Will economic compounding and compulsory licences lead to lower prices?

Do we still want to work via the system?

Dutch association Innovative Medicines

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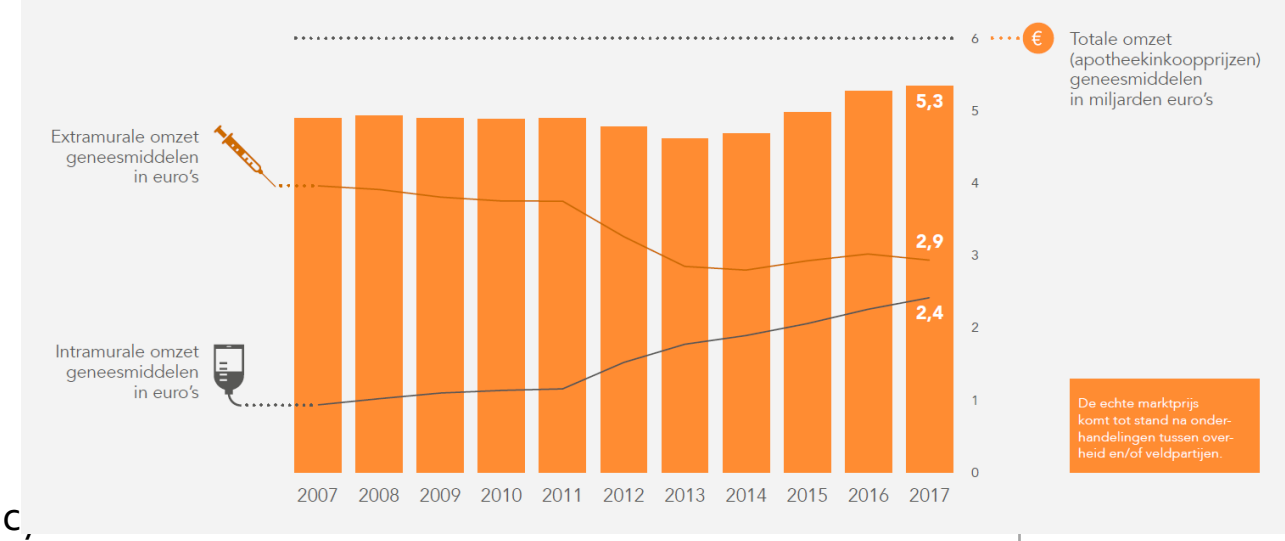
Axon Seminar

17 April 2019

Setting the scene

- Financial sustainability of the health system perceived to be under pressure
- Outline Agreement (hoofdlijnenakkoord) specialist medical care: growth curve to 0% (up to 2022)
- Due to the financial system, savings out of hospital cannot be used inside hospital



- Discussions about transparenc
- Polarization of the public debate – talking about pharma, not with pharma

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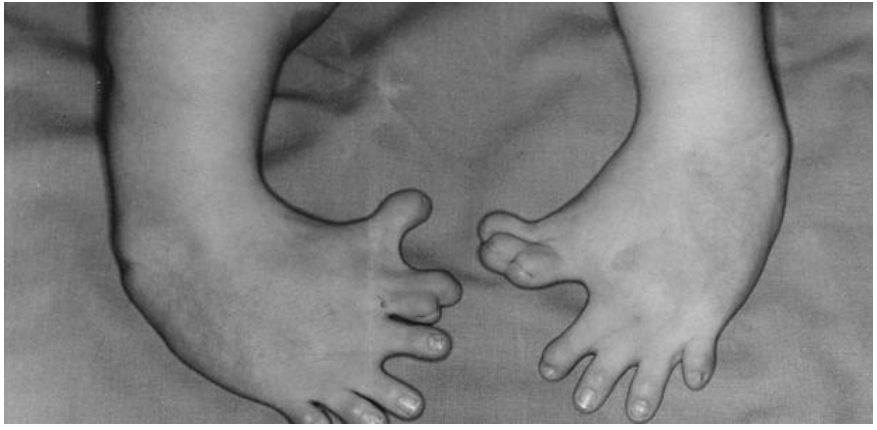
Why and how do we regulate pharmaceuticals?



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Why and how do we regulate pharmaceuticals?

Website European Commission

"Much of the impetus behind the adoption of the legal framework stemmed from the determination to prevent a recurrence of the thalidomide disaster of the late 1950s, when thousands of babies were born with limb deformities as a result of their mothers taking a medicinal product during pregnancy.

This experience, which shook public health authorities and the general public, made it clear that to safeguard public health, no medicinal product must ever again be marketed without prior authorisation.

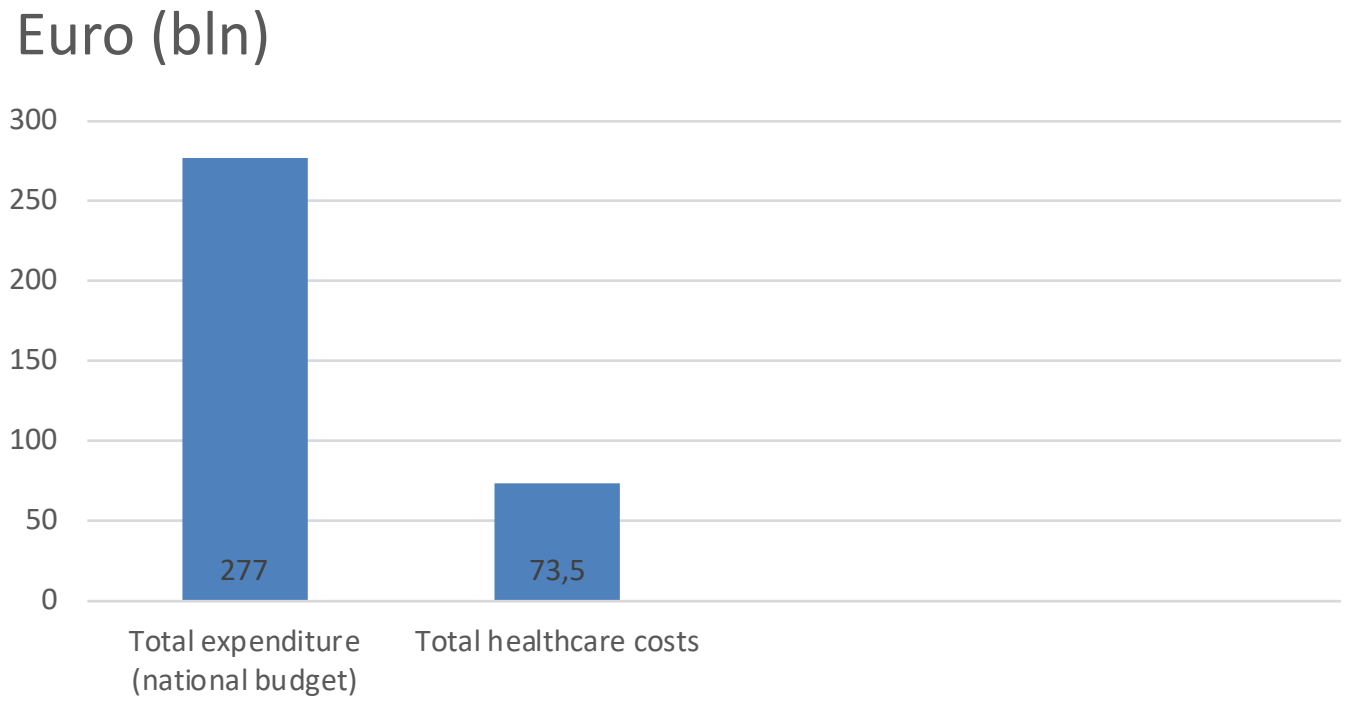
Since then, a large body of legislation has been developed around this principle, with the progressive harmonisation of requirements for the granting of marketing authorisation, and post-marketing monitoring, implemented across the entire European Economic Area (EEA)."

