
# prevention and management of availability problems: An industry perspective

9 November 2018

Multi-stakeholder workshop

HMA/EMA task force on availability of authorised medicines for human and veterinary use

# Medicines shortages

- Causes & main drivers of shortages
- Scenarios leading to shortages
- Communication of shortages
- Availability of medicines

# Causes and main drivers of shortages

| | | Regulatory | Manufacturing | Quality | Economic | Supply chain |
|---|---|---|---|---|---|---|
| Products not authorized | | Regulatory time lag | NA | NA | NA | NA |
| Products authorized but not launched | | National requirements | Manufacturing capacity<br>Natural disasters | NA | Market attractiveness<br>Company size | NA |
| Products authorized and marketed but unavailable due to shortages | Temporary | NA | Manufacturing lag times<br>GMP issues<br>Surges in demand | API and excipient supply | Pricing mechanisms<br>Tender practices<br>Cost-containment measures | Supply quotas and parallel export<br>Logistical Inefficiency |
| | Permanent | NA | Manufacturing capacity | NA | Commercial withdrawals | NA |

# Scenarios leading to shortages: Pricing mechanisms

- Low price policies
- Inadequate volumes
- Price regulation that do not allow for price adjustments to reflect changes in costs of:
  - Goods (e.g. ingredients)
  - Manufacturing (e.g. FMD)
  - Regulatory procedures (e.g. Art 57)
  - Distribution (e.g. increased cost of ingredients)

# Scenarios leading to shortages:
# Tender practices

Price-only tender

Single supplier (single-winner tenders)

