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Risk of overdose with venlafaxine associated with alcohol consumption

Venlafaxine is an antidepressant belonging to the group of serotonin and norepinephrine reuptake inhibitors (SNRIs), used in the treatment of major depressive episodes, as well as for the treatment of panic disorder and anxiety.

Cases of venlafaxine overdose have been reported to the European Eudravigilance database (including reports from the Portuguese National Pharmacovigilance System), some of which had fatal outcomes. The most frequently reported adverse reactions associated with overdose include mydriasis, tachycardia, vomiting, seizures, and altered consciousness (from drowsiness to coma).

Individuals undergoing treatment with venlafaxine should be advised **not to consume alcohol**, due to the potential worsening of underlying psychiatric conditions, as well as the risk of adverse interactions with the drug, including central nervous system depressant effects. This recommendation is particularly important considering that most cases of overdose were associated with simultaneous use of alcohol and/or other medications.

To minimize the risk of overdose, it is recommended to prescribe the lowest dose of venlafaxine necessary to adequately control the patient's condition, as severe intoxication symptoms can occur in adults after ingesting approximately 3 grams of venlafaxine. Severe intoxication may require complex emergency treatment, and in cases of suspected venlafaxine overdose, immediate contact with the **CIAV – Portuguese poison Information Center** (800 250 250) - is advised.

Any case of drug overdose should also be reported to the National Pharmacovigilance System in order to contribute to increasing the knowledge on the safety profile of medications and to identifying any new associated risks.

João Paulo Fernandes

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Communications to Healthcare Professionals published on the Infomed product information webpage

Click on the links.

INN Medicinal product	Target	Materials Online publication date
Nirmatrelvir + Ritonavir *Paxlovid*	**Physicians:** hospital emergency, internal medicine, infectioius diseases, pneumology, oncology, haematology, nephrology, cardiology and transplantation units **Pharmacists:** hospital	Strengthening of information about fatal and potentially fatal drug interactions with certain immunosuppressants, including tacrolimus 21-03-2024
Pseudoefedrina *Aerinaze, Actifed, Aspirina Complex, Bisolgripal, Cegrinaso, Claridon, Dinaxil, Grinhals, Holsigrip, Sinutab II*	**Physicians:** general/family medicine, allergology, ENT, neurology, pneumology, internal medicine, and corresponding Medical Societies **Pharmacists**	Medicines containing pseudoephedrine - risks of reversible posterior encephalopathy syndrome (RPES) and reversible cerebral vasoconstriction syndrome (RCVS) 09-02-2024
Valproic acid/ semi-sodium valproate *Ácido Valpróico Generis, Ácido Valpróico Ratiopharm 300 mg, Ácido Valpróico Ratiopharm 500 mg, Depakine, Depakine Chrono 300, Depakine Chrono 500, Depakine Chronosphere, Diplexil, Diplexil 150, Diplexil 300, Diplexil 500, Diplexil 1000, Diplexil-R, Valproato de sódio Altan*	**Physicians:** neurology, psychiatry, general/family medicine, child psychiatry, and neuropaediatrics **Pharmacists:** community and hospital pharmacies	New measures regarding the potential risk of neurodevelopmental disorders in children conceived by men treated with valproate during the three months prior to conception 19-02-2024

Compiled by Patrícia Catalão

Quality of data in ADR reports

Spontaneous reporting of Adverse Drug Reactions (ADRs) is the cornerstone upon which the National Pharmacovigilance System (NPS) relies. According to national legislation, any suspected ADR can be reported to the NPS by healthcare professionals and/or citizens. The importance of ADR reporting is reflected in the possibility of identifying safety issues associated with the use of medications that were not detected during their development. The collected information is evaluated in an aggregated manner to help characterize the overall safety profile of the medication.

This assessment may result in updates to the Summary of Product Characteristics (SPC) and corresponding Patient Information Leaflet, or in the implementation of additional measures to manage certain important risks, including Educational Materials or Direct Healthcare Professional Communications (DHPC).

The preferred reporting method is online through the **RAM Portal,** which is available on the INFARMED website. Other communication methods are accepted, as described in the Patient Information Leaflet included in the packaging of each medication, as well as in the medication's profile in the INFARMED **INFOMED** Medicines Database.

The RAM Portal allows for easy, accessible, and rapid reporting/insertion of suspected adverse reactions through its **link**. It has two online forms: one for healthcare professionals and one for patients. Some health units have web services that allow direct connection to the RAM Portal; in these cases, the report is transmitted directly to the NPS.

