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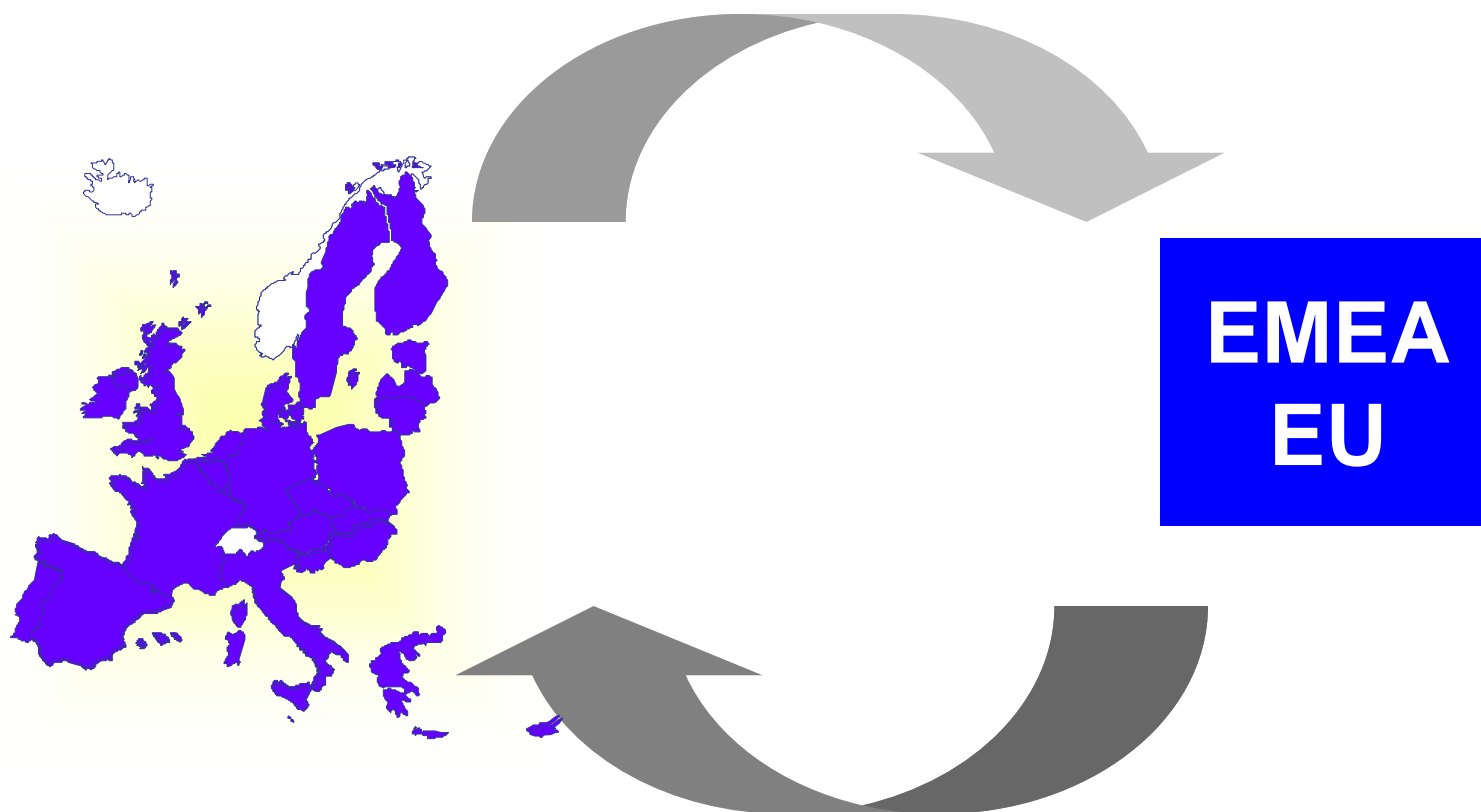
EURORDIS SURVEY ON ORPHAN DRUGS AVAILABILITY IN EUROPE

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Eurordis Therapeutic Development Officer

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Barcelona 9 July 2007

Availability from the patients' point of view

Designation, M.A. : European process



National availability for patients ?

4th Eurordis' survey on OMPs availability in the EU

- 1. Objectives, methods and data collection**
- 2. Analysis by country**
- 3. Analysis by product**

4th Eurordis' survey on OMPs availability in the EU

Objectives of the study:

- **To diagnose the limitations in access for patients**
- **To identify possible solutions**
- **To allow EU patients to really benefit from the scientific, financial and administrative investments made at the EU level.**

Methods (1): Requested data

- **Date**
 - National registration
 - First availability for patients
 - First sales
- **Price**
 - Ex-factory
 - For pharmacies
 - For patients
- **Reasons of unavailability**
- **Level of reimbursement**
- **Population of treated patients (provided amount of drug)**

Methods (2): Parameters of analysis, normalised for each drug

- **National/European Price** (*% of the European Price Mean*)
- **Time from European MA to national availability** (ΔT vs *European Mean Time*)
- **Maximal population treated per country** (*Availability, prevalence, population*)
- **1-year cost of treatment per patient** (*National price, drug dosage*)
- **Total 1-year cost of treatment of all nationally available OMP per inhabitant** (*Price, dosage, prevalence, population*)
- **National 1-year cost of treatment according to country GDP** (*Price, dosage, prevalence, population*).

Methods (3): Targets of the survey

22 drugs x 28 countries : 616 possible situations

	A U T	B E L	C Y P	C Z E	- --	D E U	D N K	E S P	E S T	F I N	F R A	G B R
Aldurazyme												
Busulvex												
Carbaglu												
Fabrazyme												
Glivec												

S V K	S V N	S W E	N O R	I S L	C H E

Ventavis												
Xagrid												
Xyrem												
Zavesca												

Methods 4: The tartan of collected information

	A U T	B E L	C H E	C Y P	C Z E	D E U	D E N K	E S P	E S T	F I N	F R A	G B R	H U N	I R L	- - -	P R T	S V K	S V N	S W E
Aldurazyme																			
Busulvex																			
Carbaglu																			
Fabrazyme																			
Glivec																			
Litak																			
Lysodren																			

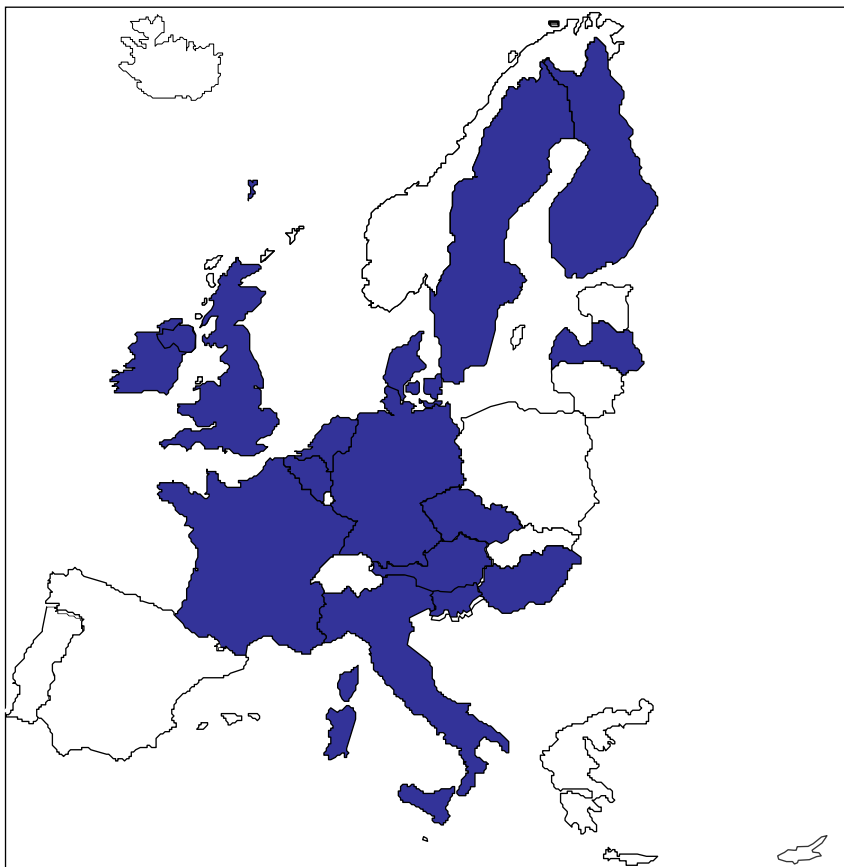
Xagrid																			
Zavesca																			

Methodology (5): The last bastion of secrecy

	A U T	B E L	C Z E	D E U	D N K	FI N	F R A	S V N	S W E	H U N	I R L	C H E	C Y P	E S P	E S T	G B R	S V K
Aldurazyme																	
Busulfex																	
Glivec																	
Zavesca																	
Carbaglu																	
Revatio																	
Somavert																	
Ventavis																	
Xagrid																	
Xyrem																	



