Pharmacovigilance considerations of COVID-19 vaccines

Μαρία Πολυδώρου – Γιώργος Χρηστιάς

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EMA guidance

EMA/544966/2020

Consideration on core requirements for RMPs of COVID-19 vaccines

coreRMP19 guidance

30 October 2020
EMA/174312/2020
Data Analytics and Methods Taskforce

Detailed guidance on ICSRs in the context of COVID-19

Validity and coding of ICSRs

EMA/333964/2020

Pharmacovigilance Plan of the EU Regulatory Network for COVID-19 Vaccines

1 9 April 2013
2 EMA/109434/2013

3 Guideline on good pharmacovigilance practices (GVP)

4 P I: Vaccines for prophylaxis against infectious diseases – Definitions for
5 inclusion in GVP Annex I Rev 2

World Health Organization

COVID-19 Vaccines: Safety Surveillance Manual

Module: Responding to adverse events following COVID-19 immunization (AEFIs)

Vaccine pharmacovigilance

- **The science and activities relating to the detection, assessment, understanding and communication of adverse events following immunisation and other vaccine- or immunisation-related issues, and to the prevention of untoward effects of the vaccine or immunisation**
- In this definition, immunisation means the usage of a vaccine for the purpose of immunising individuals which in the EU is preferably referred to as vaccination (in the report of CIOMS/WHO Working Group on Vaccine Pharmacovigilance the terms immunisation and vaccination are used interchangeably.
- Usage includes all processes that occur after a vaccine product has left the manufacturing/packaging site, i.e. handling, prescribing and administration of the vaccine.
- **An adverse event following immunisation (AEFI) is any untoward medical occurrence which follows immunisation and which does not necessarily have a causal relationship with the usage of the vaccine**. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease. While this AEFI definition is compatible with the definition of adverse event applied in the EU, the AEFI definition is not needed to describe pharmacovigilance for vaccines in the EU. However, EU guidance on pharmacovigilance for vaccines makes use of the terminology suggested by CIOMS regarding possible causes of adverse events, turning them into suspected adverse reactions. A coincidental event is an AEFI that is caused by something other than the vaccine product, immunisation error or immunisation anxiety.

Cause-specific definitions of AEFI and its implications in the COVID-19 context

- *Vaccine product-related reaction:* An AEFI that is caused or precipitated by a vaccine due to one or more of the inherent properties of the vaccine product.
- *Vaccine quality defect-related reaction:* An AEFI that is caused or precipitated by a vaccine that is due to one or more quality defects of the vaccine product including its administration device as provided by the manufacturer.
- *Immunization error-related reaction:* An AEFI that is caused by inappropriate vaccine handling, prescribing or administration and thus by its nature is preventable.
- *Immunization anxiety-related reaction:* An AEFI arising from anxiety about the immunization.
- *Coincidental event:* An AEFI that is caused by something other than the vaccine product, immunization error or immunization anxiety.

Routine pharmacovigilance activities

- **Signal detection** methodological considerations and requirements are described in GVP Module IX, which should be read in conjunction with GVP P.I. Signal management; further considerations related to the description in the RMP include:
  - Data sources for signal detection should be specified
  - Routine signal detection methods and practices may be insufficient to efficiently screen the expected high volumes of ADR reports also taking into consideration the situation of a mass vaccination campaign
  - Leveraging the infrastructure and results of global efforts to define lists of AESI and background analyses should be part of MAHs' signal detection activities

Routine pharmacovigilance activities

ICSR reporting requirements are described in GVP Module VI, which should be read in conjunction with GVP P.I. and Detailed guidance on ICSRs in the context of COVID-19 Data sources for signal detection

- **Specific follow-up questionnaire(s)**
- **Summary Monthly Safety Reports**
- **Traceability**

Additional pharmacovigilance activities

- Continuation of safety surveillance from **ongoing clinical trials** should be a priority and included as additional pharmacovigilance activities.
- Considerations should be given whether routine activities will be sufficient to provide adequate data to further characterise important identified and potential risks and investigate missing information or if, in addition to ongoing or planned clinical trials, an observational **post-authorisation safety study (PASS)** is required
- **Effectiveness studies** should be included in this section of the RMP.

