Supply Shortages of Medicines in Europe

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Meeting with all eligible organisations

11 December 2013, EMA

Disclaimer

EURORDIS is one of the signatories of the

"*Code of Practice between Patients' Organisations and the Healthcare Industry*"

Read here

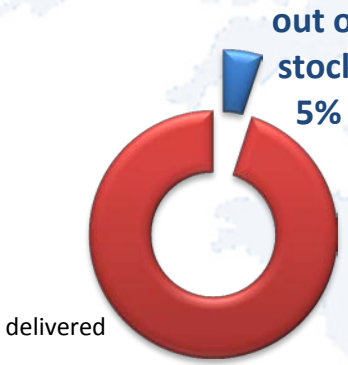
Few facts

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)
539 for pharmacists

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

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



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

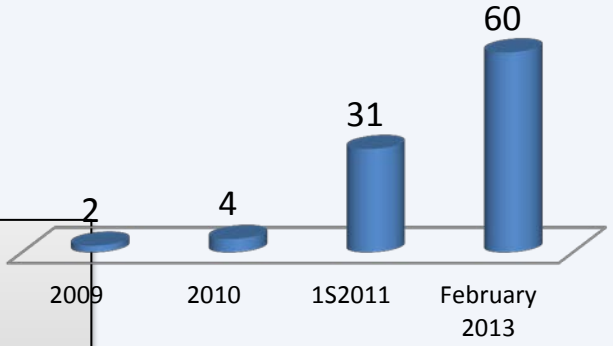
European survey, 300 hospital pharmacists
- 99% had shortages
- 63% reported problem to be weekly or daily
- 73% problem grown worse past year
- 44% emergency medicine = common shortage

(EAHP 2012)

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

(FDA)

Shortage notifications to ANSM



Le Quotidien du Médecin
25 March 2013

Manufacturing causes

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

Medical causes

More "natural" causes

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

In some cases, regulatory changes may impact on supply

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

Economic causes

Parallel exporting of medicine	The increasingly globalised nature of pharmaceutical manufacturing
	Lack of priority given to smaller markets by industry
	Economic crisis and health budget control, where speculation encourages parallel import
	Market withdrawal for economic reasons
	Policy to reduce production costs, often to the detriment of quality and quality control

Price differences

- Listed prices of medicines vary substantially across EU Member States:
  - According to EUROSTAT (2007), price levels in the EU varied by 60 percentage points in 2005
  - East European countries had the lowest average prices (around 70% of EU average)
  - whilst Germany had by far the highest price level of all EU Member States
- Based on more recent data, Kanavos et al. (2011) found ex-factory price gaps for a sample of expensive medicines of 93% between highest and lowest priced countries

Drug market organisation

Political action needed	Increase in demand due to another shortage
	The abolition of public service obligation for a minimum national stock in some countries
	Quotas of medicines by country, with inaccurate estimates of the demand
	Tendering and procurement with selected wholesaler unable to find medicine at the proposed price

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

EMA with NCAs should:

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- Create an unit to facilitate prevention, coordination of resolution and of communication on shortages
- Create a public catalogue on supply shortages
- Conduct market research to improve the understanding of the causes and the scale of shortages
- Work more closely with industry to prevent shortages and to better organise the end of a shortage (no aggressive competition)
- Reinforce Good Manufacturing Practices (GMP) inspections and dedicate more resources to this activity
- Involve patients and HCPs in decision making and communication

Public authorities should

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- 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
- Examine causes of shortages, including economic ones, formulate recommendations to prevent or alleviate them

Industry: preventing shortages

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- 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 on compassionate use
- Adapt production capacity to the planned dates of marketing authorisation

Industry: managing shortages

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- Inform the EMA and relevant HCP and patients' organisations when a shortage is possible (even if false alerts)
- Involve POS and HCPs in all aspects of the shortage 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

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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

Legal obligations

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- Legislation should require companies to notify the EMA of shortages even when the shortage is only possible
- To strengthen the provisions of Article 81 of the EU Directive on Medicines for Human Use
- GMP inspections should be more frequent for all medicines on the EU market
- 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
- National initiatives e.g. ANSM board

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
- Petitioning right of EU citizens to ask EC to take initiative?

Common Position on Supply Shortages of Medicines

Signed by 21 organisations as of 06/12/2013

- AGE Platform Europe (AGE)
- Alzeihmer 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)

21 October 2013

Thank you.

World 2009-today?

