EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA Initiatives on Product Shortages Due To Manufacturing/GMP Issues

QP Forum, Dublin April 2015

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Shortages - public awareness


Monday 20 February 2012

The Telegraph

HOME » HEALTH » HEALTH NEWS

Drug shortages cause delays for cancer patients

Patients are being forced to wait for vital drugs - including treatments for cancer - because of desperate shortages of medicines across Britain.


FiercePharma

NEWS TOPICS ANALYSIS FEATU

Topics: Supply Chain and Manufacturing

Ipsen warns of shortages of its orphan drug Increlex

Drug treats children who are short for their age


The Gazette

montrealgazette.com

Pharmacists warn of drug shortage

'Significant reduction' at sandoz; Generic drug maker must upgrade plant to meet U.S. FDA requirements

BY WILLIAM MARSDEN, THE GAZETTE FEBRUARY 20, 2012 2:06 AM

Radium-223 Production Halted Due to Manufacturing Glitch

Beth Fand Incollingo @fandincollingo

Published Online: Wednesday, October 15, 2014

The New York Times

SundayReview | The Opinion Pages

EDITORIAL

A Frightening Shortage of Vital Drugs

Published: February 18, 2012

A severe shortage of a drug used to treat childhood leukemia appears

Often start as acute or national and develops into long-lasting and/or worldwide

Supply of Medicines to EEA

- Increase in the supply chain complexity

- Perception of an increase in the number of shortages due to manufacturing, quality and compliance problems in the supply chain.

- EEA is important destination and source of medicines and ingredients.

Importance of the Supply Chain

- Supply chain is frequently a complex path
- Every stage in the process there is an opportunity for a problem to arise
- Supply chain disruption due to manufacturing/GMP and quality problems also have an economic impact due to increased costs e.g recalls and decreased public confidence in the organisation = ⇓ shareholder value.

EMA Actions

- Discussions at CHMP and CMD(h), PDCO, COMP
- Discussions at HMA
- Regulatory authority Workshop in September 2012
- In November 2012 EMA published a reflection paper and implementation plan with 2 main objectives;
  - Provide a framework for assessment
  - Raising Awareness and seeking solutions

Shortages – reflection paper

Virtual group on shortages created in 2012

- First phase: Identify tools to assess reports of shortages
- Second phase: Industry to come up with plan
- Third phase: extended implementation

EUROPEAN MEDICINES AGENCY
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22 November 2012
EMA/590745/2012
Patient Health Protection

Reflection paper on medicinal product supply shortages caused by manufacturing/Good Manufacturing Practice Compliance problems

1. Introduction

Ensuring the security and Good Manufacturing Practice (GMP) compliance of the manufacturing supply chain is an important responsibility of the Marketing Authorisation Holder (MAH) to ensure appropriate and continued availability of medicinal products for human use to meet the needs of patients in accordance with Article 81 of Directive 2001/83.

There is evidence that disruption in supply of medicines can lead to inter alia, a failure to treat; the use of less desirable, often expensive, unfamiliar alternative medicinal products; an increased potential for errors and poorer patient outcomes, caused by absent or delayed treatment or incidence of preventable adverse events associated with alternative medicinal products or dosage forms[1].

Recent unexpected disruptions to the manufacturing supply chain due to manufacturing/GMP compliance problems have resulted in acute and chronic shortages of important medicinal products in the European Union (EU) requiring changes to prescribing information, and initiation of patient allocation programs[2].

EU legislation currently requires mandatory pre-notification by MAHs of disruption of supply in the case of permanent or temporary cessations[3,4] and for manufacturers of medicines in the case of any defect that could lead to an abnormal restriction in supply[5].

In the United States (US), as a result of a high number of shortages of medicinal products, the Food and Drug Administration (FDA) have published at the end of last year a draft "Interim Rule" regarding

23 November 2012
EMA/708575/2012
Patient Health Protection

Reflection paper on medicinal product supply shortages caused by manufacturing/Good Manufacturing Practice compliance problems
Implementation plan 2012-2015

A Framework for assessment

- Developed common understanding of critical medicine/develop decision tree/clarify national input into EU advice/communication (public catalogue)
- Facilitate Benefit / Risk evaluation through template AR (points to consider) and closing AR (retrospective impact of shortage) plus resource guidance.
- Risk indicators for shortages (manufacturing and quality) developed to identify products at risk.
- Crisis situations resulting from product shortages addressed in context of EU Incident Management Plan (IMP)
- Develop international co-operation to foster sharing of information
- Revision of GMP Guide / Compilation of Community Procedures

Raising Awareness / Proactive approach

- Raise awareness of the impact of product shortages and stimulate industry reaction and improvement in Business Continuity Planning.

- Promote better and proactive risk management by Marketing Authorisation Holders – resilience in supply chains.

- Held a workshop with stakeholders

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/events/2013/10/event_detail_000796.jsp&mid=WC0b01ac058004d5c3

Stakeholder Workshop

- Held in London, 14th October 2013.
- Attended by Competent Authorities, HCP's, PCG's, Industry Associations;
- A challenge to the industry associations to;
    1. formulate proposals to enhance risk-control measures for preventing supply disruptions caused by Manufacturing / Quality problems.
    2. propose the means to communicate such issues to authorities.
- Report back to the Agency and the network.
- Q4 2014 / Q1 2015 – Industry Associations have reported back.