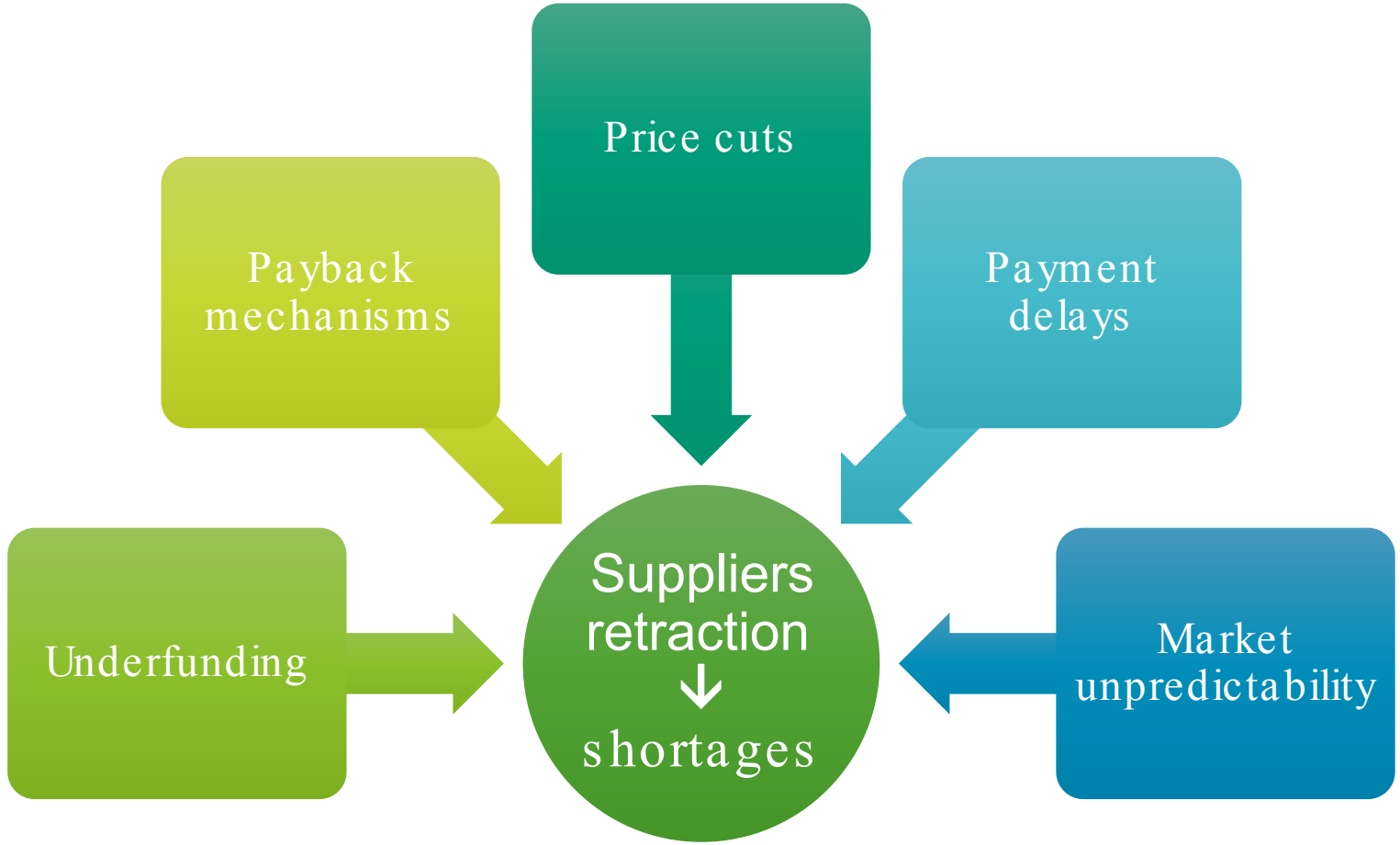
Short lead times

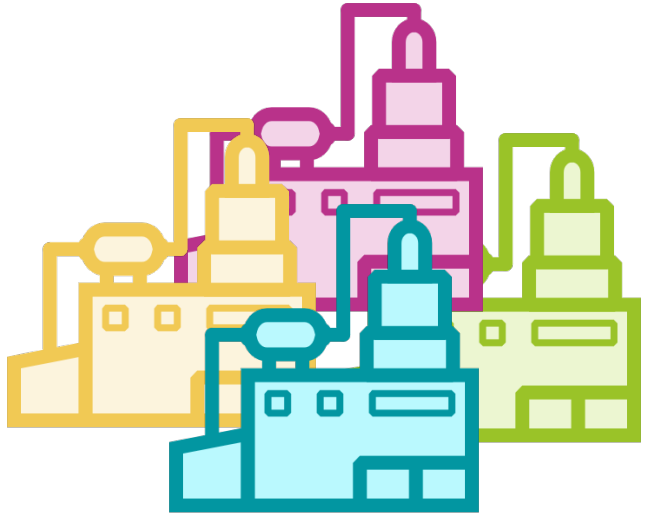
Severe penalties

Less suppliers on the market

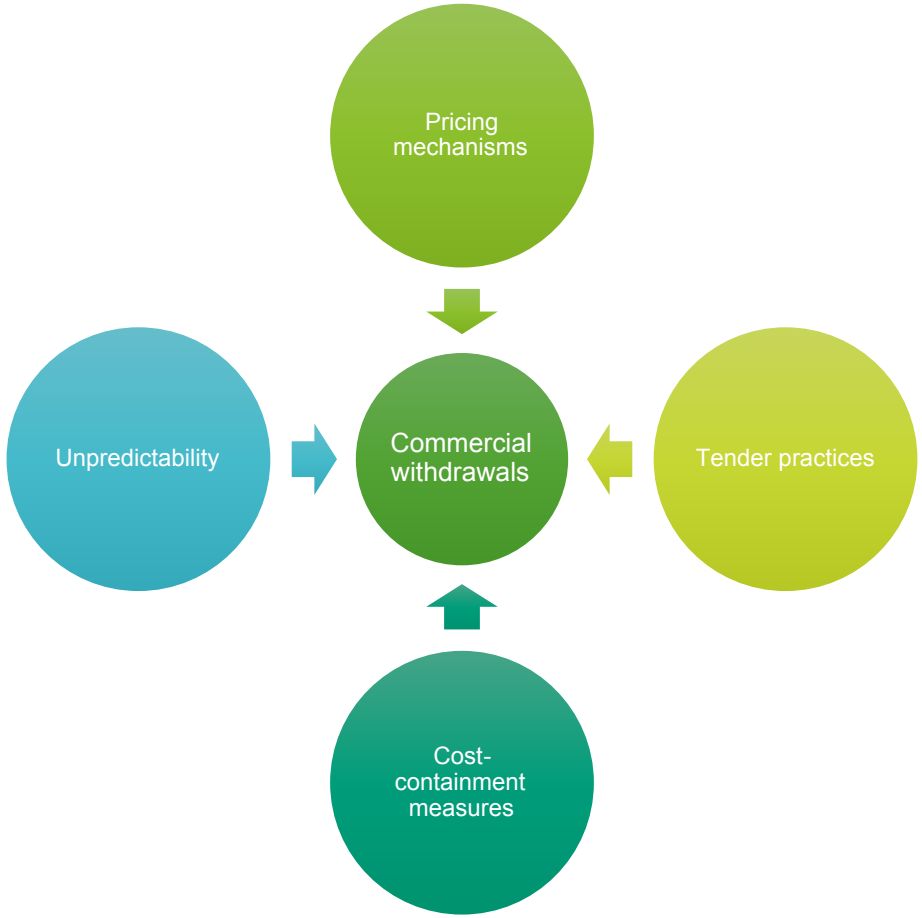
More frequent **medicines shortages**

# Scenarios leading to shortages:
# Cost -containment measures

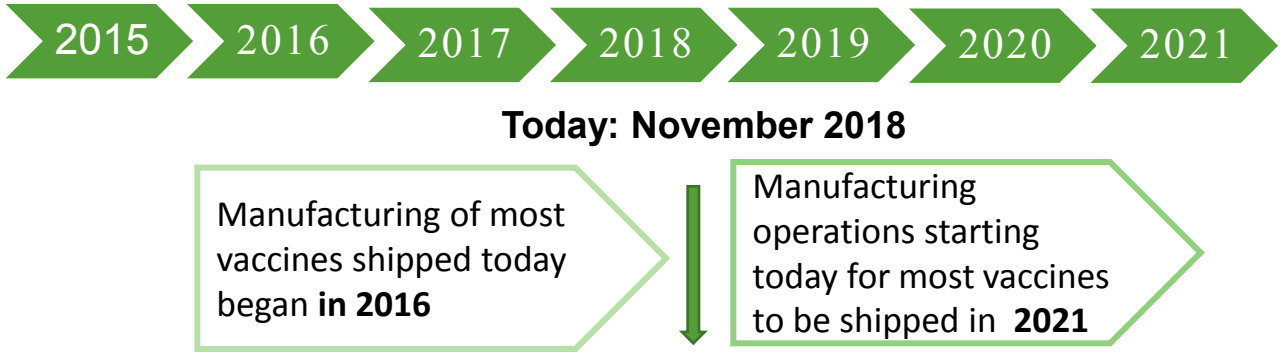


# Scenarios leading to shortages:
# Commercial withdrawals




# Vaccine supply example




- Vaccine manufacturing is highly complex with long lead times and can be unpredictable.
- Short-term response to unexpected changes of demand is difficult.
- Significant increase of capacity post-autorisation:
  - takes time (5 to 10 years are needed to build and license a new facility)
  - results from decision based on assumptions and taken at risk.

# Vaccine supply specificity

- What are manufacturers doing to improve vaccine supply?
  - continuously invest in more robust and efficient manufacturing and control processes to increase production of high quality vaccines meeting European standards
  - invest in additional capacity (expansion of existing facilities and establishment of new facilities ).
- Industry measures alone will not be sufficient as the root causes of vaccine shortages/unavailability are driven to a significant extent by external factors:
  - changes of national immunisation programmes in the world
  - unpredictable changes of epidemiology
  - complexity of worldwide regulatory requirements.

# Vaccine supply specificity

- Vaccines Europe recommendations* to establish sustainable vaccine supply:
  - establish early and continuous dialogue between manufacturers and public health authorities to better anticipate the evolution of vaccine recommendations
  - introduce procurement practices which would enable to better manage risk and optimise vaccine supply
  - optimise existing capacity by streamlining regulatory requirements in Europe and across regions.
- Vaccines Europe stands ready to work:
  - with all relevant stakeholders on feasible solutions to improve vaccine supply (eg. in Joint Action on Vaccination)
  - with HMA/EMA taskforce on implementation of the guidance on notification of shortages for vaccines.

* http://www.vaccineseurope.eu/wp-content/uploads/2017/06/VE-paper_priorities_vaccination_policy-22-05-2017.pdf

# Good practices in communication of shortages

**11. Are there specific penalties for interruption of supply/shortages? If yes, did you impose sanctions during the last 10 years ? Have the penalties for shortage resulted in reluctance from the MAH to inform you about shortages, or in deregistration of the medicinal product?**

- Most authorities foresee sanctions:
  - Not applied in the last 10 years in most cases. Some exceptions for non reporting of interruption of supply or for non-compliance to the public service obligation leading to warning letters, suspensions of authorisation or financial penalty.
  - No reluctance from the MAH to inform the authorities/deregistration has been reported.
- 8 MS have no specific sanctions for interruption of supply.

