



Supply Shortages of Medicines in Europe

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EAHP, Brussels, 17 November 2014



World 2009-2013

- Quality defect at Genzyme's manufacturing facilities
- Company unable to manufacture Fabrazyme[®], Cerezyme[®]... (ERT)
- For Fabry: patients put on a reduced dose, or switched to alternative, or stopped
- 12% of patients experienced worsening of the disease, with strokes, unbearable pain, collapse, loss of consciousness...
- Causes:
 - Officially: manufacturing issue, financial pressure, quality assurance neglected
- Issues:
 - How to select the happy few who could continue treatment?



World 2011-2013

- Severe quality issues at Ben Venue laboratories (GMP inspection)
- 12 medicines suspended
- 2 not suspended because no alternative: Caelyx[®], Ceplene[®]

Caelyx[®] indicated for breast neoplasms, multiple myeloma, ovarian neoplasms or Kaposi sarcoma.

Causes:

- shortcomings in quality assurance at Ben Venue lab.

Issue

- To suspend or not a potentially defective product?



The screenshot shows the European Medicines Agency (EMA) website. The main headline reads: "European Medicines Agency recommends transfer of manufacturing sites for Caelyx and Ceplene". Below the headline, there is a Q&A section with a table of questions and answers. The table has columns for Name, Language, First published, and Last updated. One entry is visible: "Questions and answers on final recommendations on Caelyx and Ceplene manufactured at Ben Venue Laboratories" in English, published on 16/03/2012. To the right, there is a "Related information" section listing links to EPAR pages for Caelyx and Ceplene, and a link to a precautionary recall of a batch of Vistide manufactured at Ben Venue Laboratories.

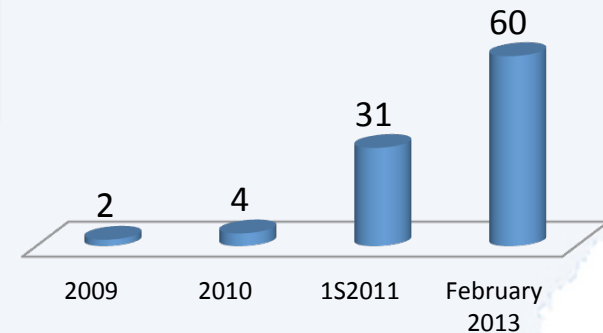
Few facts 2013

30 to 40 medicines
in short supply at any
given time in the UK
(PNSC)

37 active substances
in short supply
2012-2013
France (ANSM)

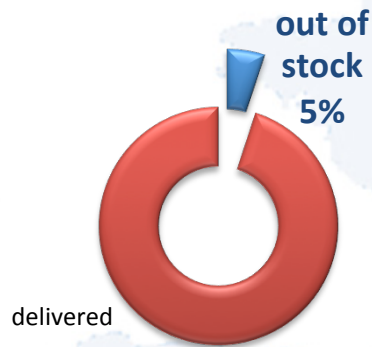
Of which 10 = orphan
medicinal products
(authorised to treat life-threatening
and severe rare diseases) (EURORDIS)

Shortage notifications to ANSM



Le Quotidien du Médecin
25 March 2013

Community pharmacies orders to
wholesalers (France, 2012) (PGEU)



27 medicines
in short supply
12/07/2013
Netherlands
(KNMP)

USA (FDA)

- 178 shortages were notified in 2010
- 132 involved sterile injectable medicines
- Increase of 192% since 2005

Medicines Shortages Characteristics

All Member States

All types of medicines

All durations

All distribution chains

National,
European and
international
measures needed

Causes are various

Manufacturing issues

Medical causes (shift in demand...)

Economic causes (market withdrawal, price differences among countries...)

Disorganisation of the distribution chain...

Concerns for the patients (main ones)

Information

- ✓ Often only at pharmacy to renew prescription
- ✓ “out of stock” and no other information
- ✓ Reporting
- ✓ Getting more information

Consequences

- ✓ Disease evolution can start again
- ✓ Clinical impact rarely measured
 - ✓ Anxiety
- ✓ Going from one pharmacy to the next
- ✓ Medication errors (substitution with unfamiliar products)
- ✓ What is the cost to public health?

Management

- ✓ Transparency on causes
 - ✓ Transparency on available supplies
- ✓ Transparency on duration and on measures taken
- ✓ Participation in decision-making
 - ✓ Legal Liability (Obligations of MAH and Distributors, Article 81 of Directive 2001/83)

A reflection by patients, consumers & healthcare professionals in Europe

- Patients', consumers' and healthcare professionals' organisations are adopting a common position
- Draft presented at the PCWP/HCPWP, EMA, 25/09/2013
- Drafting group:
 - Françoise Charnay-Sonnek
 - Roberto Frontini & Richard Price
 - David Haerry
 - Dr Carla Hollak
 - François Houÿez
 - Sascha Marschang
 - Jurate Svarcaite
 - European Specialist Nurses Organisations ([ESNO](#))
 - European Association of Hospital Pharmacists ([EAHP](#))
 - European Aids Treatment Group ([EATG](#))
 - Academic Medical Centre, Amsterdam ([AMC](#))
 - European Organisation of Rare Diseases ([EURORDIS](#))
 - European Public Health Alliance ([EPHA](#))
 - Pharmaceutical Group of the European Union ([PGEU](#))



