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From the Editor

INFARMED once again organized an event to disseminate and discuss the latest developments in pharmacovigilance at national and international level, under the motto **Pharmacovigilance: Towards an Integrated Approach**. The event, which took place in the Infarmed Tomé Pires Building Auditorium in Lisbon, on 6 June, also provided a renewed opportunity to present scientific research work, which has been gaining increasing importance in this area in Portugal. In this issue of the Pharmacovigilance Bulletin, we are beginning to publish the work presented in poster form. Since this was a meeting within the scope of the National Pharmacovigilance System, we begin with **risk minimisation measures**, a topic that was the subject of no less than seven of the works presented. Several researchers sought to find out the real-life impact of this type of measure, particularly in terms of the incidence and profile of adverse reactions to drugs with special safety issues. Two groups investigated the effectiveness of educational materials published for the anticoagulants **apixaban** and **rivaroxaban**. In the field of prevention of adverse pregnancy outcomes, two other groups of researchers analyzed the impact of educational materials related to both relatively commonly used drugs – **oral retinoids** – and the drugs **thalidomide**, **lenalidomide and pomalidomide**, all of which are medicines whose risk management includes **Pregnancy Prevention Plans**.

Risk minimization measures of a broader scope were studied with regard to both **oncological** pharmacotherapy in general and the use of monoclonal antibodies in other complex conditions such as **rheumatoid arthritis**.

The authors of the last poster published in this issue specifically studied the impact of communications addressed to health professionals (which resulted from the evolution of the old Dear Doctor Letters) on the spontaneous reporting of adverse reactions to **fluoroquinolones**, a class of antimicrobials commonly used in clinical practice.

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.

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

INDEX CARD

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EFFECTIVENESS OF RIVAROXABAN'S PORTUGUESE EDUCATIONAL MATERIALS – A QUALITATIVE STUDY

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INTRODUCTION

The Importance of Educational Materials on Rivaroxaban

- Relevance of additional risk minimization measures
- Efficient dissemination and comprehension of safety information are essential for the protection of individual and public health
- As an anticoagulant, Rivaroxaban has a very narrow therapeutic window
- It is essential that those involved in prescribing, dispensing and using this medicinal product understand the safety information present in the educational material

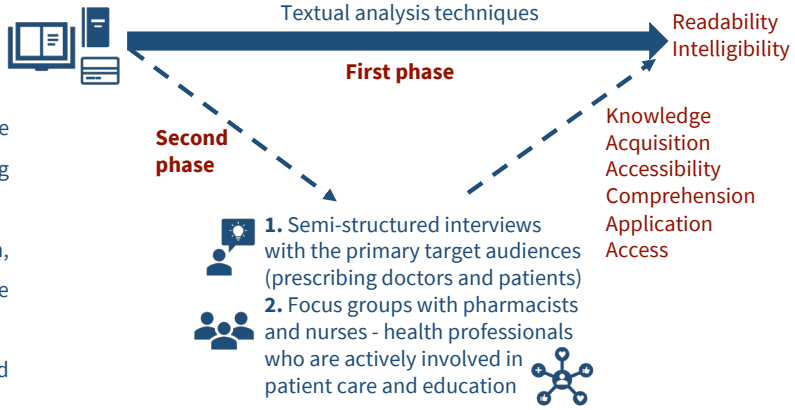
AIMS

To evaluate the legibility, intelligibility, and comprehension of Rivaroxaban educational materials, as well as how this information is transmitted to and understood by healthcare professionals and patients in Portugal

The main objective was to analyze the Rivaroxaban prescriber's guide (PG) and patient alert card (PAC)

METHODS

- Qualitative methodological approach
- **First phase:** the readability and intelligibility of the text in the educational materials under examination were assessed using textual analysis techniques
- **Second phase:** evaluating the readability, knowledge acquisition, accessibility, comprehension, application, and access of the written and illustrated information in the documents
- The software utilized included ALT, Coh-Metrix-Port 2.0, and MAXQDA 24



RESULTS

First Phase

- Both the PG and the PAC exhibited a moderate level of readability and intelligibility
- In terms of lexical analysis, emphasis was placed on issues concerning medication administration and risk management, particularly bleeding, within the texts of the educational materials

