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From the Editor

In the third part of the publication of the papers presented at the INFARMED event **Pharmacovigilance: Towards an Integrated Approach**, the following topics are addressed: **drug interactions**, the relationship between adverse reactions and treatment compliance in **diabetes mellitus** and **multidrug-resistant pulmonary tuberculosis**, the safety profiles of **hormonal implants (etonorgestrel)**, and CGRP antagonists used in ***migraine***.
Opening this issue is a new call for attention to measures to minimize reproductive risk when using medicines containing **valproate**.
Note: Only posters presented in English or with a version in English are published in this issue. For the remainder, please refer to the Portuguese language edition.

Valproate and valproic acid: measures to prevent in utero exposure and pre-conceptional paternal exposure

Medicines containing valproate/valproic acid are used in the treatment of epilepsy, bipolar disorder, and additionally in the prevention of migraine attacks. These medicines are known teratogens, capable of causing congenital malformations and developmental disorders of the nervous system. Recent data also suggest an increased risk of these disorders in children conceived by men who were treated with valproates in the three months prior to conception. Therefore, strict measures are in place to prevent these risks::

Use in female patients of childbearing age (enhanced measures)

- Initiation of therapy and supervision by a specialist experienced in treating the indicated conditions.
- Use only when other treatments have been ineffective or not tolerated.
- Contraindicated during pregnancy unless no suitable alternative treatment for epilepsy is available.
- Compliance with the **Pregnancy Prevention Programme**.

INDEX CARD

Director: Márcia Silva
Editor: Rui Pombal
Contributors: Adriana Gamboa, Ana Severiano, Ana Sofia Martins, Cristina Mousinho, Fátima Bragança, Fátima Hergy, Magda Pedro, Márcia Silva, Patrícia Catalão, João Paulo Fernandes
Publishing Assistant: Inocência Pinto
Advisory Board: Conselho Diretivo do INFARMED, I.P.
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Parque de Saúde de Lisboa, Av. do Brasil, N.º 53, 1749-004 Lisboa
Phone: +351 217 987 100
E-mail: farmacovigilancia@infarmed.pt
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Key measures to be ensured by prescribers

1.Assess the patient's potential for pregnancy.

2.Explain the risks of the medication to the patient and her partner, ensuring they fully understand them.

3.Confirm a negative pregnancy test (blood analysis) before starting and during treatment, as needed.

4.Advise on the necessity of correct and effective contraception throughout the treatment period.

5.Explain the importance of planning a pregnancy.

6.Emphasize the need to urgently consult a doctor in the event of pregnancy.

7.Stress the importance of regular treatment reviews (at least annually) by a specialist.

8.Provide the Patient Guide.

9.Discuss and complete the annual Risk Acknowledgement Form with the patient at the start of treatment and during each review.

Use in Male Patients (New Measures)

• Therapy initiation and supervision by a specialist experienced in treating the indicated conditions.

Key measures to be ensured by prescribers:

1. Inform the patient about the potential risk and discuss the need to consider effective contraception, including for the partner, during treatment and for at least three months after discontinuation.
2. Advise against sperm donation during treatment and for at least three months after discontinuation.
3. Explain the importance of regular treatment reviews.
4. Consider and discuss alternative treatments if the patient plans to conceive.
5. Provide the Patient Guide.

Under no circumstances should treatment be discontinued without consulting a doctor.

To assist in the management and monitoring of these patients, risk minimization tools are available for healthcare professionals – including the **Healthcare Professional Guide** and the **Annual Risk Acknowledgement Form**. A patient card is included in the medication package, intended for female patients of childbearing age and male patients. Additionally, the **outer packaging contains a warning** about the risks of exposure during pregnancy.

It is essential that all parties involved adhere to the risk minimization measures to prevent exposure during pregnancy and paternal exposure before conception. For complete information, refer to the Summary of Product Characteristics (SmPC) for the medications and the educational materials available on Infomed at https://extranet.infarmed.pt/INFOMED-fo /.

Ana Severiano, Ana Sofia Martins

Educational Materials published on the Infomed product information webpage

Click on the links

INN Medicinal product	Target	Materials Online publication date
Anakinra *Kineret*	**Healthcare professionals:** physicians: rheumatology, internal medicine and paediatric rheumatology; nurses experienced in the diagnosis and treatment of CAPS, Still's disease and FMF	Guide
	Patients	Patient/Caregiver guide
		02-09-2024
Avalglucosidase alfa *Nexviadyme*	**Healthcare professionals:** neurologists, pneumologists, internists, neuropaediatricians and paediatricians subespecialized in metabolic diseases and involved in the diagnosis and treatment of Pompe's disease; nurses involved in the treatment of patients with avalglucosidase; National Coordinating Centre for the Diagnosis and Treatment of Lysosomal Storage Disorders	Guide – home infusion Guide for immunogenicity testing services
		30-08-2024
Dabigatran etexilate *Dabigatrano etexilato Sandoz, Dabigatrano etexilato Mylan*	**Physicians:** general/family medicine, internal medicine, haematology, immuno-haemotherapy, cardiology, neurology, vascular surgery, neuro surgery, general surgery, clinical pathology, gastroenterology, and anaestesiology	rescriber's guide for cardiovascular indications (NVAF, DVT and PTE)
	Physicians: orthopaedics	Prescriber's guide for primary prevention of VTE in adult patients submitted to total elective hip arthroplasty or total elective knee arthroplasty
	Physicians: general/internal medicine, internal medicine, haematology, immuno-haemotherapy, orthopaedics, cardiology and neurology; paediatric cardiology and haematology	Prescriber's guide for paediatric use
		12-07-2024
Daratumumab *Darzalex*	**Physicians:** haematology dpt directors, prescribing haematologists, immuno-haemotherapy dpts using this medicinal product	Guide
	Healthcare professionals: blood banks	Guide
	Patients	Card
		05-09-2024

