EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Additional monitoring of medicines and direct patient reporting – impact on the package leaflet

EMA Human Scientific Committees' Working Party with Patients' and Consumers' Organisations (PCWP) - 30th November 2011

Deadline for comments: 20th December 2011

Ana Sempere
Product Information Quality Section/Medical Information Sector

Implementation of the PhV legislation
Impact on the package leaflet

- Introduction
- Draft proposals
  - Black symbol and explanatory sentence for additional monitoring
  - Standardised text to encourage the reporting of suspected adverse reactions
- Next steps

Introduction

- There are certain aspects of the implementation of the new pharmacovigilance (PhV) legislation, which have an impact on the product information:
  - **Additional monitoring of medicines:** Black symbol and standardised explanatory sentence to be included in the summary of the product characteristics (SmPC) and in the package leaflet (PL) for medicinal products subject to additional monitoring.
  - **Direct patient reporting:** Standardised text to encourage adverse reactions reporting to be included in the summary of the product characteristics (SmPC) and in the package leaflet (PL).

Introduction

- The Working Group on the Quality Review of Documents (QRD), together with the Medical Information Sector, has worked on the **draft proposals** to be implemented in the product information.
- Development of the draft proposals:
  - Compilation of information about the pharmacovigilance activities currently in place at national level through a questionnaire.
  - The information provided by the Member States has been used to help setting up the principles to be used as the common basis to draft the proposals.
  - First draft has been agreed in November 2011.
- Final proposal to be provided to the Product Risk Assessment Committee (PRAC) after further internal and external consultation.

Black symbol and explanatory sentence on additional monitoring

Legal scope

'For medicinal products included in that list, the summary of product characteristics and the package leaflet shall include the statement **"This medicinal product is subject to additional monitoring".** That statement shall be preceded by a **black symbol** which shall be selected by the Commission following a recommendation of the PRAC by 2 January 2012, **and shall be followed by an appropriate standardised explanatory sentence'**

Draft proposal

Draft proposal to cover the following aspects:

- Selection of a **black symbol**.
- **Location** within the product information of the symbol + “This medicinal product is subject to additional monitoring” + the standardised explanatory sentence.
- **Definition of the standardised explanatory sentence**; which should follow the statement “This medicinal product is subject to additional monitoring”.

Black symbol
Information provided by Member States

Member States have provided the following information on:

- Symbols **already in use** at national level to identify pharmacovigilance activities.
- Established **symbols** used on the labelling of medicines approved nationally for other purposes than pharmacovigilance activities, which need to be considered **to avoid any risk of confusion**.
- **Alternative symbols** which could be developed to identify the products under additional monitoring.

Black symbol
Information provided by Member States

Current symbols used for PhV activities at national level:

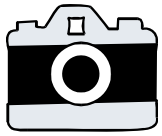
- Two symbols are currently being used in Spain () and United Kingdom (▼).
  - Triangular shape but different position and colours.
- Documents where the symbols appear displayed
  - Advertising material.
  - SmPCs to be distributed or used by healthcare professionals, as part of publications and/or websites, including the Agency's websites.
- Measurements and location
  - Set measurement criteria to ensure the prominence of the symbol.
  - Always displayed next to the name of the medicine.

Black symbol
Information provided by Member States

- List of examples of **established symbols** used for other purposes than PhV activities on the labelling of medicines approved nationally, which need to be considered to avoid risk of confusion:
  - **Triangle**:
    - Triangle with an exclamation mark = warning for driving and using machines (AT)
    - Black empty triangle symbol = moderate influence on driving ability (SL)
    - Red full triangle symbol = major influence on driving ability (SL)
    - Red triangle = products which may reduce the ability to drive or operate machines. In use since 1983. Known and recognised by a majority of the population (DK).
  - **Circle**:
    - Black empty circle = product subject to medical prescription (ES).
    - Black full/half empty circle = psychotropic substances (ES).
  - **Asterisk** = product to be stored under refrigeration (ES).