Methods (6): Countries responding...or not



- « **reluctant countries** »
 - Most mediterranean countries
 - Swiss & Luxembourg
 - Some new europeans
 - Associated countries

Methods (7): Companies responding... or not

- « **Confidential OMPs** »
 - Busilvex
 - Litak
 - Onsenal
 - Prialt
 - Replagal
 - Revatio
 - Somavert
 - Ventavis
 - Xagrid
 - Xyrem
- **Reluctancy to communicate:
more cultural than industrial (professional)
hurdle**
 - Chemicals drugs
(59% for chemicals vs 25% for biologics)
 - Geographical origin
(70% for EU vs 33% for non-EU
companies)
 - Unrelated to company size
(46% for Major, 56% for Medium or Small)

Methods (7): Discussion

- **Shortcomings**

- Missing data
- False data
- Prevalence >> treated population
- Drugs for same/similar indications (Fabry dis., HTAP)

- **Added value**

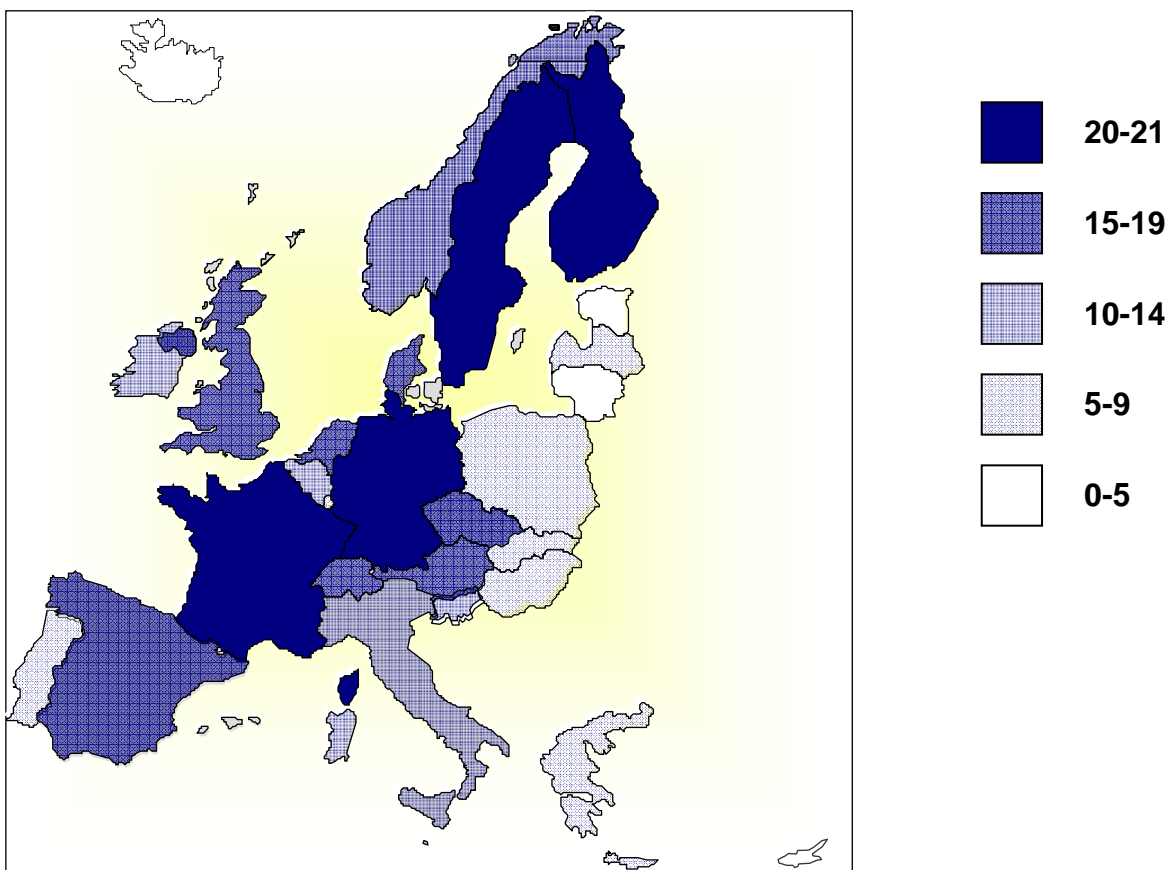
- Presentation of a collective point of view
- Origin of the limitations on availability

Availability by country: the current situation

- **Number of OMPs**
- **Time to availability**
- **Price/Cost**

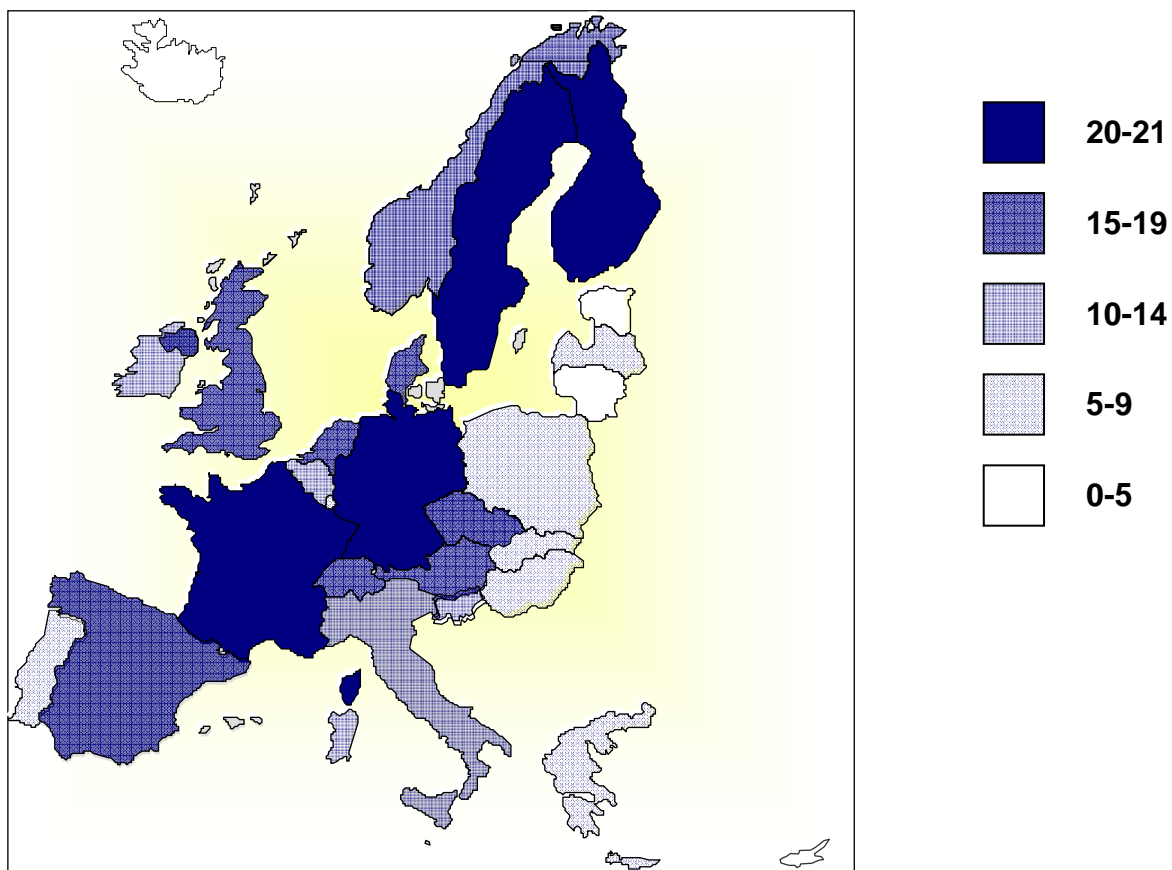
Available OMPs by country: the current situation