Second Phase

Prescribing Doctors (*n*=10)	• Were more aware of the existence of the PG • More than half of the interviewed reported not using the PG
Pharmacists (*n*=10) and Nurses (*n*=10)	• Most were more aware of the PAC • Most reported not having access to educational materials in their professional practice but believed that their use would be beneficial
All healthcare professionals	• Unanimously acknowledged the importance of having educational materials for Rivaroxaban • They considered, in terms of readability, both materials to have adequate typographical elements, as well as being perceptible, understandable, concise, complete, and easy to read
Patients (*n*=10)	• Only half (*n*=5) were aware of the PAC, and most of them had never used it • Nevertheless, those who regularly carried the PC found it to have a positive impact on their medication use

CONCLUSION

- Overall, healthcare professionals and patients considered the educational materials to be materials that are legible, intelligible, with an appropriate design and typographic factors
- However, it is noteworthy that doctors showed a lack of knowledge and reading of the educational material intended for them - the PG
- Regarding patient's engagement, only three had read the educational material aimed at them – the PAC.
- This study serves as the foundation for the development of a pilot intervention aimed at testing new educational formats with both patients and healthcare professionals

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2. EUPATI Open Classroom - Pharmacovigilance and Risk management. 6. Direct healthcare professional communication. Communicating medicines safety information directly to healthcare professionals an introduction to DHPC. In 2023 [cited 2023 Oct 11]. Available from: https://learning.eupati.eu/mod/book/tool/print/index.php?id=828

Effectiveness of Additional Risk Minimization Measures when using baricitinib (Risk-Bari) - Preliminary analysis

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[1]Unidade de Farmacovigilância dos Açores, Açores, Portugal; [2]INFARMED - National Authority of Medicines and Health Products, I.P., Porto, Portugal

INTRODUCTION

Baricitinib is a selective and reversible inhibitor of Janus kinase (JAK) 1 and JAK2, which is approved for the treatment of moderate to severe active rheumatoid arthritis and atopic dermatitis, as well as severe alopecia areata, in adult patients.[1] Additional risk minimization measures (aRMMs) include educational materials to mitigate the risks of malignancies, major adverse cardiovascular events (MACE), serious infections, venous thromboembolism (VTE), and mortality.[2] These educational materials include a Healthcare Professionals (HCP) Guide, a Patient Alert Card (PAC), and Direct Healthcare Professional Communications (DHPC).

AIM

To assess awareness and knowledge among professionals most involved in prescribing this product in Portugal about the risks associated with the use of this product in Portugal, as well as to determine the accessibility of educational materials.

METHODS

Cross-sectional and Non-interventional	Dermatologists, rheumatologists, and immunoallergologists were invited to complete an online questionnaire in order to assess their awareness, knowledge, and adherence to aRMMs.
The recruitment strategy for completing the questionnaire included professional and social networks, and collaboration with professional associations.	Data collection occurred over a period of 105 days between 09/2023 and 12/2023.
A descriptive analysis was performed with *software Statistical Package for the Social Sciences*® (IBM SPSS Statistics) 29.0 version.	

RESULTS

77 questionnaires

→ Excluded:
- 5 questionnaires not valid
- 2 questionnaires because physicians did not provide medical appointments to patients with rheumatoid arthritis/atopic dermatitis/alopecia areata

