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Medizin mit Qualität und Seele
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Drug Shortages

A Hospital Pharmacist´s Perspective

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Dr. Thomas Langebner, MBA
thomas.langebner at vinzenzgruppe.at

Krankenhäuser Barmherzige Schwestern Wien, Linz, Ried • Orthopädisches Spital Speising • St. Josef-Krankenhaus Wien • Krankenhaus Göttlicher Heiland
Herz-Jesu Krankenhaus • Barmherzige Schwestern Pflege • Kurhaus Marienkron • Herz-Kreislauf-Zentrum Bad Ischl

Disclosures

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- Chief pharmacist at Krankenhaus Barmherzige Schwestern Linz
- Co-ordinator of pharmaceutical purchasing activities at Vinzenz Gruppe
- Relationship with pharmaceutical companies
  - none

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Agenda

- introduction
- consequences of drug shortages
- causes of drug shortages
- basic concepts in theory of markets
  - product life cycle
  - pricing
  - quality
  - customer
- take home messages

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tu felix Austria
paradise lost

- a lecture on drug shortages (EAHP congress 2008)
  - a message from a different planet?
  - a preview of things to come!
- 2011: fosfomycin, iv-prednisolone; 5-FU, calciumfolinate, ...
- Jan 2012: Austrian Association of Hospital Pharmacists (AAHP): letter to the Minister of Health
- Austria today
  - no big disasters recently,
  - a significant decrease in overall supplier reliability,
  - numerous (short term) shortages

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- **consequences of drug shortages**
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- points to consider

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Consequences of drug shortages

- Drug shortages put **patients at risk**.
- Drug shortages cause **significant extra costs** for health-care systems.
- Drug shortages are **a major threat** to European health-care systems.
- Drug shortages are **not a trivial offence**.

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Characteristics of pharmaceutical industry
Anything new?

- Production of (iv-)medicines is a challenging task,
  - but it always was.
- Production of (iv-)medicines requires high technical and financial efforts,
  - but it always did.
- Production of (iv-)medicines requires compliance with strict regulation,
  - but it always did.

- What´s new?
  - expiry of major patents
  - empty pipelines (the end of the “era of blockbuster drugs”)
  - reduction of profits
  - cost pressure
  - concentration processes
  - increased complexity of manufacturing and supply chains
  - increased capacity utilisation
  - increased (exaggerated?) return on equity-expectations (J. Ackermann: 25% RoE/y)

The main cause of drug shortages is economic.

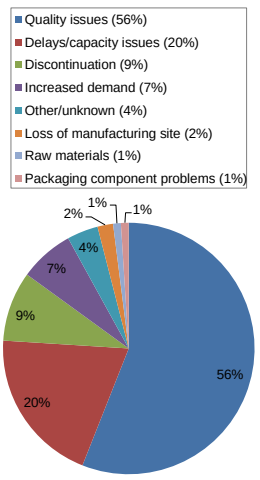
If manufacturers don't make enough profit, they won't make generic drugs.

[Gatesman/Smith 2011]

- failure of quality management
- a reactive approach to quality management
- cheaper sources for active pharm. ingredients (APIs)
- contracting practices
- ageing facilities
- leaner inventory (just-in-time practices)
- lack of redundancies
- discontinuation
- new production opportunities
- stockpiling by end users
- increased demand caused by another drug shortage (domino effect)

[ASPE 2011, Cherici/Frazier 2011, Woodcock/Wosinska 2012]

Reasons for iv-Drug Shortages (FDA 2012)



[redrawn from Kweder/Dill 2013]

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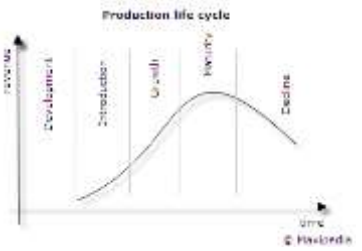
The misleading Logic of Product Life Cycle



- Despite dramatic progress in medicine there is a substantial body of "mature" active pharmaceutical ingredients (APIs) that are still essential in therapy.
- **Adequate supply with "mature" medicines is (at least) as essential to health-care systems as adequate supply with innovative medicines.**

"mature" APIs, e.g.

- busulfan (1954)
- methotrexate (1955)
- dexamethasone (1958)
- cyclophosphamide (1958)
- vincristine (1958)
- cytarabine (1959)
- 5-fluorouracil (1960)
- bleomycin (1966)
- etoposide (1973)
- cisplatin (1979)
- ondansetron (1990)
- paclitaxel (1992)
- … [Newman/Cragg 2007 mod]

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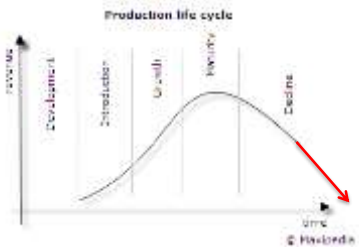
Product Life Cycle – a smooth landing



- Essential but "mature" medicines require a **steady state equilibrium**,
  - i.e. a **fair price level** allowing for
  - continuous and **adequate supply**
  - as well as **adequate revenue**.