Number of available OMPs



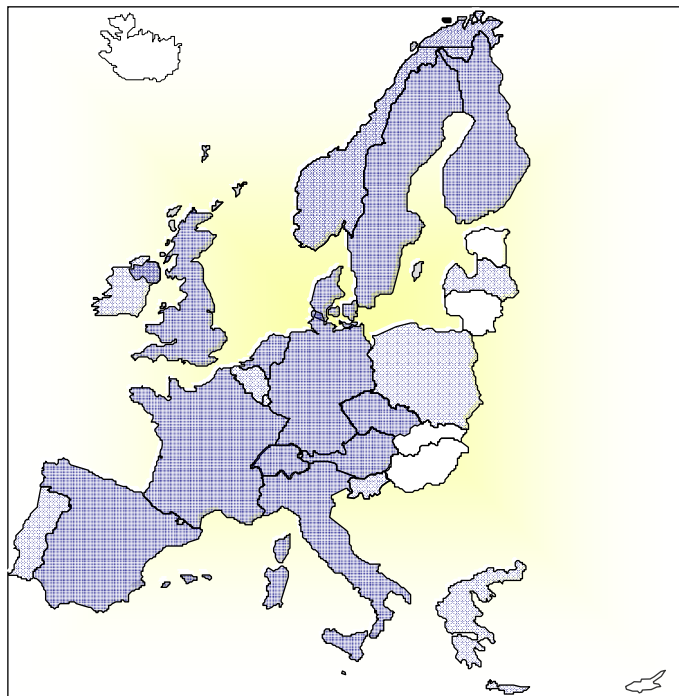
Available OMPs by country: the current situation

Number of available OMPs

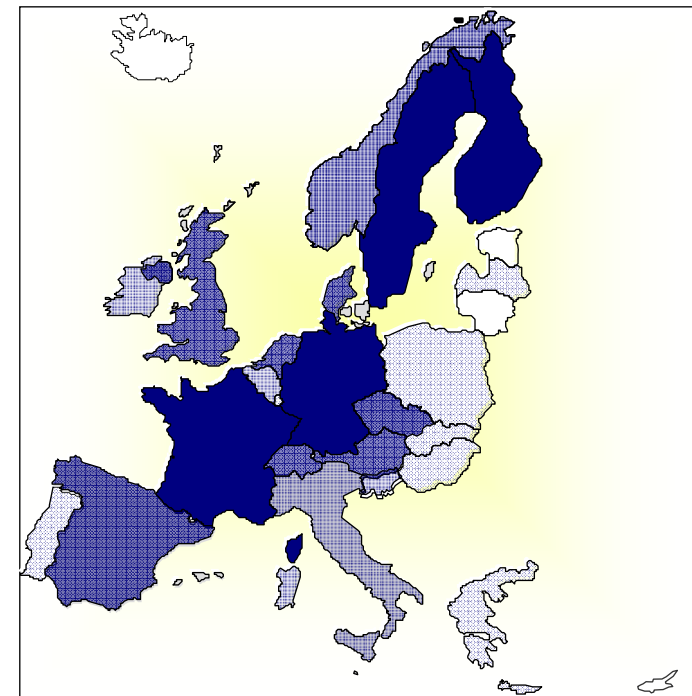
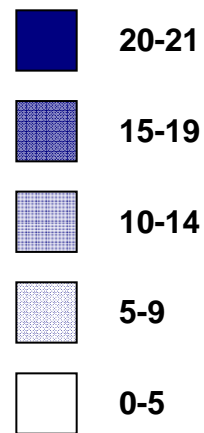


Availability of OMPs by country: the current situation

Number of available OMPs



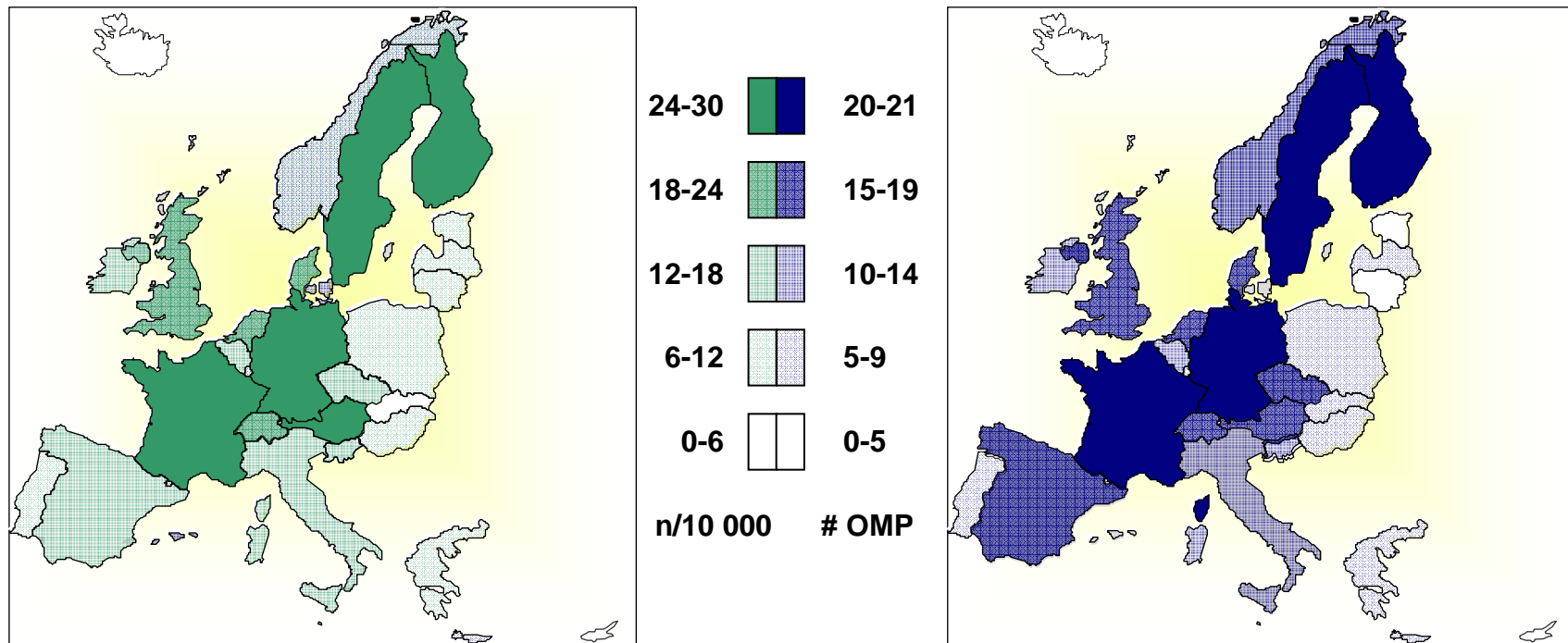
OMP authorised before 01/01/04



OMP authorised before 01/01/06

Availability of OMPs by country: the current situation

How many patients for how many OMPs ?