EMA: Informing the public of suspected and confirmed side effects

- Committed to **transparency** and keeping patients and healthcare professionals fully **informed** to make their choices, for example:
  - Public access to **EudraVigilance** in place since 2012 through www.adrreports.eu
    - Publication of data from reports of suspected side effects to vaccines will be **updated weekly**
  - Regular public COVID-19 vaccines **safety updates**
  - Publish **risk management plans (RMPs)** for COVID-19 vaccines
  - Established side effects will be **included in the package leaflet**
- Network of **national medicines agencies** and of **stakeholders** will be strong channels for communication

Collection of exposure data

- A timely availability of aggregated exposure data for each COVID-19 vaccine will be essential for several PV activities including observed-to-expected analyses
- Member states are gathering this data in various manners, for instance by implementing national health data registers to collect information on individual vaccinations. EMA will collect and compile this data from Member States
- An important requirement for the safety monitoring of all biological medicines in the EU (GVP P.II) is the need for product/batch traceability during clinical use. The traceability requirement covers the release by the manufacturer, the entire distribution chain & the actual vaccination

Spontaneous reporting of suspected adverse reactions (1/2)

- The regulatory requirements for collection, data management & submission of individual reports of suspected adverse reactions associated with medicinal products are addressed in GVP Module VI. With respect to vaccines, there are also specific recommendations in GVP P.I
- A single report of a SAE[1] occurring in temporal association with vaccination, especially if event is unexpected or fatal, could have a detrimental impact on vaccination programmes due to perception of unsubstantiated risks or risk amplification
- A single report of a SAE should be processed as a signal only if there is a possible causal association to the vaccine. This requires adequate information on clinical course of event (time to onset, signs/symptoms, results of relevant laboratory/diagnostic tests, evolution, & treatment of event), medical history, vaccination history, co-medication & details of vaccine(s) administered (including brand name, batch number, route of administration & dose)

[1] SAE : Serious Adverse Event

Spontaneous reporting of suspected adverse reactions (2/2)

- EMA has also published detailed guidance on individual case safety reports (ICSRs) in the context of COVID-19, which takes into account the guidance regarding COVID-19 related terms (ref. to updated MedDRA, since v23.0)
- Upon authorisation, COVID-19 vaccines are subject to additional monitoring, which aims at enhancing the reporting of suspected adverse reactions
- Quality & completeness of information in ICSRs[1] are important for any meaningful causality assessment & will be crucial in this context of mass vaccination. Beyond the minimum criteria required for ICSR validation, reports should ideally contain precise information on demographics, vaccine brand, batch number, vaccination/reaction dates, outcome, concomitant drugs etc
- Submission of ICSRs with AESIs[2], or fatal or life-threatening reactions in a shorter timeframe than 15 days should be considered when feasible

[1]ICSR: Individual Case Safety Report / [2]AESI: Adverse Event of Special Interest

EMA COVID-19: reporting suspected side effects of medicines

Help us understand how medicines act in COVID-19

We count on you to continue to report any suspected side effects your patients may experience with medicines they are taking while infected.

Please report all suspected side effects your patients experience while infected, including with medicines intended to treat the disease or pre-existing conditions.

Suspected side effects should be reported even if the medicine is not authorised for use in COVID-19.

For a reminder of how to report to your national authority, please visit the relevant website:
www.adrreports.eu/en/report_side_effect.html

When reporting side effects, healthcare professionals are encouraged to provide information that is as accurate and complete as possible.

