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PRAC celebrates its 10th anniversary

The European Medicines Agency (EMA) Pharmacovigilance Risk Assessment Committee (PRAC) is in charge of assessing and monitoring the safety of medicinal products for human use. It was created in 2012 to reinforce monitoring of the safety of medicines across Europe.

The PRAC's work encompasses every aspect of risk management, including adverse drug reaction detection, assessment, risk minimization and communication. The PRAC assesses post-authorization safety studies (i.e., studies undertaken when medicines are already in the market) and issues recommendations on pharmacovigilance and risk management system issues, including effectiveness monitoring.

The Committee has a chairperson, elected by its serving members, one member and an alternate nominated by each of the EU Member States and EEA-EFTA States, six independent scientific experts, one member and one alternate representing patients organisations, and one member and an alternate representing healthcare professionals, the ten latter being nominated by the European Commission.

The central role of the PRAC in safeguarding medicinal product safety in Europe is well mirrored by the number of meetings it has conducted since its inception – a total of 249 meetings to discuss more than 3,900 safety topics over ten years. In this period of time the following were undertaken:

- 6,996 Periodic Safety Update Reports
- 5,673 Risk Management Plans
- 3,945 Post-Authorization Safety Studies
- 2,117 sundry in-depth Reports
- 1,859 Responses to requests for advice etc
- 722 Safety Signals
- 67 Safety Assessments

The plenary meeting from last July marked the 10th anniversary of the PRAC. EMA's Executive Director, Emer Cooke, gave a speech to underscore the relevance of PRAC work all these years. She praised and thanked the dedication and contribution of the Committee members and highlighted how even more effort has had to be made in the last few years to face up to new public health protection challenges in a context of rapid developments and urgency in decision making.

Ana Sofia Martins and Márcia Silva, from the Medicines Risk Management Dpt, have been representing Infarmed at the PRAC since 2016.

PRAC meeting highlights, agendas and minutes can be found here

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Excipients: safety information in patient leaflets – part 7

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Excipient	Route(s) of administration	Information in Patient Leaflet	Comments
Lactitol (E966)	Oral	*If you have been told by your doctor that you have an intolerance to some sugars contact your doctor before taking this medicinal product.* *May have a mild laxative effect.* *Calorific value 2.1 kcal/g lactitol.*	• Used as a non-cariogenic substitute for sucrose and as a diluent for solid formulations. In high doses it can be used in the treatment of hepatic encephalopathy and as a laxative. • It is not absorbed by the small intestine but is degraded by colonic microflora. • Stable in hot and humid environments. • Patients with rare hereditary problems of fructose intolerance, galactose intolerance, galactosaemia or glucose-galactose malabsorption should not take lactilol-containing medicines.
Lactose	Oral	*If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.* *Contains x g lactose (x/2 g glucose and x/2 galactose) per dose. This should be taken into account in patients with diabetes mellitus.*	• It can be used as an excipient in tablets and capsules as well as in powder for inhalation. • Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take lactose-containing medicines.
Lanolin (wool fat)	Topical	*May cause local skin reactions (e.g. contact dermatitis).*	• Widely used in topical pharmaceutical formulations and in cosmetics. It can be homogeneously mixed in twice its weight of water, thus producing stable emulsions for storage.
Latex (natural rubber)	All	*The container of this medicinal product contains latex rubber. May cause severe allergic reactions.*	• Not a common excipient.

Ribociclib
adverse events of special interest

Ribociclib is a selective inhibitor of cyclin-dependent kinase (CDK) 4 and 6. These kinases play a crucial role in signalling pathways that lead to cell division and cellular proliferation.
Ribociclib is indicated for the treatment of women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer in combination with an aromatase inhibitor or fulvestrant as initial endocrine-based therapy, or in women who have received prior endocrine therapy.

The final results of the recent **MONALEESA-2** clinical trial, including global survival figures, have confirmed the long-term benefits of the combination of ribociclib with letrozole as first line therapy for HR-positive, HER2 receptor-negative post-menopausal women.
Follow-up has demonstrated that global survival has gone beyond the 5 year mark. No new safety signals emerged but grade 3 and 4 adverse events of special interest were detected for the **ribociclib + letrozole combination** compared to letrozole in monotherapy, namely: **neutropenia, hepatobiliary toxicity with raised transaminases, QT interval prolongation, and pulmonary interstitial disease or pneumonitis.**
Given the above adverse events, section 4.2 Posology of the Summary of the Product's Characteristics as well as the corresponding section of the Patient Information Leaflet now include a "dose modifications" option with adjustment tables according to the grade (1 to 4) of the ADRs.
The safety results from MONALEESA-2 highlight the need for ADR monitoring in that ADRs can have an impact on the medicine's dose and/or posology, thus affecting the drug's benefit-risk ratio.

Rita Baião

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 hospital healthcare professionals don't report ADRs more

ADR underreporting is a worldwide problem. This Australian study using a mixed methodology survey tried to identify factors associated with reporting decisions.

