EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Impact on the product information of the additional monitoring of medicines

5th Stakeholders forum on the implementation of the new pharmacovigilance legislation

An agency of the European Union

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  - Mandatory scope.
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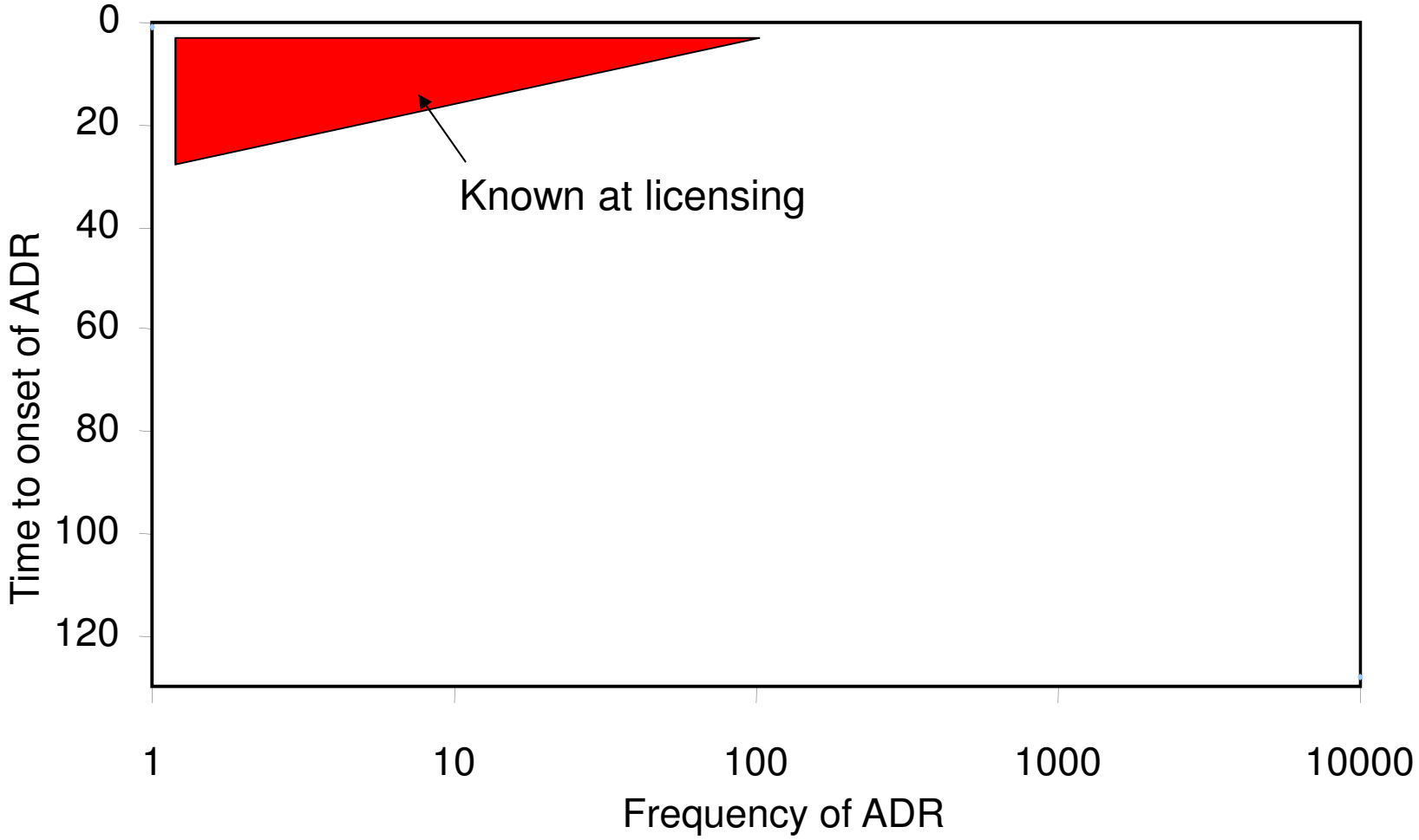
Background – the need for monitoring

- Limitations in pre-clinical toxicology and phase 1-3 clinical trials
  - Lack of experience on adverse effects
  - Exposure in small numbers of people
  - Short duration
  - Unlikely to detect ADRs:
    - Less frequent than 1/1500
    - With long latency
  - Lack of experience in special patient groups
    - Elderly, children, pregnancy, multiple disease, polypharmacy

Background – the need for monitoring



Background – the law (Reg 726/2004 whereas clause 17)