When reporting a suspected side effect in a patient, you should tell us:

- ☑ The age and sex of the patient
- ☑ Whether the infection was diagnosed through testing or based on clinical symptoms alone
- ☑ A description of the side effects
- ☑ The name of the medicine (brand name as well as active substance) suspected to have caused the side effects
- ☑ Dose and duration of treatment with the medicine
- ☑ The batch number of medicine (found on the packaging)
- ☑ Any other medicines being taken around the same time, including non-prescription medicines, herbal remedies or contraceptives
- ☑ Any other health conditions your patient may have

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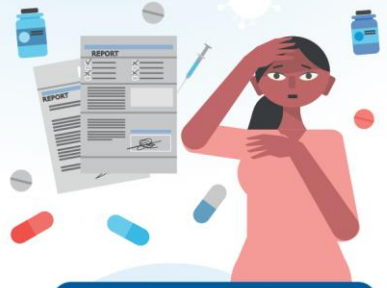
EMA COVID-19: reporting suspected side effects of medicines

Help us understand how medicines act in COVID-19

Report suspected side effects of medicines taken while you have COVID-19 to your doctor, nurse, pharmacist, directly to your national medicines authority or to the manufacturer of your medicine.

Patients with COVID-19 should report all suspected side effects they experience while infected, including with medicines intended to treat the disease or pre-existing conditions.

Suspected side effects should be reported even if the medicine is not authorised for use in COVID-19.



If you are worried about any suspected side effects with your medicine, please speak to your doctor or pharmacist for advice.

To find out how to report to your national authority, please visit the relevant website:
www.adrreports.eu/en/report_side_effect.html

When reporting a suspected side effect, you should provide at least the following information:

- ☑ Your age and sex
- ☑ Whether the infection was diagnosed through testing or based on clinical symptoms alone
- ☑ A description of the side effects
- ☑ The name of the medicine (brand name as well as active substance) suspected to have caused the side effects
- ☑ Dose and duration of treatment with the medicine
- ☑ The batch number of medicine (found on the packaging)
- ☑ Any other medicines being taken around the same time, including non-prescription medicines, herbal remedies or contraceptives
- ☑ Any other health conditions you may have

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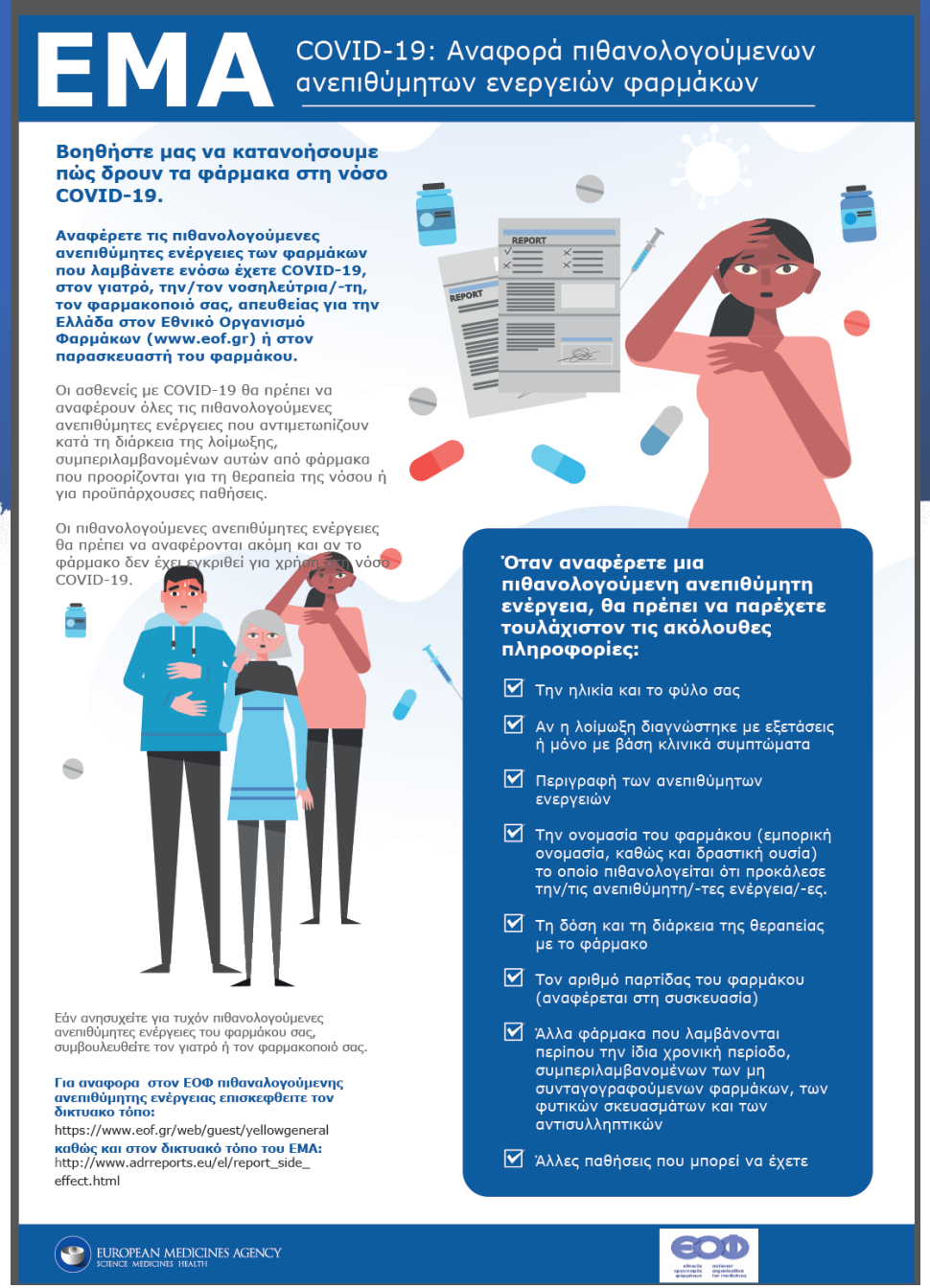