15

Ad-hoc technical meeting under the Pharmaceutical Committee on shortages of medicines, 25 May 2018

**Concerning Art.23 of Directive 2001/83/EC, Member states (EC) consider:**

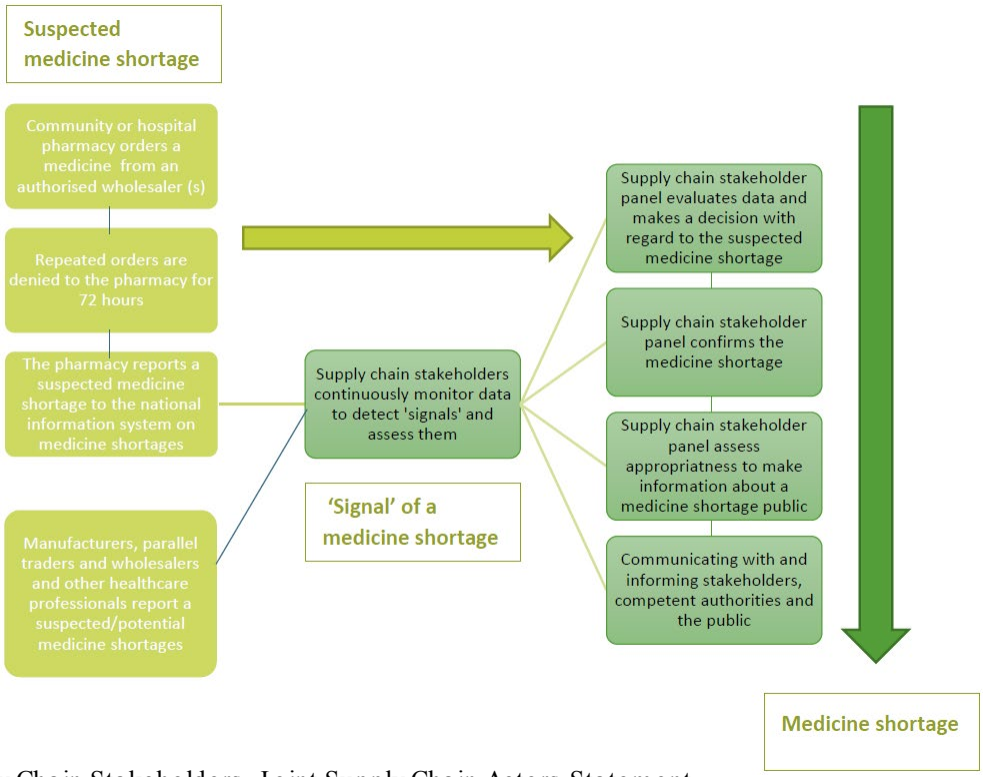
- Communication between MAHs and NCAs is generally functioning
- MS communicate with industry to monitor shortage situations

