MEDICINES SHORTAGES

TOPICS PATIENTS AND HEALTHCARE PROFESSIONALS PROPOSE TO FOCUS ON IN 2020-20205

- Why this presentation?
  - Patients, consumers, healthcare professionals agreed on a common position to address medicines shortages back in 2013
  - EMA and NCAs issues recommendations and established a task force
  - Industry set up working groups
  - International Coalition of Medicines Regulatory Agencies added shortages to their agenda
  - Regular workshops kept all stakeholders up-to-date
  - A European Cooperation in Science and Technology was launched (COST Action 15105)

Nevertheless

- Number of shortages doubled between 2018 and 2019
- A twenty-fold increase since 2008

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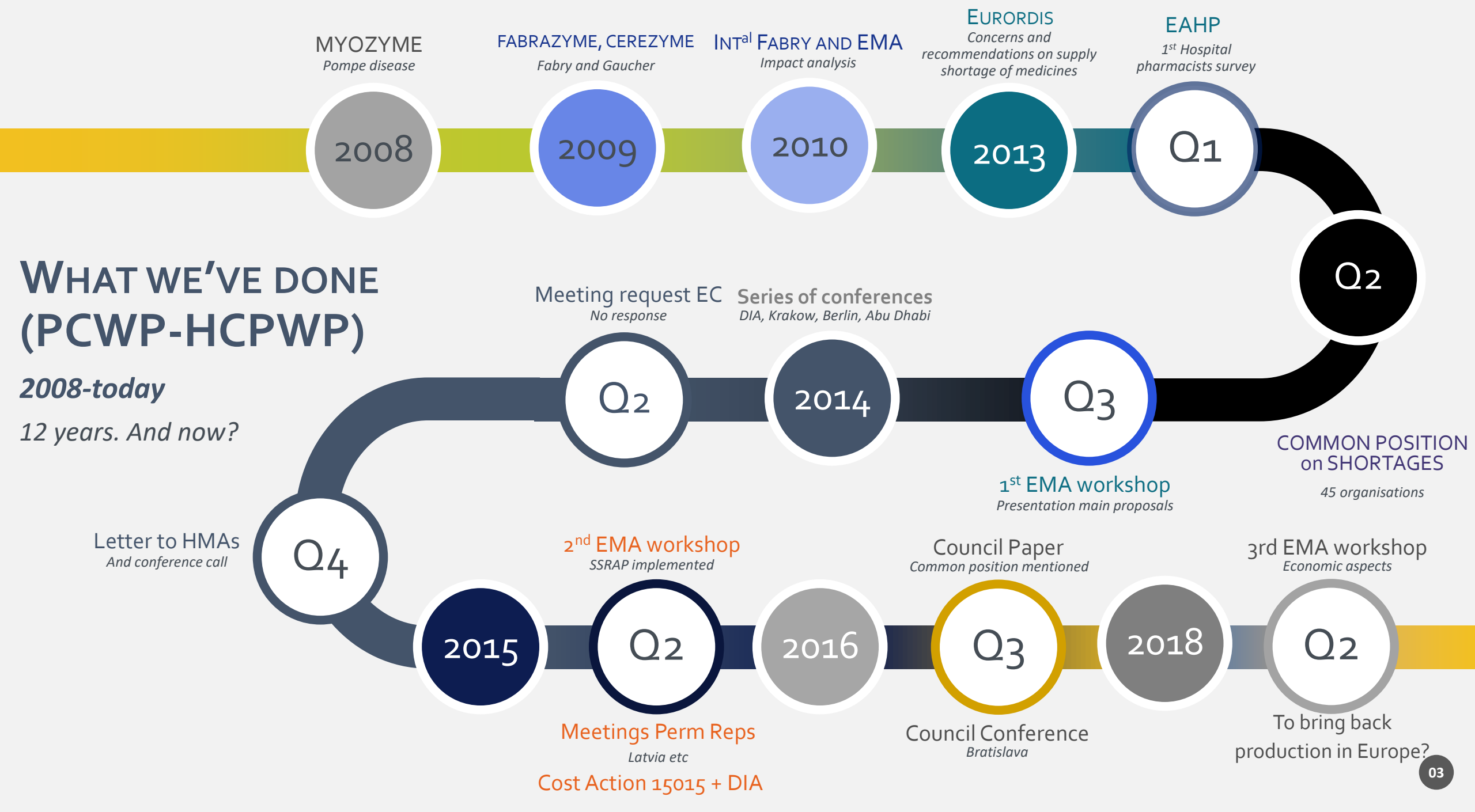
WHAT WE'VE DONE (PCWP-HCPWP)

2008-today

12 years. And now?