Mixing up 3 pillars of the pharmaceutical system

- Pricing & reimbursement
- Research & development (IP)
  - Adjustment of the SPC system
  - Compulsory licences
- Regulatory
  - Stimulate compounding (no manufacturing authorization or marketing authorization needed)

Are we in a crisis that requires such drastic measures?

The context – healthcare costs in the Netherlands



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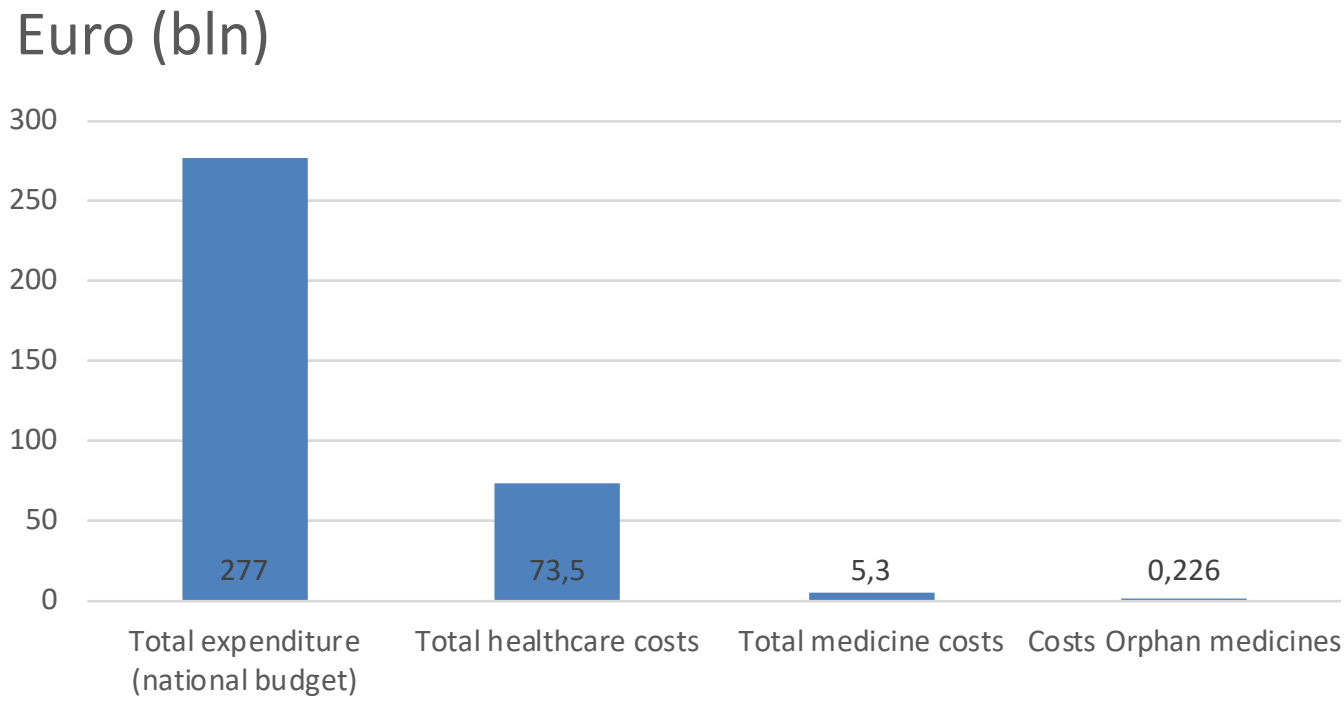
The context – healthcare costs in the Netherlands