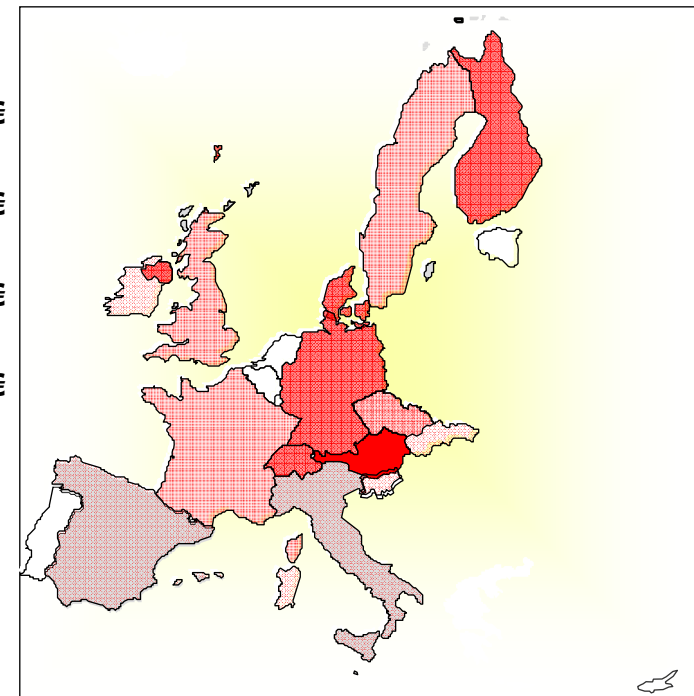
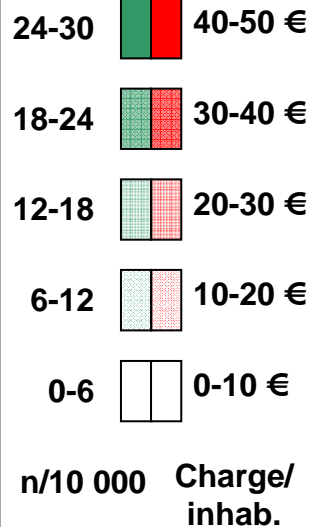
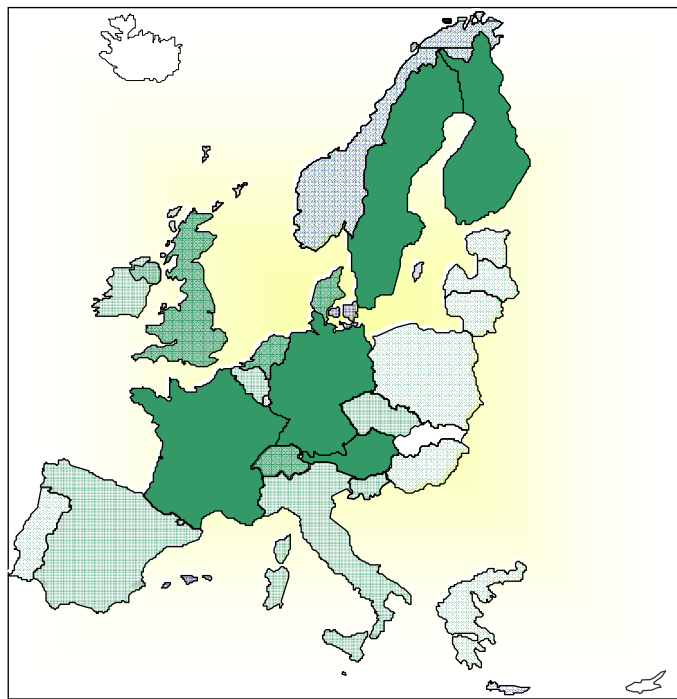


Cumulated prevalences of diseases

Number of OMP authorised before 01/01/06

Availability of OMPs by country the current situation

How many patients for which cost ?

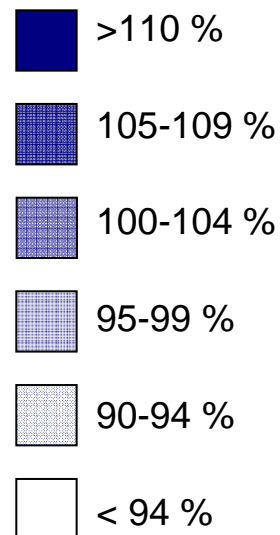
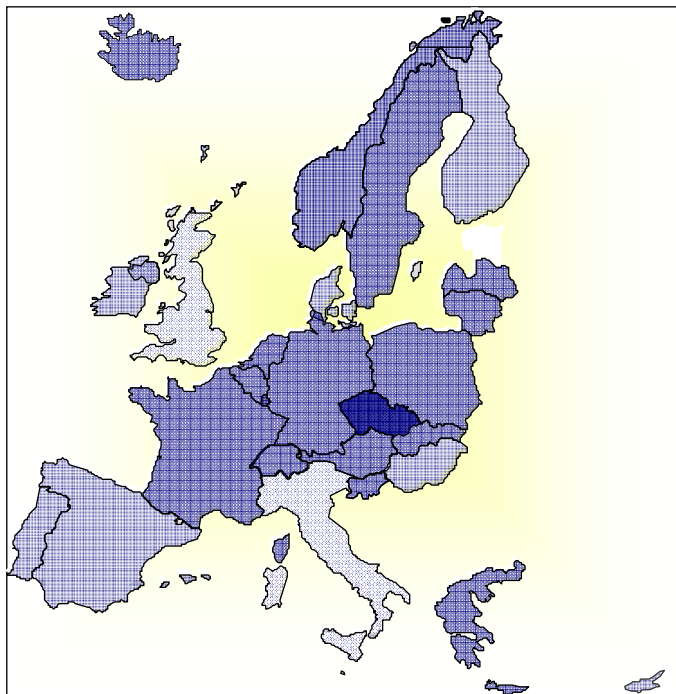


Patients concerned / 10 000 inhabitants
Cumulated prevalences of concerned diseases