Signed by 45 organisations as of 12/06/2014

- AGE Platform Europe (AGE)
- Alzheimer Europe
- Asociación de Addison y Otras Enfermedades Endocrinas-Adisen (Spain)
- Association Surrénales (France)
- Behcet Syndrome Society UK
- DEBRA International
- European Association of Hospital Pharmacists (EAHP)
- European Aids Treatment Group (EATG)
- European Association of Urology (EAU)
- European Federation of Allergy and Airways Diseases Patients associations (EFA)
- European Federation of Neurological Associations (EFNA)
- European Federation of Internal Medicine (EFIM)
- European Institute of Women Health (EIWH)
- European Multiple Sclerosis Platform (EMSP)
- European Organisation for Rare Diseases (EURORDIS)
- European Public Health Alliance (EPHA)
- European Specialist Nurses Organisations (ESNO)
- European Union of Geriatric Medicine Society (EUGMS)
- International Patient Organisation for Primary Immunodeficiencies (IPOPI)
- Patients Network for Medical Research and Health (EGAN)
- The European Consumers' Organisation (BEUC)
- The European Society of Oncology Pharmacy (ESOP)
- European Patients Forum (EPF)
- Spinal Muscular Atrophy Europe (SMAE)
- European Heart Network (EHN)
- European Haematology Association (EHA)
- European Working Group on Gaucher Disease (EWGGD)
- European Gaucher Alliance (EGA)
- European AIDS Clinical Society (EACS)
- European Liver Patient Association (ELPA)
- Pulmonary Hypertension Association Europe (PHA Europe)
- Standing Committee of European Doctors (CPME)
- European Academy of Paediatrics (EAP)
- Rett Syndrome Europe (RSE)
- European Foundation for the Care of Newborn Infants (EFCNI)
- European Federation of Neurological Societies (EFNS)
- European Society for Medical Oncology (ESMO)
- International Diabetes Federation European Region (IDF Europe)
- European Cancer Patient Coalition (ECPC)
- Thalassaemia International Federation (TIF)
- European Haemophilia Consortium (EHC)
- Myeloma UK
- European Association for Clinical Pharmacology and Therapeutics (EACPT)
- Myeloma Patients Europe (MPE)
- Rare Voices Australia Ltd.



EMA with NCAs should:

Create an unit to facilitate prevention, coordination of resolution and of communication on shortages

Create a public catalogue on supply shortages ([catalogue](#))

Work more closely with industry to prevent shortages and to better organise the end of a shortage







Involve patients and HCPs in decision making and communication

e.g. in the Netherlands:







<http://farmanco.knmp.nl/>

Farmanco

Special reports

Type	Active substance	Brand	Form of administration	Revision Date	Impact
	Typhoid Vaccine, parenteral and oral	Typherix, Typhim Vi, Vivotif	injection, gastro-resistant capsule	15-07-2013	Alternatives are not available
	Varicella Vaccine	VARIVAX	Powder for suspension for injection	17-06-2013	Alternatives are not available
	Cefotaxime	Cefotaxime	powder injection	14-06-2013	Import possible
	Vinblastine	Vinblastine	Liquid Injection	08-07-2013	Import possible
	Vincristine	Vincristine	Liquid Injection	08-07-2013	Import possible
	Bleomycin	Bleomycin	powder for solution for injection	10/06/2013	Import possible

Latest Reports

Type	Active substance	Brand	Form of administration	Revision Date	Impact
	Typhoid Vaccine, parenteral and oral	Typherix, Typhim Vi, Vivotif	injection, gastro-resistant capsule	15-07-2013	Alternatives are not available
	Corifollitropin alfa	Elonva	Liquid Injection	08-07-2013	Substitution is possible
	Levothyroxine (sodium)	Euthyrox 75 mcg	tablet	08-07-2013	Solved
	Epirubicin	Epirubicin PCH	infusion, injection	09-07-2013	Substitution is possible
	Lactulose	Lactulose PCH, RP	syrup, powder for oral use	09-07-2013	Substitution is possible
	Enalapril	Enalapril PCH, Apotex, CF	tablet	09-07-2013	Substitution is possible

Public authorities should

Explore the establishment of buffer stocks to be held by wholesalers for more flexibility to the supply chain

Ensure fair distribution of the remaining supply

When a MS stockpiles some supply, this should not pre-empt stocks to the detriment of others

Establish a mechanism for stakeholders to report evidence of a product shortage to the authorities

Industry: preventing shortages

Supply Shortage Risk Assessment Plan with MA submission (SSRAP)

Inform EMA , HCP and patients' organisations when a shortage is possible (even if false alerts)

Involve POS and HCPs in the crisis management: guidelines, programmes, communication

Treat all countries equally, and within countries, each hospital / wholesaler equally

Initiatives

- Common position on medicines supply shortages by all stakeholders
- EMA workshop 14/10/2013
- Meeting at the European Commission DG SANCO/ DG ENTERPRISE 30 June 2014

Desired initiatives:

- EC reflection on the organisation of the drug market and distribution chain
- Maybe a legislation proposal to better coordinate measures, to better inform the public, and to better prevent shortages
- Discussion for the agenda of the Presidency of the Council of MofH 2014 (Italy) – 2015 (Rep. Slovak)