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Educational Materials published on the Infomed product information webpage

Click on the links

INN Medicinal product	Target	Materials Online publication date
Dienogest + Ethinylestradiol *Kelzy*	**Physicians:** gynaecologists general/family physicians providing family planning services	Checklist
	Patients	Card
		30-08-2024
Eculizumab *BEKEMV*	**Physicians:** haematology, nephrology	Guide Vaccination / Antibiotic prophylaxis certificate
	Patients	Guide Card
		23-08-2024
Eliglustat *Cerdelga*	**Physicians:** haematology, internal medicine, neurology and hepatology (gastroenterology)	Guide
	Patients	Alert card
		23-09-2024
Fenfluramine *Fintepla*	**Physicians:** neurology and paediatric neurology	Guide
	Patients	Guide
		03-08-2024
Fumarate, dimethyl *Skilarence*	**Physicians:** dermatology	Guide
		03-08-2024
Gilteritinib *Xospata*	**Physicians:** haematology	Guide
		24-08-2024
Hydroxicarbamide *Siklos*	**Physicians:** haematology and paediatrics	Treatment guide
	Patients	Guide Dosing leaflet
		16-08-2024
Iptacopan *Fabhalta*	**Physicians:** haematology and internal medicine	Guide
	Healthcare professionals: Prescribing haematologists and internists, and hospital pharmacists	Vaccination certificate
	Patients	Guide Card
		26-09-2024

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Educational Materials published on the Infomed product information webpage

Click on the links

INN Medicinal product	Target	Materials Online publication date
Laronidase *Aldurazyme*	**Healthcare professionals:** neurologists, paediatricians and internists managing patients with a confirmed diagnosis of Mucopolysaccharidosis I, to treat non-neurological manifestations of the disease at home; nurses administering the medicine at home	Guide – home infusion therapy
	Patients	Guide for the patient/caregiver – home infusion therapy 26-09-2024
Lenalidomide *Lenalidomida Grindeks*	**Healthcare professionals:** haematologists and hospital pharmacists	Safety information
	Patients	Booklet for female patients with potential to become pregnant Booklet for female patients without potential to become pregnant Booklet for male patients 26-09-2024
Natalizumab *Tysabri 20 mg/ml, concentrado para solução para perfusão, Tysabri 150 mg/ml, solução injetável em seringa pré-cheia* *Tysabri 150 mg/ml, solução injetável em seringa pré-cheia*	**Physicians:** neurologists undertaking a multipl sclerosis clinic **Healthcare professionals:** administering Tysabri subcutaneously out of hospital	Safety information Checklist for out-of-hospital administration Out-of-hospital supplementary information 25-07-2024
Onasemnogene abeparvovec *Zolgensma*	**Physicians:** prescribers at centres treating spinal muscular atrophy **Patients**	Risk minimization guide Caregiver's guide 26-09-2024
Ozanimod *Zeposia*	**Patients**	Guide 15-08-2024
Paracetamol *Paracetamol Accord Solução para perfusão 10 mg/ml, Parafusiv*	**Healthcare professionals:** pharmaceutical, paediatric and paediatric emergency services	Administration guide Dosing ruler 12-09-2024

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Educational Materials published on the Infomed product information webpage

Click on the links

INN Medicinal product	Target	Materials Online publication date
Quetiapine *Seroquel, Seroquel SR*	**Physicians:** neurology, psychiatry, internal medicine, general/family medicine	Educational material 20-09-2024
Teriflunomide *Aubagio, Teriflunomida Accord, Teriflunomida Krka, Teriflunomida Mylan, Teriflunomida Pharmakern, Teriflunomida Sandoz, Teriflunomida Stada, Teriflunomida Teva, Teriflunomida Zentiva*	**Physicians:** neurology **Patients**	Guide Card 26-08-2024
Tocilizumab *RoActemra*	**Patients**	Brochure 24-09-2024
Trastuzumab deruxtecan *Enhertu*	**Patients**	Card on potential pulmonary issues 21-09-2024
Valproic acid/valproate semisodium *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, Epixival, Valproato de sódio Altan*	**Physicians:** neurology, psiquiatria, medicina geral e familiar, psiquiatria infantil e neuropediatria **Patients**	Guide for healthcare professionals who treat female children, women of childbearing age, and male patients Contraception and pregnancy guide Guide for male patients 23-09-2024

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

Drug-drug interactions as a public health problem:

A retrospective study of adverse drug reaction reports submitted to the National Portuguese Pharmacovigilance system

Maria Inês Gouveia[1]; João Paulo Fernandes [2]; Sandra Queiroz[2]; Márcia Silva[2]

1- Faculty of Pharmacy, University of Lisbon, Lisbon, Portugal
2-INFARMED - National Authority of Medicines and Health Products - I.P, Lisbon, Portugal

1 INTRODUCTION

According to the World Health Organisation, above 50% of patient harm is preventable, with half of this harm being attributed to medications. [1] Drug-drug interactions (DDIs) are an important cause of adverse drug reactions (ADRs), which can have a significant impact at the public health level.