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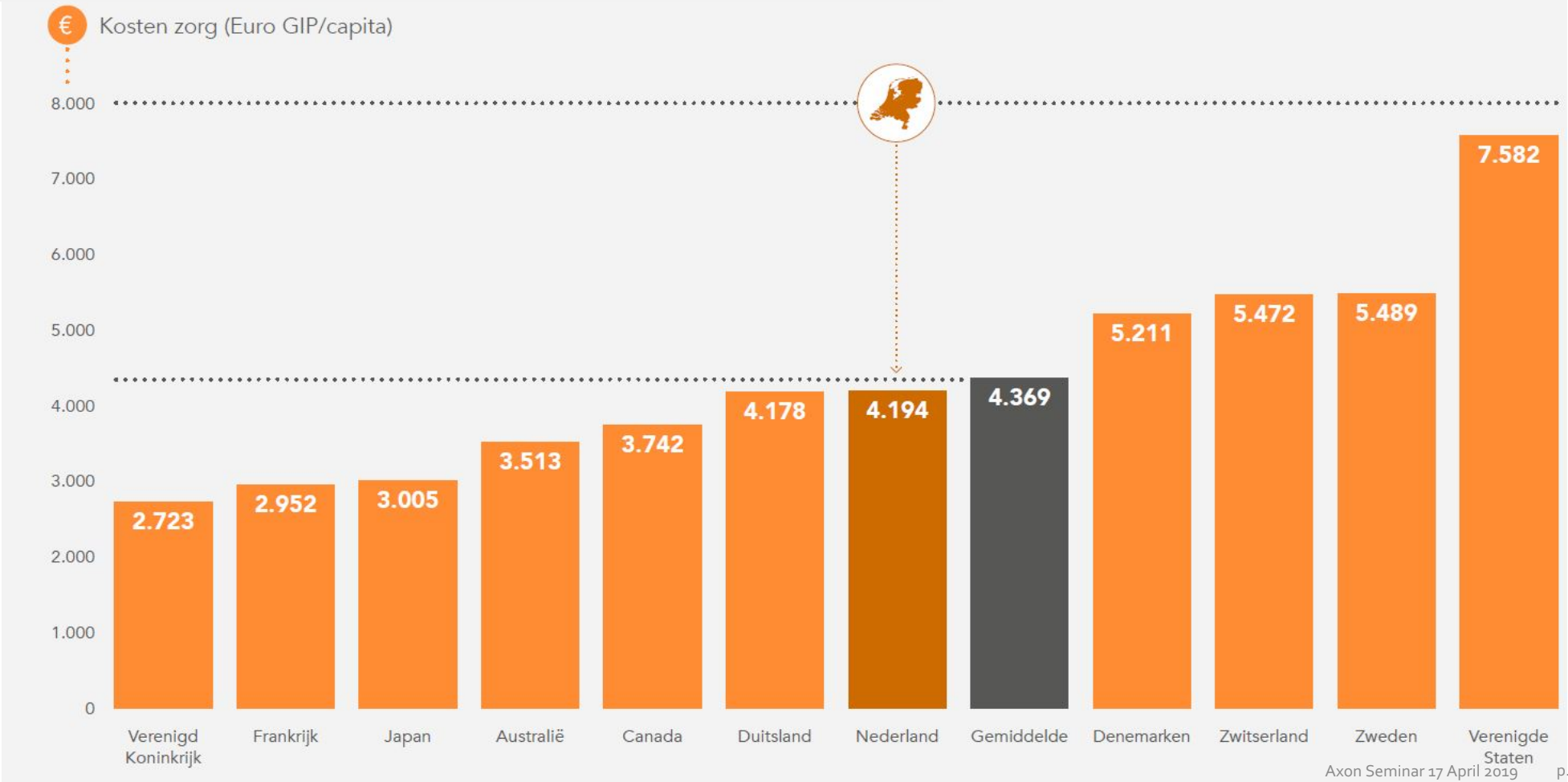
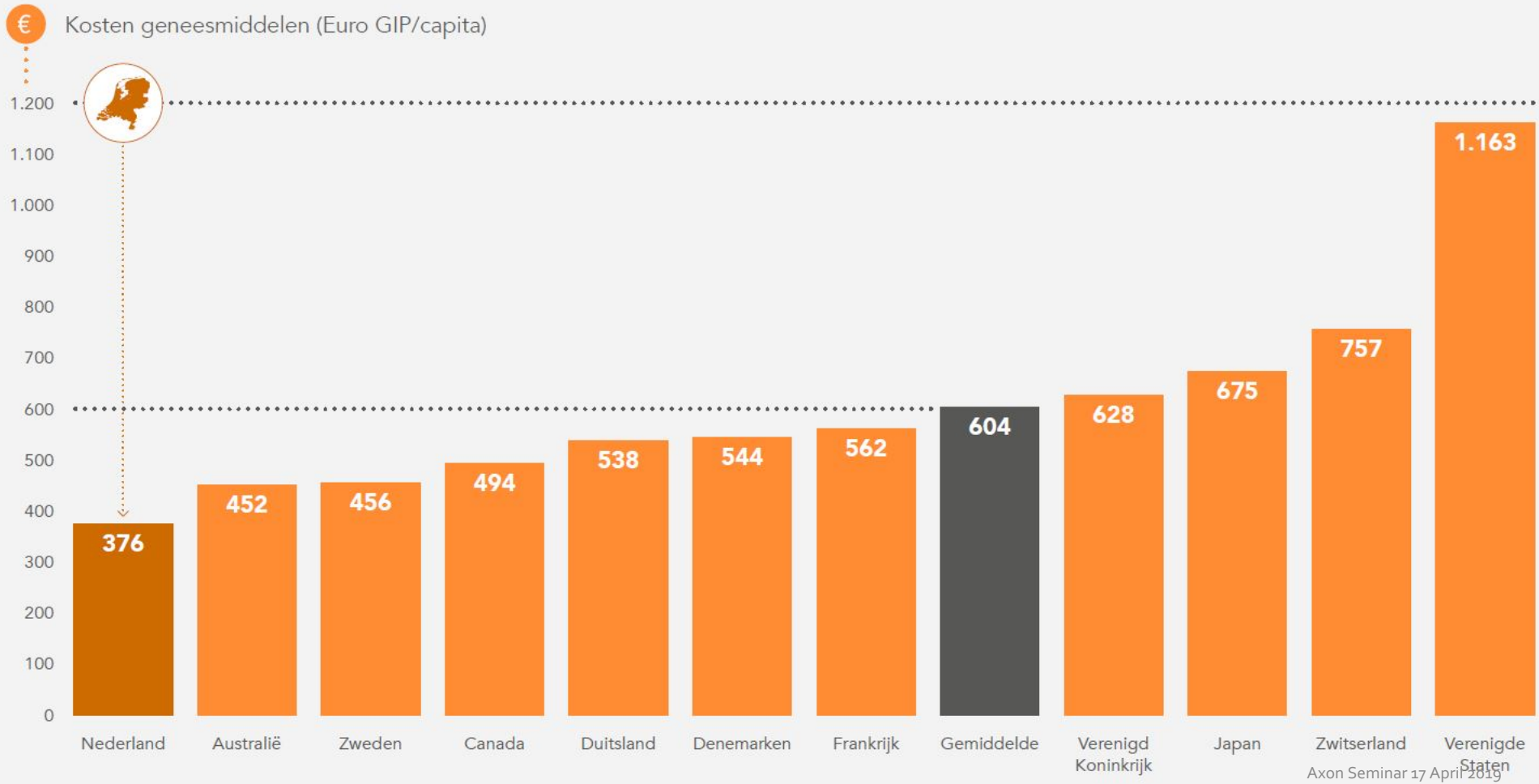
Cost of healthcare per capita