… some medicinal products are authorised subject to additional monitoring. This includes all medicinal products with a new active substance and biological medicinal products, including biosimilars, which are priorities for pharmacovigilance. Competent authorities may also require additional monitoring for specific medicinal products that are subject to the obligation to conduct a post-authorisation safety study or to conditions or restrictions with regard to the safe and effective use of the medicinal product. Medicinal products subject to additional monitoring should be identified as such by a black symbol and an appropriate standardised explanatory sentence in the summary of product characteristics and in the package leaflet. A publicly available list of medicinal products subject to additional monitoring should be kept up to date by the European Medicines Agency ……

Mandatory Scope

- Article 23(1) of Regulation (EC) No 726/2004

The list shall include the names and active substances of

- (a) medicinal products authorised in the Union that contain a new active substance which, on 1 January 2011, was not contained in any medicinal product authorised in the Union;
- (b) any biological medicinal product not covered by point (a) that was authorised after 1 January 2011.

Optional Scope

Can include at the request of the Commission or a National Competent Authority, and following consultation with PRAC, MAs where

- granted with conditions
- measures in the RMP, such as conducting Post Authorisation or Efficacy Studies
- Concerns over the adequacy of the PV system
- Exceptional circumstances

Due consideration should be given to the inclusion of generics

Creating & maintaining the list

- For mandatory scope products the EMA and NCAs will be responsible for automatic inclusion
- EMA will update CAPs within 15 days of grant
- RMS or NCA shall inform EMA within 15 days of grant for MR, DCP and national licenses
- For optional scope products CHMP, RMS, NCA shall consult PRAC before inclusion on the list
- PRAC recommendation will be sent to relevant body
- Final decision will be incorporated within 15 days

Creating & maintaining the list

- products will normally remain on the list for 5 years
- for mandatory scope products removal will be tied to the renewal procedure
- for optional scope products review will be tied to fulfillment of obligations i.e. RMP measures, PASS etc
- removal should apply to all generics unless there are different conditions
- extensions will take into account the completion of milestones, or as considered necessary
- products removed from the list can be added again

Black symbol and explanatory statement

- Products on the list shall state on the SmPC and PIL

  "This medicinal product is subject to additional monitoring"

- This shall be preceded by a black symbol, approved by the EC following PRAC recommendation
- This shall be followed by a standardised explanatory statement
- SmPCs shall be updated by way of variation to include/remove the symbol and statement

Black symbol and explanatory statement

- The Quality Review of Documents (QRD) group has worked on a proposal to be included in the product information (SmPC and PL) regarding:
  - Black symbol and its location.
  - Location and wording of the explanatory statement.
- As part of the preparatory work, the draft proposal has already undergone a consultation with:
  - National Competent Authorities.
  - Patients, consumers and healthcare professionals organisations.
  - Pharmaceutical industry associations.
- The proposed QRD human annotated template shall be published for a one month consultation on the EMA website (likely in June 2012).
- The final proposal and all the views expressed during the consultations, will be provided to PRAC for their consideration when drafting the recommendation on the black symbol for the Commission.

Transparency

- List to be published on EMA web portal
- Relevant products to be published on NCA web portals
- Links to product information and summary RMP to be established
- NCAs to have appropriate communications in place to inform patients and healthcare professionals
- NCAs to encourage reporting of ADRs

Obligations - EMA

- For the inclusion of CAPs on the list
- For the automatic removal of products unless there is a recommendation to extend
- For publishing the list and product information
- Co-coordinating activities regarding maintenance of the list

Obligations - NCAs

- Informing EMA which mandatory scope products should be included on the list
- Identify optional scope products for PRAC recommendation
- Recommend time period for inclusion on the list
- Recommend removal or extension
- Publish relevant products on web portals with product information and summary RMP
- Communicate and encourage reporting

Obligations - PRAC

- Make recommendations for optional scope products inclusion on the list
- Recommend extension or removal from the list
- Recommend black symbol for identifying products on the list
- Recommend explanatory wording for PIL and SmPC

Obligations - MAH

- Include black symbol and approved wording on PIL and SmPC
- Include information on additional monitoring status in any material distributed to healthcare professionals or patients
- Encourage reporting of ADRs
- Submit relevant variations to maintain marketing authorisation as applicable

Processes

- GVP module X to be released in phase 2, June 2012
- Black symbol and wording consultation June 2012
- Development of list up to Sept 2012
- Consideration at PRAC Sept 2012
- PRAC recommendations considered by EC, CHMP etc
- Adoption and publication of list
- Procedure for variations and timescales

Conclusions

- Additional monitoring is a key public health deliverable of the new legislation
- Signal management activities must be appropriate
- GVP Module X makes clear the responsibilities
- Optional scope should be proportionate to risk
- Still unanswered questions, next few months should provide clarity
- Transparency and communications are key to delivering success
- Feedback welcomed

Thank you

Questions?