2 AIM

This study aims to analyze Individual Case Safety Reports (ICSRs) submitted to the National Portuguese Pharmacovigilance System and identify ADRs that may result from DDIs.

3 METHODS

Retrospective study which analyzed ICSRs received by the Portuguese National Pharmacovigilance System in January 2023.

ICSRs with more than one drug (classified as either suspect or concomitant) were selected.

Assessement of whether the clinical implications of DDIs aligned with the provided description of ADRs in each ICSR.

How?

The **Summary of Product Characteristics** for each drug was consulted, as well as the **UptoDate database**.

4 RESULTS

- Our research retrieved a total of 727 ICSRs of which 307 contained more than one drug involved and were analysed.

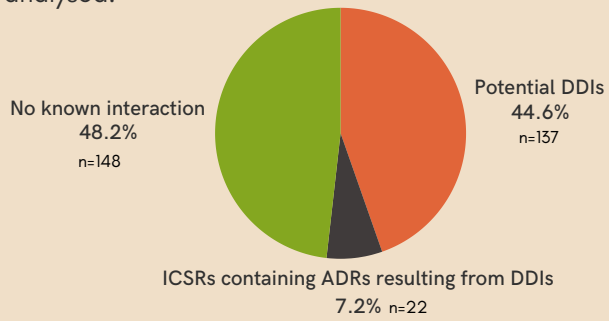


Fig.1-Analysis of the 307 ICSRs that contained ≥ 1 reported drug

- Most of DDIs were due to cumulative class effects. Very few cases were due to CYP alteration and mechanism interference. **Only one** ICSR was coded as DDI.

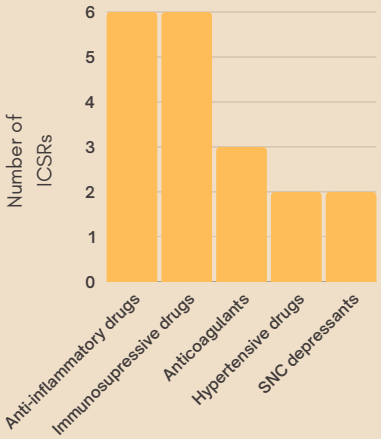
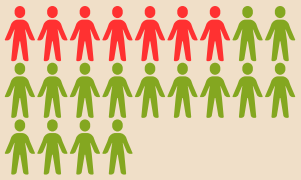


Fig.2- Number of ICSRs resulting from class cumulative effect DDIs



7 out of the 22 ICSRS that resulted from DDIs were considered serious

Fig.3- ICRs seriousness classification

- Regarding the potential DDIs, the majority included cases where therapy is possible with close monitoring. The potential incorrect use of drugs from the same classes was also verified, but the ADRs were not related.

5 CONCLUSIONS

Our study highlights the importance that ADRs resulting from DDIs have in Public Health. Healthcare professionals face an important challenge with the increasing prevalence of polypharmacy, particularly in aging populations with multiple comorbidities which accentuates the importance of understanding and managing these interactions and avoiding placing an additional burden on healthcare systems and resources.

References

[1] - World Health Organisation - Patient Safety Key Facts, 11 Sept, 2023 - Hodkinson, A.,Tyler, N., Ashcroft, D.M. et al. Preventable medication harm across health care settings: a systematic review and meta-analysis. BMC Med 18, 313 (2020). https://doi.org/10.1186/s12916-020-01774-9

[2] - UpToDate. (2023). UpToDate. https://www.uptodate.com/contents/search

Feeling Interactive?

A 10-year review of reports to the Portuguese National Pharmacovigilance System

Marta Loureiro[1], Joana Machado[2], Patrícia Gomes[2], João Paulo Fernandes[3], Márcia Silva[3]

[1]Faculdade de Farmácia da Universidade de Coimbra, Faculty of Pharmacy, Coimbra, Portugal
[2]Unidade Local de Saúde São José, Lisbon, Portugal
[3]INFARMED – National Authority of Medicines and Health Products, I.P., Lisbon, Portugal

Introduction

Drug interactions refer to changes in the pharmacokinetics of a medicinal product that are a consequence from the **simultaneous use of one** or **more medicinal products**, or **their use with the the intake of dietary supplements, foods, alcohol,** or with the **use of recreational substances** [1]. These interactions can pose risks as they can heighten the product's toxicity or diminish its effectiveness [2].
Clinical trials often fail to identify all potential interactions, highlighting **the need for real-world monitoring** [3].

Aim

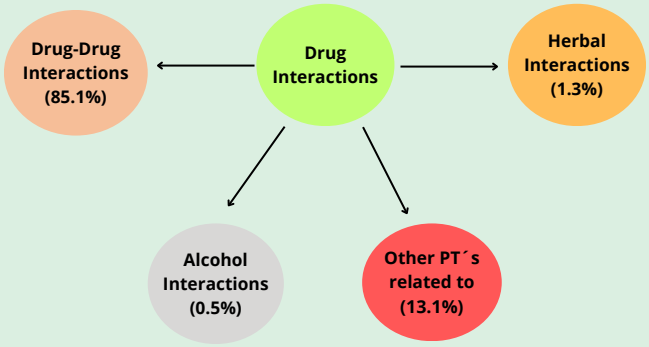
To **characterise** and **analyse** reports received by the **National Pharmacovigilance System** concerning **drug interactions**.