To discuss where we are in 2020

An abundance of measures already taken, but do they work?

EMA/HMA task force

- On the availability of authorised medicines for Human and Veterinary Use
- Presentation of the task force deliverables and national measures
  - Discussion on their implementation at national level
  - Discussion on follow-up actions with stakeholders

Industry Inter-Association Task Force

- Risk-based approach for the prevention / management of shortages (product based, systems based)
- ISPE Drug Shortage Assessment and Prevention Tool
  - Collected success stories of implementation of deliverables
  - Asked EMA to provide baseline metrics on the number of shortages due to manufacturing/quality issues so that impact can be measured

Communication on shortages

- Implementation of the Guidance
  - Are MS implementing it?
  - Do we have concrete examples to share?
  - Are MS informing the EMA?
  - Recent report from the Dutch governement
- Notification rules: are they now harmonised?

Example of an action by industry : Product Level Assessments

Risk-based triage approach

Patient impact first

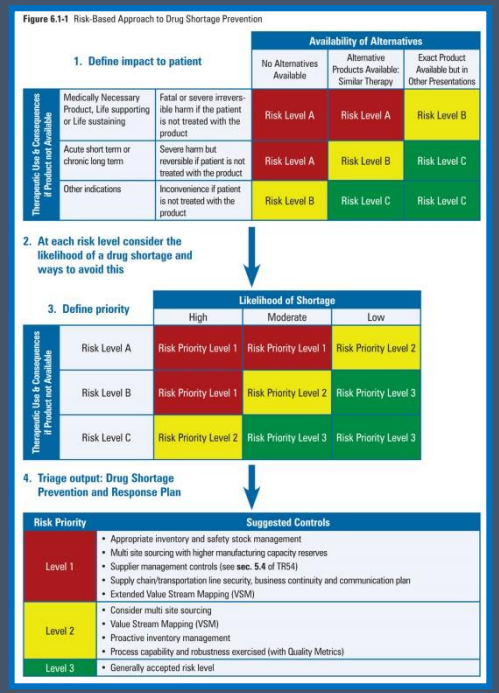


Figure 6.1-1 Risk-Based Approach to Drug Shortage Prevention

1. Define impact to patient

Therapeutic Use & Consequences if Product not Available		Availability of Alternatives: No Alternatives Available	Alternative Products Available: Similar Therapy	Exact Product Available but in Other Presentations
Medically Necessary Product, Life supporting or Life sustaining	Fatal or severe irreversible harm if the patient is not treated with the product	Risk Level A	Risk Level A	Risk Level B
Acute short term or chronic long term	Severe harm but reversible if patient is not treated with the product	Risk Level A	Risk Level B	Risk Level C
Other indications	Inconvenience if patient is not treated with the product	Risk Level B	Risk Level C	Risk Level C

2. At each risk level consider the likelihood of a drug shortage and ways to avoid this

3. Define priority

Therapeutic Use & Consequences if Product not Available	Likelihood of Shortage: High	Moderate	Low
Risk Level A	Risk Priority Level 1	Risk Priority Level 1	Risk Priority Level 2
Risk Level B	Risk Priority Level 1	Risk Priority Level 2	Risk Priority Level 3
Risk Level C	Risk Priority Level 2	Risk Priority Level 3	Risk Priority Level 3

4. Triage output: Drug Shortage Prevention and Response Plan

Risk Priority	Suggested Controls
Level 1	• Appropriate inventory and safety stock management • Multi site sourcing with higher manufacturing capacity reserves • Supplier management controls (see sec. 5.4 of TR54) • Supply chain/transportation line security, business continuity and communication plan • Extended Value Stream Mapping (VSM)
Level 2	• Consider multi site sourcing • Value Stream Mapping (VSM) • Proactive inventory management • Process capability and robustness exercised (with Quality Metrics)
Level 3	• Generally accepted risk level