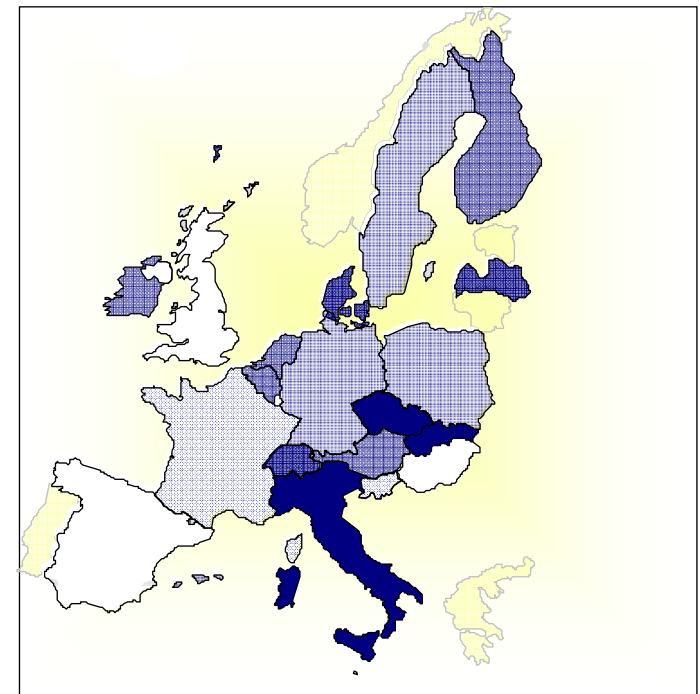
cost / inhabitant / year

Averaged OMP price compared to European mean price

Ex factory price

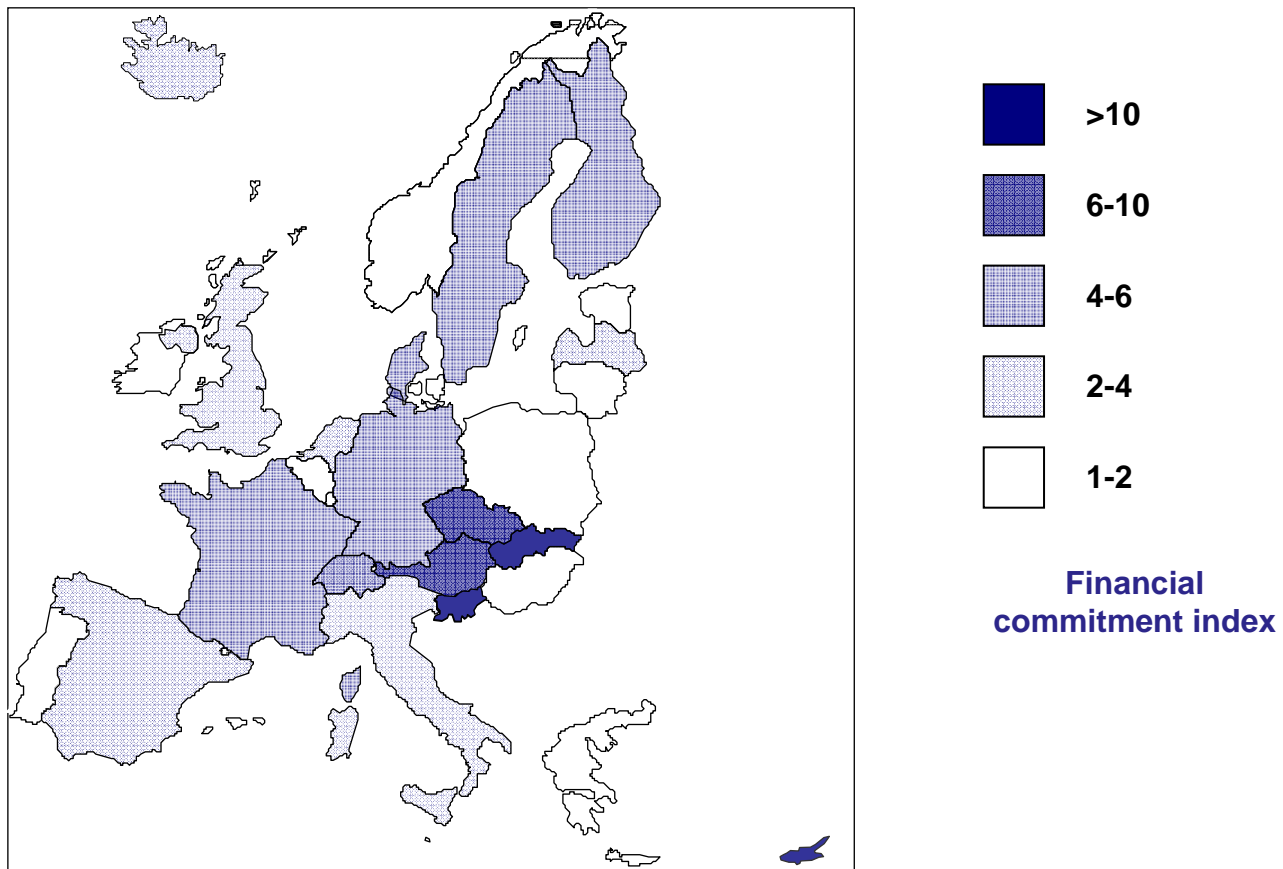


Users price



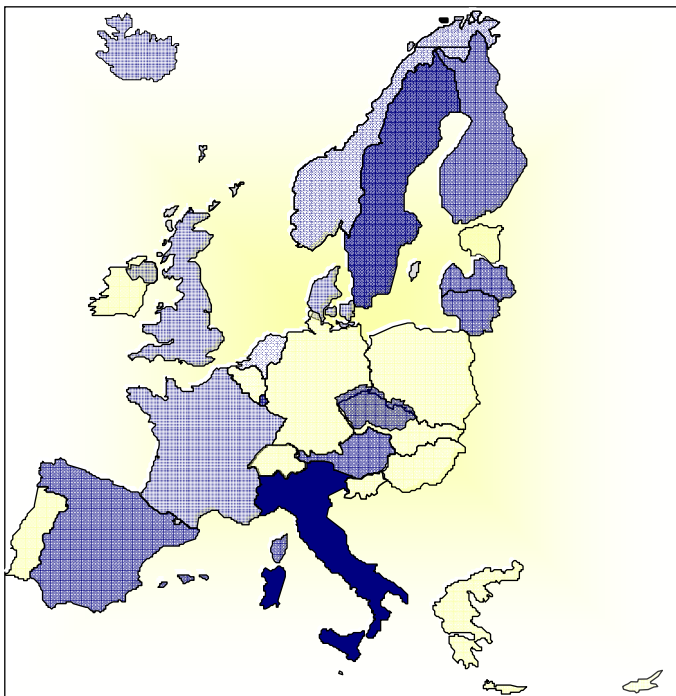
National commitment

Relative values according to the GDP

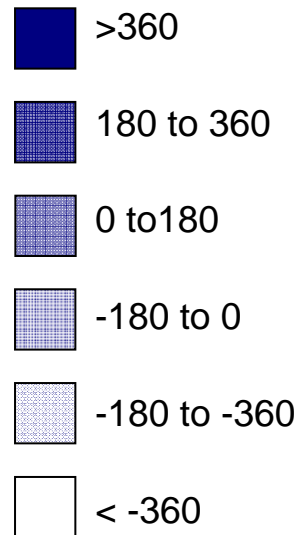


Averaged time to availability compared to European mean

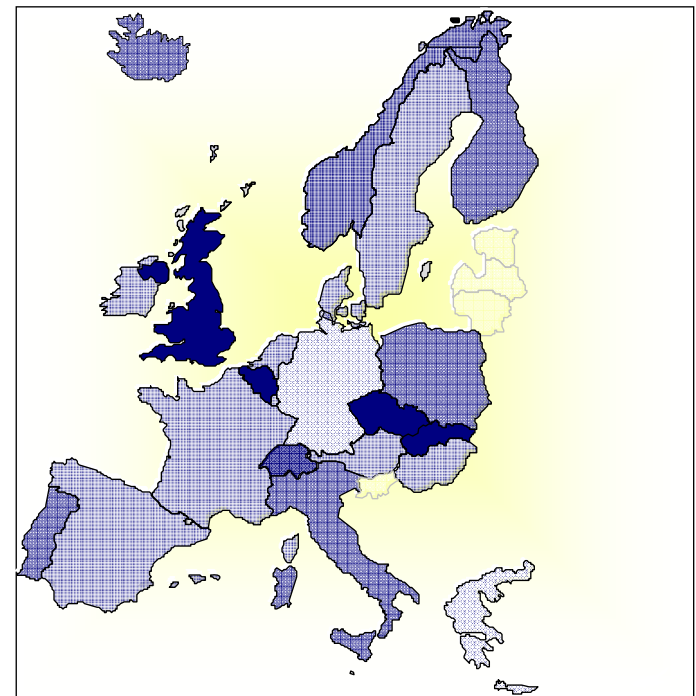
MA → National registration



Number of days



MA → First sales



Conclusions

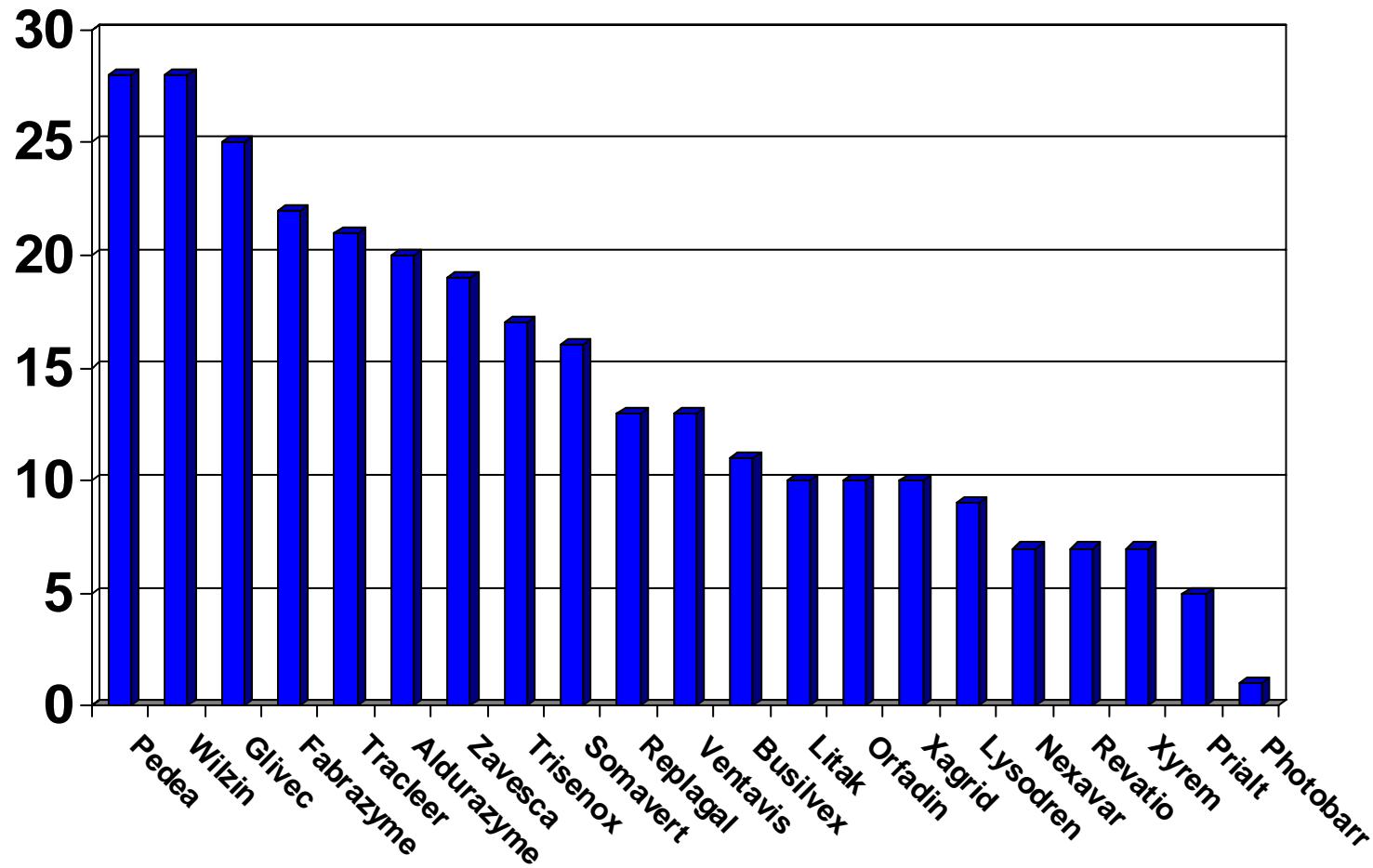
- **Large differences in the number of available OMPs**