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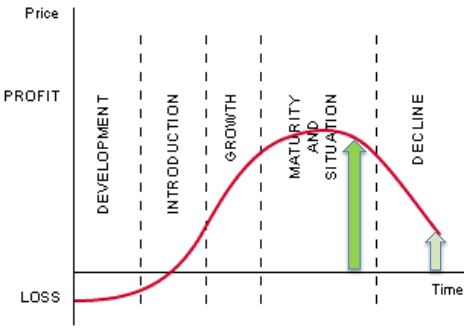
The "sales decision"



- Why shouldn't you **produce** and **sell** while a product is still making profit?

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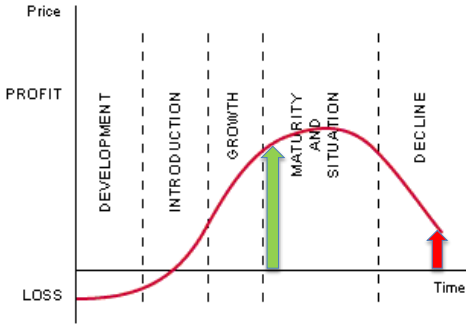
The “investment decision”



“mature” medicines:
price levels after patent expiry

- zoledronic acid: 7%
- docetaxel: 2%
- gemcitabine: 5%
- …

- Why should you **(re)invest** in a product if there is a more profitable alternative?
- In a setting of capacity restraints (expected) (excessive) benefit from new products discourages the production of old, essential but less profitable medicines.

Price elasticity (responsiveness)
How to react on changing prices

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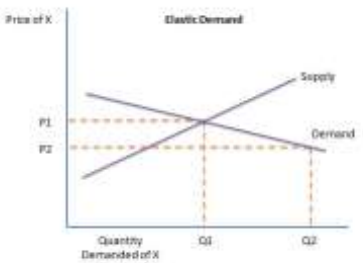

- High elasticity (responsiveness) means that
  - decreasing prices will stimulate a prompt increase in demand.
  - increasing prices will stimulate a prompt increase in supply.

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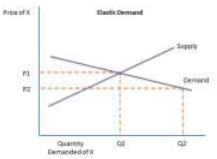
Price elasticity of supply
How suppliers react



- Decreasing prices for “mature” medicinal products obviously contribute to decreased supply.
  - typ. suddenly due to discontinuation, disruption of production or secondary shortage
- Is a (moderate) increase of prices going to stimulate a (fast) increase in supply?
- Empirical data show the price elasticity for prescription drugs to be very low.
  - approx. 0,2 in UK and US [Opderbeck 2005]
  - i. e. doubling the amount supplied requires a 5-fold price

Determinants of elasticity
- availability of raw material
- length and complexity of production
- mobility of factors
- time to respond
- inventories
- spare/excess production capacity
- …

[Gabler]

Pricing medicines
The end lies in the beginning

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“mature” medicines:
price levels after patent expiry

- Zoledronic acid: 7%
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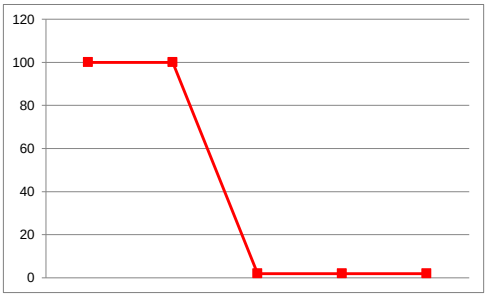

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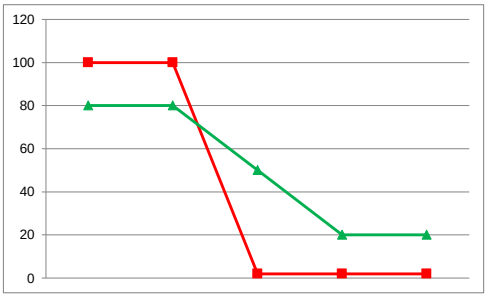
Pricing medicines
The end lies in the beginning



- Excessively high pricing for new medicines discourages the production of “mature” medicinal products.
- Re-shaping (i.e. flattening) the price-curve will set the right signal for a long-term perspective and stimulate continuous and adequate supply with essential medicines.
- Pricing medicines is a matter of trade-offs taking into account the legitimate interests of customers (i.e. good supply with good medicines at a fair price) and of suppliers (i.e. good revenue, clear perspectives).

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Quality
What you see is what you get!

- the total set of characteristics of a thing.
- the standard of something as measured against other things of a similar kind;
- the degree of excellence of something

[Duden, Oxford Dictionary]

Quality
What you see is what you get?

