EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Shortages of medicinal products due to manufacturing and quality problems

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An agency of the European Union

Overview

- Introduction
- Consequences of drug shortages
- Actions taken by the EU Regulatory Network and the CHMP
- Next steps
- Your contribution

Drug shortage – definition(?)

American Society of Health-System Pharmacists (ASHP):

"A supply issue that affects how the pharmacy prepares or dispenses a drug product or influences patient care when prescribers must use an alternative agent"

Am J Health-Syst Pharm 2009;66:1399-1406.

FDA:

"A situation in which the total supply of all clinically interchangeable versions of an FDA-regulated drug is inadequate to meet the current or projected demand at the user level. In general - focuse on shortages of medically necessary products that have a significant effect on public health"

FDA, Manual of Policies and Procedures, 6003.1. September 26, 2006, version Feb2012

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.


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


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 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

Reasons/Causes

- Manufacturing failure
- Closure/planned maintenance of the manufacturing site
- Quality defect (product, packaging)
- Raw material unavailability
- GMP con-compliance at a manufacturing site
- Contamination
- Unexpected increase in demand in clinical practise due to a supply shortage of a different medicinal product
- Drug recall, discontinuation
- Natural disaster, fire…

Experience so far…

- Permanent
- Temporary
- Planned
- Sudden
- Local/national
- Pan-European

- Single drug
- Multi drug
- Serious condition
- Rare indication
- Lack of alternatives

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

Consequences of drug shortages

- Failure to treat adequately
- Delay/denial of treatment to patients
- Exposure to defective product
- Increased risk of medical errors
- Change in prescribing
- Restricted use
- Use of alternative product
  - Availability
  - Interchange (efficacy, safety, administration route, etc.)
  - Adverse profile

Communication

- Targeted for various stakeholders
- Timely
- Corrective measures
- Format:
  - DHPC + PhV communication plan
  - CHMP dedicated press release
  - Q&A
  - Educational material

- Consultation and feedback received from patients and healthcare professionals (Fabrazyme, Increlex, Depocyte, etc.)

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 as an economic impact due to increased costs e.g recalls and decreased public confidence in the organisation = **-7%** drop in shareholder value.

EU Legal Framework

- EU legislation currently requires mandatory pre-notification by;
  - MAHs of disruption of supply in the case of permanent or temporary cessations *(Financial penalties possible for centrally authorised products)*
  - Manufacturers of medicines in the case of any defect that could lead to an abnormal restriction in supply.
  - Distributors and MAH's - Continued availability of medicinal products for human use : Article 81 of Directive 2001/83 *(Financial penalties may be possible depending on national legislation)*
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EMA Actions

- Discussions at CHMP and CMD(h)
- Discussions at HMA
- Regulatory authority Workshop in September 2012
- GMDP IWG Interested parties discussions in November 2012
- In November 2012 EMA published a reflection paper and implementation plan;

Implementation Plan

- Develop common understanding of "essential" medicine/develop decision tree/clarify national input into EU advice/communication
- Explore if crisis situations resulting from product shortages should be addressed in context of EU Incident Management Plan (IMP)
- Develop international co-operation to foster sharing of information

Implementation Plan

- Raise awareness of the impact of product shortages and stimulate industry reaction and improvement in Business Continuity Planning
- Facilitate Benefit / Risk evaluation
- Promote better and proactive risk management by Marketing Authorisation Holders
- Investigate how to measure the impact of drug shortage in patients

What else do EU authorities do to prevent shortages?

Primary

- Expedited variations
- Waived inspections
- Rational risk-benefit decision making more frequently with consultation

Secondary

- Transparency about GMP status of manufacturers via EudraGMP

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.
- Industry associations : develop and share methodologies for assessment, information sharing, communication.
- Marketing authorisation holders : develop supply chain **RESILIENCE**

What can healthcare providers and patients do?

Assist with the communication

Reducing the demand

- Identifying alternatives using clinical pharmacology strategies

Rational reallocation

- Using alternatives that are in greater supply
- Sharing information to assist in identifying priority patients for allocation

Expert meetings and consultation

Clinical/treatment feedback

Follow up monitoring