The survey was completed by 133 healthcare professionals. The following factors were identified as **ADR reporting predictors:**

- knowing how to report an ADR
- having received training in ADR reporting
- dealing with ADR cases in clinical practice

Reporting promotion **interventions** should consider the following three action categories:

- changing the reporting process
- enabling clinicians to report ADRs
- creating a positive ADR reporting culture

• Li R et al. Why hospital-based healthcare professionals do not report adverse drug reactions: a mixed methods study using the Theoretical Domains Framework. Eur J Clin Pharmacol. 2022 Jul;78(7):1165-1175.

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
Adalimumab *Amgevita*	**Patients**	Patient safety card (adult) Paediatric patient safety card 10-06-2022
Yuflyma		Adult patient safety card Paediatric patient safety card 01-06-2022
Avelumab *Bavencio*	**Patients**	Information brochure Alert card 08-06-2022
Belantamab mafodotin *Blenrep*	**Physicians:** haematologists **Physicians:** ophthalmologists **Patients**	Guide on corneal adverse reactions Guide on corneal adverse reactions Guide on corneal undesirable effects Eye screening form Patient card Eyedrop card for pharmacies 02-07-2022
Brolucizumab *Beovu*	**Patients**	Guide Audio guide 23-06-2022
Daratumumab *Darzalex*	**Physicians:** haematology department directors, haematologists and immunohaemotherapy directors at departments where this product is used **Healthcare professionals:** at blood banks **Patients**	Guide Guide for blood bank professionals Patient card 31-07-2022

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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
Emicizumab *Hemlibra*	**Healthcare professionals:** immunohaemotherapists treating patients with haemophilia, or in exceptional cases, haematologists who are expected to prescribe Hemlibra; emergency department and nursing service directors at reference centres for the treatment of congenital coagulopathies	Guide
	Laboratory professionals: at reference centres for the treatment of congenital coagulopathies	Guide
	Patients	Guide for patients/caregivers Patient card 09-07-2022
Fentanyl *Breakyl 200 µg, 400 µg ou 600 µg, película bucal*	**Physicians:** at pain units, palliative care units and oncology services	Important information on risk minimization
	Pharmacists: hospital pharmaceutical services and community pharmacies	
	Patients and Caregivers	Important information on risk minimization 21-06-2022
Hemin *Normosang*	**Healthcare professionals:** at reference centres for porphyria , including internists, specialists in metabolic diseases, haematologists, gastroenterologists, hepatologists	Guide 20-07-2022
Ozanimod *Zeposia*	**Physicians:** neurologists and gastroenterologists	Checklist for the prescribing physician
	Patients	Patient/caregiver guide Specific pregnancy alert card 01-07-2022
Quetiapine *Quetiapina Farmoz SR* *Quetiapina Sandoz*	**Physicians:** neurologists, psychiatrists, internists and general/family medicine specialists	Guide 20-07-2022 Guide 09-07-2022
Vedolizumab *Entyvio*	**Physicians:** gastroenterologists	Guide 07-07-2022

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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
Rituximab *Truxima*	**Physicians:** rheumatologists and internists **Physicians:** oncologists treating lymphomas, heamatologists, rheumatologists and internists **Nurses:** at day hospitals **Pharmacists:** hospital **Patients**	Guide for non-oncological indications Information Guide for non-oncological indications 15-07-2022
Vandetanib *Caprelsa*	**Physicians:** nuclear medicine specialists and onco-endocrinologists treating thyroid conditions **Patients**	Educational material Patient and paediatric patient caregiver dosing and monitoring guide Warning card 19-07-2022

Compiled by Patrícia Catalão

Communications to Healthcare Professionals published on the Infomed product information webpage

Click on the links.

INN Medicinal product	Target	Materials Online publication date
Cetrorrelix *Cetrotide*	**Physicians:** gynaecologists/obstetricians specialized in medically assisted reproduction techniques	Temporarily out of stock 12-07-2022
Defibrotide *Defitelio*	**Physicians:** specialized in haematopoietic stem cell transplantation **Pharmacists:** at applicable healthcare organizations	Do not use for prophylaxis of veno-occlusive disease (VOD) following haematopoietic stem cell transplantation (HSCT) 13-06-2022
Dexmedetomidine *Dexdor, Dexmedetomidina... Accord, Altan, B. Braun, Ever Pharma, Kalceks, Mylan, Teva*	**Physicians:** anaesthetists and intensivists; heads of anaesthesiology and intensive care departments; Portuguese Society of Anaesthesiology and Portuguese Society of Intensive Care Medicine **Pharmacists:** hospital	Increased risk of mortality in patients aged ≤65 years in intensive care units 16-06-2022
Obeticholic acid *Ocaliva*	**Physicians:** hepatologists, gastroenterologists, internists and immunologists	New contraindication in the treatment of primary billiary cholangitis in patients with decompensated liver cirrhosis or with a history of hepatic decompensation 09-06-2022

Compiled by Patrícia Catalão