- Οι ασθενείς και οι επαγγελματίες υγείας θα πρέπει να αναφέρουν πιθανολογούμενες ανεπιθύμητες ενέργειες απευθείας στην εθνική τους αρχή διαμέσου των στοιχείων επικοινωνίας που είναι διαθέσιμα εδώ ή στους κατόχους άδειας κυκλοφορίας (φαρμακευτικές εταιρείες) των φαρμάκων, ακολουθώντας τις οδηγίες στο φύλλο οδηγιών για τον ασθενή. Οι ασθενείς μπορούν επίσης να αναφέρουν ανεπιθύμητες ενέργειες στον ιατρό, το νοσηλευτή ή το φαρμακοποιό τους οι οποίοι θα διαβιβάσουν τις πληροφορίες στις ρυθμιστικές αρχές

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23 April 2020
EMA/192437/2020
Media and Public Relations

Αναφορά πιθανολογούμενων ανεπιθύμητων ενεργειών από φάρμακα σε ασθενείς με COVID-19

Ο Ευρωπαϊκός Οργανισμός Φαρμάκων (EMA) και οι αρμόδιες εθνικές αρχές υπενθυμίζουν στους ασθενείς με επιβεβαιωμένη ή εικαζόμενη νόσο από τον κορονοϊό (COVID-19) να αναφέρουν πιθανολογούμενες ανεπιθύμητες ενέργειες (παρενέργειες) που παρουσιάζουν με οποιοδήποτε φάρμακο λαμβάνουν. Αυτό συμπεριλαμβάνει τα φάρμακα για τη αντιμετώπιση της COVID-19, καθώς και τα φάρμακα που λαμβάνουν οι ασθενείς για να αντιμετωπίσουν χρόνιες, προϋπάρχουσες παθήσεις. Συμπεριλαμβάνει επίσης φάρμακα που ενδέχεται να χρησιμοποιούν οι ασθενείς εκτός ενδείξεων για την θεραπεία της COVID-19.

