



# Supply Shortages of Medicines in Europe

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Frequently asked questions from patients and  
responses prepared by their organisations

# 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...
- Issues:
  - How to select the happy few? By whom?
  - How to communicate on a crisis situation full of uncertainties?

# 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 EMA website with the headline "European Medicines Agency recommends transfer of manufacturing sites for Caelyx and Ceplene". The page includes a sidebar with navigation links such as "Human medicines", "Patient safety", and "Regulatory". The main content area features a "Q&A" section with tabs for "Press release", "Key facts", and "All documents". The "Press release" tab is active, displaying a list of questions and answers. The "Related information" section on the right lists links to "Caelyx: EPAR", "Ceplene: EPAR", and "Orphan designation".

European Medicines Agency recommends transfer of manufacturing sites for Caelyx and Ceplene

Q&A Press release Key facts All documents

Expand all items in this list

About

Why were these medicines reviewed?

What actions have been taken so far?

What are the final recommendations of the CHMP?

Name	Language	First published	Last updated
Questions and answers on final recommendations on Caelyx and Ceplene manufactured at Ben Venue Laboratories	(English only)	16/03/2012	

Related information

- Caelyx: EPAR
- Ceplene: EPAR
- Ceplene: Orphan designation
- European Medicines Agency recommends precautionary recall of remaining batch of Vistide manufactured at Ben Venue Laboratories

# Few facts 2012

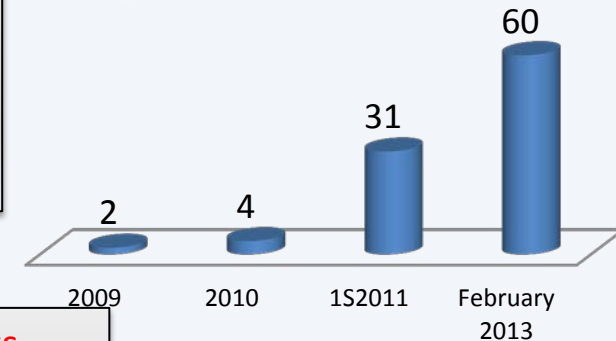
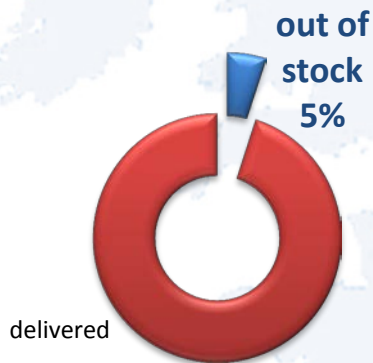
30 to 40 medicines  
in short supply  
at any given time  
in the **UK**  
(PNSC)