70 questionnaires

→ Excluded:
- 4 questionnaires for belonging to other medical specialties

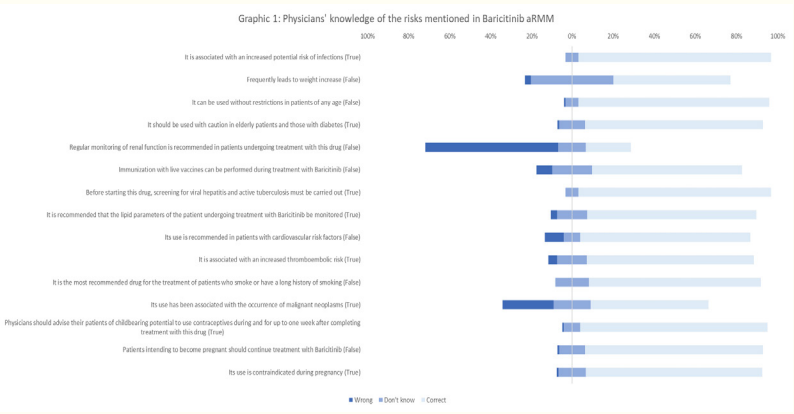
66 valid questionnaires

53 complete questionnaires

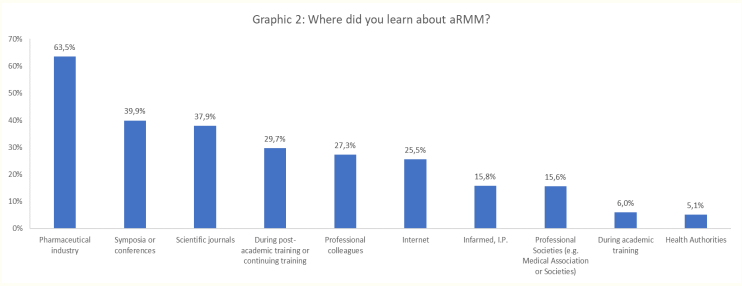
Of the 66 valid questionnaires:

- 50.0% of the responses were from immunoallergologists,
- 25.8% from dermatologists, and
- 24.2% from rheumatologists.

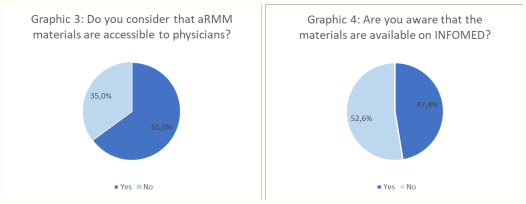
Respondents demonstrated that they were aware of most of the risks addressed by the aRMMs, with the exception of malignant neoplasms (24.8% of respondents answered incorrectly, and 18.0% were unaware of this information).



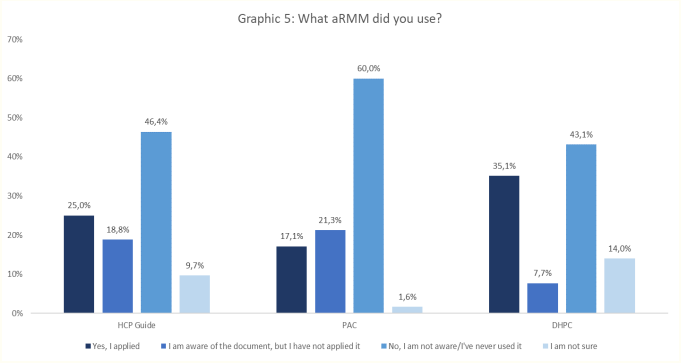
Only 27.9% of the respondents were aware of aRMMs and 63.5% recognized the Pharmaceutical Industry as the primary source of information, followed by symposia/conferences (39.9%) and scientific journals (37.9%).



Most physicians (65.0%) considered educational materials accessible, while 52.6% of respondents are unaware that they are available through the national medicines database (INFOMED).



Regarding adherence to educational materials, we verified the following:



The three main barriers to implementing aRMMs identified by respondents were:

- **lack of time** (39.2%),
- **insufficient dissemination** (32.1%), and
- **difficulty communicating with the patient** (12.3%).

CONCLUSION

The scientific evidence gathered from this study could be used to optimize communication and educational strategies, making aRMMs more accessible, understandable, and implementable. Thus, it ensures that healthcare professionals are fully informed and equipped to manage the risks associated with baricitinib, consequently improving patient safety and the quality of healthcare.

REFERENCES

[1] https://www.ema.europa.eu/pt/documents/product-information/olumiant-epar-product-information_pt.pdf

[2] https://extranet.infarmed.pt/web/fl/matedu/SEGURANCA/2023/1/60341/e0cbe17003c64a3398ff001aa5d1d87c_011.pdf (Accessed on 02-06-2024)

ACKNOWLEDGMENTS

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"Farmacovigilância: Rumo a uma Abordagem Integrada"
Dia da Farmacovigilância 2024 – INFARMED, I.P.