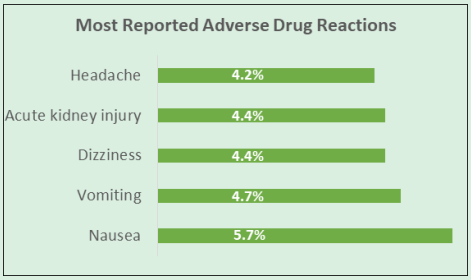
Methods

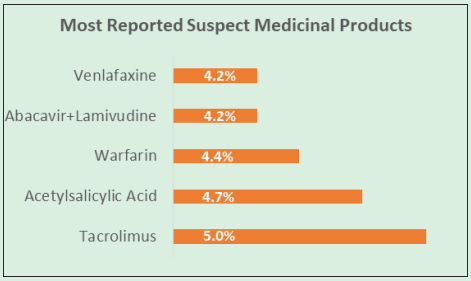
Retrospective study of **Individual Case Safety Reports (ICSRs)** indicating potential drug interactions reported to the Portuguese National Pharmacovigilance System between 2014 and 2023, enabled through the use of MedDRA High Level Term (HLT) "Interactions". Duplicate cases were excluded. Characterisation of cases considered **patient demographics, reported suspected products, MedDRA Preferred Term (PT), seriousness** and **type of reporter.**

Results

The study analysed **383** ICSRs indicating potential drug interactions (52.0% female; median age 56.8 years; interquartile range = 25.0).
Healthcare professionals reported the majority of cases **(86.7%)**, compared to **13.3%** by **patients**. Among the cases, **54.0% had at least one PT** classified as an **Important Medical Event** (IME) and **11.7%** as a **Designated Medical Event** (DME). **Acute kidney injury**, present in 4.4% of the cases, falls under both classifications and **was the most reported reaction**.







Of the ICSRs, **27%** were classified as **non-serious** and **73%** as **serious**, with 29% leading to hospitalisation.

Conclusion

In this study, a significant proportion of individuals experienced **serious adverse reactions** due to drug interactions, particularly **drug-drug interactions (DDIs)**. Therefore, this study aims to raise awareness and educate the public about potential drug interactions, an often overlooked aspect, to effectively manage and safeguard public health. Timely reporting of such events is essential for **enhancing pharmacovigilance efforts** and **ensuring patient safety.**

Literature

THE PHOLLOW COHORT: REAL-WORLD THERAPEUTIC ADHERENCE TO BLOOD GLUCOSE LOWERING DRUGS (EXCLUDING INSULINS) IN PORTUGAL

Mariana Romão[1], José Guerreiro[1], Carolina Rojais[1], Catarina Nunes[2], Zilda Mendes[1], António Teixeira Rodrigues[1,2,3,4]

[1]Centro de Estudos e Avaliação em Saúde/Infosaúde, Associação Nacional das Farmácias (CEFAR/IF, ANF); [2]Centro de Informação do Medicamento e Intervenções em Saúde (CEDIME/IF, ANF), Associação Nacional das Farmácias ; [3]Life and Health Sciences Research Institute [ICVS], School of Medicine, University of Minho, Braga; [4]ICVS/3B's-PT Government Associate Laboratory, Braga/Guimarães

Background

- The main goal of pharmacological treatment for diabetes is to achieve glycemic control. Medication adherence is key to the effectiveness of glucose-lowering drugs (GLD), given that poor glycemic controls due to medication nonadherence accelerates the development of long-term complications, leading to increased hospitalization and mortality1.
- Phollow is a real-world evidence (RWE) tool based on a cohort of community pharmacy users from about 83% of the community pharmacies (CPs) in Portugal. It allows the identification and characterization of patients undergoing treatment with prescription drugs.

Aim

This study aims at measuring therapeutic adherence to antidiabetics (excluding insulins) in a real-world setting in Portugal.

Methods

This is a retrospective, multicenter, cohort study of patients taking blood glucose-lowering drugs, excluding insulins, identified in Portuguese community pharmacies. An anonymized, random sample of 10% of all GLD-treated patients was selected from the Phollow cohort (Fig.1). Medication dispense data was retrieved between **January 2018 to December 2021** through the community pharmacy software.

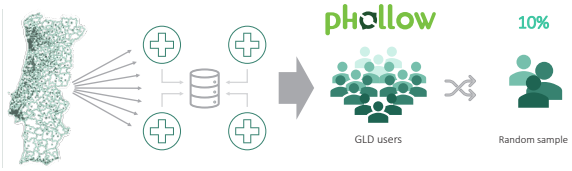


Fig. 1 – Patient selection

Analysis:

- The defined daily dose (DDD, source WHO) was used to calculate number of days of drug supply at the active substance (international nonproprietary name, INN) level.
- **Adherence** = proportion of days covered (PDC); calculated at the patient level at 1, 2, and 3 years after treatment initiation, for each INN.
- Patients were considered adherent if PDC≥80%.
- Age was calculated at the time of cohort entry.

