



IMPACT FOR PUBLIC HEALTH

PREPARING FOR THE UNEXPECTED – WHEN YOUR MEDICINE IS NOT AVAILABLE ANYMORE

HMA/EMA workshop on availability of authorised medicines

François Houyez

9 November 2018, EMA, London

EURODIS.ORG

• Medicines shortages

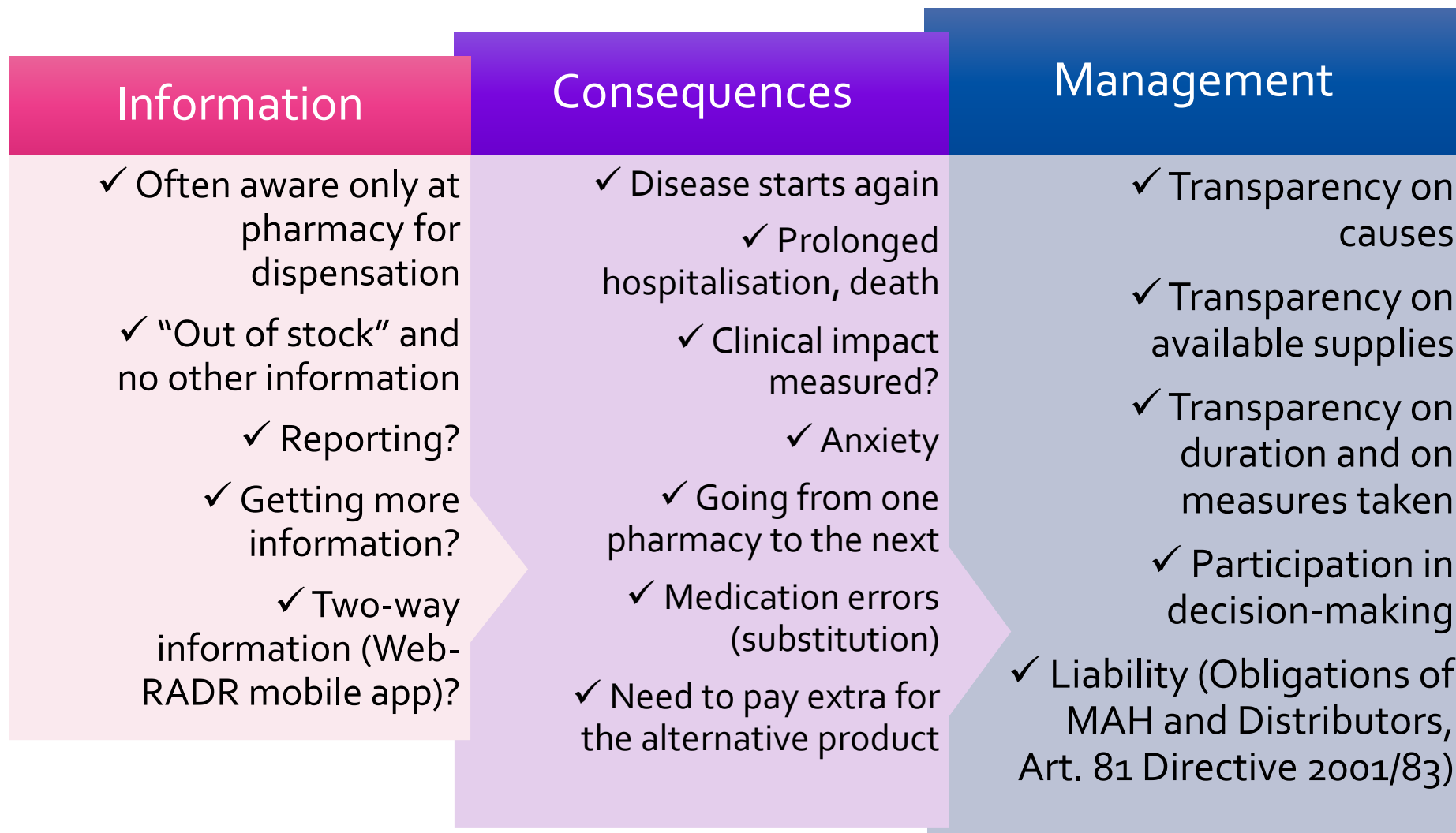
- 2008: first discussions at PCWP on shortages (ERT to treat Pompe disease)
- 2013: Common position of patients, consumers and healthcare professionals (45 organisations) (Many recommendations still valid)
 - 2013: EMA Reflection paper