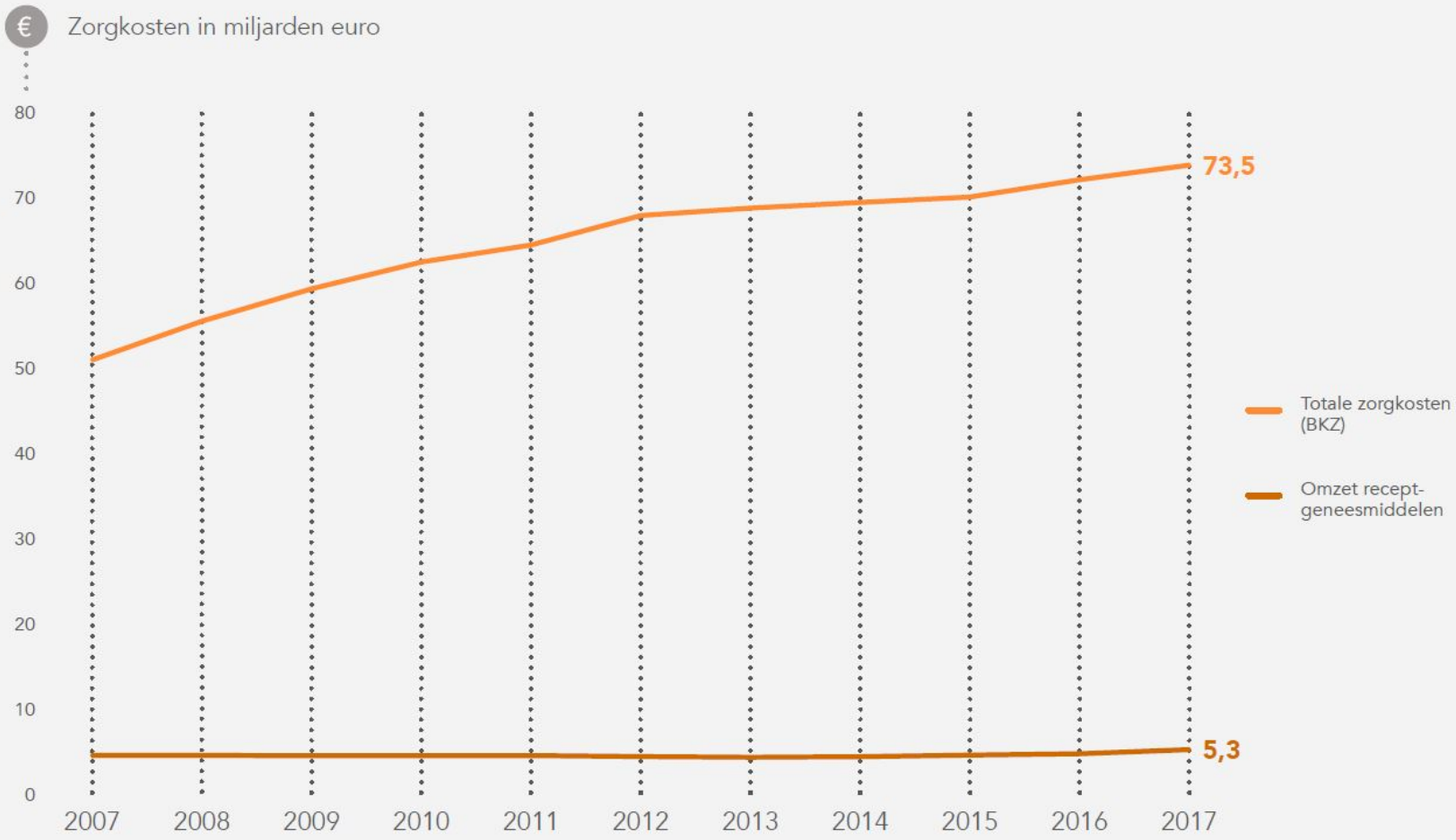


Cost of medicine per capita



Bron: Journal of the American Medical Association: Healthcare spending in the United States and other high-income countries (2017)