Communication & Transparency (1/2)

- A detailed overview of established EMA transparency practices in relation to medicinal products is provided in Guide to information on human medicines evaluated by EMA. The Agency also publishes descriptive information on suspected adverse reactions reported to EudraVigilance for all medicines authorised in the European Economic Area (EEA)
- In addition to these, the Agency has put in place Exceptional transparency measures in relation to COVID-19 vaccines/treatments approved or under evaluation. These include the publication of full RMPs[1] for these products. The scope of the meeting Highlights from PRAC[2], has also been extended to include information on other safety procedures involving COVID-19 treatments/vaccines, including signals, PSURs[3], PASS[4] & RMPs

[1]RMP: Risk Management Plan / [2]PRAC: Pharmacovigilance Risk Assessment Committee / [3]PSUR: Periodic Safety Update Report / [4]PASS: Post-Authorisation Safety Study

Communication & Transparency (2/2)

- EMA will publish regular PV updates on approved COVID-19 vaccines, with latest information. Format/contents will be developed in collaboration with NCAs[1] through PRAC[2]. Patients', consumers' & healthcare professionals' organisations will be consulted during preparation of some of these communication materials & pre-user testing will be considered
- NCAs may have webpages or websites dedicated to the pandemic, with information on suspected adverse reactions reported for COVID-19 vaccines in their territories

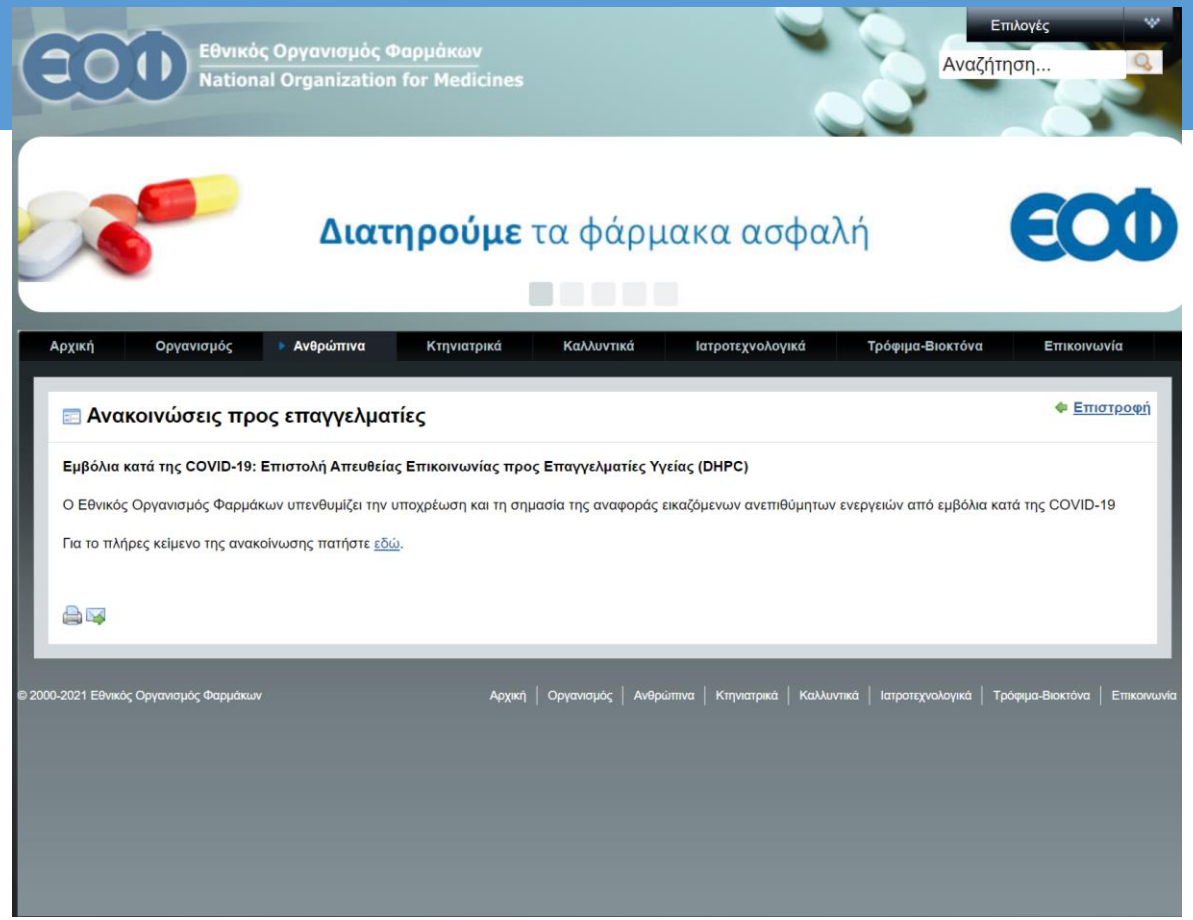
[1]NCA: National Competent Authority / [2]PRAC: Pharmacovigilance Risk Assessment Committee