 - Some countries ignored?
 - Dramatic differences in national commitment (cost vs GDP) Some countries do not consider rare diseases a priority?
- **Unexplainable differences in time to availability**
- **Very low variability in ex-factory price (need of confidentiality ?)**
 - Equity for all?
 - Inequity for « poor » countries (flexible price in a global market)
- **Low variability in user price**

Availability by product: the current situation

- **Number of Countries**
- **Time to availability**
- **Price/Cost**

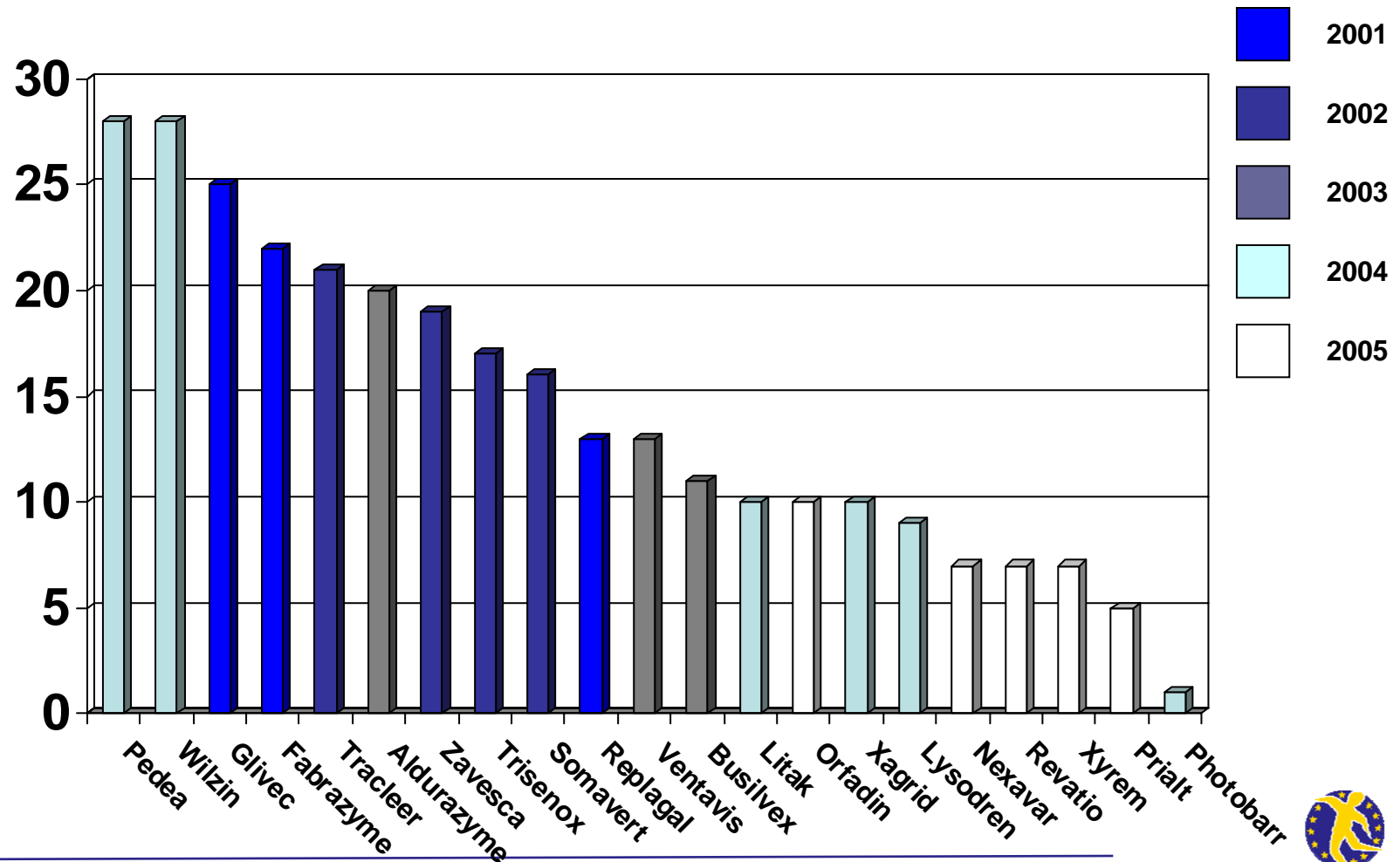
Availability by product: the current situation