Drug sales relatively stable

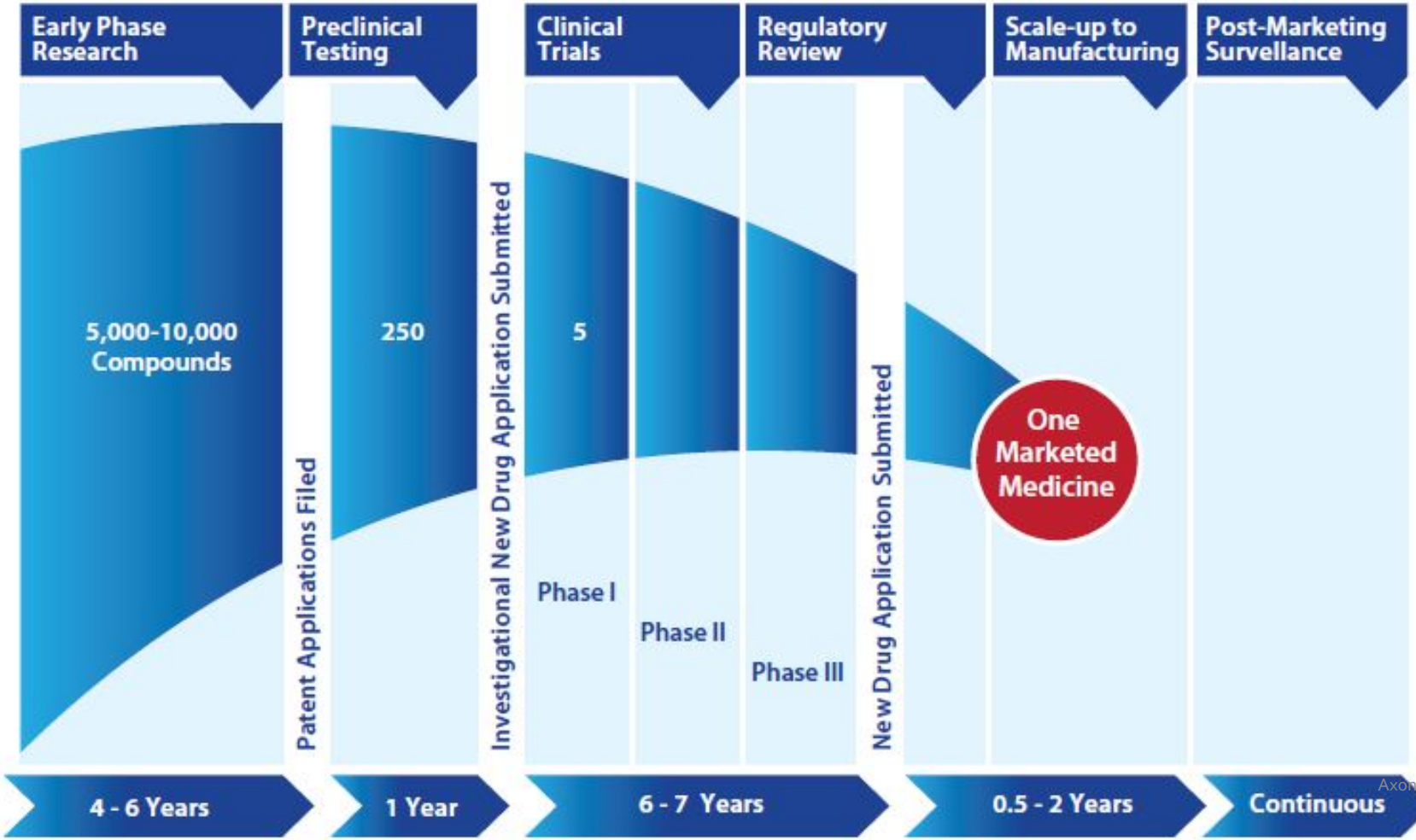


Bron: Rijksbegroting 2018; Farminform 2018

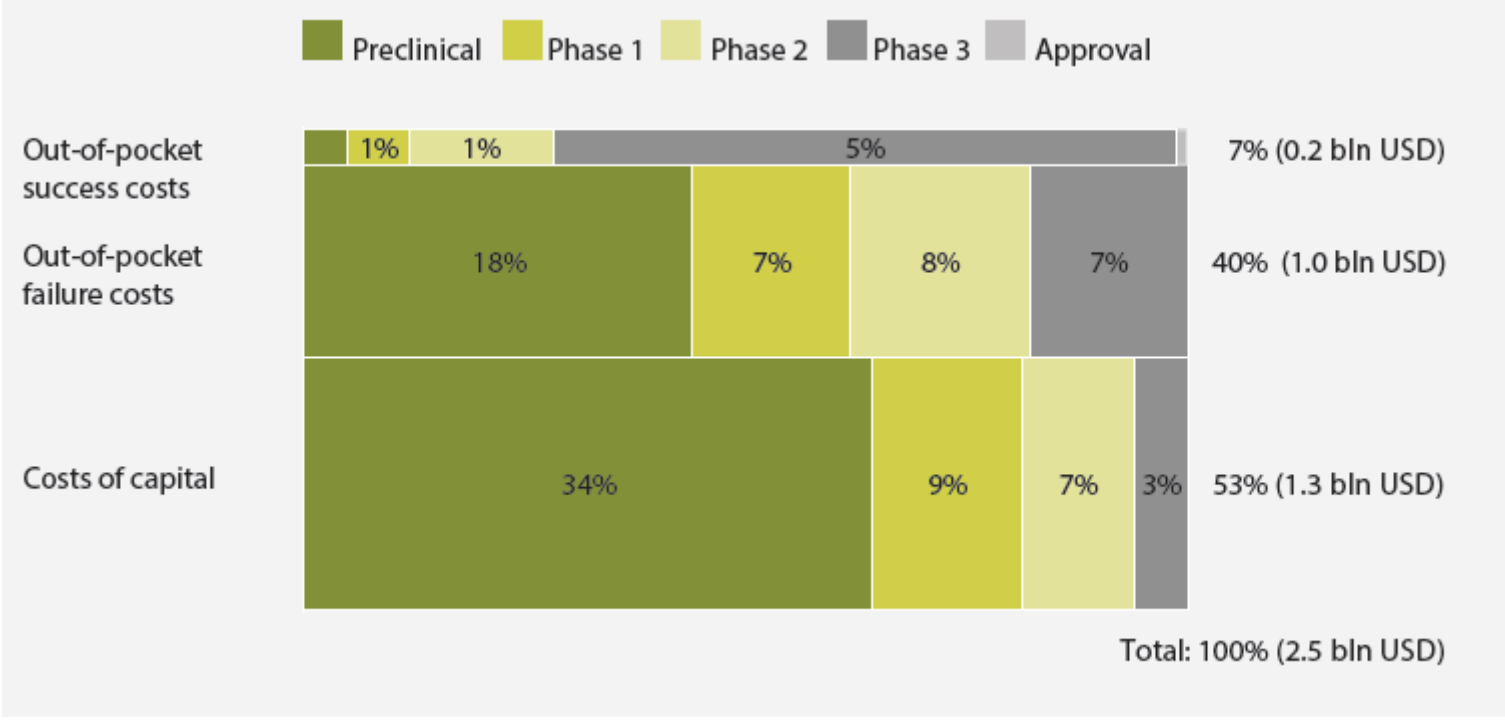
The context - Development of a new medicine

We need only three things to develop a new medicine

Development of a new medicine takes 11-14 years



The costs of developing a new medicine rises sharply



After authorization – the patient does not have access yet

Health care coverage

- Each country has its own system with respect to EU law and regulations
- Horizon scanning (selection)
- Assessment by National Health Care Institute (Zorginstituut Nederland)

Price negotiations on multiple levels

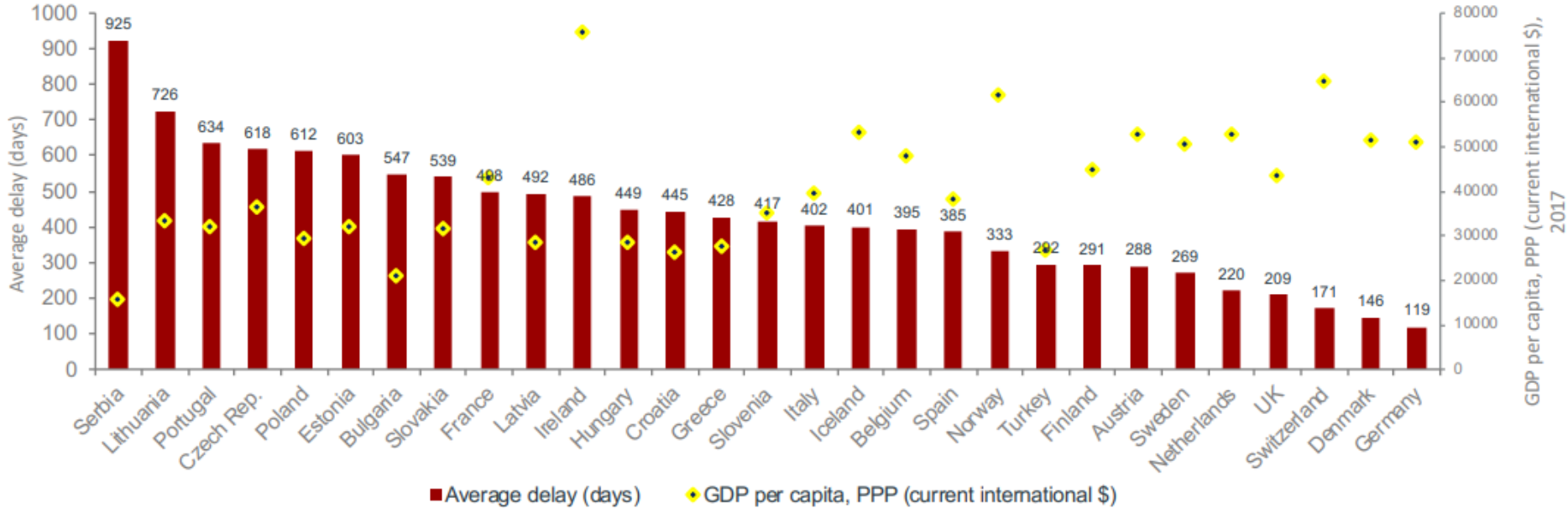
- International (Beneluxa)
- National (Bureau Prijsarrangementen Geneesmiddelen (LOCK), joint procurement health insurance companies)
- Local (hospital groups, insurance companies)

