 117 buah negara. Tahun 2025 juga merupakan ulang tahun ke-10 kempen ini berlangsung di peringkat antarabangsa.

Tema bagi #MedSafet *safer"*. Tema ini m keselamatan ubat ad dan anggota kesihat memainkan peranan untuk digunakan.

Pemantauan kesel ubatan yang berad kempen ini adalah mengenal pasti da oleh ubat-ubatan. akan dianalisis u sampingan baha tersebut. Di Ma laporan kesan s dinilai dan dikaj diambil sekiran Dengan itu, per ubat-ubatan dar

#MedSafetyWeek 2025: Malaysians urged to report drug side effects, keep medicines safe

The Star | A dose of awareness

A dose of awareness

By SYED UMAR ARIFF

FOCUS

Sunday, 09 Nov 2025

Related News

Public urged to report side-effects of medicines

PUTRAJAYA: The Health Ministry has called on the public and healthcare workers to play an active role in reporting the side effects of medicines, as part of the annual #MedSafetyWeek 2025 campaign aimed at ensuring the continued safety of medicines in Malaysia.

Held from Nov 3, the campaign is coordinated by the National Pharmaceutical Regulatory Agency and forms part of a global initiative by the World Health Organisation.

The ministry said the theme "We can all help make medicines safer" underscores that medicine safety is a shared responsibility of all parties, including healthcare professionals, pharmaceutical companies and consumers.

The ministry said monitoring medicine safety is crucial to ensure that products available in the market are both safe and effective.

"All reports of side effects received will be analysed to detect potential new safety risks such as previously unidentified side effects, or to determine appropriate risk mitigation measures," said the

Health workers reports through t Pharmacy Informatic via email at fv@ Consumers ma suspected side consulting healthca or submitting the Co Effect Reporting For email or post. – Bern

Radio Interviews

Exhibitions and Health Carnival

Collaboration: NPRA, PhAMA, Hospital Selayang & Malaysian Paediatric Association

Perlis

Penang

Johor

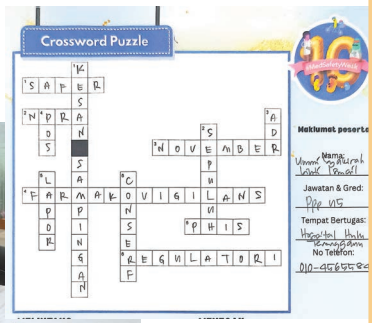
Sarawak

Malacca

Children's Activities

Colouring contest

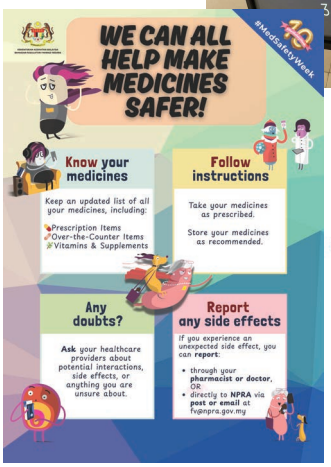
Puzzles



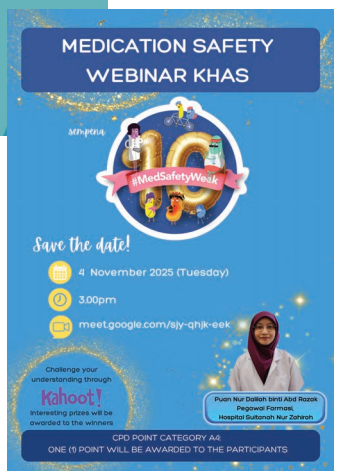
Spot the candy vs medicine

Social Media Postings

Videos, Posters & Others

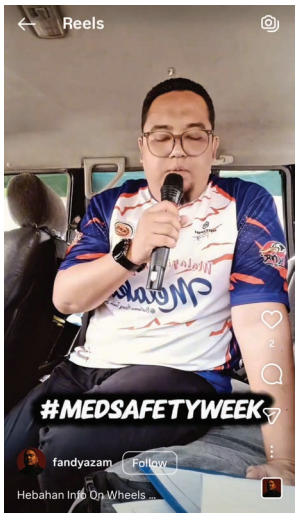


Online Webinars



Info on Wheels

by Jabatan Penerangan Malaysia



#MedSafetyWeek

3–9 November 2025

Articles 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 comprehensive but rather represents a selection of clinically relevant items that warrants dissemination.