Capacity building

- In order to continuously achieve a high quality & fit-for-purpose safety monitoring/risk management of COVID-19 vaccines, NCAs[1] & supporting EMA staff should have the necessary expertise at their disposal. To support/reinforce the knowledge of assessors/staff who will be involved in these activities, EMA, in collaboration with NCAs, have set up a dedicated training programme
- The training builds on scientific/regulatory experience gained by EMA & NCA experts through procedures for COVID-19-related products where a PV assessment was performed. The training recordings/presentations will be made available on EU Network Training Centre (EU NTC) Learning Management System platform.

[1]NCA: National Competent Authority

EOF DHPC



- Ο Εθνικός Οργανισμός Φαρμάκων (ΕΟΦ) υπενθυμίζει την υποχρέωση που έχει κάθε επαγγελματίας υγείας να αναφέρει ανεπιθύμητες ενέργειες για τις οποίες υπάρχει η υποψία ότι σχετίζονται με τη χορήγηση εμβολίου κατά της COVID-19.
- Η αναφορά των ανεπιθύμητων ενεργειών θα πρέπει να γίνεται προς τον ΕΟΦ με τη χρήση της φόρμας της κίτρινης κάρτας
  ... ιδιαίτερα η ηλεκτρονική αναφορά μέσω του ιστότοπου του ΕΟΦ **https://www.eof.gr/web/guest/yellowgeneral**
- Επισημαίνεται ότι η αναφορά επέχει θέση υπεύθυνης δήλωσης και ο αναφέρων θα πρέπει να γνωρίζει ότι ενδέχεται να ζητηθούν από τον ΕΟΦ επιπλέον στοιχεία ταυτοποίησης του ιδίου ή/και του εμβολιαζόμενου/ασθενούς, σχετικά με το ιστορικό του, την έκβαση των ανεπιθύμητων ενεργειών ή για την ταυτοποίηση του εμβολιαζόμενου, σε περίπτωση που απαιτηθεί περαιτέρω διερεύνηση για λόγους προάσπισης της δημόσιας υγείας.

EMA preparing guidance to tackle COVID-19 variants

News 10/02/2021

EMA is developing guidance for manufacturers planning changes to the existing COVID-19 vaccines to tackle the new virus variants. In order to consider options for additional testing and development of vaccines that are effective against new virus mutations, the Agency has requested all vaccine developers to investigate if their vaccine can offer protection against any new variants, e.g. those identified in the United Kingdom, South Africa and Brazil, and submit relevant data.

EMA will shortly publish a reflection paper that will set out the data and studies needed to support adaptations of the existing vaccines to current or future mutations of SARS-CoV-2 in the European Union (EU). The questions that will be addressed as part of this reflection paper include:

Which are the options for introducing a new strain into an existing approved vaccine?

What will be the minimal regulatory requirements to demonstrate the quality, safety and efficacy?

Which bridging studies will be required to provide adequate reassurance of a vaccine's efficacy against a new strain, either as first vaccination or as booster

Challenges in pharmacovigilance of COVID-19 vaccines post authorization

- Traceability
- Additional local phv responsibilities requested by HAs
- Duplicate reporting
- PIL availability to vaccine recipients
- Call for AE reporting for vaccine recipients

ΕΛ.Ε.Φ.Ι.

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ΦΑΡΜΑΚΕΥΤΙΚΗΣ
ΙΑΤΡΙΚΗΣ

Μαιάνδρου 23, 115 28 Αθήνα | T 210 7211845 | E info@elefi.gr | W www.elefi.gr