Principles of risk management

Introduction

No medicine is without risk, and the benefits of a medicine must always be weighed up against its risks. The balance of benefits and risks should be effectively considered and must not be left to chance. Failing to manage the risks may lead to crisis situations with harmful consequences for patient safety and public health.

Risk management strategies

Why do we need a risk management strategy for all new medicines?

The objective of a risk management strategy is to ensure that the balance of benefits and risks of a medicines remains positive over the time when it is used in real world settings. Randomised controlled trials rarely represent real-life experience accurately. Health authorities have increasingly adopted new regulations mandating companies to proactively manage the risk for all their medicines.

Types of risk

Identified risk

There is adequate evidence of an association between the medicine and the risk occurrence.

Potential risk

There is some basis for suspicion of an association between the medicine and the risk occurrence, but it is not confirmed.

Missing information

There is insufficient or no data. Usually additional data or evidence must be collected, using a risk management plan.

Signal detection

This is information arising from one or more sources, which suggests:

- A new, potentially causal relationship between an intervention and an event, **or**
- A new aspect of a known association between an intervention and an event (or set of related events).

The association may either be adverse or beneficial, and is judged to be likely enough to justify verification.

Risk management plan

Risk management is the process of measuring or assessing risk and developing strategies to manage it. Risk management is based on three pillars:

1. **Safety profiles**
   All risks (identified or potential) are compiled, along with a record of what is missing in terms of safety information.
2. **Risk assessment or pharmacovigilance plan**
   This is the plan for further identifying, characterising, and assessing risks. It contains both routine and additional pharmacovigilance activities.
3. **Risk Management Plan (RMP)**
   This is the plan for minimising the risk; it is an integral part of the risk management plan (see below). It contains both routine and additional risk minimisation activities.

Specific regulations in Europe

Pharmacovigilance legislation is evolving continuously. Risk management planning and related activities may differ from one country/region to another in order to be adapted to each country's healthcare infrastructure, regulatory requirements, and legal framework.

However, the ultimate goal of any risk management plan is the same: to ensure patient safety. In the European Union, it is called a Risk Management Plan (RMP). Risk management plans must be submitted by companies at the same time they apply for marketing authorisation in the European Union, although they must be continually updated and revised throughout the medicine's lifetime. Risk management plans can also be requested by the EMA at other times, or whenever there is concern that a risk may be affecting the balance of benefits and risks for a particular medicine.

Medicines under additional monitoring

As part of the pharmacovigilance legislation, the EU maintains a process which stipulates that all medicines that are subject to additional monitoring must carry a black inverted triangle '▼'. This black inverted triangle is always applied to a medicine to indicate that it is under additional monitoring, usually for a five year period. The aim of the symbol is to notify and encourage patients and doctors to report any suspected side effects through their respective national reporting systems, so that any new emerging information can be analysed efficiently. This reporting is essential and complementary to all other pharmacovigilance activities to better understand the risks and safety profile of a new medicine in a real-life setting.

Other medicines can also be placed under additional

monitoring, based on a decision by the EMA's Pharmacovigilance Risk Assessment Committee (PRAC). Data from this reporting will be analysed as part of the continuous assessment of the benefit-risk balance of each medicine during its life-cycle.

Summary

- Risk management is increasingly considered necessary to enhance the benefit-risk balance in real-life. Risk minimisation activities should be proportionate to the risks and should not prevent the use of medicine in appropriately selected patients.
- Risk management can be challenging and expensive, but is necessary and ultimately rewarding and reassuring. It allows trust to be built between companies and stakeholders (transparency).
- Risk management is increasingly becoming a cornerstone for sustainable market availability of complex medicines (for instance, advanced-therapy medicines).
- Risk management is an opportunity to protect patients, avoid crisis, and enhance the knowledge about the products.

[glossary_exclude]Resources

- European Commission (2008). *Volume 9A of the rules governing medicines in the European Union – Guidelines on pharmacovigilance for medicines for human use*. Retrieved 12 July, 2021, from https://ec.europa.eu/health/sites/default/files/files/eudralex/vol-9/pdf/vol9a_09-2008_en.pdf
- European Medicines Administration (2014). *Guideline on good pharmacovigilance practices (GVP) Module V – Risk management systems (Rev 1)*. Retrieved 1 September, 2015, from https://www.ema.europa.eu/en/documents/scientific-guidel

ine/guideline-good-pharmacovigilance-practices-module-v-risk-management-systems-rev1-superseded_en.pdf
- European Parliament (2012). *Regulation (EU) No 1027/2012 amending Regulation (EC) No 726/2004 as regards pharmacovigilance*. Retrieved 12 July, 2021, from https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2012:316:0038:0040:EN:PDF
- European Parliament (2012). *Directive 2012/26/EU amending Directive 2001/83/EC as regards pharmacovigilance.* Retrieved 12 July, 2021, from https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2012:299:0001:0004:EN:PDF[/glossary_exclude]

Attachments

- Presentation: Principles of Risk Management

  Size: 372,303 bytes, Format: .pptx

  A presentation describing the principles of risk management, which can be adapted for own use.

A2-5.18-v1.3