Report of Suicidal Behaviour with Efavirenz Use

By Syifa' Izzati Mohd Zainul Arifien

Case Report 1 [1]

A 16-year-old male adolescent, with no known prior psychiatric history, was diagnosed with retroviral disease. Antiretroviral therapy (ART) was initiated with efavirenz 400 mg once daily and a fixed-dose combination of tenofovir and emtricitabine once daily.

Five days after initiating ART, the patient developed neuropsychiatric symptoms, including spaciness, poor concentration and school refusal. He subsequently developed **suicidal ideation**, with multiple reported attempts; attempting to hang himself at home and trying to jump from both his residential flat and school building. The patient also reported persistent negative emotions, low mood, and excessive thinking since starting treatment. Following a clinical review, efavirenz was discontinued and substituted with dolutegravir. Olanzapine 2.5 mg once daily was also prescribed for three days.

During a follow-up phone call, his family member reported a significant improvement after switching to dolutegravir, noting that the patient no longer expressed suicidal thoughts or tendencies and rarely experienced low mood. However, no formal psychiatric evaluation was conducted, due to the family's reluctance to attend regular follow-ups. Given the presence of concomitant medications, the adverse events were assessed as *possibly* related to efavirenz.

AI-generated image

Discussion

Efavirenz is a non-nucleoside reverse transcriptase inhibitor (NNRTI) that suppresses replication of Human Immunodeficiency Virus type 1 (HIV-1).[2] There are currently nine (9) registered efavirenz-containing products marketed in Malaysia, available either as monotherapy or in fixed-dose combinations.[3] In Malaysia, it is indicated for the treatment of HIV-1 infection in adults and paediatric patients and is a preferred option for first-line ART regimens in treatment-naive patients.[2,5] Efavirenz is typically used in combination with two nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs).[4,5] Like other ARTs, although efavirenz does not cure HIV infection, it plays a critical role in reducing viral load, morbidity and mortality, thereby improving quality of life and life expectancy among people living with HIV.

The risk of serious psychiatric adverse events, including severe depression, **suicidal ideation** and nonfatal **suicide attempts** has been documented in local package inserts of products containing efavirenz.[2] Although a causal relationship with efavirenz has not been established, there have been occasional reports of death by suicide, delusions and psychosis-like behaviour. Commonly, patients experience nervous system symptoms such as anxiety, hallucinations, impaired concentration, insomnia, and abnormal dreams. In some cases, serious neurologic adverse events such as ataxia and encephalopathy (characterised by confusion, psychomotor slowing, psychosis, or delirium) may occur as late-onset neurotoxicity. Precise pathophysiology remains unclear, but it is believed that the high penetration of efavirenz into the central nervous system (CNS) contribute to these effects.[2,6] Cerebrospinal fluid (CSF) concentrations of efavirenz are approximately three times higher than expected based on its unbound plasma fraction.

The neuropsychiatric effects are likely driven by multiple mechanisms, involving direct effects on serotonin receptors, disruption of mitochondrial energy production, neurotoxicity from its primary metabolite, and neuroinflammatory processes.[6,7] Several factors may increase the risk of neuropsychiatric adverse events associated with efavirenz. The strongest predictor of suicidal behaviour is a pre-existing psychiatric disorder.[2,5,6,8,9] Other contributing factors include substance abuse, heavy alcohol use and conditions that elevate plasma drug concentrations, such as taking efavirenz with food, chronic liver disease and the concomitant use of medications with CNS effects. Genetic polymorphisms in the CYP2B6 gene can also result in elevated plasma concentrations or prolonged drug half-life, which subsequently increase the risk of CNS toxicity.[2,6] The onset of neuropsychiatric adverse events associated with efavirenz varies depending on the type and severity of the symptom.[2,9] Common symptoms, such as anxiety and hallucinations typically begin within 1 to 3 days after treatment initiation and generally resolve or become tolerable after the first 2 to 4 weeks. However, severe late-onset neurotoxicity may occur months to years after starting efavirenz therapy. Serious psychiatric events such as suicidal behaviour may also present with delayed onset, with one study reporting a median onset of 10.2 months after initiation.[8]