2018

- French Senate: shortages 10x more frequent in 2018 compared to 2008 (550 vs 44)
- Netherlands Farmaco: shortages 4x in 2018 compared to 2008 (720 vs 190)



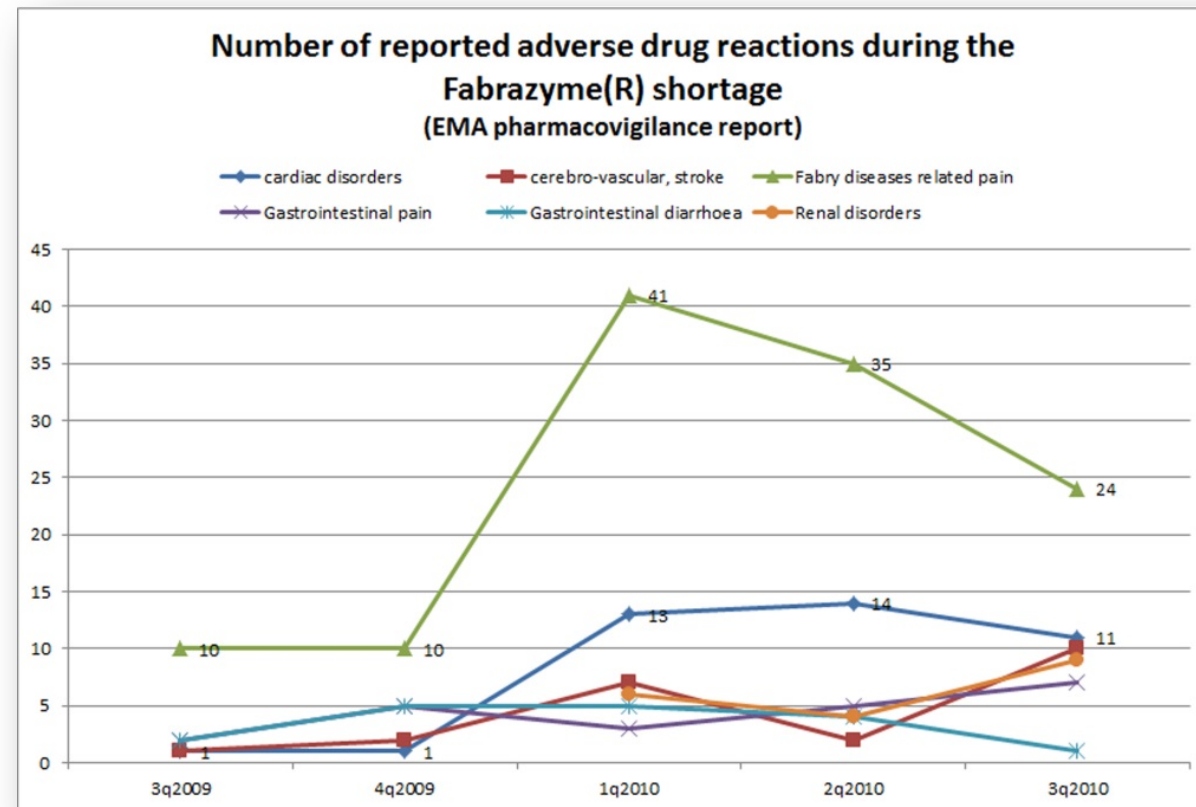
Concerns for the patients



Historic case: Fabrazyme® shortage 2010


- Fabry International Network Survey
- 24 organisations, 22 countries, 1 Dec. 2010 – 31 Jan. 2011
- 442 responses, 170 Europe (\cong 3,000 patients treated worldwide)
- 336 on treatment when shortage occurred
 - 270 changed treatment (reduced dose or switched)
 - 139 with worsening of disease or ADR (48%):
 - 3 strokes
 - 8 renal impairment
 - 13 heart disorders
 - 15 depression
 - 18 hearing/balance disorders
 - 20 stomach pain
 - 39 pain
 - 37 fatigue/lethargy