And after negotiations

- Funding (add-on)
- Uptake in treatment guidelines
- Local availability – concentration and centralization of care
- Prescription according to treatment guidelines

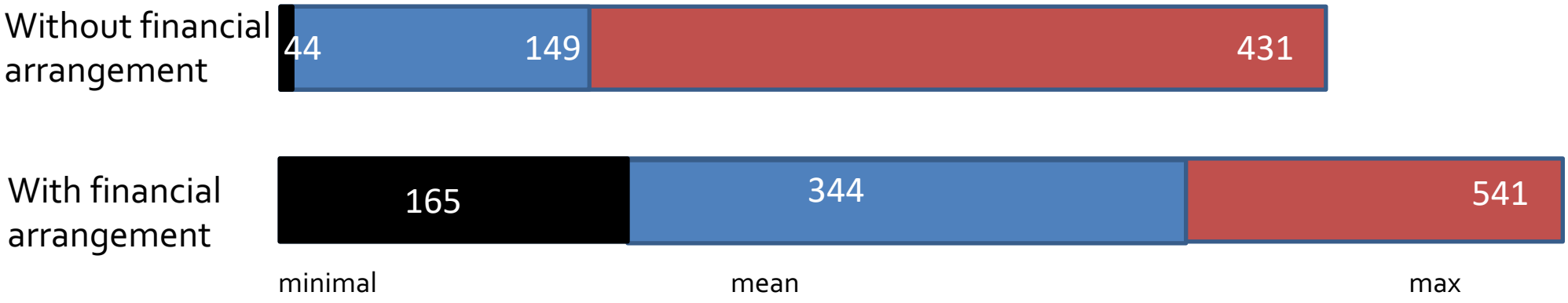
Length of market access delays (average)

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



Source: GDP per capita, PPP (current international $), 2017 - World Development Indicators, World Bank

Slow availability for LOCK products



Number of days from EMA registration until the medicine has received an add-on. Calculations do not include products with access during the reimbursement procedure (e.g. other indication). Source: EMA (2018); Z-index (2018)

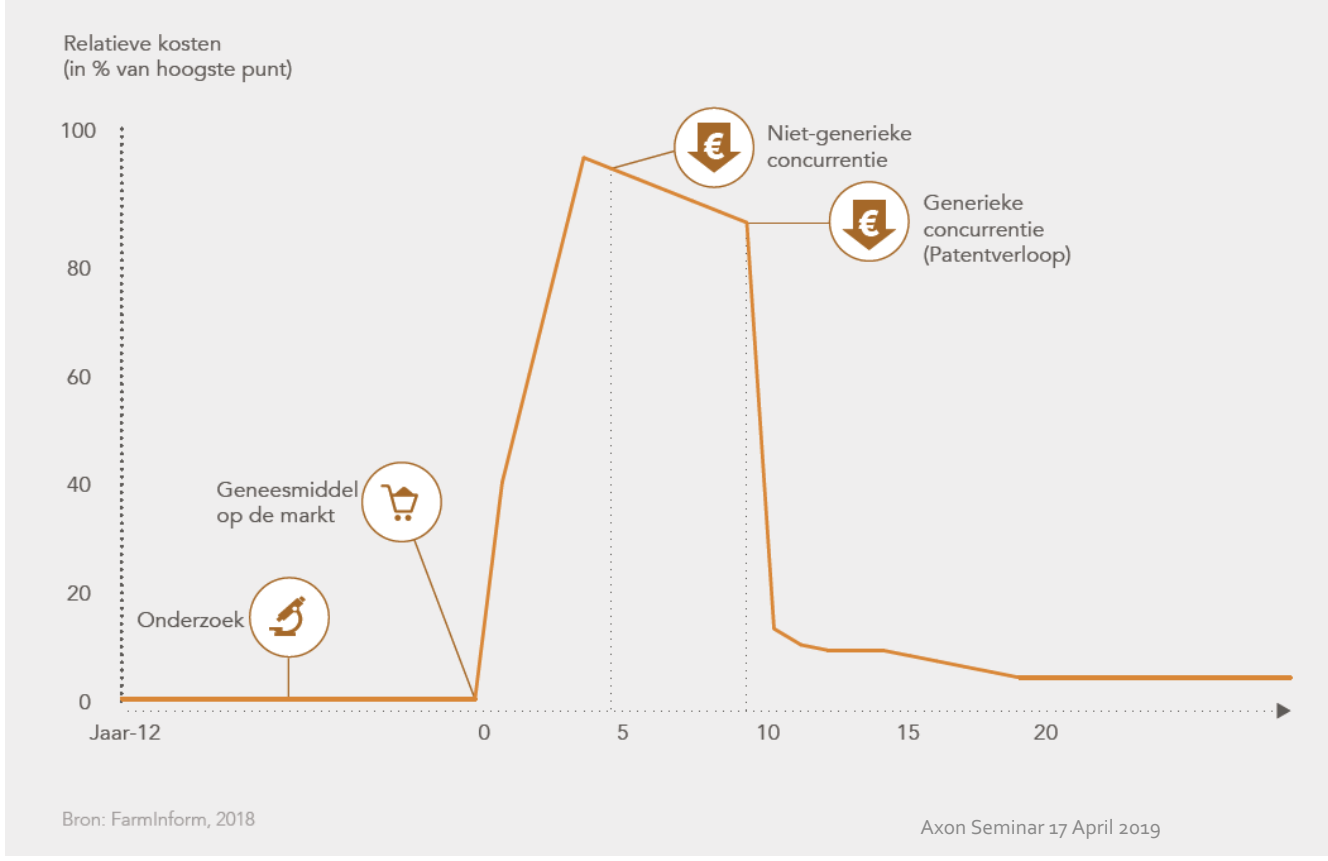
The context: the financial life cycle of a medicine