# Current communication practices

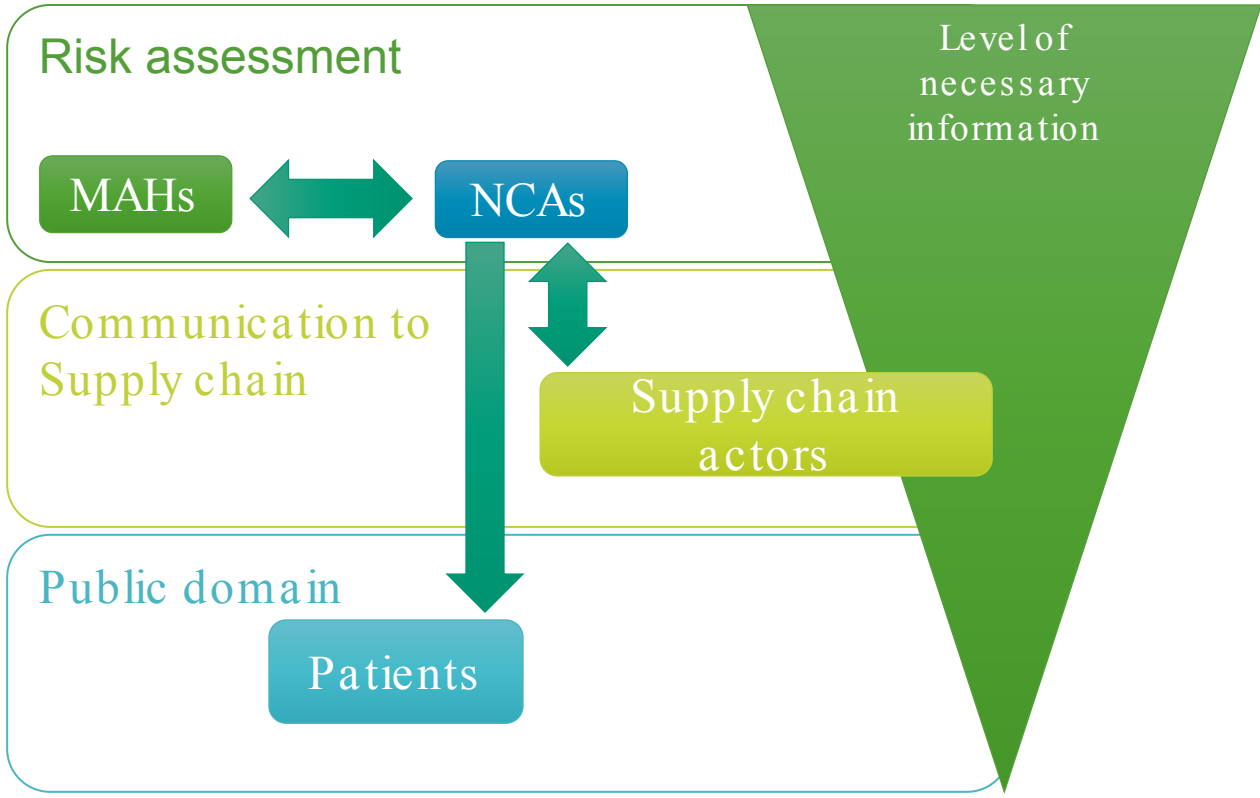
- Significant differences and variations across Member States – Need for increased convergence and harmonisation
- A need for simplification of the notification process (at the national and central level) – Development of an unique portal

# Good practices in communication of shortages

## Hypothetical system of detection and assessment of a medicine shortage




## Communication must be well planned to avoid worsening shortages




Supply Chain Stakeholders. Joint Supply Chain Actors Statement on Information and Medicinal Products Shortages. (2016).

# Good practices in communication of shortages

| Define risk to patient | | | Access to Therapies | | |
|---|---|---|---|---|---|
| | | | No alternatives | Alternative products available Similar therapy | Exact products available but in other presentations |
| Product indications | Life supporting or life sustaining | Fatal or severe irreversible harm if the patient is not treated | 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 |

# Conclusions

- Medicine shortages are a multi-factorial issue that must be tackled in strict collaboration with all stakeholders (regulators, industry, supply - chain, payers).
- Efficient communication is essential:
  - Simplification and harmonisation are needed;
  - Ensure all supply chain actors receive sufficient information.
- Product specificities should be considered when it comes to shortages
  - Single-source vs multi-source products;
  - Vaccines, sterile products, etc.
- Medicine shortages and availability are different issues that should not be confused.
- Industry and supply chain will continue working together to find solutions.

# Availability of medicinal products

- A product is available in a country if it is developed, obtains market authorization and is placed on the market in the given country.
- As an ambition companies want to launch in as many countries as possible and as fast as possible.
- However a number of factors can impact companies' ability to launch their products on all markets:
    - Availability of a functioning healthcare system with adequate expertise and infrastructure (as reflected by the level of health expenditures)
    - Pricing & reimbursement processes (including potential spill-overs through External Price Referencing – will impact on the launch sequence)
    - Level of regulatory requirements
    - Size of the population
    - Availability of IP rights
    - Cost to bring the product to the market (including whether local revenue will sustain local infrastructure)
- Availability vs delays