Limitations

This research is based on dispensing data, which may underestimate adherence due to the assumption of periods of medicine coverage (1-, 2-, or 3-year periods). It also intends to study adherence at the INN level, rather than adherence to overall diabetes treatment. Therapeutic switches or add-ons are not captured in INN-specific adherence estimates.

Results

150 914 Patients in the cohort

66 years median age (IQR: [57.0;75.0])

51.5% female

Medication exposure

Over the 4-year period, 71.2% of the patients in the cohort used metformin, 13.7% used gliclazide, 12.4% used metformin + sitagliptin, 11.4% used metformin+ vildagliptin, and 8.7% used dapagliflozin at least once during the observation period.

Adherence | **mean PDC per INN**

- The mean adherence rate (PDC) varied between 29.2% (acarbose) and 73.8% (glimepiride) in the first year of exposure, decreasing to 25.5% and 67.0% at 2-years, and to 23.7% and 64.0% at 3-years (Fig.2).

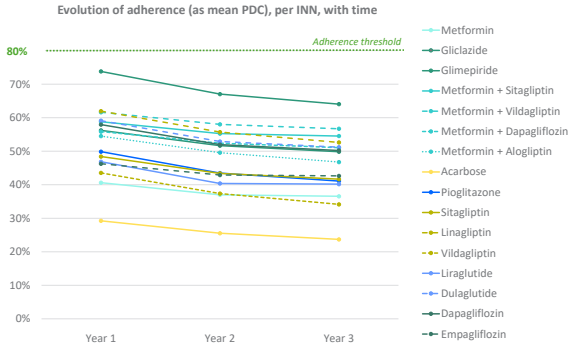


Fig. 2 – Adherence over time. The chart plots INNs with ≥1% frequency in the first year of the cohort. Substances are grouped at the ATC level 4 (therapeutic group). Each therapeutic group is represented by a color. The increasing dashing symbolizes a decreasing proportion of patients exposed to the drug within the therapeutic group in the first year of utilization.

Adherence | **proportion of adherent patients per INN**

- Glimepiride has the highest proportion of adherent patients (PDC ≥ 80%) over time, followed by two DPP-4 inhibitors (Linagliptin and Saxagliptin) (Fig.3).
- The proportion of patients considered as adherent to metformin was 12.5% at 1-year, 10.7% at 2-year, and 10.3% at 3-year.
- The INN with lowest adherence was acarbose.

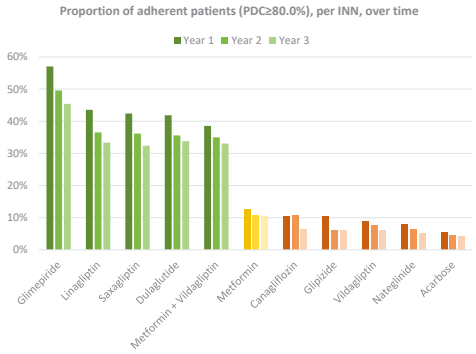


Fig. 3 – Proportion of adherent patients over time. The chart plots the top 5 INNs in green, Metformin (1st line) in yellow, and bottom 5 INNs in red.

Conclusions

- Adherence (either as mean PDC or proportion of adherent patients) **varied substantially** between INNs and generally **decreased with time**.
- There was a **very low proportion of patients achieving the adherence threshold for first-line diabetes treatment (metformin)**. This may suggest some level of nonadherence, but also medication switch before completing a full year of treatment.
- Phollow increases knowledge about the medication use patterns of the Portuguese population, which is fundamental to support pharmaceutical practice and health policies. More research is needed that accounts for switches between drug classes.

REFERENCES

1. World Health Organization (2016) Global Report on Diabetes. World Health Organization, Geneva, 1-88.

AKNOWLEDGEMENTS

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Programa de Farmacovigilância Ativa do Pretomanid

Joana Salvado[1], Cláudia Pádua Santos[2], Fátima Cimadeira[1], Raquel Inez[1], Cristina Meireles[1], Renata Afonso[1], Nadine Ribeiro[3]
[1] Farmacêutica Hospitalar, Unidade de Farmácia da Administração Regional de Saúde de Lisboa e Vale do Tejo
[2] Farmacêutica Hospitalar, Unidade Local de Saúde de São José
[3]Coordenadora da Unidade de Farmácia da Administração Regional de Saúde de Lisboa e Vale do Tejo

INTRODUÇÃO

Um dos maiores problemas associados ao tratamento da Tuberculose Multirresistente é a adesão à sua longa duração.

As *guidelines* da OMS de 2022 sugerem o uso do regime terapêutico de 6 meses com Bedaquilina, Pretomanid, Linezolide e Moxifloxacina, como tratamento de escolha para os doentes elegíveis, em oposição aos regimes mais longos, de 9 a 18 meses, referidos nas *guidelines* da OMS de 2020.[1]

O Pretomanid é um novo medicamento indicado, em adultos, para o tratamento da tuberculose pulmonar extensamente resistente ou intolerante a fármacos.[2]

A monitorização das reações adversas (RA) é fundamental para regimes de tratamento que incluam novos medicamentos. A OMS recomenda o estabelecimento de programas de Farmacovigilância Ativa (FA) para utentes em tratamento com Pretomanid, para deteção e gestão adequada de RA e prevenção de complicações decorrentes de interações medicamentosas.[2]

Neste sentido, a Comissão de Farmácia e Terapêutica (CFT) da ARSLVT elaborou o Programa de FA do Pretomanid.