New pharmaceutical medicines typically face competition after a relatively short time on the market

Take the total life cycle into account

Penicillin:

- Costs 1942: $ 800/day
- Converted to the price level of 2018, a penicillin treatment costs € 60.000 (7 days)
- Real costs 2018: € 24,57



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Goals 'geneesmiddelenagenda' Dutch Ministry of Health

Goals:

- Financial sustainability health system
- Patient access to new innovative medicines
- Affordability

How? By mixing up 3 pillars of the pharmaceutical system (with consequences for innovative, generic & rediscovered medicines)

- Pricing & reimbursement
- Research & development (IP)
  - Adjustment of the SPC system
  - Compulsory licences
- Regulatory
  - Stimulate compounding

Leading to lower prices?
Are there any side effects? Do we want these?

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Use of compulsory licences leads to a lot of (unwanted?) side effects

Leads to reduced access

- Leads to a hostile negotiating environment
- Challenges willingness to negotiate
- Most innovative medicines get competition within several years after introduction
- Length of procedure considerably (incl. appeal and objection possibilities)
- Could limit incentives for conducting clinical trials
- Limits manufacturing of new drugs

A lower price is not guaranteed

- Legal uncertainties
- There is no experience with compulsory licences for financial reasons
- The licensee has to invest considerably
  - Obtain clinical data (not available due to data exclusivity period)
  - Obtain bioequivalency / biosimilarity data
  - Obtain necessary permits (e.g. (adjustment) manufacturing license, trade license)
- Considerable disturbance of European internal market

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Compounding is important in case of a medical need

Compounding is an important exemption to the authorization process:

- Alternative dosage forms (fluid in stead of solid forms)
- Particular dosages/strengths (children)
- Alternative raw materials (intolerancies/allergies)
- Alternative organoleptic characteristics (masking of unpleasant bitter substances with syrup)
- Shortages
- Discontinued medicines
- Special combinations (polypharmacy)

Use compounding in a proper way

- Medical need
- Exceptional case
- Not a replacement for a registered medicine
- Not for financial reasons: do not mix-up the pillars

Can compounding replace registered medicines?

Comparing apples and oranges

Value of the regulatory system

- Prior assessment of the product and person responsible for preparation of the product
- Medicines are assessed on quality, safety and efficcy
- Guarantees quality throughout Europe
- Compliance with marketing authorization is verified throughout the product lifecycle

`Compounding: safety is under pressure

- No prior assessment of product and person responsible for preparation of product
- Not subject to stringent testing and pharmacovigilance rules
- Not all pharmacies are inspected on a regular basis – and neither their products

Research Belgian Consumer Organisation Test-Aankoop

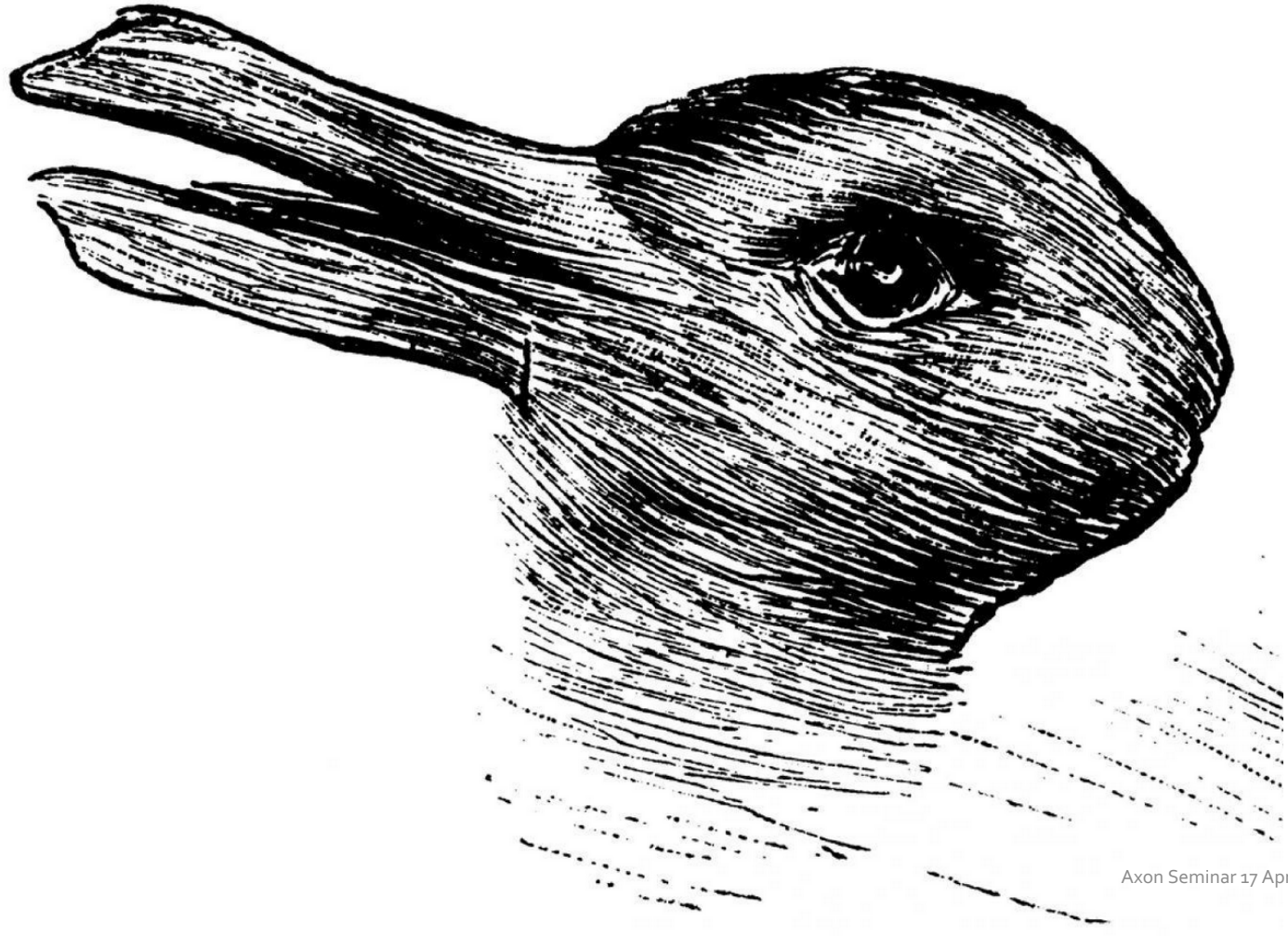
Visited 44 pharmacies in 2016 to obtain a magistral preparation of dexamethasone capsules 0.5 mg

In 35 cases the magistral preparation did not conform to the specifications of the European Pharmacopoeia (Ph. Eur.)