Drug Shortage Risk Register

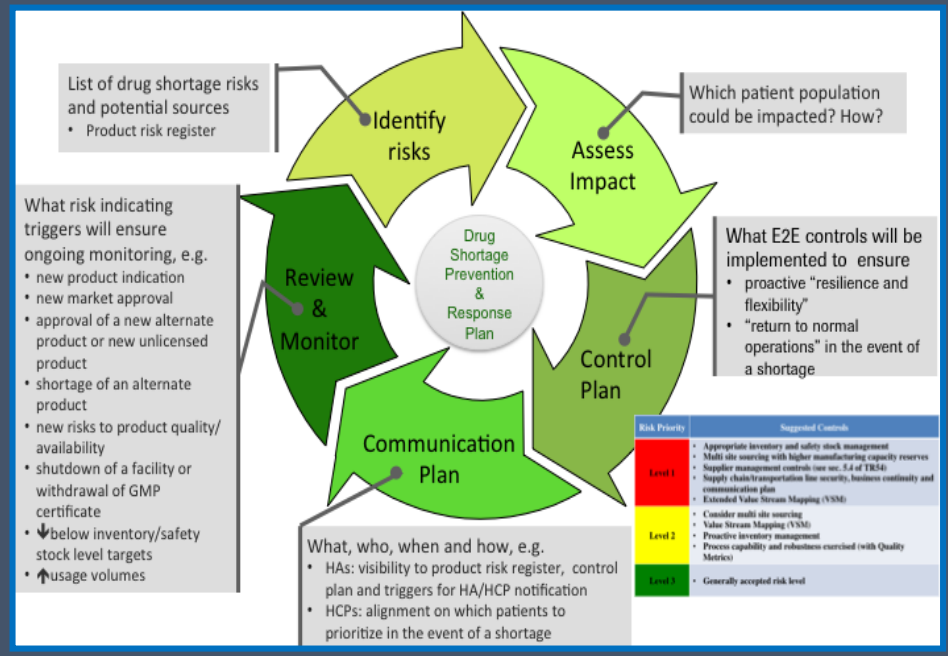
1. **Risk-based triage of products**

   How to establish preventive controls based on product criticality and patient impact

2. **Establish a Drug Shortage Risk Register & a Prevention and Response Plan**

   A holistic framework and simple templates at a product level

Drug Shortage Prevention and Response Plan



Recent measures adopted by MS

Do they work? Are they coordinated? Or do they worsen the situation?

Limiting parallel trade

re-export prior authorisation

- Slovak Presidency Conference in 2016, Cost Action 15105
  - Belgium (Laure Geslin, FAMHP, Céline Van Wetter, hospital pharmacist, Koen Straetmans, pharmacist)
  - Slovakia: National Authority, Zuzana Baťová
  - Czech Rep: Reasons for unavailability of medicinal products. State Institute for Drug Control
- How the Commission evaluates if measures are proportionate

When no alternative exists anywhere

- How frequent is this?
  - See Hospital Universitario Virgen de la Victoria, Málaga, Spain: what is the % of situations where no alternative exist and criteria must be decided upon on which patients need to stop treatment? 10%?
- Who then decides?
- Ethics committee involved?
- Coordination of supply at EU level?
- Or remaining supply sold elsewhere?

Brexit preparedness

1 year for the transition

- National viewpoint from the UK regulator: MHRA
- European viewpoint from the Industry: EFPIA / Medicines for Europe / AESGP
- Viewpoint from a country likely highly affected by Brexit such as Ireland or Malta

TOPICS WE THINK DESERVE MORE FOCUS

AND DISCUSSIONS WITH ALL PARTIES

Joint meeting of patients, consumers and healthcare professionals working parties EMA | March 2020

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More work / reflection needed

To understand the causes

EC study on the root causes of shortages

Joint EMA/EC

EPSCO meeting November 2019

Do we really need this study before proposing new actions?

See: A critical look at erroneous incentives and lacking legal framework as drivers of medicines shortages and objectors to problem-solving approaches. H Jenzer, Uni Bern

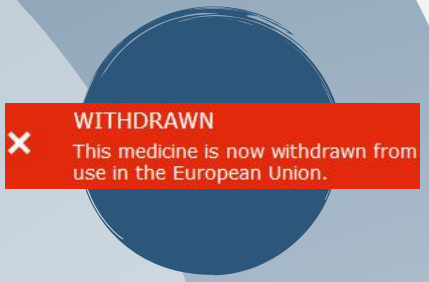
EU coordination

How can we improve the European coordination for managing what's left of the supply equally among MS, and within MS?

