Managing Core Safety Information

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The views expressed in this presentation are my own and do not represent my employer nor legal advice on practice.
Some definitions...

| RSI Reference Safety Information | No formal definition, recommendations vary from section 4.8 to whole of SmPC. |
| CCDS Company Core Data Sheet     | Can contain more information than RSI.                                    |
| SmPC Summary of Product Characteristics | EU required local licensing information.                             |
| PIL Patient Information Leaflet  | Consumer-friendly version of above.                                    |
Reference Safety Information can have massively cross-functional effects.

- Periodic Safety Update Reports.
- Periodic Benefit Risk Evaluation Reports.
- Clinical and Consumer Testing documentation.
- Investigator Brochures.
- Clinical Overview and Summary.
- Product Compliance Summary.
- Summary of Product Characteristics.
- Patient Information Leaflet.
- Pack.
- Marketing material.
Why do we have RSI?

• To ensure the minimum safety warnings are reflected on labelling to protect the consumer.
• To protect the company from mislabelling challenges.
• To provide a global, medically-approved version of labelling for use in all markets, reducing costs and promoting a consistent safety position.
Legislation varies globally

- US recommends EU SmPC as format but uses monographs for OTC products.
- AUS/NZ have started to create their own.
- Germany attempted EU Core Data Sheets.
- EU PV legislation indicates a requirement for RSI but no definition.
- UK post-BREXIT?
International Guidelines for preparing Core Clinical Safety Information on Drugs
CIOMS Working Groups III and IV 1999

- All pharmaceutical manufacturers must prepare Company Core Safety Information (CCSI) for each of their marketed products.
- Information specific to different dosage forms or uses of products should be clearly identified.
- Should include adverse effects due to excipients.
- National Data sheets may contain safety information that differs slightly from CCSI; particularly they may contain additional information pertinent to a particular country or region.
- CCSI should be determined by the needs of healthcare professionals in the context of a regulatory and legal environment.
- As soon as relevant safety information becomes sufficiently well established it should be included in the CCSI.
EU Good Pharmacovigilance Practice Module VII
2013 onwards.

“It is common practice for marketing authorisation holders to prepare their own company core data sheet which covers data relating to safety, indications, dosing, pharmacology, and other information concerning the product. The core safety information contained within the CCDS is referred to as the company core safety information (CCSI). A practical option for the purpose of the PSUR is for each marketing authorisation holder to use the CCDS in effect at the end of the reporting interval, as reference product information for both the risk sections of the PSUR as well as the main authorised indications for which benefit is evaluated.”
Stakeholders in RSI

- Global Regulatory Function
- Marketing and Commercial
- Drug Safety Officers
- Global Core Safety Group
- R&D
- Global Vigilance Group
- Local Regulatory Function
Related documentation and processes

CCDS

Market experience PSUR/RMP

Clinical Knowledge CSR

Regulatory perspective PRAC/CMDh

Medical understanding IB/CO/CS

PIPA
Big Pharma’s Big Fines

Family awarded $63 million in Motrin case
Audit impacts and responsibilities
MHRA Breakdown of Critical findings 2015-2016

Breakdown of Critical Findings

- Reference Safety Information: 28%
- Data Management: 18%
- Record Management: 9%
- Supervision and Oversight: 18%
- Signal Management: 9%
- System Failure: 9%
- CAPA Management: 9%
MHRA bottom line...

• RSI features at all levels of findings.
• 18% of critical findings relate to RSI.
• Increasing awareness that RSI is a root document that drives safety understanding of products.
Minimum, maximum or somewhere in between?
Anatomy of a Company Core Data Sheet

1. Name of the medicinal product
2. Qualitative and quantitative composition
3. Pharmaceutical form
4. Clinical particulars
   - 4.1 Therapeutic indications
   - 4.2 Posology and method of administration
   - 4.3 Contraindications
   - 4.4 Special warnings and precautions for use
   - 4.5 Interaction with other medicinal products and other forms of interaction
   - 4.6 Fertility, pregnancy and lactation
   - 4.7 Effects on ability to drive and use machines
   - 4.8 Undesirable effects
   - 4.9 Overdose
5. Pharmacological properties
   - 5.1 Pharmacodynamic properties
   - 5.2 Pharmacokinetic properties
   - 5.3 Preclinical safety data
Nearly 200 different active or active combinations for the medicinal products in the market, worldwide.

Previous consequences of missing or inaccurate safety data include factory closure, products pulled from markets, and even legal consequences.

A CCDS is an essential document to ensure our basic safety information aligns across all these markets.

It also allows for any unnecessary or out of date warnings to be removed, potentially increasing a market in a country.

A global roll out gives each market the opportunity to ensure that no safety information is missing.

Unfortunately, this information doesn’t always align.
CCDS Deployment:
Document management

• Example: 1 CCDS, for 10 licences...
• 10 gap analyses.
• 10 draft CES.
• 10 CES have Global Regulatory review.
• 10 CES have Local Regulatory review.
• 10 CES then adapted for local requirements.
• 10 CES reviewed and signed off by medic.
• Potentially 10 sets of RFI.
• All documented...
Global Core Safety
Wording or Product Safety Recommendation

Local licensing documentation

Pack and PIL
Summary

• How extensive should your RSI/CCDS be?
• Minimum or maximum content (or in between)
• What other value can be derived (compliance, consistency, reduced workload in market, aligned labels)
• Do not underestimate document management!
Watch outs

• Work sharing in EU.
• Different points of view internationally.
• Be prepared to find inconsistencies in historical documentation.
• Timeframes.
• Excipients and non-active related wording.
• PIL wording?
Thank you!

Any questions?