Health Service Reimbursement: Early Benefit Assessment of New Drugs in Germany

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Conflict of interest

Nothing to disclose

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Agenda

- IQWiG – Background
- Reimbursement of drugs in Germany
- Early benefit assessments: framework, methods, results
The German health care system I

- **Statutory health insurance (SHI) funds:** cover approx. 90% of population in Germany
- **Financing:** contributions by employers and employees
- **Structure:** public-law corporations, financially and organizationally independent
- **Solidarity principle:** each insured person receives the health care service that is medically necessary, regardless of income, amount of contributions paid, or morbidity risks

The German health care system II

- Large sections of the health care system are shaped by self-government via contracts that are concluded with the health care providers
- **Legal basis:** Social Code Book V (SGB V):
  - Provides framework for reimbursed health care services ("benefits catalogue")
Federal Joint Committee – decision body for reimbursement

Federal Joint Committee

Federal Ministry of Health (Bundesministerium für Gesundheit)
Federal Parliament (Bundestag / Bundesrat)
State ministries responsible for Health (Gesundheitsminister der Bundesländer)

Legislative frame

Statutory Health Insurance

Physicians / regional and federal organisation

Hospitals / regional and federal organisation

Insuree / Patient

SHI Funds / Umbrella organisation

Federal Joint Committee

Decisions on reimbursement

Self Administration Body

Institute for Quality and Efficiency in Health Care (IQWiG)

- IQWiG was founded as an independent scientific institute by a health care reform in 2004
- The legal basis of the work of IQWiG is the Social Code Book V (SGB V)
- IQWiG runs under the umbrella of a private-law foundation, financed through levies for inpatient and outpatient medical treatment (SHI funds)
IQWiG’s tasks according to § 139a SGB V

- IQWiG produces independent, evidence-based reports e.g. on:
  - Drugs (benefit and cost-benefit assessment)
  - Non-drug interventions (e.g. surgical procedures, medical devices, diagnostic and screening methods)
  - Clinical practice guidelines (CPGs) and disease management programmes (DMPs)

- In addition, IQWiG provides easily understandable health information for patients and the general public
  
  http://www.informedhealthonline.org/informed-health-online.2.en.html
  
  http://www.gesundheitsinformation.de/startseite.2.de.html

Legal and organizational background – HTA in Germany

G-BA may commission IQWiG to conduct HTAs using EBM methods (drugs, non-drug procedures)

Health services funded by statutory health insurances (coverage ~90% of German population)

Social Code Book (SGB) provides legal framework
General Methods

Version 4.1 of 28 November 2013

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Reimbursement of drugs in Germany

- Expenditures SHI for drugs (2012): 30 billion €
- Licensed drugs can be prescribed by physicians immediately after licensing
- Prices are specified by drug manufacturers (regulation only for margins in distribution chain)
- SHI funds must reimburse licensed drugs
- Federal Joint Committee may regulate
Instruments for cost-containment and price regulation

- Reference pricing (since 1989), predominantly for generic drugs
- Discount agreements between individual SHI funds and drug manufacturers (since 2007: obligation for pharmacies to dispense discounted drugs)
- Temporary cost-containment measures: price moratorium (until 2017), price reductions, legally implemented discounts (drug manufacturers, pharmacies), co-payments of insured persons

Regulations on drugs in the hospital sector

- Hospital-specific positive lists for drugs
- Diagnosis-Related-Groups (DRG) system: drug costs included in flat-rate reimbursement
- Special prices for expensive drugs (e.g. cancer drugs)
**Turnover of patent-protected drugs before AMNOG**

### Agenda

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AMNOG – new legislation, new HTA products

- New law to reorganize pharmaceutical market for SHI
- Came into force on 01/01/2011
- § 35a SGB V directly concerns early benefit assessment of drugs:
  - For new chemical entities / new indications
  - Requirement linked to market entry
  - Now onus of proof on drug manufacturer to demonstrate added benefit (vs. an appropriate comparator) – submission of a dossier
  - Results used for price negotiations (not for the decision: reimbursement yes/no)

Drug assessment according to AMNOG

[Diagram showing the assessment process involving patient representatives, external experts, submission of a dossier, assessment by IQWiG, and decision on additional benefit by the Federal Joint Committee]
Drug assessment according to AMNOG

Submission of a dossier by the manufacturer

Assessment (by IQWiG)

Decision on additional benefit by the Federal Joint Committee

Additional benefit?