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

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

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

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

European survey, 300 hospital pharmacists

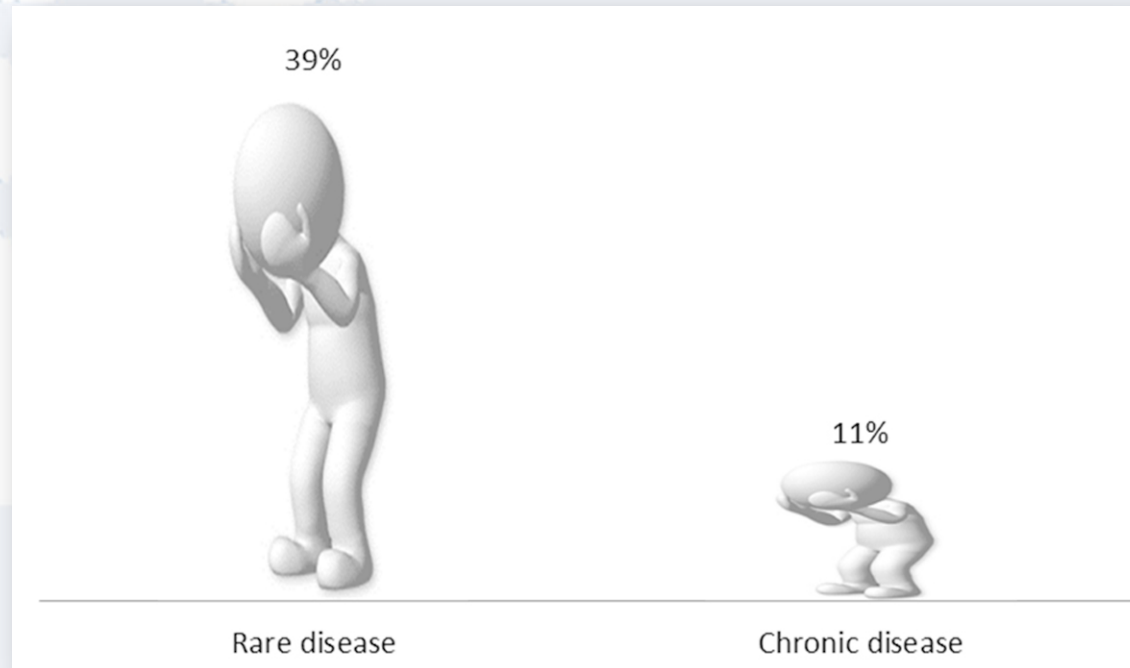
- 99% had shortages
- 63% reported problem to be weekly or daily
- 73% problem grown **worse past year**
- 44% emergency medicine = common shortage (EAHP 2012)

USA

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

# IPSOS patients' survey – Greece 2012

- People who were prescribed an orphan drug were more frequently reporting shortages: 37/96 versus 23/207 with a chronic condition





# Some causes due to manufacturing issues

## GMP

contaminations, impurities happen, due to significant quality assurance issues

And also hazards, occurrence of a quality defect despite all measures were taken according to quality standards

Raw materials produced far away from final product assembling (globalised nature of pharmaceutical manufacturing)

# Some causes are medical

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Shifts in demand, resulting from the use of the medicine which differs from what was expected (e.g. a paediatric medicine also used in adults)

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Early communication on promising new drugs in scientific conferences creating a hype for the medicine in question

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# Some causes are economic

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Lack of priority given to smaller markets by industry

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Economic crisis and health budget control, where speculation encourages parallel import

(Kanavos 2011: ex-factory price gaps for a sample of expensive medicines of 93% between highest and lowest priced countries)

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Market withdrawal for economic reasons

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Policy to reduce production costs, often to the detriment of quality and quality control

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# Some causes due to the drug market

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Increase in demand due to another shortage

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The abolition of public service obligation for a minimum national stock in some countries

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Quotas of medicines by country, with inaccurate estimates of the demand

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Tendering and procurement with selected wholesaler unable to find medicine at the proposed price

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Sometimes not optimal organisation of the distribution chain

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# 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](#))

Proposals which

# Can be implemented in the current legal framework

(see full list of proposals in the Common Position)

# 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 ([done](#))

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)

Consider multiple manufacturing sites

When possible shortage: confidentiality because of business sensitive information not accepted

When communicating on CT results, anticipate potential consequences

# Industry: managing shortages

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

Communicate the exact figures (production capacity, remaining stocks...)

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

# Other recommendations

Alternative unlicensed treatments should be made available through compassionate use programs if considered sufficiently safe

General guidelines might be helpful, developed with support of ethicists and legal advisors, how to distribute a small supply of a medicine when prioritisation is impossible (randomisation?)

The scope of pharmacy practice should be extended when medicines are in short supply. Where a medicine is not available, to establish the right to substitute with another one

Proposals which require

# Changes to the framework

(see full list of proposals in the Common Position)

# Legal obligations

Legislation should require companies to notify the EMA of shortages even when the shortage is only possible

For medicines that are life-saving, or to treat severe conditions, with no substitution product: SSRAP

Review of the operation of the pricing system in Europe including its impact on medicines shortages

In situations of extreme shortage: as a last resort, consider legislate on random allocation of remaining supply

Legally binding coordination at European level (by the EMA) to ensure fair distribution of the remaining supply

# 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



# 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 Immuno-deficiencies (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.

Thank you!