What can industry do?

- Shift focus from reactive to proactive risk management and more explicitly assess supply chains and transport risks as part of procurement and contract management and corporate governance processes.
- Improve pre- and post-incident communication on disruptions.
- Marketing authorisation holders : develop supply chain **resilience**
- Challenge to Industry Associations : develop and share methodologies for prevention, risk assessment, communication.

What have industry associations done

A positive response

•Formed an Inter-Association Task Force

•ISPE – ISPE Drug Shortages Prevention Plan – October 2014

•AESGP/EFPIA/EGA/PPTA – Industry Communication Principles to Authorities – Q4 2014

•PDA – Technical Report on "Risk-Based Approach for Prevention and Management of Drug Shortages" – Q4 2014

Drug Shortages Prevention Plan– a holistic approach to prevention of shortages due to manufacturing quality problems

Features

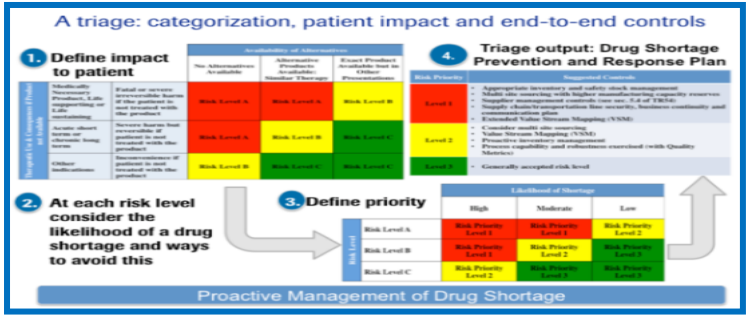
- Follows ISPE's unique shortages survey
- Discussions at every ISPE conference during 2014
- A toolbox and best practice examples to help stakeholders correct and prevent manufacturing quality issues that can create supply disruptions & respond to and manage such disruptions should [illegible]y occur.

Risk-Based Prevention of Drug Shortage

Foundational concepts

1. **Risk-based triage of products**
   - establish preventive end-to-end controls for drug shortage risks based on criticality of the product, patient impact and overall product risk evaluation.
2. **Establishment of a Product Risk Register and a product Drug Shortage Prevention and Response Plan**
   - A holistic framework and simple templates at product level

1.



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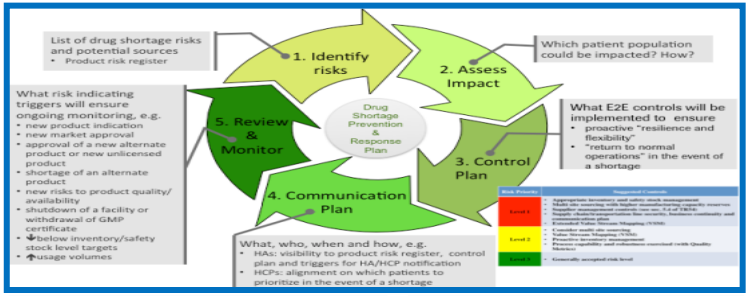


PDA Parenteral Drug Association

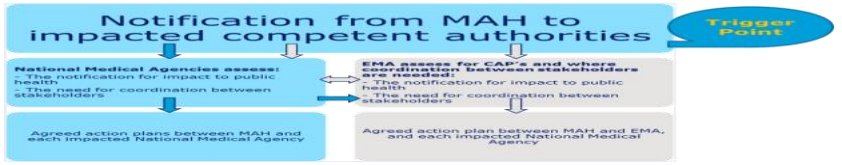
Communication Principles

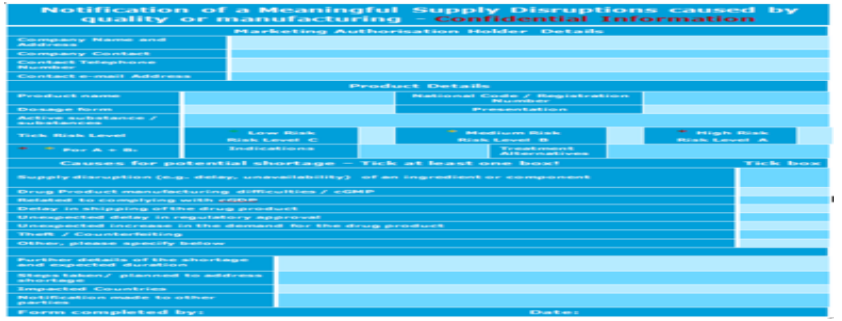
Deliverables

1. **Harmonised definition of a meaningful disruption to supply**

2. **Harmonised reporting template with initial categorisation based on PDAs triaging model**

3. **Harmonised time point and recipient of the information at NCA and EMA**





What next?

- Update to the EMA implementation plan – 3rd Phase.
- Developing a response to the association papers.
- Maintaining the positive engagement of the industry associations in the future – raising awareness of the industry to take up and use the documents developed.

Conclusion

- Public Health and patient safety are our main concerns
- Public health and patient safety are linked to supply chain security
- Initiatives have been/are being taken by Regulators
- Initiatives have been taken by industry associations.
- Need for pharmaceutical manufacturing industry to implement tools developed with goal of building more resilient supply chains and establishing more effective communication processes.

Thank you for your attention

Any Questions?

Further information

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