Serious and/or severe



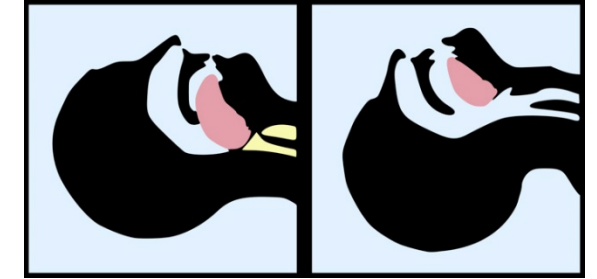
12% of patients experienced worsening of the disease

Serious

Document(s)	Status	First published	Last updated
 Cinryze (C1 inhibitor, human)	Ongoing	06/08/2018	

- To treat angioedema attacks, or prevention of those attacks – typically in 12 - 17 y.o.
- Shortage due to : demand which outweighs current production capacities
- Austria, Denmark, France, Germany, Ireland, Italy, Spain, Sweden, United Kingdom, Iceland and Norway
- Alternatives: Ruconest® (authorised to treat attacks, not for prophylaxis) – or Berinert®
- Clinical manifestations of angioedema (hereditary form, \cong 5,000 in EU):
 - Intestinal occlusion syndrome, sometimes with ascites and hypovolemic shock
 - Laryngeal oedema can be life-threatening with a risk of death of 25% if not treated
 - Dental procedures are a triggering factor for laryngeal oedema

- Patient organisations report (Cinryze® shortage):



- Substitution with Ruconest® or Berinert®
-

Tensions on supply for those products as demand increased

Supply preferably shipped to higher price countries

Ruconest® authorised for attacks, not for prophylaxis

- Duration and impact?
-

No information on duration

In some MS: Cinryze® batches sent in Summer 2018 (thousand doses) – enough to avoid problems

No report of severe effect from patients

- Other actions
-

8 Oct. 2018: National Regulatory Agency ANSM granted temporary use authorisation for lanadelumab (ATU)

For prophylaxis. Report on b/r

Number of patients enrolled: extent of the problem

- Patient organisations report (blood derived products):

- Immunoglobulin replacement therapies

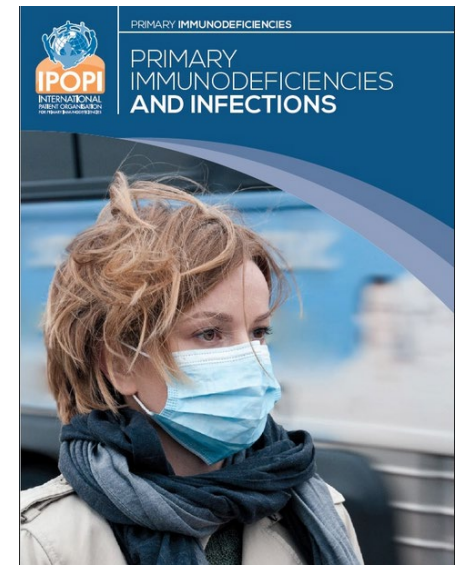
Used by 70% of patients affected by Primary Immune Deficiencies (PID)

- Causes of shortages

Tender system restricting the number of products (no available alternative in case of shortage)

New tax introduced causing market withdrawals (e.g. Nov 2017 in Romania, report of one death)

Market withdrawal for safety reasons for some batches



- Impact

Can affect any Member State, large or small pop

Long manufacturing process (fractionation): 6 to 12 months

Availability of the raw material, the plasma – a scarce material everywhere, especially in the EU

In general, are patients informed?