# EFPIA Market Access Delays analysis

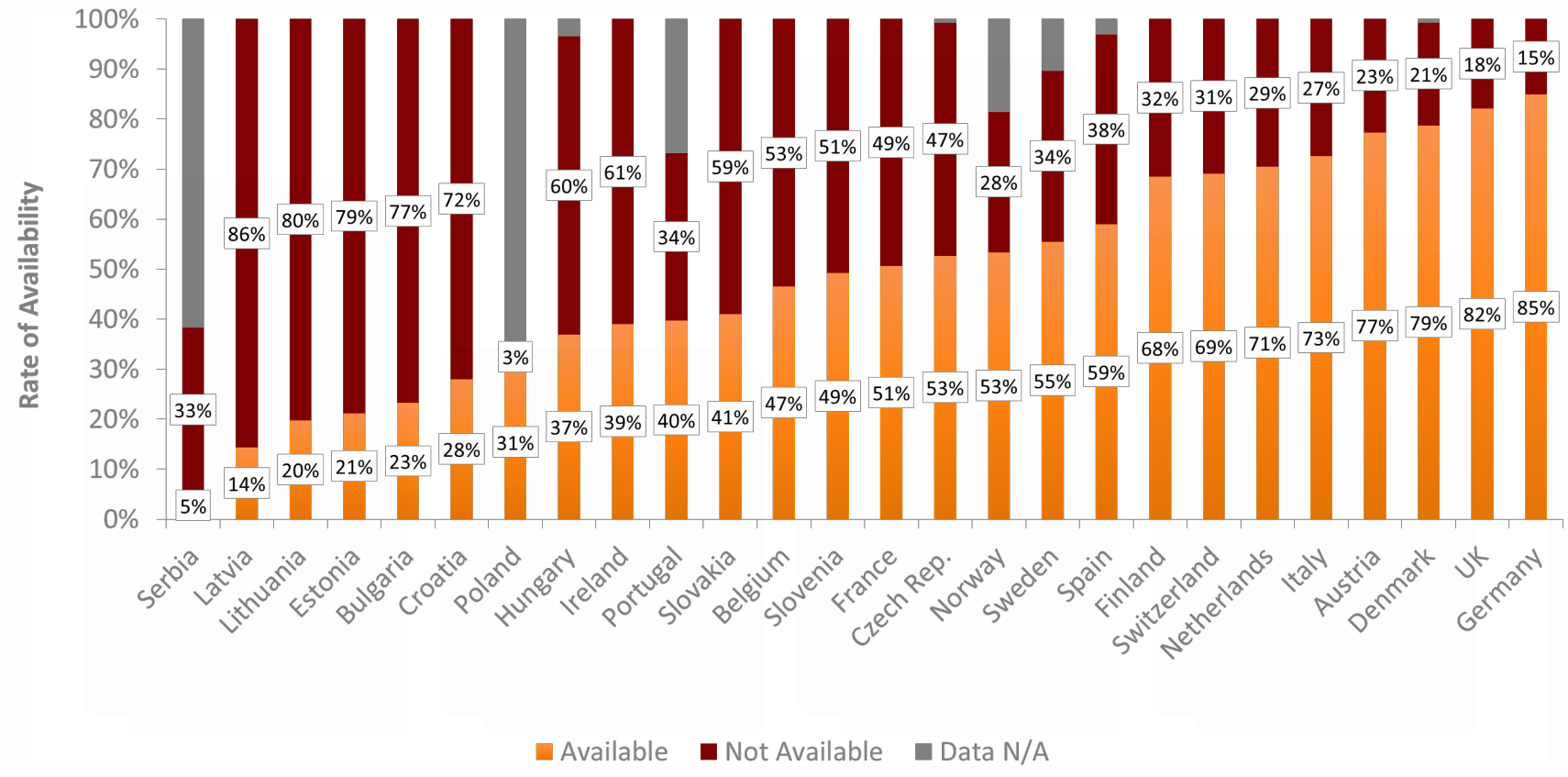
The Patients W.A.I.T. Indicator gives a snapshot of the 2 parameters at a cut-off date (December 2017)– data from medicines cohorts dropping out of the reference period are not updated in subsequent surveys.

Waiting times reflected in the Patients W.A.I.T. Indicator include any delay, whether attributable to companies or to competent authorities.

**The Patients W.A.I.T. Indicator is not a measurement of the delays as defined in the "Transparency" Directive.** Delays under the "Transparency" Directive reflect the number of days that national competent authorities need to make their decisions regarding price and inclusion of medicines in the positive list, where applicable. These delays do not include the time needed to prepare submissions under relevant national regulations, which may also include clock-stops for supply of additional information during the process; neither do "Transparency" Directive delays include time required to complete other formalities before a new medicine can be made available in a given country.