Review of studies evaluating effectiveness of risk minimisation measures for oncology medicinal products registered in the European Medicines Agency (HMA-EMA) Catalogue: findings and lessons learned

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I. Introduction

Medicinal products are one of the most successful health interventions. Nonetheless, medicines may also have undesirable and/or unexpected risks and side effects, and new risks can be identified, for any medicine, after authorization (1). In 2005 the European Commission began a review of the European system of safety monitoring, which eventually led up to the introduction of a guideline in Good Pharmacovigilance Practices (GVP), divided into modules, which are a set of measures drawn up to facilitate the performance of pharmacovigilance in the European Union (EU) (2, 3). The GVP guideline Module XVI outlines that planning and implementing risk minimisation measures (RMMs) and assessing their effectiveness are essential elements of risk management (1,4).

Pharmacovigilance activities play a crucial role in oncology, given the potential for toxicity, narrow therapeutic windows and strict dosing schedules associated with many of the medicinal products used. The lack of an overview of the application of RMMs for these medicines and their effectiveness evaluation highlights the need for a comprehensive assessment (5).

II. Objective

This study aims to **review post-authorization studies targeted at evaluating the effectiveness of RMMs (routine and additional) of oncology medicinal products**, registered in the HMA-EMA Catalogue of real-world data (RWD) sources and studies.

III. Methods

Eligibility

RMMs effectiveness evaluation studies concerning medicines categorized under the Anatomical Therapeutic Chemical (ATC) code "L (Antineoplastic and Immunomodulating Agents)" and "V10 (Therapeutic Radiopharmaceuticals)", with a therapeutic indication in oncological medical conditions, up to February 2024.

Data Sources

HMA-EMA Catalogue of real-world data sources and studies.

Variables Extracted

HMA-EMA RWD Catalogues study ID, EU PAS Number, official title, study status, last updated date, availability of the protocol and study report, medicinal product identification, risk management plan category, participating countries, study design, timeline, primary and secondary objectives, type of RMM evaluated, target population and their respective size, data collection method and sources, process and outcome indicators, pre-defined effectiveness criterion threshold (if available), target population size reached, effectiveness of the RMMs and the respective evaluation conclusion .

IV. Results

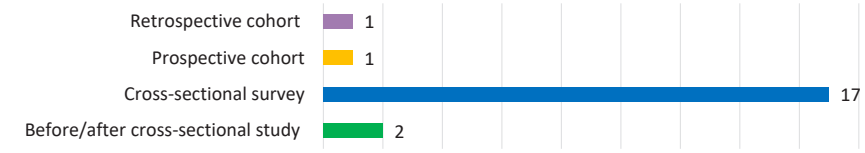

Figure 1. Study design type

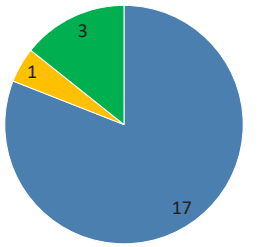

Figure 2. Type of RMM evaluated

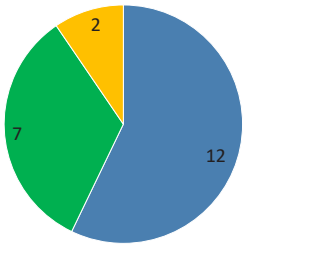

Figure 3. Target population

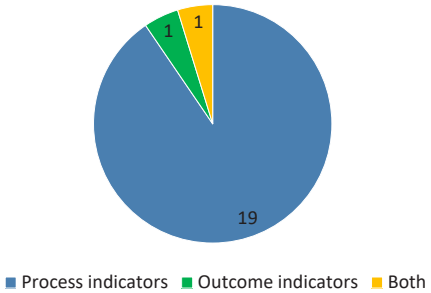

Figure 4. Assessed indicators

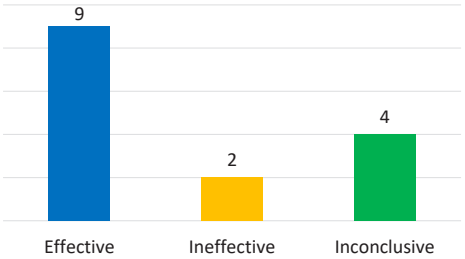

Figure 5. Effectiveness of RMMs conclusion, by sponsor (of the 15 studies with an available study report)

V. Conclusions

Most analyzed studies were cross-sectional surveys and evaluated additional RMMs. The GVP guideline (Module XVI) recommends outcome indicators (safety outcomes) as the ultimate measure of success of a risk minimisation programme, with process indicators complementing the assessment of outcome indicators. Such factor was not observed in our review, since most studies assessed process indicators, with only one assessing both process and outcome indicators. More than half of the studies with available results were reported as effective by the Sponsor and a quarter of them were inconclusive. Continuing to develop future regulatory guidance regarding effectiveness evaluation of RMMs, particularly for process and outcome indicators and the pre-definition of success thresholds, could be beneficial in establishing better measures of success.

