MINUTES of the EL.E.F.I. Pharmacovigilance day
10-05-2019

- **EOF: What's new in Pharmacovigilance**

Eleni Papaioannou, Physician, Adverse Drug Reaction Department, Pharmaceutical Studies and Research Division, National Organization for Medicines

-Regular meetings between EOF- Pharmacovigilance (PV) parties are essential as there is a need for a common language / common interpretative vocabulary in PV.
-The purpose of PV is expanded to support patient safety with wise therapeutical options concerning the use of drugs.
-In PV we progress from data collection to properly informed therapeutic decisions by transforming simple data into knowledge along with the help obtained from the development of bioinformatics

Agni Kapou, Pharmacist, Head of the Adverse Drug Reaction Department, Pharmaceutical Studies and Research Division, National Organization for Medicines

1) AWARENESS CAMPAIGNS:

-Via the European Medicines Agency (EMA)'s and EOF;s awareness campaign, awareness and involvement in PV among patients and health professionals is promoted by way of receiving more qualitative reports.
-The EMA recently (05/2019) launched its campaign in the use of social media.
-Emphasis is given on informing patients on adverse drug reactions (AE) reporting by patients themselves (opening to patients to submit their experience with the use of drugs).

2) NEW PV LEGISLATION OBJECTIVES OF THE YEAR 2012:

- Collection of better safety data, higher quality data (e.g. via awareness campaigns)
- Faster and more efficient evaluation of safety matters
- More efficient regulatory actions
- Clear communication on drug safety

3) CONSULTATION SIGN-UP:

Possibility for public active participation in the open consultations regarding decisions on the approval and safe use of drugs (e.g. broad consultation between scientific disciplines, Healthcare Professionals, female patients and their families and patient organizations on the risk of damage to the fetus by using valproate during pregnancy - 09/2017: EMA public hearing on valproate in pregnancy.

4) New Eudravigilance live and GVP Module IX update (11/2017)

5) ACCESS TO ALL (patients and health professionals) to adverse drug reactions reports by term through a broad reports' database of possible drugs' ADR

6) EOF follows up and adopts to the actions of the EMA as well as to the information occurring from Brexit by:

- Updating its quality system
- Developing electronic applications for the management of its obligations
- Participating in European PV campaigns (SCOPE 2016-2018)
- Releasing a new electronic yellow card
- Undertaking more European evaluation procedures at a local level
- Staffing additional personnel in order to improve processing time

-Management of pediatric safety data, concerning mainly non-reported SmPC data, is a priority for EOF.
-PV and quality defects are of utmost importance and are referred to in the Business Continuity Plan of the EMA.

Sofia Trantza, Pharmacist, Adverse Drug Reaction Department, Pharmaceutical Studies and Research Division, National Organization for Medicines

Next steps, especially during 2019:

- Guidelines for pregnancy-lactation (Q1/Q2 2019) and the geriatric population are expected to be put to public consultation (to be announced).
- Investigation of safety data collection for regulatory purposes through patient records, which can call for legislation regulations.

➢ **"Dear Healthcare Professional" Communication (DHPC)**

Virginia Makrigianni, Head of Pharmacovigilance, Bayer Hellas ABEE

Case study presentation: joint DHPC, multiple MAH coordination:

Case study presentation concerning sending a joint DHPC letter on behalf of a large number of Marketing Authorization Holders (MAH) who had preparations with the same active substance. The objective is to highlight the importance of cooperation between the companies involved as occurs by assigning the role of a coordinator at a company/MAH, which undertakes the representation of all MAHs. The role of the coordinator is to suggest translation, to receive the necessary approvals from the other companies, to communicate with the Authorities and the other MAHs, to adhere to the short approval time-frame, to manage material distribution as well as to submit to the Authorities the necessary proof for successful distribution.

Cleopatra Dipla, Senior PV Officer, Sanofi-Aventis S.A.C.I.

Internal management and involved parties:

This presentation aims to highlight the importance of cooperation between the involved departments as well as the challenges we face in everyday practice: Necessary internal approvals, communication with the Authorities, short time frames as well as cost management, in order to ensure the efficiency of the procedure and by extension the correct and timely information of healthcare professionals.

Xenia Michael, Senior Manager Pharmacovigilance/ LSO GR, CY & MT, Teva Pharmaceuticals

Distribution methods: inhouse vs outsourcing:

Focus was on choosing an external 3rd vector party vendor for the process of material preparation and shipment.
She cited the pros and cons concerning having management performed by an external partner compared to having it done internally either by the PV department or in cooperation with other departments of the company (e.g. medical/sales&marketing), as well as the partner selection criteria (to the extent to which these can be shaped by the GVPs).