Reference price

Permissible for reference price?

Price negotiations SHI and manufacturer

Agreement?

Discount on sales price

Decision by arbitration body

On request of SHI or manufacturer: health economic evaluation
Appropriate comparator therapy (ACT)

- Specified by G-BA
- If requested, advice on ACT is offered by G-BA to drug manufacturer
- Precondition for ACT: approved and reimbursable
- Decision criteria for selection of ACT:
  - Evidence of benefit for patients; tested in clinical practice
Early benefit assessments

- Legal obligation for the manufacturer of the drug under assessment to provide all available evidence for the HTA
  - Study reports (including study protocols) of all studies on the drug under assessment which have been sponsored by the manufacturer
  - All available information on ongoing and terminated studies which have been sponsored by the manufacturer or in which the manufacturer was financially involved
  - Assessment reports of regulatory authorities
  - Corresponding information about studies by third parties as available

General steps from formulating question to decision on therapeutic value

- Identify PICO
- Appropriate comparator used?
- Identify relevant clinical trials (direct / indirect comparison)
- Identify patient-relevant outcomes (selection and assessment of outcomes following EbM methods)
- Determine treatment effects
- Consider benefits and harms
- Consider uncertainty / risk of bias
- Aggregate information on various outcomes
GOAL:

⇒ Adequately capture benefits AND harms…
AMNOG – extent of ‘added benefit’

Criteria in accordance with AM-NutzenV*

- Major added benefit
- Considerable added benefit
- Minor added benefit
- No added benefit has been proven
- Less benefit

*Regulation for Early Benefit Assessment of New Pharmaceuticals

- in the therapy-relevant benefit, which has not previously been achieved versus the appropriate comparator

sustained and great improvement# (cure, major increase in survival time, long-term freedom from serious symptoms, extensive avoidance of serious side effects)

AMNOG – extent of ‘added benefit’

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AMNOG – extent of ‘added benefit’

Criteria in accordance with AM-NutzenV*

- **Major added benefit**
  - sustained and great improvement# (cure, major increase in survival)
  - marked improvement# (perceptible alleviation of the disease, moderate increase in survival time, alleviation of serious symptoms, relevant)

- **Considerable added benefit**
  - moderate and not only marginal improvement# (reduction in non-serious symptoms, relevant avoidance of side effects)

- **Minor added benefit**
  - marked improvement#

- **No added benefit has been proven**

- **Less benefit**
  - moderate and not only marginal improvement#
  - sustainable and great improvement#

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*Regulation for Early Benefit Assessment of New Pharmaceuticals
#In the therapy-relevant benefit, which has not previously been achieved versus the appropriate comparator
Results of IQWiG’s early benefit assessments

- Added benefit determined in 45% of assessments

Status: 9 Jan 2014 (without orphan drugs): maximum added benefit due to consideration of addenda (n = 58)

Results of IQWiG’s early benefit assessments

- No added benefit determined in 55% of assessments

Status: 9 Jan 2014 (without orphan drugs): maximum added benefit due to consideration of addenda (n = 58)
How to access IQWiG reports

www.iqwig.de

English abstracts available soon

How to access the manufacturers’ dossiers

www.g-ba.de

Only German versions available
Summary

- Early benefit assessments:
  - provide basis for price negotiations for outpatient sector (price discounts negotiated are not binding in inpatient sector)
  - close the evidence gap in the assessment of new drugs
  - support informed decision-making by physicians and patients
- So far, 58 early benefit assessments (or “dossier assessments”) have been performed: 45% show added benefit

