cBG MEB

# Risk Minimisation

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# Outline of the presentation

1) Introduction

2) Risk Minimisation Plan

3) Educational Material

4) Effectiveness of Risk Minimisation Measures

# Introduction

Approval Decision

=

Critical Juncture

**Beginning of lifecycle**

pursue and manage **emerging** knowledge about

**risk–benefit**

**uncertainty**

# Introduction

New pharmacovigilance legislation in 2005

The definition of a Risk Management Plan (Volume 9A):

“A risk management system is a set of pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to medicinal products including the assessment of the effectiveness of those interventions.”

## Introduction

Ultimate goal:

The benefits must outweigh the risks in the largest possible way

- by increasing the benefit
- OR
- by decreasing the risk

# Introduction

- **PART I**
  - ✓ Safety specification
  - ✓ Pharmacovigilance plan

- **PART II**
  - ✓ Evaluation of the risk and the need for risk minimisation
  - ✓ Risk Minimisation Plan

# Evaluating the need for Risk Minimisation

- Determine acceptable level of risk
  - *Varies according to perceived benefit, drug class, risk*
- Define the process (i.e. likely treatment pathways and stakeholders)
  - *This may vary per market*
- Anticipate real world usage
- Identify desired behaviour and potential failure modes
  - *Failure Modes and Effects Analysis (FMEA)*
- Evaluate potential for risk mitigation and identify potential tools
- Rationale for additional activities outside of SPC and PIL
- Describe tools and assessment of them

# Risk Minimisation Plan

- Details the risk minimisation activities
- Should include both routine and additional risk minimisation activities
- A safety concern can have more than one risk minimisation activity
- Should include details how the effectiveness will be assessed

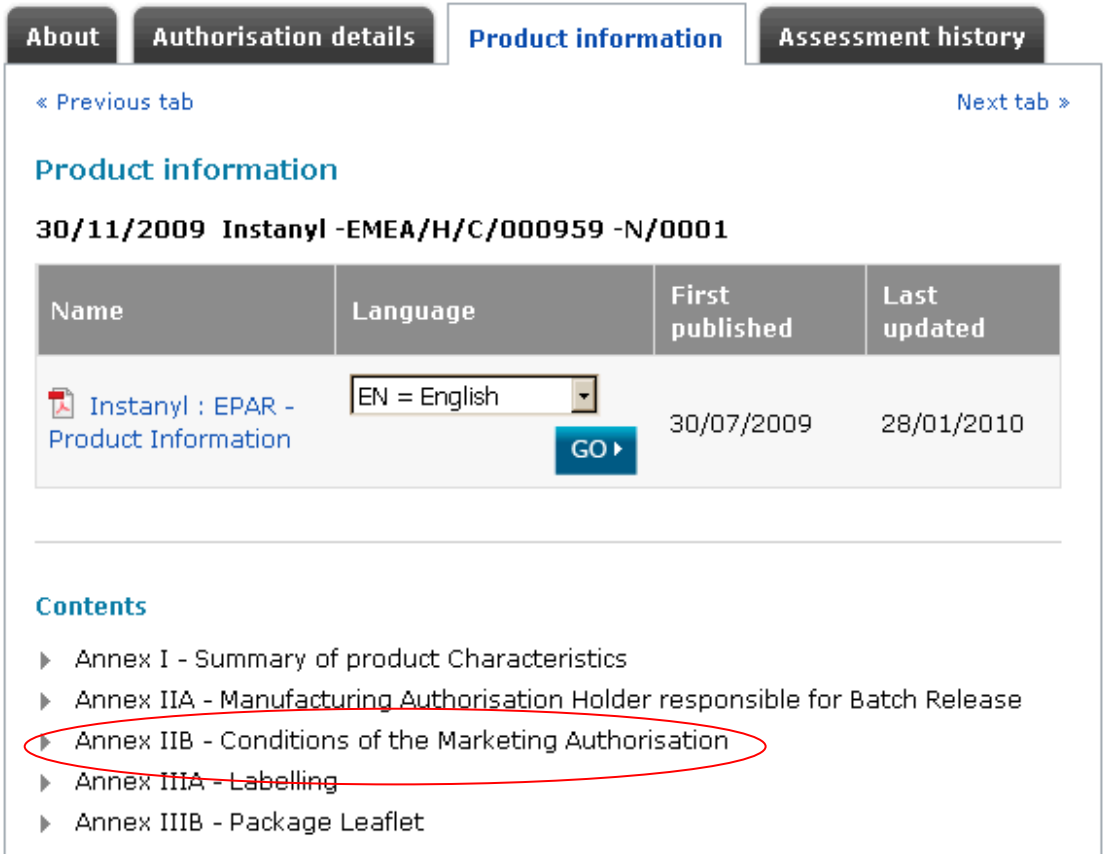
# 4. RISK MINIMISATION PLAN

For each important identified or potential risk for which additional risk minimisation measures are planned, provide the following:

| | |
|---|---|
| Safety concern | |
| *Routine risk minimisation activities* (i.e. product information, labelling and packaging) | *<Short description of what will be put in the SPC, labelling etc to minimise risk e.g. warning in 4.4 that caution should be used in patients with cardiac failure etc>* |
| *Additional risk minimisation activity 1* (e.g. educational material or training programmes for prescribers, pharmacists and patients, restricted access programmes) | *Objective and rationale* |
| | *Proposed actions* |
| | *Criteria to be used to verify the success of proposed risk minimisation activity* |
| | *Proposed review period* |

# Risk Minimisation Plan

- If Risk Minimisation Measures are needed, the requirements are laid down in Annex II (**www.ema.europa.eu**)



# Risk Minimisation Plan

- Routine Risk Minimisation
  - Summary of Product Characteristics (SPC)
  - Patient Information Leaflet (PIL)
  - Legal status of a medicine

- Additional Risk Minimisation
  - Provision of information (educational material)
  - Control at pharmacy level
  - Control of prescription size
  - Restricted access
  - Registries
  - .....

**Additional Risk Minimisation Measures can be complex, and are context dependent.**

# Risk Minimisation Plan

What kind of products need Risk Minimisation?

1) Serious adverse drug reactions
   - E.g. immune system disorders

2) New (difficult) method of administration
   - New patch in neuropathic pain

3) High potential for abuse / off-label use
   - Risk for addiction

# Risk Minimisation Plan

| | | | |
|---|---|---|---|
| Abseamed | Aclasta | Arava | Arcalyst |
| Arepanrix | Atripla | Benefix | Binocrit |
| Celvapan | ChondroCelect | Cimzia | Ecalta |
| Effentora | Efient | Epoetin alfa | Evoltra |
| Exjade | Fablyn | Firmagon | Focetria |
| Gliolan | Humira | Ilaris | Increlex |
| Instanyl | Ionsys | Leflunomide | Lucentis |
| MabCampath | Macugen | Mircena | Multaq |
| Mycamine | NovoSeven | NPlate | Nymusa |
| Onbrez | Opgenra | Optimark | Pandemrix |
| Photobarr | Prevenar | Qutenza | Ranexa |
| Refacto | Remicade | Renvela | Retacrit |
| Revatio | Revlimid | Revolade | RoActemra |
| Scintimun | Siklos | Silapo | Silodyx |
| Simponi | Soliris | Stelara | Tasigna |
| Thalidomide | Thelin | Thymanax | Tysabri |
| Urorec | Valdoxan | Volibris | Zypadhera |