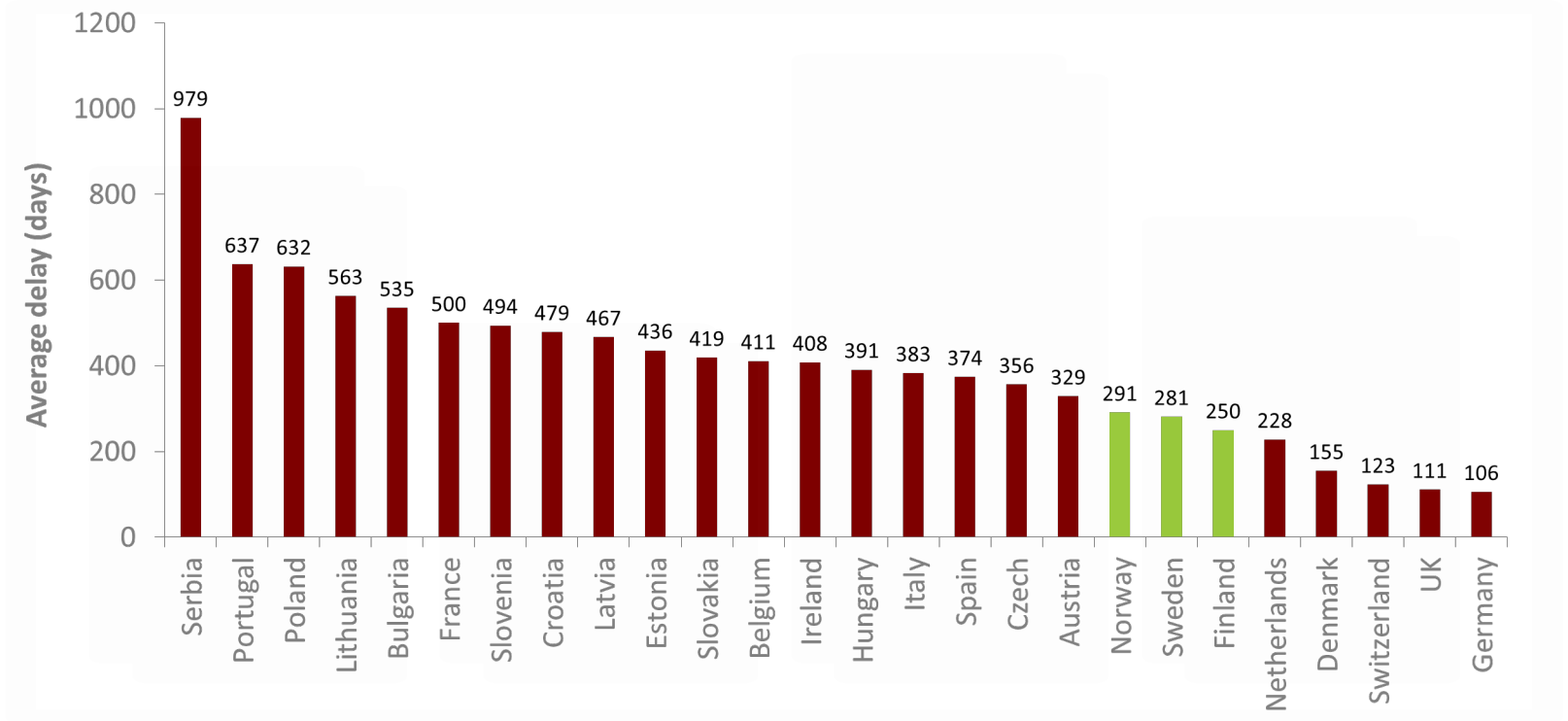
# Rate of Availability (%)

The rate of availability, measured by the number of medicines available to patients in European countries as of 2017: for most countries this is the point at which the product gains access to the reimbursement list.



