Medication-errors workshop

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European Medicines Agency, London, United Kingdom

CHMP Position Paper on Medication Errors in the Context of Benefit/Risk

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Committee for Medicinal Products for Human Use (CHMP)

Position paper on potential medication errors in the context of benefit risk balance and risk minimisation measures

Draft

Focus on medication errors caused by confusion of a newly introduced medicinal product with an existing one, similar in active substance but different in some aspects.

Adoption by CHMP for release for consultation	24 May 2012
Start of public consultation	1 June 2012
End of consultation (deadline for comments)	30 November 2012
Adoption by CHMP	<DD Month YYYY>
Date of coming into effect	<DD Month YYYY>

Comments should be provided using this template. The completed comments form should be sent to thomas.goedecke@ema.europa.eu.

Trigger

Centralised hybrid application for MA

- concentrate for solution for infusion, to be diluted
- higher strength than the originator and other generics

Clinical data

- **Major concerns regarding safety**
  - ⇨ potential for medication errors (confusion)
  - Risk minimisation measures such as
    - PI: very clear labelling and instructions for dilution
    - RMP: specific educational activities (user testing for Health Care Professionals, DHPC letter)
- B/R discussion prompted the CHMP to draft a focussed position paper on medication errors

Introduction

- **Changes** on use of a product in clinical practice arise from:
  - Variations, line extensions, extensions of indications
  - different formulation, presentation, route of administration, strength or composition, different indication or target population
  - new products referring to but deviating from authorised product on the market
- **All such applications** should be compared to existing products as regards potential medication errors
- **Aim**:
  - raise awareness on **B/R evaluation** of such products
  - discuss measures how to address this risk of medication errors

B/R - Potential benefits

- Additional products as a **valuable expansion** of the therapeutic armamentarium
  - satisfy a well motivated medical need
- On the other hand, such additional products carry an **inherent potential risk of inadequate use** due to confusion
- Drug therapy is generally advocated and performed by **well-trained experienced personnel**
  - based on expert decision for treatment
  - applied according to standardised working procedures (if not taken by the patient him-/herself)

B/R - Potential benefits

Examples of possible benefits:

- Preservatives and/or antioxidants avoided or reduced ⇨ reduced undesirable effects
- Improved (in-use)stability ⇨ reduced undesirable effects
- Facilitations in preparation (e.g. dilution of a concentrate) ⇨ enhanced safety of the pharmacist/HCP, indirect benefit for patients because of reduction of potential preparation errors
- More appropriate concentration giving flexibility (ready to use rather than requiring dilution)
- Different formulations, e.g. liposomal, extended release, ...
- Different indications requiring different dosing
- Use in specific populations, e.g. children, older people, ...

B/R - Evaluation of risks

- **Risk and effects** of medication errors **depend on:**
  - the extent of deviation from the established product,
  - the therapeutic window of the active substance,
  - the severity of adverse effects
  - and the steps taken to avoid any possible confusion
- Certain circumstances impact the **probability of a medication error** ⇨ to take into account:
  - product administered by health care professional or patient?
  - person undergone some kind of special training?
  - product intended for emergency use, prepared in stress situations?
  - product intended for use in children?

B/R - Evaluation of risks

Parameters for evaluation of the B/R ratio:

- Occurrence and/or severity of adverse events
- Loss of efficacy
- Question of narrow therapeutic index drug, to be judged case-by-case on clinical considerations (e.g. cytotoxic drugs)
- Use in particularly vulnerable patient population (e.g. immunocompromised patients, paediatric population, etc.)
- Extent of the possible over- or under-exposure (double strength leading to two times higher dosage)
- Proposals in the RMP to clearly differentiate the products – e.g. vial size, packaging warnings on vials, etc.

Risk minimisation / monitoring

Risk minimisation strategies discussed case-by-case:

Importance of preventive action

- Very clear highlighting in SmPC, PIL and labelling (most important routine risk minimisation)
- Different vial sizes, packaging, names, etc.
- „User testing“ (clear instructions for use, submitted before approval)
- Training to pharmacists/healthcare professionals (approved educational material offered by the MAH, will require a complete EU-RMP to be approved prior to approval)

Risk minimisation / monitoring

Monitoring of effectiveness of risk minimisation measures:

- Routine monitoring of medication errors resulting in adverse reactions (signal detection)
- PSURs in accordance with regular periodicity (every 6 months after authorisation until at least two full years of marketing experience in the EU)
- Shortening of PSUR cycle
- **Effectiveness** of all risk minimisation measures (product information, educational material, user testing) should be **re-evaluated within specifically agreed time-intervals**, e.g. in PSURs, milestones or up-dates of the RMP, etc.

Recommendations

- CHMP particularly accentuates the need for a **critical** assessment of **agents with a narrow therapeutic index or** intended for a **special population**
- Applicant to **justify** such an application by demonstrating a prevailing benefit to **counterbalance** the product-associated increased risk of medication error
- B/R balance based on a comprehensive **case-by-case B/R evaluation**
- Advice for **early meetings with regulatory agencies** when considering to develop and to submit an application involving a product that introduces changes to the already established clinical practice

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Overview of comments received on 'Position paper on potential medication errors in the context of benefit risk balance and risk minimisation measures ' (EMA/274183/2012)

Interested parties (organisations or individuals) that commented on the draft document as released for consultation.

Stakeholder no.	Name of organisation or individual
1.	German Pharmaceutical Industry Association (BPI), Boris Thurisch
2.	Association of the European Self-Medication Industry (AESGP), Helga Blasius
3.	Prescrire, Florence Vandevelde
4.	a.r.c. pharma, Jeanne Ducorroy
5.	NHS Commissioning Board, David Cousins
6.	Gilead Sciences International Limited, Carol Walker
7.	The Guild of Healthcare Pharmacists, Scott Savage
8.	European Industrial Pharmacists Group, Jane Nicholson
9.	European Federation of Pharmaceutical Industries and Associations (EFPIA), Isabelle Clamou
10.	Merck Sharp & Dohme (MSD), Angelika Joos
11.	Mundipharma Research GmbH & Co., Michael Sturm
12.	Health Canada, My-Yen YU

Comments – for discussion

General comments, e.g.

- Definition of medication errors
- Widen the scope to all products before market introduction
  - all products in general? plus OTC products? plus biologicals and vaccines (including traceability issues)?
- More consistent terminology
- Measures in RMPs may come too late

Specific comments on the text, e.g.

- Level of expertise and errors made by health care professionals
- Expand lists of examples
- Clarify the place of user testing
- PSURs questioned as monitoring tools

Thank you for your attention