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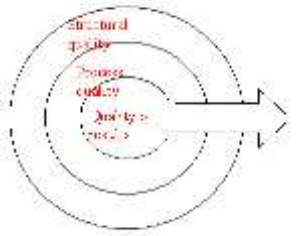
Quality
What you get is more than what you see



- "You can´t inspect quality into the product; it is already there."
  W. Edwards Deming (1900-1993)
- You can´t inspect good quality into a medicine, you can only produce it.

"The FDA said groups that buy drugs, such as hospitals and group purchasing organizations, **rarely take quality into account when making purchasing decisions**, …"
[Reuters, Oct 2013]

- Why should they?!
  - „When applying for a marketing authorisation, companies, inter alia, **must document that the product will be of appropriate quality**." [EC DG Health & Consumers]
  - „**It is forbidden to produce** or to market medicinal products or active pharmaceutical ingredients **if quality is not in accordance** with the current state of science."
    [Austrian Law on Medicines § 4 par. 1]
- Should there be an extra fee for quality of supply?
  - The marketing authorisation holder has the **obligation to guarantee adequate and continuous supply** in order to meet the demand of domestic patients.
    [Austrian Law on Medicines § 57a par. 1]
- Product quality and quality of supply are integrative and mandatory elements of the total quality of a medicine, and are **not an "extra feature"**.
- Exercising adequate control over the total quality of medicines is **the core task of medicines agencies**.

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The customer of pharmaceutical industry
Anatomy of a complex figure

- **Patient**: the one who consumes the medicine

- **Doctor**: the one who defines demand (by prescribing medicines)
- **Health insurance** etc.: the ones who pay
- **Hospital & hospital pharmacy**: the ones who purchase and provide resources
- **Medicines agency**: the one to take care of safety and quality issues
- **Health-care system, government & society**: the ones to define the framework

- The patient is the "**primary customer**".
- All others mentioned are acting on behalf of patients ("**agents**").

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How to influence market behaviour

	discourage	encourage
hospitals	suppliers evaluation, contractual fines	long-term contracts, higher prices
authorities	inspections, sanctions	incentives

Hospitals and governmental authorities

- should encourage good market behaviour (i. e. reliable supply of medicines of good quality) and
- should discourage bad market behaviour
- by use of
  - market instruments and
  - legal means

On effects and side-effects

	remedies	limitations, side-effects
information	- co-ordination of suppliers - (early) information to customers - information to the general public - quality rating system	- symptomatic mitigation - self fulfilling prophecy - irritation, panic - passing on the hot potato
inspections	- strict control - regulatory flexibility	- causing shortages - encouraging malpractices
contracting	- guarantees - failure to supply clauses	- no increase in overall supply - shifting the hole

- **Medicines agencies are no "restaurant guides".** They act as regulatory bodies on behalf of patients. Quality rating is useful , but only for medicines agencies to take action against "low scorers".
- Customers and medicines agencies can mitigate the consequences of drug shortages but are **not able to address the underlying causes of drug shortages**.

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The principal

All State power emanates from the people …

- Society is the "**meta-customer**" ("**principal**") and there is an (implicit) contract with pharmaceutical industry about the provision of required health-care services.
- Governmental authorities are the legal representatives of society. They act on behalf of the members of society (e. g. patients) to define **the framework of common well-being**.
- When markets fail to provide the desired results (e.g. reliable supply with medicines) it is the duty of governmental authorities to modify the framework.

"**Union action** … shall be directed towards improving public health, … and obviating sources of danger to physical and mental health" [Article 168 of the Treaty]

Changing the Framework

- Address drug shortages as **a matter of priority**.
- Take proper steps to (re-)establish a **sustainable supply situation**.
- Ensure **fair pricing for new medicines**.
- Establish **a price range-scheme for generic medicines**.
- Incentivize (re-)establishment of **production sites (including APIs) within the EU**.
- Incentivize **a more resilient EU drug market** (infrastructure, inventory, redundancies).
- Establish a concept of "**strategic reserves**" for essential drugs.
- Enforce mechanisms to **ensure total product quality** of medicines.
- **(Re-)Empower medicines agencies** to exercise adequate control.
- Establish **notification processes** (planned interruptions, discontinuations).
- Establish a **special scheme for rare drugs** (i.e. low volume of production drugs).

[ASCO 2011, Baumann 2013, Chabner 2011, Friske 2013, ISPE 2013, Link/Hagerty/Kantarjian 2012]

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Take home messages

- Drug shortages are **a major threat** to EU health-care systems.
- Customers (i.e. purchasers) and medicines agencies have **limited means to react on drug shortages**, and can´t address the underlying causes.
- It is the duty of **EU authorities to re-adjust the framework** of pharmaceutical markets in order to re-establish continuous and adequate supply with essential medicines.

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Thank you for your attention.

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