References:

To access the references, please scan the provided QR Code

Fluoroquinolone Antibiotics

The Impact of Direct Healthcare Professional Communications on Spontaneous Reporting

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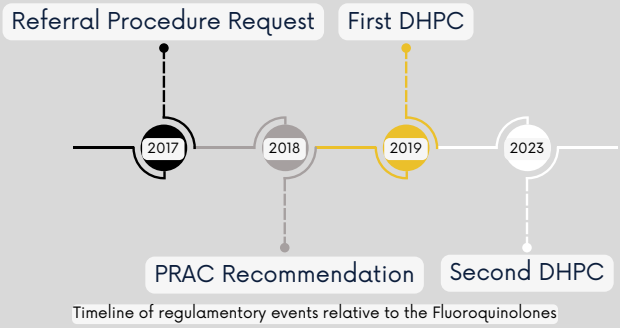
Introduction

Reports of long-lasting musculoskeletal side-effects motivated the German medicines authority to request a referral procedure to the PRAC (Pharmacovigilance Risk Assessment Committee), in 2017, for systemic and inhaled medicines of the quinolone and fluoroquinolone classes of antibiotics [1].
This culminated in the suspension of all quinolones, the emission of a Direct Healthcare Professional Communication (DHPC) restricting the use of fluoroquinolones (2019) [2], and the commissioning of the study EUPAS37856 [3], which results led the PRAC to issue a second DHPC (2023) [4].



Timeline of regulamentory events relative to the Fluoroquinolones

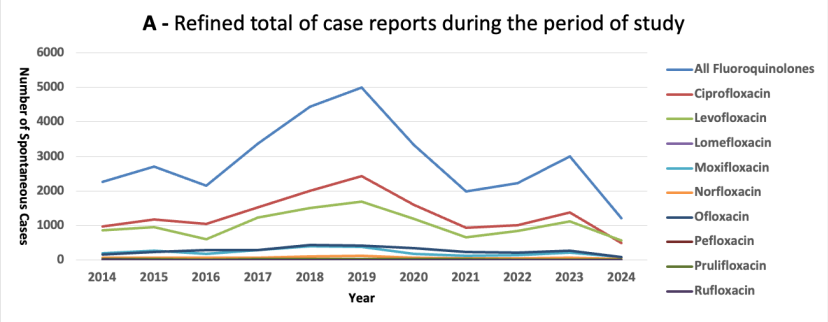
Objectives

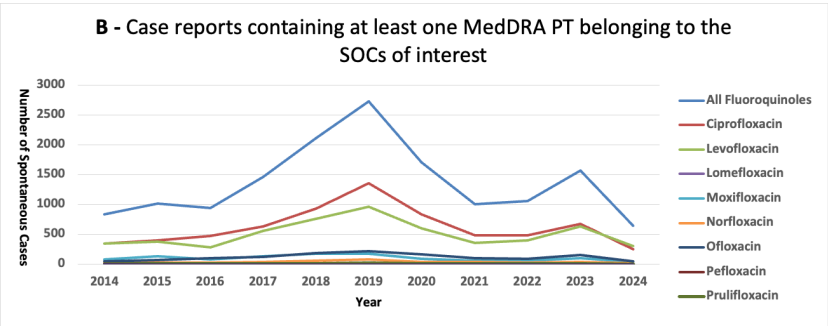
This descriptive study aims to explore the effect of these regulatory actions on the overall pattern of spontaneous notifications for the drugs contemplated by both DHPCs, and on the pattern of spontaneous notification of the side-effects.