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- Quality defect at Genzyme's manufacturing facilities
- Company unable to manufacture Fabrazyme®, Cerezyme®… (ERT)

For Fabry: rare disease, severe

- 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: don't know
- Unofficially: financial pressure pushed company to neglect quality assurance

Issues:

- How to select the happy few? By whom?

EURORDIS Rare Diseases Europe

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?

Frequent cause: parallel import

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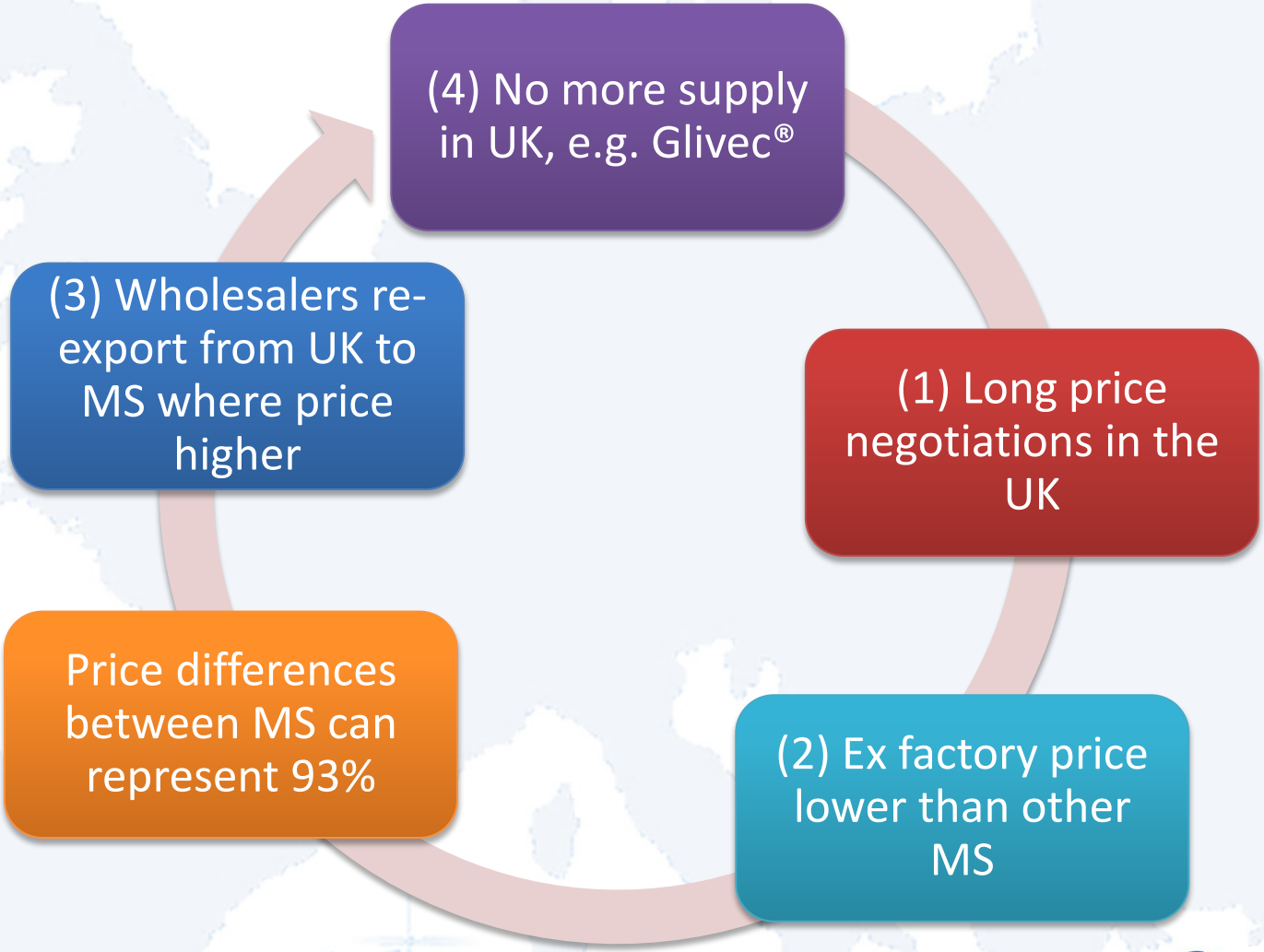

e.g. in the Netherlands:

http://farmanco.knmp.nl/

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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