Number of countries



Availability by product: the current situation

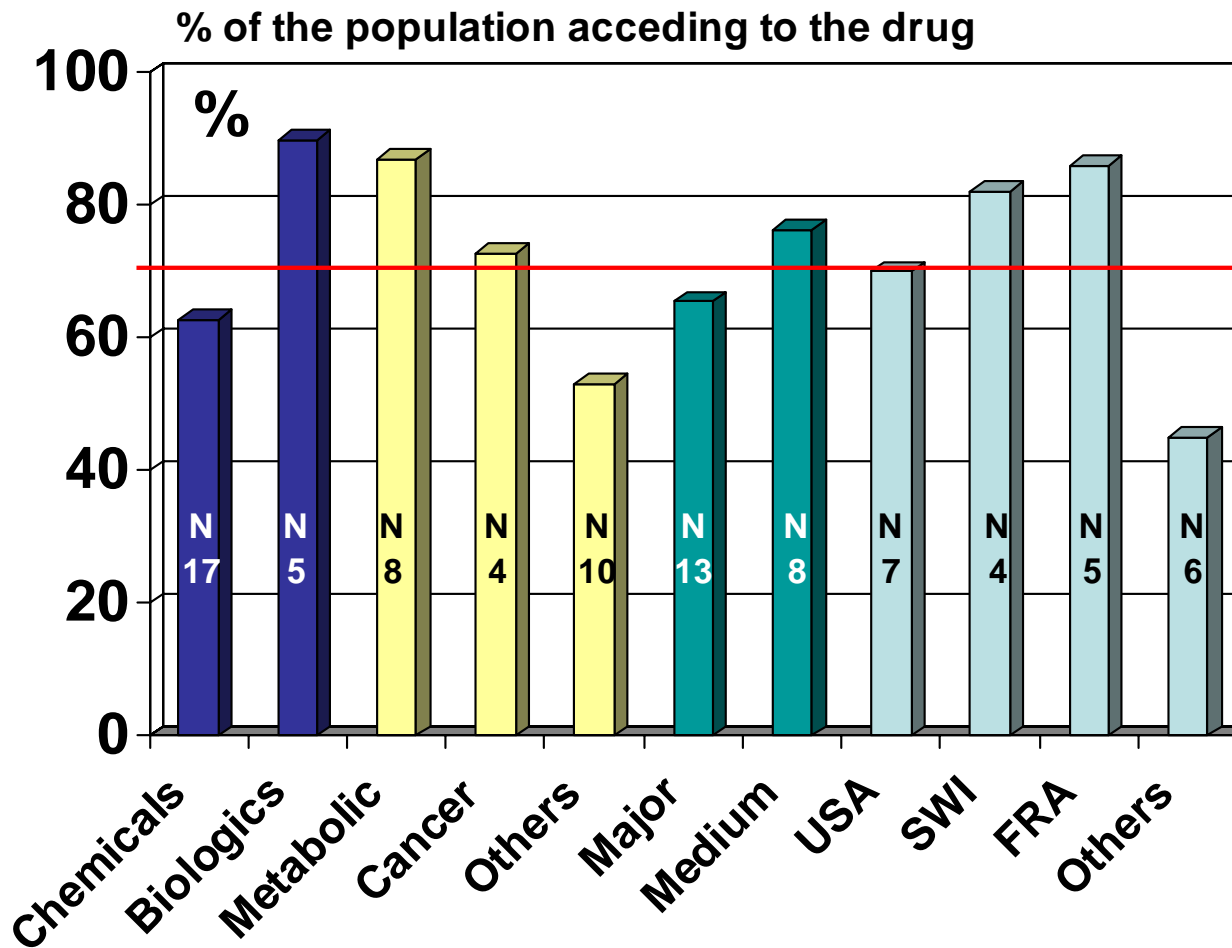
Number of countries



Strategy to cover the European market

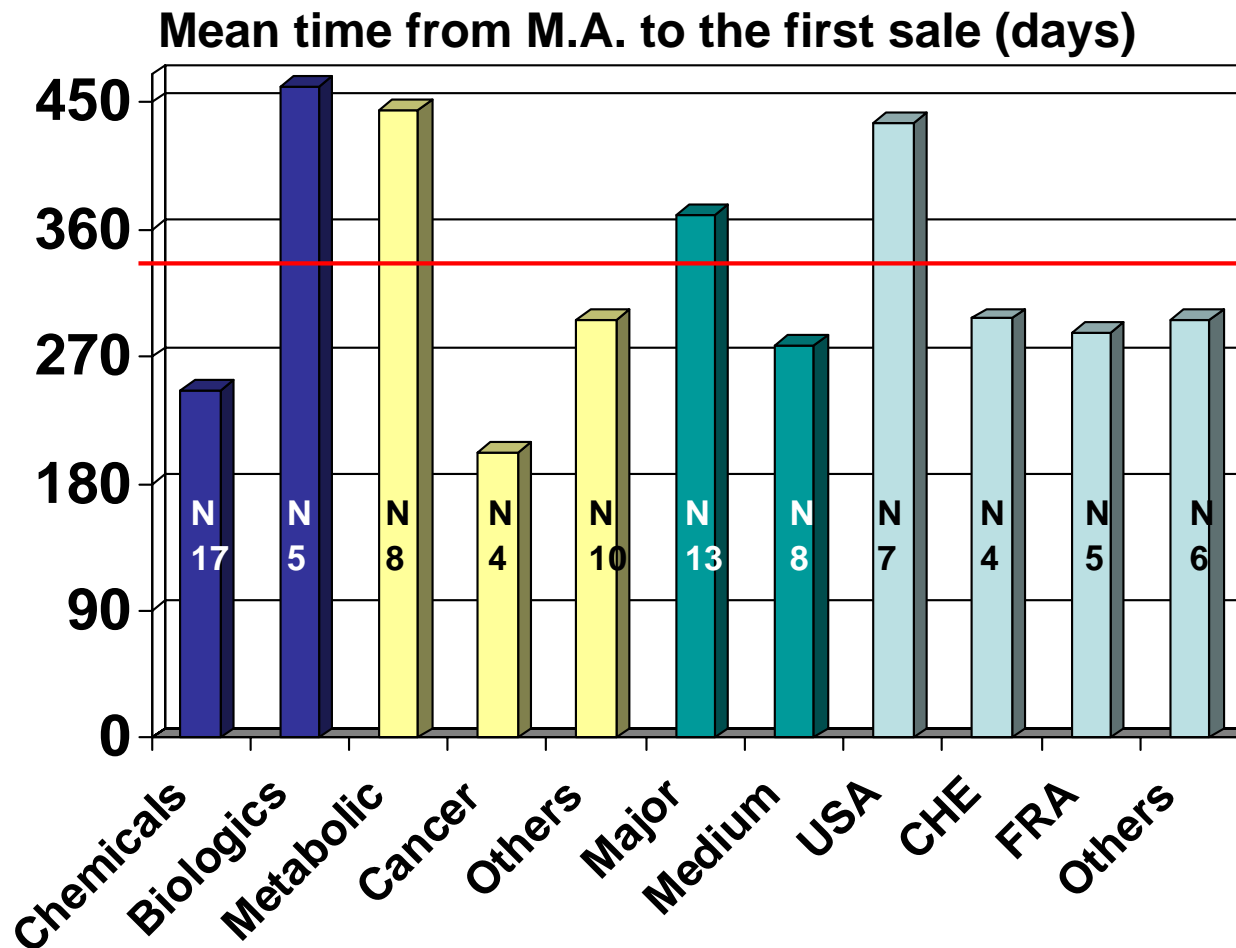
- **The smaller the country, the less attractive it is :**
 - Drugs available in 7 countries: 50% of the global population
 - Drugs available in 14 countries: 75% of the global population
 - Drugs available in 21 countries: 90% of the global population
 - Drugs available in 28 countries: 100% of the global population
- **A dynamic process: the older the M.A., the higher the # of countries**
 - Overall: 6 countries fast served, then 3 new countries/year
(# countries = $5.7 + 0.24$ months; $p < 0.02$)

