Risk Management Plans and ways of working with

DHCP letters and aRMM

Direct Healthcare Provider letters and additional risk minimisation activities

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DHCP (Direct Healthcare Professional Communication) definition and purpose

Putting Patients First

A DHPC is a communication by which important safety information is delivered directly to healthcare professionals (HCPs) to inform them of the need to take certain actions or adapt their practices in relation to a medicinal product.

It is intended to

- change healthcare practices, attitudes, decisions and behaviours in relation to the use of products
- support risk minimisation behaviour
- facilitate informed decisions on the rational use of products
- support public confidence in the regulatory system

DHCP background

Proactive Sharing of Risk

European Union (EU) pharmacovigilance (PV) legislations in July 2012 imposed new challenges on pharmaceutical companies to be proactive in minimising risks of adverse drug reactions (ADRs) for all medicinal products throughout their life cycle. A **Risk Management Plan (RMP)** should be created at initial approval and updated through the lifecycle of the product.

The Marketing authorisation holders (MAHs) are required to put risk minimisation measures (RMMs) in place and evaluate their effectiveness to ensure that the **benefits of a medicinal product outweigh the risks** by the greatest achievable margin.

RMMs are useful for consistency in identifying safety issues across generic and non-generic companies. The majority of safety concerns may be adequately addressed by routine RMMs such as pack size restrictions, suitable wordings in patient information leaflets (PILs) and summary of product characteristics (SmPC).

Additional risk minimisation measures (aRMMs) may be necessary to address specific safety issues which may not be practically achieved through routine RMMs alone including potential for medication errors, off-label use and safety concerns in a special population such as the elderly.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5376384/

Does it work as intended ?

Is the information shared?

This study examines the implementation of additional risk minimisation measures (aRMMs) and effectiveness assessment on an EU level with practical examples from the UK. Low response rates to questionnaires indicate a limitation of voluntary feedback. Pharmacists and patients should be actively involved in measuring effectiveness of aRMMs.

Despite detailed legislation, the implementation and determination of effectiveness of aRMMs can be a challenge.

There is the need for additional regulatory guidance in defining the threshold for success in relation to aRMMs.

Pharmaceut Med. 2017; 31(2): 101–112.
Additional Risk Minimisation Measures for Medicinal Products in the European Union:
A Review of the Implementation and Effectiveness of Measures in the United Kingdom by One Marketing Authorisation Holder
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5376384/

Challenges with DHCP cooperation

The preparation of a DHPC involves cooperation between the appropriate Health Authorities (HAs) and other Marketing Authorisation Holders (MAHs) of the same active substance

- Agreement of the information to share - Approval of material
- Agreement of who to share it with – Identify relevant stakeholders
- Distribute – Reaching the right Stakeholder
- Follow up – Have the intended recipients received it

Challenges with the DHCP distribution

Doing the right thing

After implementation of the legislation and trying out the process there were challenges in managing the DHCP letters in Denmark

- Scope of target group
- It was not clear who the Lead MAH should be or how the Lead MAH was defined
- The information sharing was slow since distributed by postal service
- The DHPC letters were not read despite the envelope were marked it contained safety information and that is was shared in collaboration with the authorities

In end 2018 the DKMA decided it would take the responsible for sharing the DHCP letters with the relevant stakeholders

How is it done currently in Denmark

Doing the right thing

- The Danish Medicines Agency distributes the information electronically and directly to the affected health professional's own personal digital mailbox, thus ensuring fast communication of targeted information. The distributed safety information can also be found on the authority website.
- The information is in additionally distributed to relevant hospital departments, to private hospitals and to medicinal products committees and medical societies.
- The information will in future be made available via a link from the relevant medicine's page at pro.medicin.dk.
- To ensure the DHPC notices can be identified easily, the subject field is titled "Safety information from the Danish Medicines Agency – [substance name/medication] and [safety concern]

Managing the information sharing in Denmark

- The Danish Medicines Agency has created a process that is a good, fast and painless procedure where the information to be shared in the usual format. The relief of the administrative burden for the companies is markable.
- There have been a couple of minor challenges after implementation
  - The letters cannot have the company logo so the industry cannot use there company templates, but that is manageable, it is the information in the letters that is key to share.
  - Identification of the Lead MAH can be challenging where it would be a great support to the industry if the DKMA appointed the market leader to drive the local process

Cooperation in trade association to create good conditions for Pharma companies

Why ?

Ensuring the Pharma companies common challenges both locally, European and globally are addressed within the regulatory environment

How ?

- Information sharing is key
- Identifying the administrative burdens
- Finding solutions
- Agreement
- Implementation

Danish Regulatory Affairs group at LIFDK

Strong together

Who ?

A large committee 25 approx. Regulatory Affairs Professionals

Organisation:

Meet four times a year

Leadership: One Chair, Two co-chairs, One consultant from LIFDK secretariat

Four focus groups consisting of group members, meet as needed

- Increasing Dialogue with the Danish Medicines Agency
- Pharmacovigilance legislation focus incl off label use
- Big data
- Digitalization

Annual meetings with the Danish Medicines Agencies and ad hoc dialogue on hot topics

Examples of achievements

Celebrations

What ?

- Sounding board for authorities
- Eliminating national interpretation of EU legislation
- Nordic guidelines on information on packaging material
- Sharing information on falsified medication in a simple way
- Implementation of serialisation (FMD)
- And most recently, now aligned with rest of Europe, implementation of variations at QP release.

What is next ?

The future

- Clinical trials directive implementation
  - One assessment
- Health Technology Assessments
  - Evaluation of data
- Digitalisation
  - Up to date information and organised in a smart way
- Sustainability
  - Releasing the paper burden

Questions and Suggestions

Time to get it clear

Recommended reading:

Quality of Reporting on the Evaluation of Risk Minimization Programs: A Systematic Review.

Russell AM, Morrato EH, Lovett RM, Smith MY.Drug Saf. 2020 May;43(5):427-446. doi: 10.1007/s40264-020-00905-8.
PMID: 32020558 Review.