# Length of market access delays (average)

The average time between marketing authorisation and patient access - the number of days elapsing from the date of EU marketing authorisation (or effective marketing authorisation in non-EEA countries) to the day of completion of post-marketing authorisation administrative processes

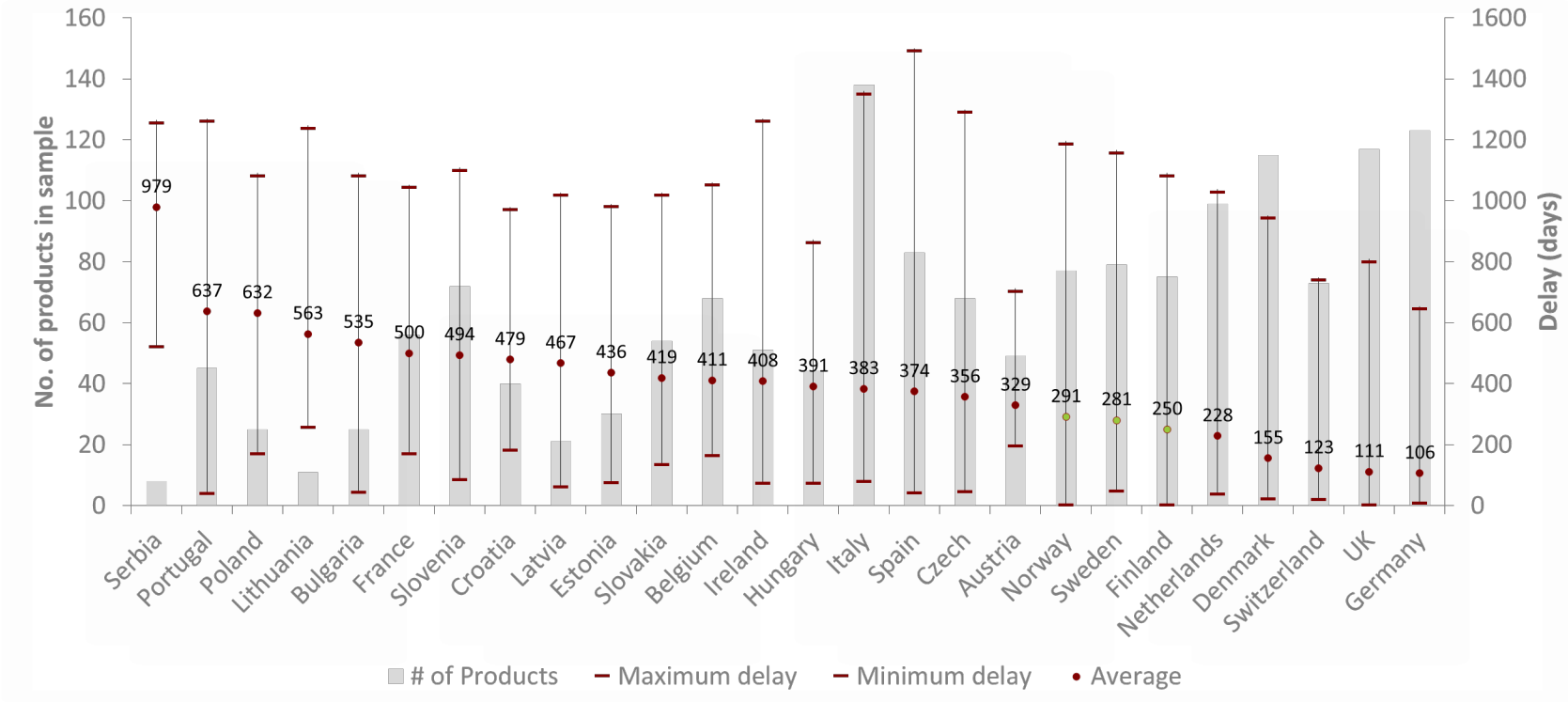



For most countries patient access equates to granting of access to the reimbursement list, except for hospital products in FI, NO, SE where some products are not covered by the general reimbursement scheme and so the zero-delay is artificially declining the median and average.

In France, some innovative products without competitors can be made available prior to market authorisation under the system of Temporary Authorisations. As these are not taken into account in the analysis, the average for France is higher than in reality.

# Length of market access delays (average)

The average time between marketing authorisation and patient access - the number of days elapsing from the date of EU marketing authorisation (or effective marketing authorisation in non-EEA countries) to the day of completion of post-marketing authorisation administrative processes




In most countries patient access equates to granting of access to the reimbursement list, except for hospital products in DK, FI, NO, SE where some products are not covered by the general reimbursement scheme and so the zero-delay is artificially declining the median and average.

In France, some innovative products without competitors can be made available prior to market authorisation under the system of Temporary Authorisations. As these are not taken into account in the analysis, the average for France is higher than in reality.