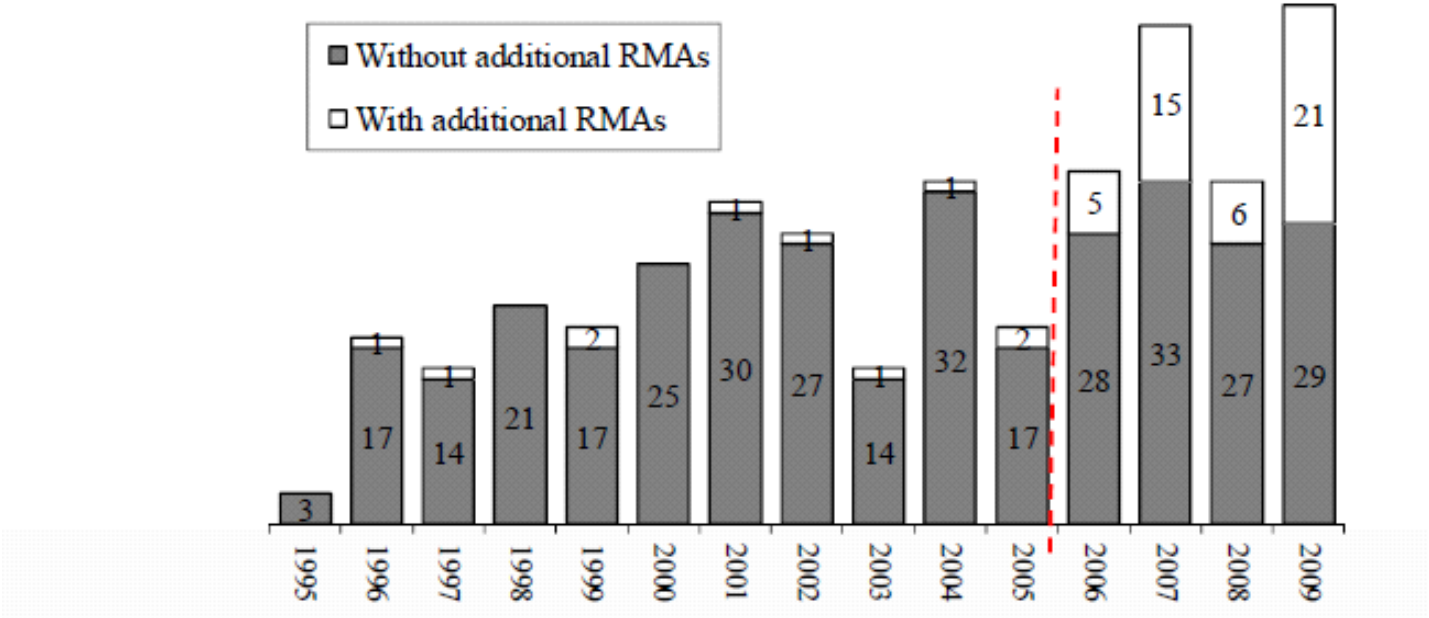

# Risk Minimisation Plan

Centrally authorised new active substances in the period January 1995 till January 2010: **391**

Active substances with additional risk minimisation activities (of the 391): **57**

**15 %**

# CAPs and additional RMA



# Risk Minimisation Plan

| Additional risk minimisation activities | No active substance [n=57] |
|---|---|
| Provision of educational material | 57 |
| * To health care professional | 56 |
| * To the patient | 31 |
| Patient monitoring/screening | 18 |
| Controlled distribution | 9 |
| Pregnancy Prevention activities | 5 |
| Special packaging / extra label | 7 |
| Others | 6 |

# Educational Material

Who needs to be educated?

1. Health Care Professionals
   - Prescribers (specialists, general practitioner)
   - Pharmacist
   - Nursing staff

2. Users
   - Patients
   - Parents, care-givers


Depending on the audience, different ways to communicate

# Educational Material

Advantages of Educational Material?

- Additional focus on the key messages
- Information more accessible than in SPC/PIL (due to pictures, different lay-out)
- As a check-list
- To give detailed instructions on how to administer

# Educational Material

Disadvantages of Educational Material?

- Advertisement in disguise
- Lot of repetition
- Important information can still be missing
- Documents can be very voluminous

# Educational Material

- Readability / language
- Length
- Clear key message
  - SPC contains ALL information
  - Educational Material only the key message(s)
  - Message of reference product and of generic product should be the same
- No advertisement (or suggestion thereof)

*Will it be effective as Risk Minimisation Measure?*

# Risk Minimisation Plan

**Current Challenges in additional risk minimisation activities**

- Additional risk minimisation
  – Guidance not always clear
  – If no additional Risk minimisation activities deemed necessary this should be discussed and supported by evidence
  – Differences in perception between MAHs and Regulators

- National implementation
  – Differences in interpretation between MSs
  – MSs requesting additions to agreed RMP
  – Practical issues with implementations due to national legislation

- Evaluating effectiveness difficult

- Additional work: should have added value

# Effectiveness

New Pharmacovigilance legislation (2012):

- Measurement of effectiveness of the additional risk minimisation measures will be mandatory

New legal requirement:

- EMA /Member States shall monitor the outcome of risk minimisation measures contained in risk management plans and of conditions….'

- As part of the pharmacovigilance system, the MAH shall monitor the outcome of risk minimisation measures which are contained in the risk management plan or which are laid down as conditions of the marketing authorisation ***(Annex IIB)*** pursuant to Articles 21a, 22 or 22a ;

# Effectiveness

"How well does the Risk Minimisation Measure work in minimising the risk?"

1. Show that a risk has been minimised (direct outcome)

2. Measurement of the implementation (performance measurement, surrogate outcome)

Important!:
**Performance measurement will never replace the need for assessment of the direct outcome!**

Successful implementation is no guarantee for effectiveness.

# Effectiveness

Examples of effectiveness measurements:

- Cognitive testing of the educational material
- Testing of knowledge
- Surveys (patients, pharmacists, physicians)
- Audit in a pharmacy
- Web-panels
- Use of medical databases
- Use of claims databases
- Drug utilization studies

# Effectiveness

- How to keep the healthcare professionals motivated?
- Baseline-measurements are lacking
  (how do you know that your results are a sign of success?)
- How do you know the healthcare professional/patient is using the Risk Minimisation Activities?
- Internet (social media) and smart phones are booming – can we use them in the Risk Minimisation Plan?
- Can spontaneous reporting be an indication of success?
  (if the adverse event is reported less, is it a success?)

# Risk Minimisation:

Work in progress…

# Questions?