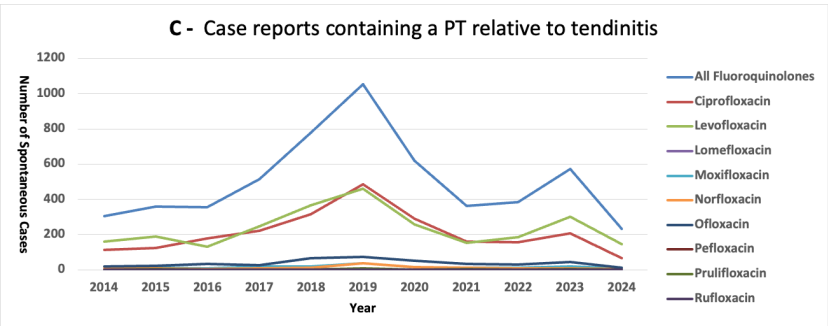
Methods

Case reports from the 1st of April 2014 to the 30th of April 2024, from the European Economic Area (EEA) [5], related to the systemic and inhaled forms of the nine fluoroquinolones covered on both DHPCs were gathered from the EudraVigilance database. Cases collected from literature review, as well as those concerning fluoroquinolones in any other pharmaceutical forms were excluded. The refined set of reports was then submitted to a tripartite analysis: an analysis of all the received notifications, a second analysis of cases which contained at least one MedDRA (Medical Dictionary for Regulatory Activities) PT (Preferred Term) belonging to the "Musculoskeletal and connective tissue disorders" and "Nervous system disorders" SOCs (System Organ Class), and a third analysis covering cases which contained a PT relative to tendinitis.

Results







Conclusion

The observed peaks in case reports concerning the fluoroquinolones matched the dates of emission of DHPCs. The lower intensity of the second peak might be due to the first DHPC lowering of the use of fluoroquinolones, and thus decreasing the number of case reports relating to these drugs. DHPCs may lead to a significant increase in the visibility or perceived importance of spontaneous reporting, which emphasizes the importance of these additional risk minimisation measures.

References:

Communications to Healthcare Professionals published on the Infomed product information webpage

Click on the links.

INN Medicamento	Target	Materials Online publication date
Etoposide *Etoposido Accord, Etoposido Hikma, Etoposido Sandoz*	**Physicians:** oncology and hematology **Pharmacists:** hospital service directors	Risk of of infusion-related hypersensitivity reactions when in-line filters are used during administration 02-05-2024

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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
Axicabtagene ciloleucel *Yescarta* **Brexucabtagene autoleucel** *Tecartus*	**Healthcare professionals:** multidisciplinary teams at qualified centres in charge of managing patients on Yescarta or Tecartus **Patients**	Guide on management of serous neurological adverse reactions and Cytokine Release Syndrome Alert card 06-05-2024
Cemiplimab *Libtayo*	**Patients**	Guide Alert card 23-05-2024
Edoxaban *Lixiana*	**Physicians:** ardiology, internal medicine, neurology, haematology, immuno-haemotherapy, general surgery, angiology and vascular surgery, general/family medicine	Guia do prescritor 27-05-2024
Normal human immuno-globulin *HyQvia*	**Healthcare professionals:** allergy specialist physicians, paediatrics, haemato-oncologists and neurologists; nurse teams caring for patients on immunoglobulins at hospitals and organizations procuring this medicinal product **Patients**	Guide Patient/caregiver guide Patient's diary 08-05-2024
Mavacamten *Camzyos*	**Physicians:** cardiology **Pharmacists:** hospital **Patients**	Checklist Guide Card 14-05-2024

Cont'd overleaf ▶

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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 *Quetiapina Mylan,* *Quetiapina Ratiopharm,* *Quetiapina Teva (comprimidos de libertação prolongada)* *Quetiapina Teva (comprimidos revestidos por película)*	**Physicians:** neurology, psychiatry, internal medicine, general/family medicine	Educational material for prescribers 01-05-2024
Tebentafusp *Kimmtrak*	**Physicians:** oncologists and dermato-oncologists specializing in the treatment of patients with metastatic uveal melanoma **Patients**	Treatment guide Guide 31-05-2024
Tocilizumab *Tyenne*	**Nurses:** administring this medicine	Administration guide 20-05-2024

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Portal RAM

Notificação de Reações Adversas a Medicamentos

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