To date, the NPRA has received 1,301 local adverse drug reaction (ADR) reports involving 2,381 adverse events suspected to be related to efavirenz.[1] The most commonly reported adverse events include dizziness (282), maculopapular rash (268), and rash (236). There were six (6) local reports of suicidal ideation, two (2) reports of suicide attempt, and one (1) report of suicidal behaviour, including the case discussed above. As of July 2025, the World Health Organization (WHO) global ADR database has recorded 141 reports of suicidal ideation, 138 reports of suicide attempt, and three (3) reports of suicidal behaviour suspected to be associated with efavirenz.[10*] Suicidal behaviour among people living with HIV is multifactorial and may be influenced by psychosocial factors such as HIV-related stigma, discrimination, substance abuse, and lack of social support.[11] Healthcare professionals are advised to remain vigilant for neuropsychiatric symptoms in patients receiving efavirenz, particularly those with a history of mental illness, and provide early psychological support and intervention when necessary to reduce the risk of suicide and optimise treatment outcomes.

*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.

Advice for Healthcare Professionals

- **Assess** patients for a history of psychiatric illness before initiating efavirenz and **avoid** its use in those with current, past or severe psychiatric illness, as they are at a higher risk of developing serious adverse effects such as depression and suicidal ideation.
- **Monitor** patients closely for neuropsychiatric symptoms, particularly during the initial weeks of efavirenz therapy and in those with known risk factors such as mental illness, substance abuse or liver impairment.
- **Counsel** patients and caregivers to promptly report any concerning behavioural or psychological changes.
- **Advise** patients to take efavirenz on an empty stomach, preferably at bedtime, to minimise potential adverse effects.
- **Consider** switching to an alternative antiretroviral agent (e.g., dolutegravir) if persistent, severe, or late-onset neuropsychiatric symptoms occur.
- **Report** any adverse drug reactions suspected to be related to the use of efavirenz to the NPRA.

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What's New

List of Safety Alerts and 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 and DCA directives that were recently issued, which are available on the NPRA website.

	Active Ingredients	Safety Alerts		Directive Ref. No. [Date]
		Title	Date	
1	Doxycycline	Fixed Drug Eruption (FDE)	13-Oct-2025	NPRA.600-1/9/13 (65) Jld.1 [18 Aug 2025]
2	Amiodarone	Risk of Primary Graft Dysfunction after Heart Transplantation	14-Nov-2025	NPRA.600-1/9/13 (69) Jld.1 [7 Oct 2025]
3	Sulfamethoxazole, Trimethoprim (Cotrimoxazole)	Risk of Circulatory Shock	14-Nov-2025	-
4	Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)	Risk of Persistent Sexual Dysfunction	14-Nov-2025	NPRA.600-1/9/13 (70) Jld.1 [7 Oct 2025]
5	Cyclin-Dependent Kinase Inhibitors (CDKIs)	Interaction with Statins Leading to Potential Risk of Rhabdomyolysis	17-Nov-2025	-

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** by

   Downloading the **ADR manual form** and submit the completed form via email or post:

   fv@npra.gov.my

   Pharmacovigilance Section,
   National Pharmaceutical Regulatory Agency (NPRA),
   Ministry of Health, Malaysia.
   Lot 36, Jalan Prof Diraja Ungku Aziz (Jalan Universiti),
   46200 Petaling Jaya, Selangor, Malaysia.

NPRA Safety Information Mailing List

To join the mailing list:

a) scan the QR code to complete the **subscription form** available on the NPRA website, or

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