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Evidence-based medicine

- Precise formulation of questions to be addressed (Patient Intervention Comparator Outcome)
- Systematic (i.e. reproducible, transparent) procedure (search and evaluation of clinical trials)
- Reliability assessment of the result as the basis for a recommendation (‘How credible are the results?’)
  - Qualitative component (risk of bias)
  - Quantitative component (precision, significance level)
  - Magnitude (and nature) of the (observed) effect

Hierarchy of evidence

Systematic Reviews (of RCTs)
Randomized Controlled Trials

Controlled Trials (non-RCTs)
Uncontrolled studies
Case series / case reports
Opinions
Uncertainty
Reference prices - most effective instrument for stabilizing drug prices

Outcomes

German Social Code Book V

‘… Regarding patient benefit, an
➤ improvement of the medical condition,
➤ a shortening of the duration of the disease,
➤ an increase in life expectancy,
➤ a reduction in side effects, as well as
➤ an improvement of the quality of life are especially to be considered. …’
Benefits catalogue of SHI

- Health care services must be sufficient, appropriate and efficient (12 SGB V)
- Approved drugs are basically reimbursable; exceptions (acc. to G-BA):
  - OTC drugs for adults (only in exceptional cases)
  - Lifestyle drugs (e.g. for improvement of erectile dysfunction, smoking cessation, weight reduction)
- Therapy advice, reimbursement restrictions and exclusions by the G-BA must be considered

![Determination of the extent of added benefit](image_url)
## Determination of the extent of added benefit

<table>
<thead>
<tr>
<th>Added Benefit</th>
<th>Outcome Category</th>
<th>Survival Time (Mortality)</th>
<th>Serious (or Severe) Symptoms (or Late Complications) and Adverse Effects</th>
<th>Quality of Life</th>
<th>Non-Serious (or Non-Severe Symptoms or Late Complications) and Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major</td>
<td>Survival time</td>
<td>Major increase in survival time</td>
<td>Cl: 0.85 (RR: 0.50)</td>
<td>Major improvement</td>
<td>Not applicable</td>
</tr>
<tr>
<td></td>
<td>Long-term freedom or extensive avoidance</td>
<td>Cl: 0.05 (RR: 0.17) and risk ≤ 5%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Death avoidance</td>
<td>Cl: 0.75 (RR: 0.17) and risk ≤ 5%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Considerable</td>
<td>Increased survival time</td>
<td>Cl: 0.95 (RR: 0.83)</td>
<td>Aversion or relevant avoidance</td>
<td>Important improvement</td>
<td>Important avoidance</td>
</tr>
<tr>
<td>Marked</td>
<td>Cl: 0.99 (RR: 0.67)</td>
<td>Important improvement</td>
<td>Cl: 0.90 (RR: 0.67)</td>
<td>Cl: 0.80 (RR: 0.33)</td>
<td>Important avoidance</td>
</tr>
<tr>
<td>Minor</td>
<td>Any statistically significant increase in survival time</td>
<td>Cl: 1.00</td>
<td>Any statistically significant reduction</td>
<td>Relevant improvement</td>
<td>Relevant avoidance</td>
</tr>
<tr>
<td></td>
<td>Cl: 1.00</td>
<td>Cl: 1.00</td>
<td>Cl: 0.90 (RR: 0.67)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Additions to AM-NutzenV in tables:
1. The precondition is the use of a validated instrument and a validated response criterion. Values count for non-response.
2. For at least one of the groups to be compared.

AM-NutzenV: Regulation for Early Benefit Assessment of New Pharmaceuticals. Cl: threshold value for the upper limit of the 95% confidence interval, RR: actual relative risk.

* Table 3.2 in the German Appendix.