If tomorrow a major antibiotic disappears for a long time, what will happen?

Do we need a stress test?

EU legal tools?



Market withdrawal for commercial reasons

Obligation on MAH to notify regulators a few months ahead

Is it enough? Does it provide enough time to find another MAH/manufacturer?

What about military pharmacies?

Relocating manufacturing in the EU

Russia doing it (bringing back from Eastern Siberia to Moscow region)

Germany and France exploring it

What about the EU?

Substitution

In some MS, pharmacists can substitute a missing product by themselves, under conditions (not systematic, and based on a risk assessment)

This is helpful, no need to wait for a new prescription.

Can we generalise this practice?

An abundance of published literature on drug shortages

Time to act, more than to write

29 references on Causes, plus Thesis

Active pharmaceutical ingredients
Globalisation of production
Lack of capacity / responsibility

General Causation, e.g. Hazard, turbulences
- LFB Lille, 11/2018 electricity failure
National shortage of blood products

Mergers to maximise gains / lower production costs
- Genzyme 2009, ERTs

Manufacturing
Defect, contaminations
- Trisenox 2017, Sartan 2019

Closure manufacturing site
- MACI in 2014

Issues at GMP Inspections
- Ben Venue laboratories 2013, 12 medicines suspended
- GVK Bio 12/2014 and 25 generic suspended (substandard ECG in bioequivalence CTs)

Wholesaling and retail trade
- Arbitrage and parallel import/expert provoke secondary shortages in low price countries (e.g. Greece 2008)
- Tendering / taxes
- Belgium, Romania 2017
- Disorganisation of distribution chain (HIV products, France 2010)

Outcomes
Financial outcomes
Price of alternative, product at "too low" price (vaccines)
Market withdrawal

Clinical needs
New standards / medical knowledge
- Myozyme 2008, for early onset Pompe disease, high demand late onset

Stress tests?

Banking industry

Financial crisis

Analysis to determine whether a bank has enough capital to withstand an economic or financial crisis, using a computer-simulated scenario

Financial authorities require banks of a certain size to regularly conduct stress tests and report the results

Banks that fail their stress tests must take steps to preserve or build up their capital reserves

US $ **50** bio+ in assets

Pharma industry

Risk based

Analysis to determine whether a MAH has enough agility to withstand an economic or technical crisis (using a computer-simulated scenario?)

Regulatory authorities require MAHs of a certain risk to conduct stress tests and report the results

Level 1 Industry drug shortage risk register

RETURNING API PRODUCTION OF ANTIBIOTICS TO EUROPE IS NOT ECONOMICALLY VIABLE IN CURRENT MARKET CONDITIONS

INVESTMENTS	Comparatively high costs in plant construction
PERSONEL COSTS	German wages comparatively high, resulting in higher operating and administrative costs
STANDARDS	High safety and environmental standards, thus comparatively costly production
REVENUE POTENTIAL	Fluctuations in demand for antibiotics and prices for APIs increase challenges to maintain operations according to plan

RESULT OF PRODUCTION SCENARIOS

Low scenario
100t
EUR -55M

Medium scenario
500t
EUR -78M

High scenario
1,000t
EUR -55M

Sources: Roland Berger. Study on the security of antibiotics supply: Pathways towards a production of antibiotic APIs in Germany and the EU. Study report. (2018).

Other topics

Do we also want to address:

Liability

- Obligations of MAH and Distributors, Art. 81 Directive 2001/83
  - The MAH and the distributors shall, within the limits of their responsibilities, ensure appropriate and continued supplies to pharmacies and persons authorised to supply medicines so that the needs of patients are covered

Others

- Epidemiology of shortages, their clinical impact?
- A mobile app for patients to receive information and comment on the shortages?
- Dialogue with HCP when looking for alternatives?
- Transparency on remaining supply?
- Patients who need to pay extra for alternative product?

An in-depth multi-stakeholder workshop

Addressing all topics, including economic issues – over 2 days?