Stella Korouli, Drug Safety Manager/ Local Safety Responsible, Roche (Hellas) SA

Digital distribution of DHCPs:

Presenting to the audience how the idea for digital DHPCs distributions came about, what partnerships were needed to design the change and what are the main parameters/requirements for the implementation of such a project. Through this presentation we wish to encourage other pharmaceutical companies towards such a change, but also to achieve the maximum possible commitment on behalf of EOF.

Sofia Trantza, Pharmacist, Adverse Drug Reaction Department, Pharmaceutical Studies and Research Division, National Organization for Medicines

-Conclusions:

- The DHCP letter plays an important role in the communication of safety concerns
- It must be ensured that DHCP letter is received by all the pre-defined recipients
- Collaboration between the parties (EMA, PRAC, CMDh, CHMP, MAH, LHA) is of utmost importance targeting the most effective management possible
- In case of important risk, the time frame is even smaller (2 days)
- Establishing means of evaluation for the information received from Healthcare Professionals also consists a challenge and an area for improvement.

-The possibility of sending "Dear Healthcare Professional" letters digitally or mixed (digital and non-digital) under a strictly defined framework is being examined by EOF, upon request of a pharmaceutical company.

- **Materiovigilance**

Eleni Papaioannou, Physician, Adverse Drug Reaction Department, Pharmaceutical Studies and Research Division, National Organization for Medicines

- Since 2015 there has been a gradual increase in the number of reports on medical devices which end up to EOF.

- The legal framework in Europe is changing.

- Being re-defined:
  - Guidelines (MEDDEV series)
  - CE Marks (Competent Authorities, Notified Bodies)
  - Harmonised standards (EN series)
  - Post-approval safety data (Post-Market surveillance / vigilance)

Maria Katsimpoula, Chemist, Adverse Drug Reaction Department, Pharmaceutical Studies and Research Division, National Organization for Medicines

1. Role of the Medical Advice Manufacturer (M/D) & the Competent Authority

According to the MEDDEV 2.12/1 rev.8 Guidance form (Guidelines on a medical devices vigilance system, January 2013), the investigation is done by the Manufacturer and not by the Competent Authority, and also suspicious M/D must not be sent to the Competent Authority. The role of the Competent Authority includes the evaluation of the investigation of the Manufacturer and of the corrective measures laid down and of course there is the possibility of discussing the issue with the Vigilance- Post Market Surveillance Working Group of MDCG.

2. Report submission by users

Users' reports to EOF concerning M/Ds have been shown to increase. However, only 20% of M/D cases in Greece are reported to EOF via the white card. Healthcare Professionals are asked to report the M/D cases to EOF via the white card. The development of a white card electronic application by EOF aims towards this direction as well.

3. New European database for M/D (EUDAMED):

- Central role in the regulation application
- 7 electronic systems
- Electronic vigilance system and post-market surveillance
  → submission, cross-validation and processing of information

➢ **Lecture**

Georgios Papazisis, *AUTh Associate Professor of Clinical Pharmacology*

Detecting safety signs based on the pharmacodynamic profile: The example of a pharmacovigilance-pharmcodynamic study on the FDA's reports' database (FAERS pharmacovigilance-pharmacodynamic study)

➢ **Pharmacovigilance and personal data protection**

Stella Korouli, Drug Safety Manager/ Local Safety Responsible, Roche (Hellas) SA
Eutuxia Augoklouri, Healthcare Compliance Contact/ Data Privacy Coordinator, Roche (Hellas) SA
Konstantina Pateli, LLM Lawyer, Legal Advisor, Zeincro Hellas S.A.

The Regulation for Personal Data Protection affects:

- Sending "Dear Healthcare Professional" letters, regarding the consent to use the data of Healthcare Professionals.
- The management and obligatory information of patients in PV. As such, PV constitutes a legislative obligation of the Marketing Authorization Holder (MAH) and therefore subject/patient approval is not necessary for the purpose of processing spontaneous reports.
- MAH cooperations. In the case of delegating PV tasks of the MAH to a third-party (e.g. CRO), the requirements for the Processor and the Controller are differentiated. The CRO company is required to assist the MAH in personal data retention.
- The global action of the MAH in third countries (outside E.U.).

➢ **Audits & Inspections in Pharmacovigilance**

Errietta Oikonomou, Head of Pharmacovigilance, Creative Pharma Services

- Legislation (GVP) on audits
  GVP Module I: Pharmacovigilance systems and their quality systems
  GVP Module II: Pharmacovigilance system master file
  GVP Module IV: Pharmacovigilance audits
- Type of audits
  System or process audit
  Internal/External
  Routine audit/For-cause audits (triggered)/Verification audit

Eleonora Sarikou, Head of Pharmacovigilance, GlaxoSmithKline S.A.C.I.