Black symbol
Information provided by Member States

- List of **alternative symbols proposed** by the Member States:
  - Magnifying glass
  - Eye
  - Exclamation mark (in a box or in a triangle)
  - Camera symbol
  - Black triangle
    - With a magnifying glass inside



Black symbol
Draft proposal

Provision of all the information stated by the Member States:

- General information
  - Symbols currently in place to identify products under intensive surveillance.
  - Other established symbols, which may pose a risk of confusion.
  - Alternative proposed symbols provided by the Member States.
- Specific information:
  - If a symbol currently in place is to be selected by the PRAC, the Member States would not object to the use of the UK black inverted triangle.
  - If an alternative symbol is to be developed, the Member States would not object to the use of a magnifying glass.

Explanatory sentence
Points to consider

- Explanatory sentence should be **non-alarmist** and should help to increase **transparency** about the PhV activities.
- National websites (ES/UK) emphasise three aspects within the information published about intensive surveillance:
  - **Criteria** that the product should meet to be included in the list of intensive surveillance.
  - **Reasons** for performing the additional monitoring:
    - To further establish the safety profile of the medicines, once the product is used at a larger scale, and to also ensure the rapid identification of previously unrecognised side effects.
  - **Reporting of adverse reactions** is also encouraged to help establishing the safety profile of the medicinal product.

Explanatory sentence
Points to consider

- The development of the explanatory sentence runs in parallel with the discussions held by other groups on other related PhV activities:
  - **Criteria**: already set by the PhV legislation for new active substance and biological medicines approved after 1st January 2011.
  - However, the PhV legislation also states that other medicines may be included in the list of additional monitoring after consultation with the PRAC, hence, **further criteria needs to be defined** for these cases (e.g. medicines with post-authorisation **efficacy** studies as a condition).
- Based on the above the proposed explanatory sentence is rather **general** and does not specify neither the criteria nor any safety or efficacy aspects of the information to be gathered. However, this might need to be revisited at a later stage once the criteria is fully defined.

Location and explanatory sentence
Draft proposal (package leaflet)

Package leaflet: Information for the <patient> <user>

<{Black symbol}> {(Invented) name strength pharmaceutical form}
{Active substance(s)}

<{Black symbol} This medicinal product is subject to additional monitoring. This means that this medicine has to be closely monitored to allow for any new information on the medicine to be captured rapidly. You are encouraged to report any side effects you may get. See section 4.>

Encouragement of the reporting of suspected adverse reactions

Legal scope

A standardised text shall be included in the SmPC and package leaflet of all medicines, expressly asking to communicate any suspected adverse reaction.

- **SmPC:** It should expressly ask **healthcare professionals** to communicate any suspected adverse reactions, according to the national spontaneous system.
- **PL**: It should expressly ask **patients** to communicate any suspected adverse reactions to his/her doctor, pharmacist, healthcare professional or directly to the national spontaneous reporting system. The different **ways of reporting available*** (electronic reporting, postal address and/or others) should also be specified.
  - [*Such alternative reporting formats in addition to web-based formats should be available to facilitate the patient reporting.]

Draft proposal

Draft proposal to cover the following aspects :

- **Location** of the standard text within the product information.
- Definition of the **standardised text** to be included in SmPC and package leaflet.

Standard text
Points to consider

Based on the information provided by the Member States, there seems to be three points to consider when drafting the statements for the package leaflet:

- To **specify** that some patients may have side effects when taking the product.
- To **refer the patients to the doctor, pharmacist or healthcare professional**, if experiencing any side effects.
- To **encourage the reporting** of side effects, including the different ways or reporting (web based formats + alternative formats).

Location and proposed standard text
Draft proposal (package leaflet)

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

<Additional side effects in children <and adolescents>>

If you get any side effects, talk to your <doctor> <or> <,> <pharmacist> <or nurse>. This includes any possible side effects not listed in this leaflet. You can also report any side effects directly to the national reporting system via <the internet at 'national reporting system website>; alternatively you can report via <alternative reporting systems to be defined at national level>. By reporting side effects you can help to make sure that medicines remain as safe as possible.

Next steps

Next steps

- December 2011 – Consultation with the QRD group, healthcare professionals and patients/consumers.
- January 2012 – Consultation with the pharmacovigilance project team.
- February 2012 – Status update to healthcare professionals and patients/consumers at the Joint meeting.
- March 2012 - Status update to the QRD group.
- April 2012 - Short external consultation on the statements (1 month).
- May 2012 - To finalise the proposals with the QRD group.

Any questions?