Concrete examples

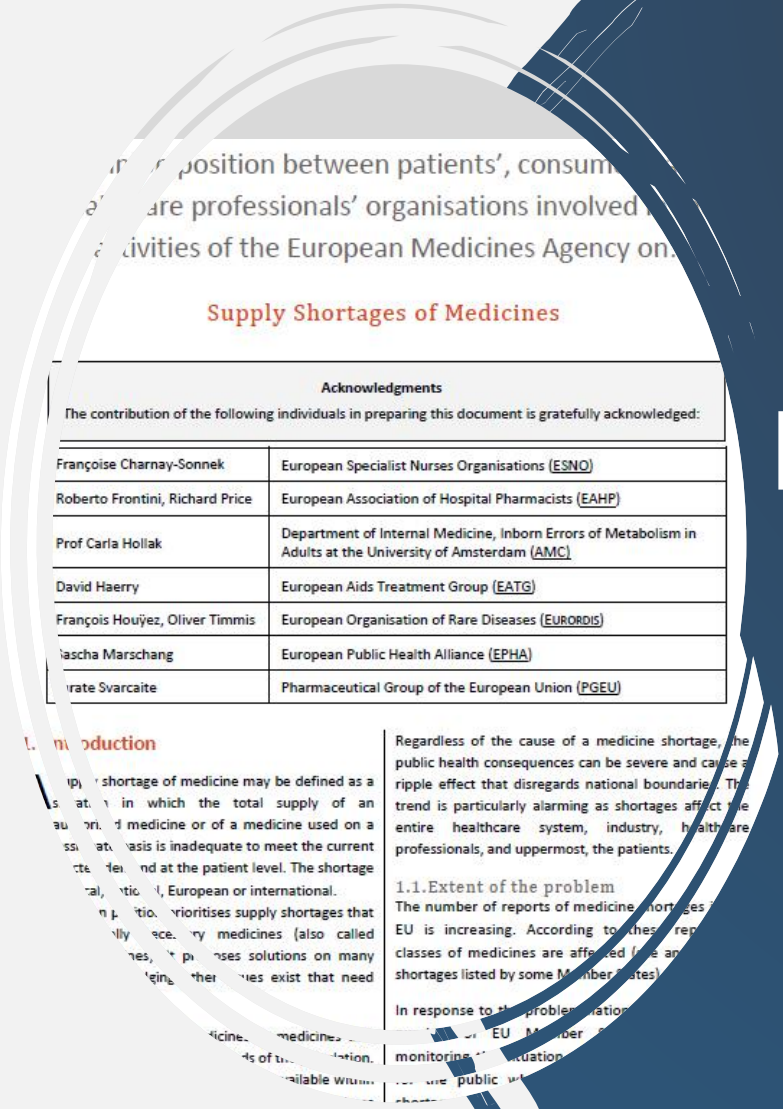
- Different shortages from which important lessons can be learned

All stakeholders

- Regulators
- National authorities (regulatory, market organization)
- Industry (MAH, distributors, exporters..)
- European Commission
- Other international actors
- Patients
- Healthcare professionals
- Communication expert
- …

To update the Common Position signed from 2013?

And better communicate about it?



...position between patients', consum...
...are professionals' organisations involved ...
...ivities of the European Medicines Agency on...

Supply Shortages of Medicines

Acknowledgments

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...rate Svarcaite	Pharmaceutical Group of the European Union (PGEU)

...oduction

...shortage of medicine may be defined as a ... in which the total supply of an ...d medicine or of a medicine used on a ...asis is inadequate to meet the current ...nd at the patient level. The shortage ..., European or international. ...prioritises supply shortages that ...ry medicines (also called ...ses solutions on many ...ues exist that need ...

Regardless of the cause of a medicine shortage, the public health consequences can be severe and can... ripple effect that disregards national boundaries. ... trend is particularly alarming as shortages affect the entire healthcare system, industry, healthcare professionals, and uppermost, the patients.

1.1.Extent of the problem

The number of reports of medicine ...hortages ... EU is increasing. According to these ...rep... classes of medicines are affected (...e an... shortages listed by some M...ber ...tates).

In response to the problem ...latio... ...EU M...ber ... monitoring ...cuation ... the public ...

- We could elaborate more on some topics
  - Substitution
  - Information
  - Liabuility
  - Relocation in the EU
  - Economic aspects….

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THANK YOU