Audits in Pharmacovigilance What is required in order for a pharmacovigilance department to stand ready for receiving an audit?
Reference to preparation, procedures during and at the closing of an audit and finally, reference to the most common audit findings.

Andreas Kourvetaris, Senior Safety Manager, Zeincro Hellas S.A.
His presentation concerned pharmacovigilance audit's design, where the following were discussed: Criteria for assessing non-compliance risk, challenges regarding collaborators-suppliers, course of action for the programming of and the steps for successful audits' completion.

Agni Kapou, Pharmacist, Head of the Adverse Drug Reaction Department, Pharmaceutical Studies and Research Division, National Organization for Medicines

EOF Legislation and good practices

1. Shift in perspective

   -Opportunity to confirm the effectiveness of our work
   -Identification of areas for improvement and taking measures, as needed

2. Objective

   -Determination of MAH compliance with the requirements regarding PV and the need for certain corrective actions
   -Special interest is given to GVP Modules I-IV

3. Main factors determining the inspection program (scheduled or urgent):

   -Previous inspections and results thereof
   -MAH compliance history with PV obligations
   -Marketing Authorization Holder / MAH
   -Product (e.g. of special interest)
   -QPPV change

4. Main inspection points

   -Maintaining and Updating the PSMF
   -QPPV and supervision
   -Quality system and audits
   -Individual case reporting management
   -Brand management
   -Continuous safety evaluation
   -Compliance with obligations towards the Authorities

➢ **Adverse event reporting & awareness campaigns on Pharmacovigilance**

Eleni Papaioannou, Physician, Adverse Drug Reaction Department, Pharmaceutical Studies and Research Division, National Organization for Medicines

Adverse Events Reporting:

1. Adverse Events (A.E.) Reporting
   The electronic application of the yellow card is available from 11/2017.

2. What do we report?
- Obligatory information:
  Suspect drug
  A.E. description
  Patient information (e.g. age, weight, sex)
  Reporter information
- Important Information:
  Dose & suspect drug indication & dates of treatment
  A.E. Start & End dates
  A.E. outcome
  Other drugs received during the last 3 months prior to A.E. initiation
- Additional Information:
  Relevant Medical history
  Laboratory Results

3. SCOPE: Strengthening Collaborations for Operating Pharmacovigilance in Europe
   3-Year project (11/2013-11/2016) funded by the European Committee and collecting information on the way the Authorities implement PV functions (available reports at SCOPE's site)

Awareness campaigns on Pharmacovigilance:

1. Conclusions of the Pan-European campaign

   -Participation of 21 competent authorities
   -13% increase in reports (1,056 reports) within the week of the pan-European campaign
   -the message reached 2,562 individuals
   -337,781 individuals saw the graphics
   -22,584 likes, clicks, retweets & shares on Twitter, Facebook, LinkedIn & YouTube
   -all participants concluded that it was worth it
   -88% would support a new campaign anew

2. EOF's public awareness campaigns on PV in the respective years resulted in:

- 350 A.E. reports in 2016
- 525 A.E. reports in 2017
- 661 A.E. reports in 2018

3. The main source of A.E. reports are physicians, followed by patients. Other Healthcare Professional categories (e.g. Pharmacists) contribute little to promoting A.E. reports Sub-reporting by physicians is observed mainly (not only) due to:

- Uncertain causality
- Concerns regarding breaching patient confidentiality
- Concerns on legal responsibilities
- Guilt
- Failure to recognize the A.E.
- A.E. that is already known

4. Conclusions from international studies lead to the following:

- Positive Healthcare Professional behavior
- Low level of knowledge concerning PV
- Healthcare Professionals usually prefer an online A.E. reporting tool & seek some sort of feedback upon A.E. reporting

5. In general there is a lack of...

- Information
- Good report forms
- Routine
- Reporting culture
- Motivation

(Time pressure forces physicians to prioritize patient care instead of "paperwork")

Patients prefer not to fill in the yellow card, but usually exchange information on A.E. mainly via social media.

All the representatives of the organizations participating in the discussion {Head of the ELEANA Patients' Association, Mrs.Ath.Pappa, Dr. Eleni Papaioannou - PV Department, EOF, Head of the Panhellenic Association of Hospital Pharmacists (PEFNI) Mrs. D.Makridaki and the Head of the Panhellenic Pharmacists Association (PEF) Mr.N.Coleman} agreed that a change in mentality and a continuous update of patients and Healthcare Professionals is necessary, concerning reporting adverse events, which helps patients on a wide scale and protects public health