Considering the potential impact that ADR reporting can have on characterizing a medication's safety profile, it is extremely relevant to focus on reporting cases with **quality**. In this sense, providing as much data as possible is encouraged. The information provided should be consistent and properly filled in the fields of the RAM Portal (Table 1)

Patient	Medicinal product	ADR
• Initials • Sex at birth • Date of birth or age at the date of the ADR • Clinical history • Weight • Height	• Trademark name /DCI • Batch • Pharmaceutical form • Dosage • Posology • Route of administration • Start and end dates • Dose reduction or suspension • Therapeutic indication • Concomitant medication	• Description • Start and end dates • Duration • Evolution • Seriousness criteria • Treatment • Causal relation with the medicine

Table 1. Relevant information to be filled in on RAM Portal for communication of the ADR case

Although, for the report to be valid, as few as four data points only are necessary (some information about the patient, the suspected medication, the description of the ADR, and the reporting person's name and contact details), information related to the medical history, concomitant medication, procedures/tests performed, and the patient's clinical evolution are all also relevant for the assessment of the case. Despite patient anonymization, it is essential to obtain the reporting person's contact details to clarify any queries and/or request additional information. Personal data sent is kept secure and confidential, serving only for the case assessment.

The cases received on the ADR Portal are transmitted to the European pharmacovigilance database **Eudravigilance**, allowing for greater data aggregation and the earlier detection of potential new safety issues. Reporting ADRs with quality information is not only an ethical and deontological duty, essential in monitoring the safety of medicines, but also an act of altruism in defence of Public Health.

Andreia Ascenso, Cristina Mousinho, Fátima Bragança

Portal **RAM**

Notificação de Reações Adversas a Medicamentos

Report an adverse drug reaction here.
Find answers to your questions about the ADR Portal here.

Educational Materials published on the Infomed product information webpage

Click on the links

INN Medicinal product	Target	Materials Online publication date
Aflibercept *Eylea*	**Physicians:** ophthalmologists who prescribe Eylea	Recommendations for the physician Intravitreal injection technique – video Intravitreal injection technique pictogramme
	Patients	Guide for the therapeutic indications of mCNV, BRVO/CRVO, DME, AMD 05-02-2024
Apixaban *Apixabano Mylan*	**Physicians:** cardiology, neurology, internal medicine, haematology, immuno-haemotherapy, anaesthesiology, orthopaedics, vascular surgery, family medicine and gastroenterology, as well as corresponding clinical directors **Pharmacists:** hospital pharmacy services directors	Prescriber's guide 05-02-2024
Apixabano *Apixabano Mylan*	**Médicos:** cardiologistas, neurologistas, internistas, hematologistas/imuno-hemoterapeutas, anestesistas, ortopedistas, cirurgiões vasculares, médicos de família e gastroenterologistas, bem como diretores clínicos respetivos **Farmacêuticos:** diretores dos serviços farmacêuticos hospitalares	Guia do Prescritor 09-04-2024
Brigatinib *Alunbrig*	**Patients**	Alert card 28-03-2024
Dabigatrano etexilato *Pradaxa*	**Physicians:** cardiology, internal medicine, haematology, immuno-haemotherapy, Family medicine, paediatrics, oncology	Paediatric prescription guide 29-04-2024
Darvadstrocel *Alofisel*	**Physicians:** surgery and gastroenterology **Healthcare professionals:** surgery, gastroenterology, nursing **Pharmacists:** hospitalares	Potencial contaminação microbiana e passos em caso de cultura positiva Método de administração Método de administração (vídeo) Instruções de receção e armazenamento 02-04-2024

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Educational Materials published on the Infomed product information webpage

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INN Medicinal product	Target	Materials Online publication date
Deferasirox *Deferasirox Accord, Deferasirox Generis, Deferasirox Mylan, Deferasirox Teva*	**Physicians:** immuno-haemotherapy, haematology and paediatrics	Prescriber's guide Posology and biological monitoring checklist
	Pattients	Guide 29-02-2024
Elranatamab *Elrexfio*	**Patients**	Card 06-03-2024
Foslevodopa + Foscarbidopa *Duodopa, solução para perfusão*	**Patients**	Guide 01-04-2024
Gilteritinib *Xospata*	**Physicians:** haematologists who may prescribe Xospata	Guide for healthcare professionals 01-02-2024
Isotretinoin *Isotiorga*	**Physicians:** dermatology, general/family medicine and GYN/OBS	Prescriber's checklist and consent form for prescription to female patients
	Farmacêuticos	Pharmacist's checklist – guidance for dispensing to female patients
	Doentes	Alert card 19-02-2024
Lenalidomide *Revlimid*	**Physicians:** haematology **Pharmacists:** dos Serviços Pharmacists dos hospitais	Informação de Segurança para Profissionais de Saúde Risk awareness form - female patient with childbearing potential Risk awareness form - female patient without childbearing potential