OBJETIVOS

Monitorização das reações adversas dos doentes em tratamento com Pretomanid na região de Lisboa e Vale do Tejo (LVT), garantindo o acompanhamento adequado dos doentes e a notificação das reações adversas à autoridade regulamentar.

MÉTODOS

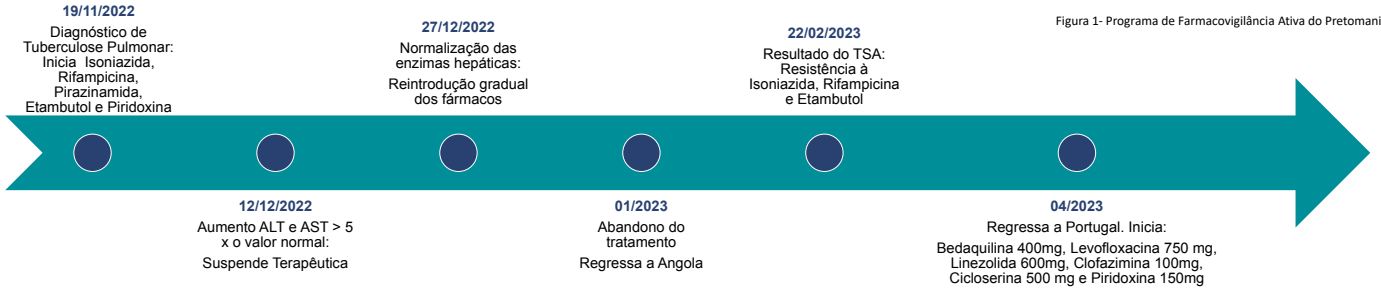
Realização do programa de FA em consulta presencial, pelo médico e farmacêutico, aos doentes em tratamento com Pretomanid na região de LVT.


Programa de Farmacovigilância Ativa

Figura 1- Programa de Farmacovigilância Ativa do Pretomanid

RESULTADOS E DISCUSSÃO

Doente do sexo feminino, 51 anos, 55kg, natural e residente em Angola, com hipertensão arterial, medicada com Losartan 100mg e Bisoprolol 2,5mg.



Em maio de 2023, foi submetido à CFT da ARSLVT o pedido de introdução do medicamento Pretomanid para início do esquema curto com Pretomanid 200mg, Bedaquilina 200mg, Linezolide 600mg, Moxifloxacina 400mg e Piridoxina 150mg, que inicia a 06/06/2023.

Tabela 1-Descrição das RAM reportadas pela utente durante o tratamento

Data	RAM	Intervenção	Evolução	Duração
06/2023	Mal-estar geral	Monitorização	Melhoria com o continuar no tratamento	Totalidade do tratamento (6 meses)
	Parestesias nos membros inferiores	Monitorização	Melhoria com o continuar no tratamento	
	Anorexia	Metoclopramida 10mg em SOS	Sem melhoria com Metoclopramida; Melhoria com o continuar do tratamento, referindo não necessitar de alternativa	
	Náuseas			
07/2023	Palpitações	Monitorização	Frequentes 1-2h após a administração da medicação	
	QT = 424ms	Monitorização	Normalizou no mês seguinte, Mantendo-se normal durante o restante tratamento	Valor pontual
10/2023	Tonturas	Monitorização	Mais frequentes nas primeiras horas após a toma da medicação, revertendo espontaneamente	Até ao fim do tratamento (2 meses)
	Diminuição da acuidade visual	Consulta de oftalmologia que não detetou alterações a nível do nervo óptico. Suspensão de Linezolida a 03/11/2023		Recuperação progressiva da visão após suspensão da Linezolida

Após 6 meses de terapêutica, a 5 de dezembro de 2023, a utente terminou o tratamento.

CONCLUSÕES

Todos os sintomas apresentados estão descritos no RCM do Pretomanid. Contudo, a implementação de programas de FA por equipas interdisciplinares é fundamental na identificação e gestão precoce de RA.

REFERÊNCIAS

1. WHO consolidated guidelines on tuberculosis: Module 4: treatment – drug-resistant tuberculosis treatment, 2022 update
2. Resumo das Características do Medicamento Dovprela 200 mg comprimidos

Adverse events related to etonogestrel implant: an old but still current issue?

