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Safe vaccination:
COVID-19 vaccine pharmacovigilance

The use of novel vaccine technological developments for COVID-19 may potentially be associated with the occurrence of **unexpected** adverse events which may be **complex** and **difficult to recognise**.

High safety standard expectations in COVID-19 immunisation mean there is a need for fast and efficient detection and investigation of any adverse event supervening after massive population administration of one or more vaccine doses. Good work coordination and use of the best technologies and methodologies available will be essential.

Post-marketing monitoring of new vaccines depends on a combination of passive and active surveillance so all stakeholders can be engaged in an expeditious response. Traditional **passive vigilance** systems are based on assessment of immunisation adverse reaction reports from spontaneous report databases. This initial assessment is followed by clinical validation of causal nexus, which will take factors into account such as type of vaccine used and interactions with other vaccines or other medicinal products, vaccinee-related factors (age, gender, comorbidities), as well as administration-related factors (needle, syringe, site and route of administration). In contrast, **active vigilance** systems follow up a representative sample of immunised subjects for adverse events.

The Portuguese National Immunisation Plan, which was set up in 1965, is one of the most successful health strategies in this country and has contributed to the eradication of vaccine preventable diseases such as polio.

However, just like any other medicinal products, vaccines are not risk free, even though the occurrence of serious adverse events is indeed rare.

Cooperation among all National Health Service stakeholders, including healthcare services and professionals, MA holders, regulators and academia, is crucial to ensure population confidence in future COVID-19 vaccines through a robust system of safety signal detection and assessment.

Real-time sharing of information on specific post-immunisation adverse events collected from various spontaneous report databases and clinical records will allow for assessment of adverse reactions, especially those which are rare and serious, as well as for early detection of safety signals and timely implementation of appropriate measures. Timely communication of relevant and reliable data is equally essential for the prevention of dissemination of false or misleading information.

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Effectiveness of COVID-19 vaccines in helping to tackle the current pandemic will greatly depend on the extent of vaccination coverage achieved in the population. Any safety concerns can have a significant impact and lead to vaccination hesitancy with subsequent compromise of immunisation rates.

Infarmed, in cooperation with other National Health Service organisations and professionals and with citizens, will ensure continuing and reinforced vaccine benefit-risk assessment. Intensive focus will be set on detecting serious and delayed reactions which need longer term safety studies and broader population samples.

Reporting any suspected vaccine adverse reactions is therefore paramount. As a minimum, the following data should be provided: vaccinee's name initials, age and gender, vaccine trademark name and batch.

Help us to know the safety profile of future COVID-19 vaccines and to promote public confidence in the immunisation plan.

Adriana Gamboa

The Portuguese National Pharmacovigilance System is counting on healthcare professionals to keep reporting any ADRs that may occur with medicinal products used in the treatment of COVID-19 – see infografic (in Portuguese)

What do they mean?

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

Leuprorelin:
new measures to prevent medication errors

Quick Read
The probability of medication errors with devices for administration of leuprorelin increases with the number of steps required for the product's reconstitution and administration. These procedures should be undertaken by professionals who are familiarised with them.

Leuprorelin is a gonadotropin-releasing hormone (GnRH) agonist. Medicinal products containing leuprorelin are administered subcutaneously or intramuscularly as prolonged release formulations every 1, 3 or 6 months. They are used for the treatment of prostate cancer, breast cancer, endometriosis, uterine myomas and precocious puberty. In Portugal, the products Eligard® and Lutrate Depot® are authorised with an indication for the treatment of prostate cancer.

In the last few years several reports of medication errors with leuprorelin-containing medicinal products have been received. They are mostly related to the complex process of preparation/reconstitution that precedes actual administration to the patient, and they have resulted in subtherapeutic doses being administered which could be associated with lack of efficacy. Although the benefits of leuprorelin are well established for the approved indications, its effectiveness may be compromised should the patients not receive the intended dose. This issue has prompted a Europe-wide safety review led by the EMA's Pharmacovigilance Risk Assessment Committee (PRAC).

The reconstitution process for Eligard® is especially complex, with more preparation steps. It was associated with most of the medication error reports. Various risk minimisation measures have been implemented in the last few years for this product, including Educational Materials, Dear Healthcare Professional Communications (DHPC), changes to the syringe plunger and introduction of a new safety syringe. However, reports of medication errors have continued to come in.

The safety review above included data from the European database EudraVigilance, from scientific literature, as well as from the MA Holders of products containing depot leuprorelin. It was concluded that the potential for medication errors increases with the number of steps required for the product's reconstitution and administration. **PRAC** thus considered that the most effective measure to reduce medication errors with **Eligard®** was the development of a **new device** with less product reconstitution complexity. This obligation was included as a condition for marketing authorisation. For **Lutrate depot®**, on the other hand, **changes to packaging** were decided in order to facilitate access of healthcare professionals to the preparation instructions. The latter in turn are to be made clearer.

Additionally, **new risk minimisation measures** are going to be introduced, including **SPC and PIL updates**, in order to further highlight the importance of compliance with reconstitution and administration instructions, as well as to recommend preparation and administration by healthcare professionals who are familiar with the procedures.

Whenever a medication error is suspected or confirmed, patients should be monitored adequately.

Sílvia Duarte

Educational Materials published in the Infomed product information webpage

Click on the links.

INN Medicinal product	Target	Materials? Online publication date
Artenimol + Piperaquine Eurartesim	**Physicians:** infectious diseases and tropical medicine specialists, other potential prescribers	Prescription checklist Information guide 5-09-2020
Lenalidomide Revlimid	**Physicians:** haematologists **Pharmacists:** pharmaceutical services at organisations where this medicinal product is prescribed and dispensed	Safety information for healthcare professionals Pregnancy report form ADR report form
	Patients	Booklet for women of child-bearing potential Booklet for women of non-child-bearing potential Booklet for male patients 19-09-2020
Propranolol Hemangiol	**Patients**	Caregiver guide 30-09-2020
Upadacitinib Rinvoq	**Physicians:** rheumatologists and internists	Healthcare professional guide
	Patients	Alert card 21-09-2020

Compiled by Patrícia Catalão