Determining factors for patient's access to OMP



Overall mean :
69 %

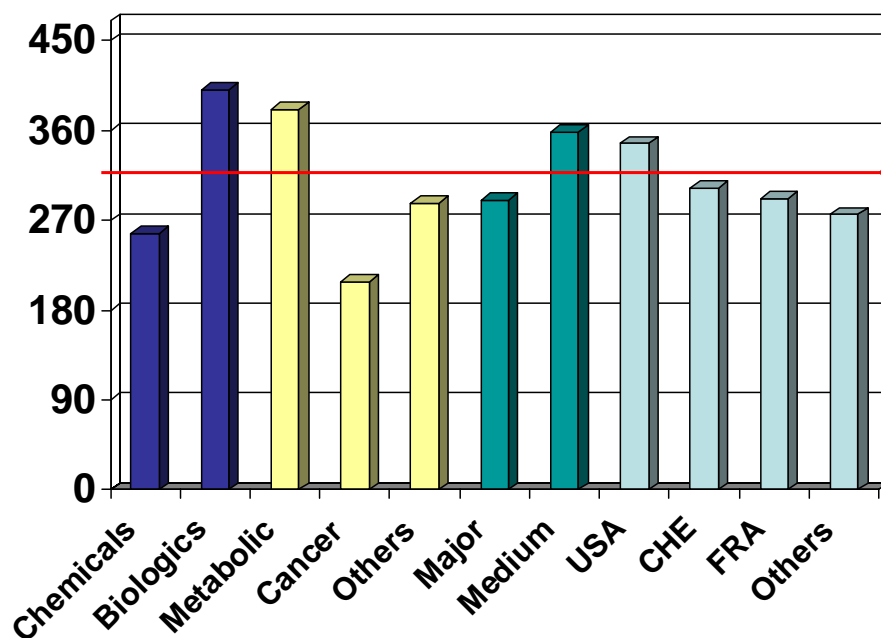
Time from European M.A. to first sale of OMPs



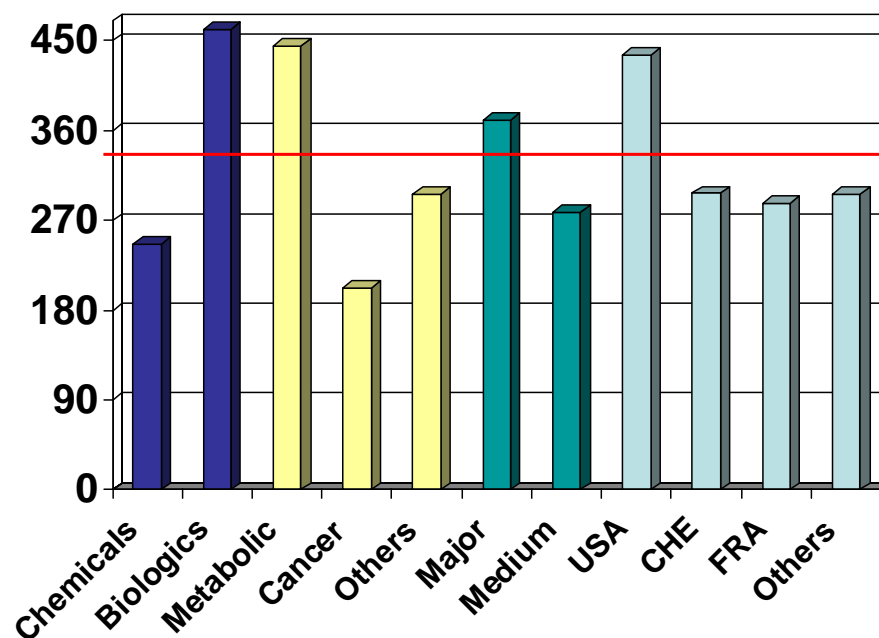
Overall mean :
341 days

Which hurdles for access to OMPs?

Time from M.A. to Registration (days)



Time from M.A. to First sale (days)



Effect of rarity on price: fear or reality ?

One year-cost for a patient

- The rarer the indication, the higher the individual cost

but not proportionally

- 100 times lower the prevalence
10 times higher the individual cost

Individual cost = 14 K€/prevalence^{0,53}
p<0.02

Global cost for a country

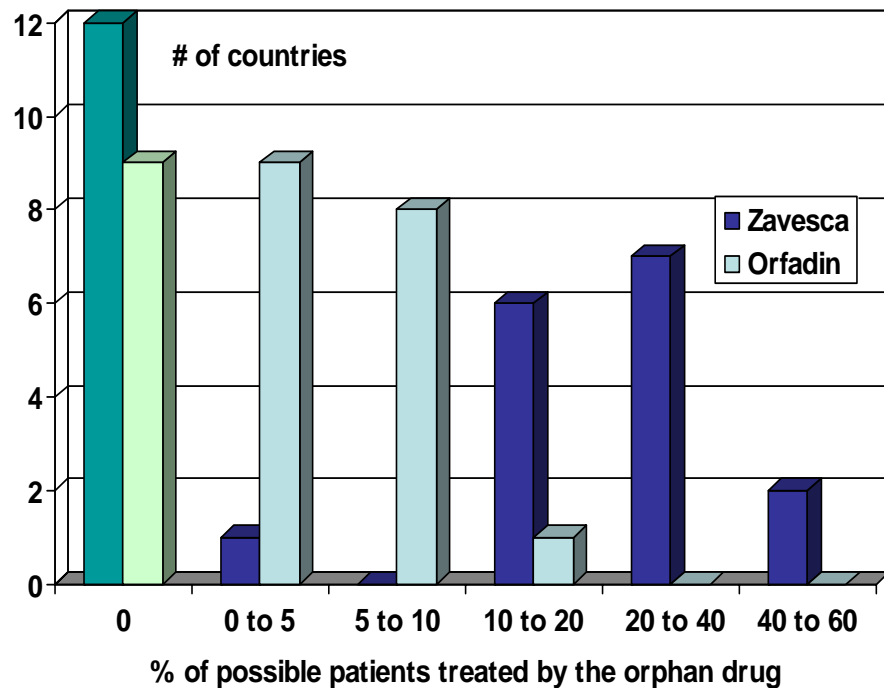
- The more frequent the indication, the higher the global cost

but not proportionally

- 100 times higher the prevalence
10 times higher the global cost.

Cost/million inhabitants = 1400 K€ x prevalence^{0,47}
p <0.05

Prevalence of the disease vs « prevalence of the use »



- Use frequency <<< prevalence
- It takes time to wide the treated population
- High variability between countries, up to 4 years after MA

Overall Conclusions (I)

Heterogeneous Access:

- **Countries with a small population suffer from a longer delay in availability of OMPs**
- **We are shocked that in some countries with high GDP there are only a small number of OMPs really available.**
- **We can understand that this situation is also a result of commercial strategies, but patients cannot accept it and it is against the legislation.**

- **MS independence is protected by the principle of subsidiarity, but they also have to respect the EU rules and the patients' rights to access their treatments.**
- **The inverse proportionality between the prevalence of the indication and the price of the product is not a rule.**
- **The number of patients treated seems to be always lower than the estimated prevalence**

Overall Conclusions (II)

- **Price policy: Is a unique price the best solution? If not risk of parallel import (not in the RD areas: small populations easy to control, hospital distribution...) psychological effect on rich countries of lower prices for poor countries?**

There are several reasons to support a complete transparency:

- **There are actually no differences in ex-factory prices.**
- **The information on the dates of availability could only help patient organisation to better access their products.**
- **After such a large EU investment, NCAs and all the other stakeholders involved have the right to know the outcome of their investment without acting like detectives.**

Why spend more money and energies to collect information that in any case is public, but just not easy to gather?

Overall Conclusions (III)

Toward a EU centralised procedure

- **The whole OMP pre-marketing process is at the EU level, so we expect access to OMP to be the same across Europe**
- **Common application forms for simultaneous transparency procedures**
- **Possibility for a central EU assessment procedure?**