João Paulo Fernandes[1]; Margarida Sousa[2]; Jani Bhikha[2]; Paula Moreira[3]; Isabel Silva[3]; Márcia Silva[1]

[1] INFARMED – National Authority of Medicines and Health Products, I.P., Lisbon, Portugal
[2] Escola Superior de Tecnologia da Saúde de Lisboa, Lisbon, Portugal
[3] Clinical Pharmacology Department, University Hospital Center São João, Porto, Portugal

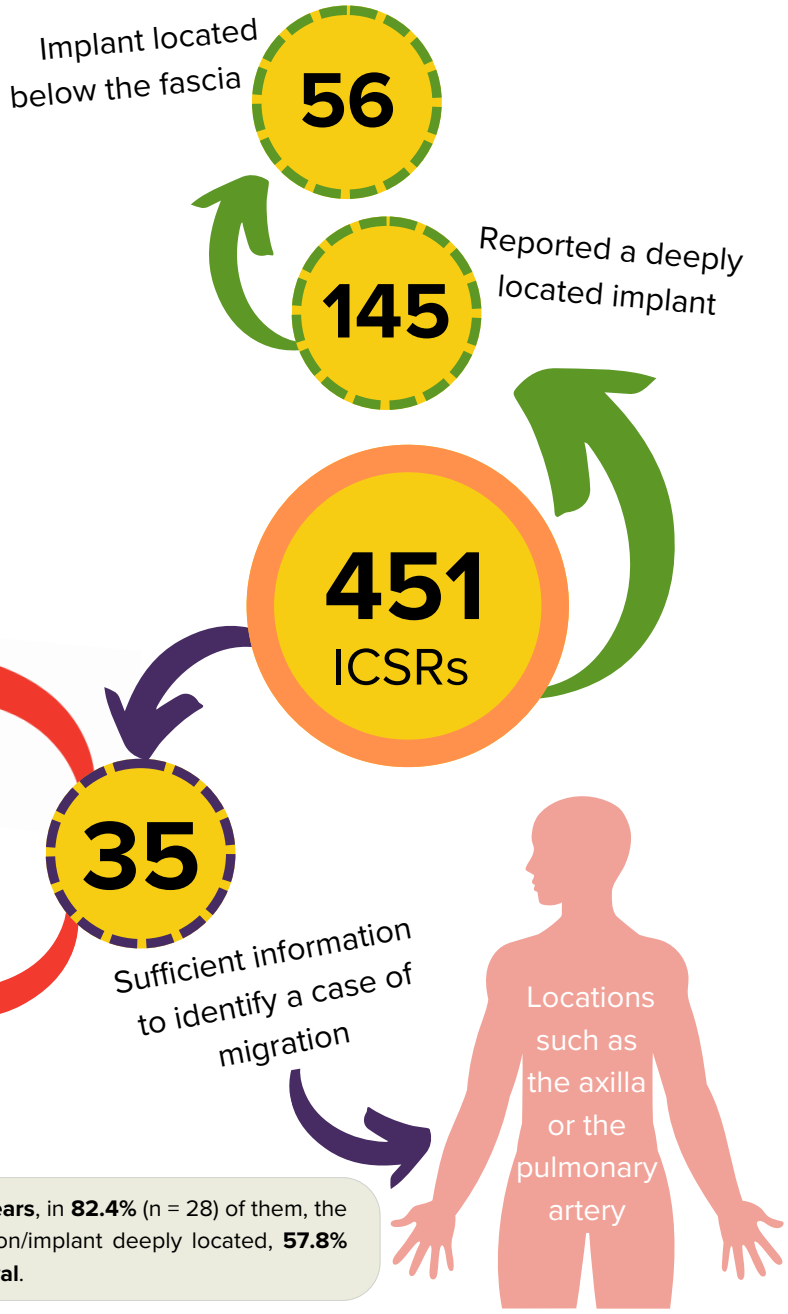
INTRODUCTION & AIM

In December 2019, in Portugal, a Direct Healthcare Professional Communication (DHPC) was approved regarding the subcutaneous implant of etonogestrel 68 mg. The genesis of this communication was based on reported cases of neurovascular injury and migration of the implant from the insertion site within the arm, or, in rare cases, into the pulmonary artery, possibly associated with deep or incorrect implant insertion. To minimize risks, the DHPC has introduced updates to the instructions for the insertion and removal of the implant [1]. The aim of our work is to conduct a descriptive analysis of the number of Individual Case Safety Reports (ICSRs) received by the Portuguese National Pharmacovigilance System (SNF) following the DHPC, related to adverse events associated with the insertion and removal of the etonogestrel implant.

MATERIALS & METHODS

Retrospective analysis of subcutaneous etonogestrel implant ICSRs reported to the Portuguese SNF, between 1 January 2020 and 31 October 2023. ICSRs were screened by 2 pharmacy students, and adverse events potentially associated with the insertion and removal of the etonogestrel implant have been flagged. All suspected migration ADR were clinically reviewed. Descriptive data analysis was performed.

RESULTS



In cases where there was an incorrect duration of use **exceeding 5 years**, in **82.4%** (n = 28) of them, the implant was **found deeply located**. Regarding the ICSRs of migration/implant deeply located, **57.8%** (n=104) **mentioned complications associated with the implant removal**.

CONCLUSION

Our results provide a general overview of adverse events associated with the etonogestrel implant. Despite inherent limitations in our study, it appears that this issue, although recognized, remains current. Further studies are needed to understand both the effectiveness of the additional risk minimization measures implemented and the potential need for new ones.