- Hospital pharmacies or emergency services
 - Patients usually receive little information on medicines dispensed during their stay
 - No copy of prescription, no package leaflet
 - Only when leaving the hospital, copy of the discharge
- When a shortage occurs
 - When harm is caused by delays in finding the appropriate alternative, are patients informed?
 - Does the discharge explicitly mention the medicine used was not the one initially prescribed due to a shortage?

Re-export x deliveries – TOP 15 MP by no. of packs in 2015

Not a
regulatory
issue, but:

Arbitrage
and re-export

Seq.	Medicinal product	No. of re-exported packs	No. of packs supplied to pharmacies	Re-export % share
1	PROCTO-GLYVENOL, RCT SUP 10	143 473	51 831	73.46
2	ALVESCO 160 INHALER, INH SOL PSS 60X160RG	130 328	106 918	54.93
3	PROCTO-GLYVENOL, RCT CRM 1X30GM	127 179	75 502	62.75
4	BETASERC 24, POR TBL NOB 50X24MG	105 177	217 844	32.56
5	GLUCOPHAGE XR 500 MG TABLETY S PRODLOUŽENÝM UVOLŇOVÁNÍM, POR	103 300	202 982	33.73
6	RECTODELT 100 MG, RCT SUP 4X100MG	101 303	57 409	63.83
7	VERRUMAL, DRM SOL 13ML	76 109	39 987	65.56
8	SPIROPENT, POR TBL NOB 20X0.02MG	74 947	59 713	55.66
9	CONTROLOC 40 MG, POR TBL ENT 28X40MG I	74 085	48 441	60.46
10	PREDUCTAL MR, POR TBL RET 60X35MG	73 636	350 564	17.36
11	GERATAM 1200 MG, POR TBL FLM 60X1200MG	72 807	25 097	74.37
12	INHIBACE 2,5 MG, POR TBL FLM 28X2.5MG	70 510	27 699	71.80
13	DILATREND 25, POR TBL NOB 30X25MG	67 315	55 097	54.99
14	NIMESIL, POR GRA SUS 30X100MG	66 994	560 531	10.68
15	INHIBACE 5 MG, POR TBL FLM 28X5MG	64 053	15 832	80.18

Pharm Dr. Zdeněk Blahuta, State Institute for Drug Control, Czech Republic
Conference "Shortages of Human Medicines in the European Union". Bratislava, 18. 11. 2016.

Outstanding issues

- Shortage management
 - Which scientific/political body to decide on the allocation of remaining supply among Member States? EMA? HMA? EC?
 - In extreme situations, Ethics committees recommend a lottery. Any other solution? Who will run it?
 - When a community pharmacy is facing a shortage (product cannot be delivered same day), how can they inform patients where to find a pharmacy that has the product?
 - Could we avoid having to go back to the doctor to prescribe the alternative product?
- Public Health impact
 - Indicators and tools to measure potential health consequences of shortages?
- A role for military pharmacies? e.g. anti-microbial products

Thank you for your attention.



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Job title

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Short list of information patients and their organisations need – and need to be involved

- Context and causes of supply shortage
- Available stock when supply shortage occurred, by country and/or hospital
- Sales volumes when supply shortage occurred
- Other countries where product is marketed and availability of the product in these countries, or other countries affected by shortage
- Estimated supply shortage duration
- Estimated date of supply resumption
- Proposed corrective measures
 - quota system, alternatives in country or available abroad, stock management between hospitals, wholesale distributors and importers, stock exchange between countries, biomedical criteria to decide which patients can continue receiving product etc.
- Communication strategy

Where to?

- 48 % Czech republic
- 17 % Germany
- 9,3 % United Kingdom
- 7,1 % Poland
- 5 % Denmark, Netherlands, Latvia

Comment: this is the state of the primary reexport – wholesalers, who buy the medicines (not the destination state)

Zuzana Baťová, State Institute for Drug Control, Slovak Rep.
Conference “Shortages of Human Medicines in the European Union”. Bratislava, 18. 11. 2016.