Only one in five preparations was in accordance with the Ph. Eur.:

- For 7 magistral preparations not every capsule contained the same amount of powder
- 5 pharmacists had not properly mixed the active substance with the inactive ingredients
- 2 pharmacists added too much active substance
- 28 pharmacists used too little active substance, causing underdosing

Letter of MoH, 9 April 2019



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What exactly does the letter say?

- Basis principle remains the use of authorized products?
- Green light for economic compounding?
- Going 60 years back in time – when the regulatory system was not yet in place

Pricing?

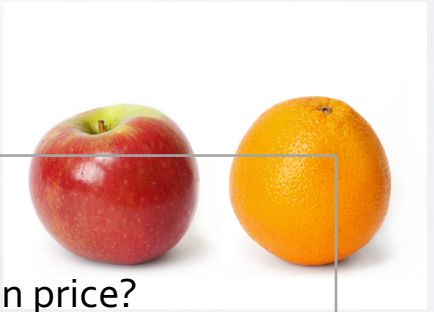
- A centralized financial arrangement between MoH and a company leads to an 'acceptable' price
- What does this mean? Can MoH enforce the use of a registered product? What is 'acceptable'?
- What will be the total financial gain?

Patient access?

- Long-term use : ~50 patients/month?
- Short-term use: ~ 150 patients/month?

  What does that mean? Total patient population? In each pharmacy? How long is long-term use? Is there a limit?
- Does MoH open the door? Or does he throw the door away?

Unwanted side effects – is it worth it?



Effects on the regulatory system

- What is the value of the regulatory system?
- Will registered medicines be compared with compounded ones on price?
- Will insurance companies start a preference policy with compounded and registered medicines?

Effects on safety?

- Safety of compounded medicines cannot be compared to registered versions
- What to do in case of shortages? What is the fall-back option for compounding?

Effects on access?

- How attractive are the Netherlands for the introduction of new medicines?
- Who will block access? Can artificial unavailability be created by parties by blocking reimbursement?
- Freeriding: want to use innovation but not pay for it?

Still … 'Basis principle remains the use of authorized products'?

Unwanted side effects – is it worth it

Effects on drug development?

- Disincentive for rediscovery/repurposing
- Disincentive for (orphan) medicine development

Economic consequences? Mixed messages!

- International reputation? (host country of both EMA and EPO)
- Will the EMA lead to more pharmaceutical business activities?
- Will this affect opportunities for Dutch start-ups and biotechs?

Are there no alternative solutions?

Respect the system

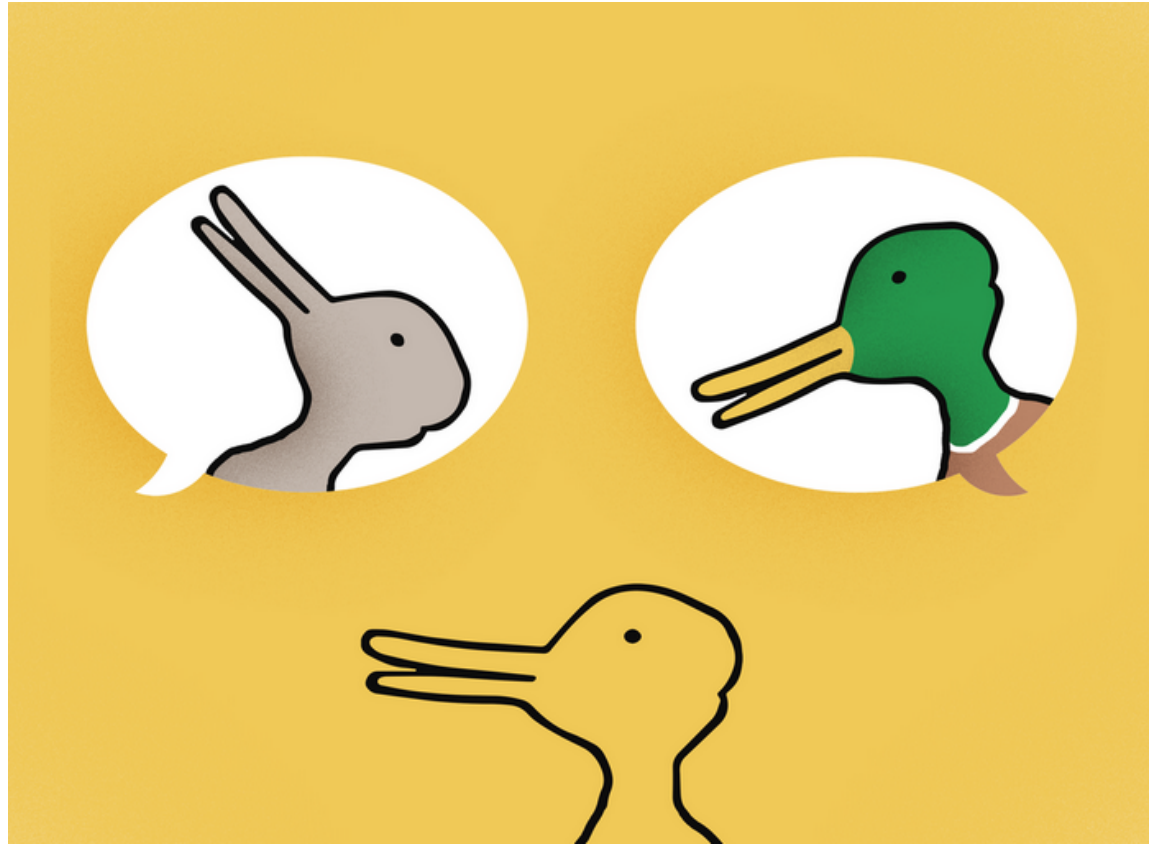
- R&D system to stimulate development of medicines
- Regulatory system for optimal quality
- Pricing / reimbursement system to obtain financial sustainability

Costs of medicines

- Develop tailor-made financial arrangements
- Use RWD to determine effect of medicine in practice
- Create one budget system for medicines

- Prepare the system for the future
  - Is the system prepared for new medicines?
  - Orphans? ATMPs?

Thank you!



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