REFERENCES

Safety First, Migraines Second

Exploring the safety profile of calcitonin gene-related peptide (CGRP) antagonists

Catarina Coxilha[1], Joana Mendonça[1], João Paulo Fernandes[2], Márcia Silva[2]

[1]ESTESL – Escola Superior de Tecnologia da Saúde de Lisboa; [2]INFARMED - National Authority of Medicines and Health Products, I.P

Introduction

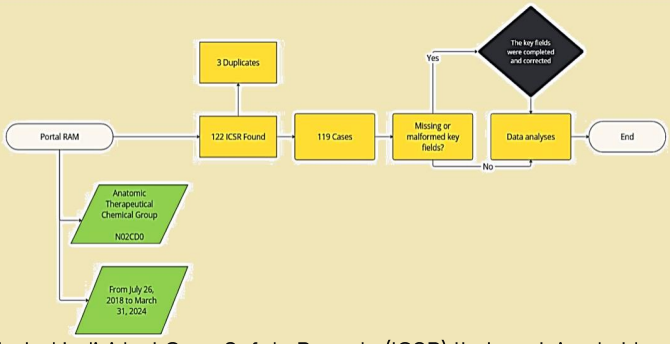
Calcitonin gene-related peptide (CGRP) antagonists are utilized in the management and treatment of migraine, which ranks among the top level-3 causes of global lost healthy life, expressed as disability-adjusted life years (DALYs), for both children, adolescents, and adults[1]. While randomized controlled trials have demonstrated a positive benefit-risk profile, ongoing monitoring of adverse drug reactions (ADRs) reported post-marketing is essential for assessing the medicinal product's safety profile in real-world settings.

Objective

We aim to analyze and characterize cases related to CGRP antagonists reported to the Portuguese National Pharmacovigilance System.

Methods

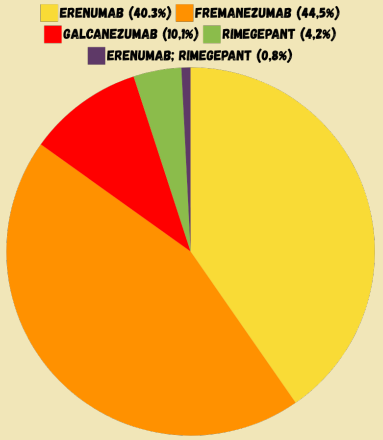
We performed a retrospective search on Portal RAM (Portuguese Pharmacovigilance Database) according to the following diagram:



We included Individual Case Safety Reports (ICSR) that contained at least one of the substances of interest coded as suspected.

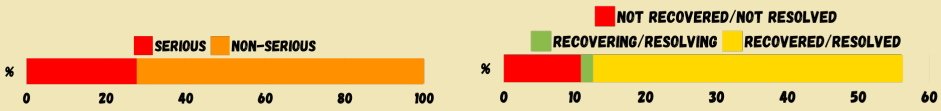
Results

Our research retrieved 119 cases of interest, with 91.6% involving females. The median age was 43.0 years (interquartile range = 9) with 97.5% of cases being reported by healthcare professionals. Fremanezumab was accounted for the highest number of cases.

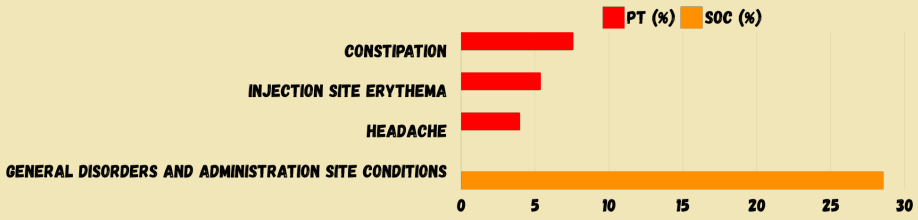


Distribution of reported CGRP by percentage of cases

Around 72.3% of the cases were classified as non-serious. The most frequently reported outcome for ADRs was "recovered/resolved", followed by "not recovered/not resolved" and "recovering/resolving".



Most frequently reported PTs were "Constipation", "Injection site erythema" and "Headache". The most frequently reported SOC was "General disorders and administration site conditions". About 11% of the cases included at least one ADR listed in the Important Medical Event (IME) list. None of the cases contained an ADR listed in the Designated Medical Event (DME) list.



Conclusions

This study contributes to our understanding of the safety profile of CGRP antagonists. Our results indicate that a significant portion of reported cases were classified as non-serious, with the most reported ADRs being related to general disorders and administration site conditions. This data supports the safety profile of these medicinal products, which have demonstrated significant efficacy in treating migraine symptoms, providing healthcare professionals and patients with valuable insight when considering migraine treatment options. However, despite demonstrating safety, it remains crucial to continuously evaluate the safety profile of these products in real-world settings to identify any potential safety concerns.

Related Literature

Communications to Healthcare Professionals published on the Infomed product information webpage

Click on the links.

INJN Medicinal product	Target	Materials Online publication date
Anti-CD19 or anti-BCMA T-CAR Cells *Abecma, Breyanzi, Carvykti, Kymriah, Tecartus, Yescarta*	**Physicians:** haematologists and oncologists	Risck of secondary malignant neoplasms originating in T cells 19-07-2024
Glatiramer acetate *Acetato de glatirâmero Mylan, Clift, Copaxone*	**Healthcare professionals:** neurologists and hospital emergency physicians, and other healthcare professionals specialized in neurology and hospital emergency	Risk of anaphylactic reactions occurring months to years after the start of treatment 14-08-2024
Obeticholic acid *Ocaliva*	**Physicians:** hepatologists, gastroenterologists, internists and immunologists	Recommendation to withdraw the Marketing Authorization in the EU due to lack of confirmation of clinical benefit 01-08-2024

Compiled by Patrícia Catalão