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INN Medicinal product	Target	Materials Online publication date
		Risk awareness form - male patient
	Patients	Brochure - female patient with childbearing potential Brochure - Female patient without childbearing potential Brochure - Male patient 01-02-2024
Mecassermin *Increlex*	**Physicians:** especialistas em endocrinology pediátrica e pediatras que fazem endocrinology nos hospitais	Informação de segurança para o médico sobre Increlex
	Patients	Informação de segurança para o Doente sobre a deficiência primária de IGF-1 e o Increlex 01-03-2024
Metreleptina *Myalepta*	**Healthcare professionals:** Who prescribe the product or are otherwise involved in the treatment of patients with lipodystrophy (endocrinologists, paediatricians, internists, nurses, and pharmacists)	Guide
	Patients	Patient/caregiver guide 11-03-2024
Pirfenidone *Pirfenidona Accord, Pirfenidona Generis*	**Physicians:** pneumology	Safety checklist 23-04-2024
Pomalidomide *Imnovid*	**Healthcare professionals:** haematologists and pharmaceutical services	Information for healthcare professionals **Risk awareness forms for:** Women with childbearing potential Women without childbearing potential Male patients

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Educational Materials published on the Infomed product information webpagE

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INN Medicinal product	Target	Materials Online publication date
	Patients	**Brochure – Important safety information for:** **Women with childbearing potential** **Women without childbearing potential** **Male patients** 09-04-2024
Quizartinib *Vanflyta*	**Physicians:** haematology	**Guide** 20-04-2024
Rivaroxaban *Epicar, Rivaroxabano Alter, Rivaroxabano Anova, Rivaroxabano Aurovitas, Rivaroxabano Azevedos, Rivaroxabano Ciclum , Rivaroxabano Farmoz, Rivaroxabano Generis, Rivaroxabano Germed, Rivaroxabano Krka, Rivaroxabano Pentafarma, Rivaroxabano Pharmakern, Rivaroxabano Ratiopharm, Rivaroxabano Sandoz, Rivaroxabano Stada, Rivaroxabano Tarmix, Rivaroxabano Tecnigen, R ivaroxabano Teva, Rivaroxabano Viatris, Rivaroxabano Zentiva*	**Physicians:** paediatric cardiology, paediatrics, paediatric oncology, haematology, paediatric surgery, cardiology, orthopaedics, general/family medicine, vascular surgery, and internal medicine	**Prescriber's guide** 27-03-2024
Teclistamab *Tecvayli*	**Patients**	**Card** 02-03-2024
Zoledronic acid *Ácido Zoledrónico Altan, 4 mg/100 ml* *Ácido Zoledrónico Altan, 5 mg/100 ml*	**Patients**	**Alert card** **Alert card** 28-03-2024

Compiled by Patrícia Catalão

What do they mean?

ADR	Adverse Drug Reaction
EMA	European Medicines Agency
MA	Marketing Authorization
PL	Patient Information Leaflet
PRAC	Pharmacovigilance Risk Assessment Committee (EMA)
SmPC	Summary of Product Characteristics

Why don't healthcare professionals report more?

This systematic review showed that, although they are easily modifiable factors, the knowledge and attitudes of healthcare professionals remain the main determinants of underreporting ADRs, namely:

- ignorance (only serious ADRs need to be reported)
- lethargy (procrastination, lack of interest, and other justifications)
- complacency (the belief that only well-tolerated medicines are allowed on the market)
- timidity (fear of appearing ridiculous by reporting what is merely a suspected ADR)
- insecurity (it is almost impossible to determine whether a medicine is responsible for a specific ADR)
- lack of feedback

Additionally, in this review, questions about confidentiality and the lack of a requirement to report emerged as new reasons for underreporting.

• García-Abeijon P et al. Drug Safety (2023) 46:625–636

... But patients are increasingly involved in reporting ADRs

... At least in France. This analysis of the French pharmacovigilance database confirms this. The reports have predominantly been submitted by women, younger age groups, and through a web portal. Mostly less serious ADRs are reported. The authors conclude that reporting activities are not only related to medical and medication factors, but also to social factors, with digital tools potentially playing an important role.

•Adopo D et al. Eur J Clin Pharm (2023) 79:229–236

What do patients describe in their reports?

The authors of this qualitative study identified six common themes in patients' descriptions of ADRs: frequency, duration, development in intensity, timing of occurrence, triggering factors, and improving factors. In other words, typically factors that are important for a professional analysis of ADRs.

• Van Lint JA et al. Drug Safety (2023) 46:1039–1047

Lost in Translation: the use of pharmacovigilance terms in different languages

This renowned researcher investigated the translation of 26 pharmacovigilance terms in 26 languages, through a panel of 83 pharmacovigilance professionals. Three types of terms emerged: those that are similar in all or almost all the languages studied (e.g., "signal," "risk"); those that are similar in form in some languages but not all (e.g., "pharmacovigilance," "surveillance"); and those for which there are significant differences between languages (e.g., "danger"/"hazard"). Misunderstandings in pharmacovigilance communication can arise due to translation difficulties. It could be interesting to have a multilingual glossary of terms and definitions, which could be used to program automatic translators.

• Aronson JK. Drug Safety (2022) 45:1363–1368