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Health Technology Assessment (HTA) for Medicinal Products (Devices, Implants, Diagnostics)

How to Cope with the Increasing Regulatory Burden?

Health Technology Assessment (HTA) im deutschen Medizinproduktemarkt:

Prinzipien, Prozesse, exemplarische Umsetzung

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MedTechDialog „Kosten-Nutzen-Bewertung / HTA für Medizinprodukte“ – Mannheim, 23. März 2017

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Note

The presentation deals with essential characteristics and peculiarities of the current German reimbursement system for new medicinal products and procedures (or methods). Given the complexity of German market access regulation, the presentation is necessarily incomplete.

Further to this, the field is rapidly evolving and undergoing continuous change.

Do keep in mind that other jurisdictions operate different systems, some of which are more explicit in certain aspects, such as the evaluation of companion diagnostics or the types and consequences of health economic analyses.

Disclaimer

The presentation was prepared in good faith.
We accept no liability for any errors or omissions.

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Regulation of Market Access

1. Inpatient (or Hospital) Market

- For each pathway to reimbursement, there are specific application procedures available – with well-defined processes and timelines
- Effective 2016, technology assessments by the JFC were introduced for high-risk and invasive methods

2. Outpatient (or Physician) Market

- A positive appraisal by the JFC is required for reimbursement of new methods in the outpatient sector
- Pathways to reimbursement may be time-consuming and difficult to predict – but new opportunities arise from a coverage with evidence development (CED) initiative

3. The Role of Health Technology Assessments (HTAs)

- is set to grow continuously; reference case: pharmaceuticals

Rationale for Systematic HTAs (Example)

Intracranial Stents

UniversitätsKlinikum Heidelberg

Heidelberg, den 24. Oktober 2007

PRESSEMITTEILUNG *Nr. 177 / 2*

Maschendraht verhindert Schlaganfall

Studie unter Federführung der Abteilung Neuroradiolo
Universitätsklinikum Heidelberg hat gezeigt: Speziell
können verengte Gehirngefäße dauerhaft erweitern

BACKGROUND AND PURPOSE:

The purpose of this study was to assess the safety and performance of the Wingspan stent system … .

METHODS:

In this prospective, multicenter, single-arm study, medically refractory patients with a modified Rankin score < or =3 and recurrent symptoms attributable to angiographically demonstrated intracranial stenosis > or =50% in a vessel 2.5 to 4.5 mm in diameter were enrolled. … .

RESULTS:

Among the 45 patients enrolled, the degree of stenosis was reduced from a baseline of 74.9+/-9.8% to 31.9+/-13.6% after stenting and 28+/-23.2% at the 6-month follow-up. The 30-day composite ipsilateral stroke/death rate was 4.5% (2/44); at the 6-month follow-up, the ipsilateral stroke/death rate was 7.0%, the rate for all strokes was 9.7%, and all-cause mortality was 2.3%. … .

CONCLUSIONS:

In medically refractory patients with high-grade intracranial atherosclerotic stenoses, … Wingspan stent system appears to be safe, may facilitate remodeling, and may contribute to favorable angiographic outcomes.

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University of Heidelberg, Press Release of Oct. 24 2007; Bose et al., *Stroke* 2007; Source: Stefan Lange, June 10, 2015

Rationale for Systematic HTAs (Example)

Intracranial Stents

Randomized Clinical Trial 2011:
"Enrollment was stopped after 451 patients underwent randomization, because the 30-day rate of stroke or death was 14.7% in the PTAS group (nonfatal stroke, 12.5%; fatal stroke, 2.2%) and 5.8% in the medical-management group (nonfatal stroke, 5.3%; non–stroke-related death, 0.4%) (P =0.002)."

n = 451: Stroke or Death (within 30 days): 14.7% vs. 5.8% (p= 0.002)

n = 112: Repeat Stroke (same region; within 12 months): 34.5% vs. 9.4% (p= 0.003)

Randomized Clinical Trial 2015:
"Among patients with symptomatic intracranial arterial stenosis, the use of a balloon-expandable stent compared with medical therapy resulted in an increased 12-month risk of added stroke or TIA in the same territory, and increased 30-day risk of any stroke or TIA. These findings do not support the use of a balloon-expandable stent for patients with symptomatic intracranial arterial stenosis."

Chimowitz et al., *N Engl J Med* 2011; Zaidat et al., *JAMA* 2015; Source: Stefan Lange, June 10, 2015

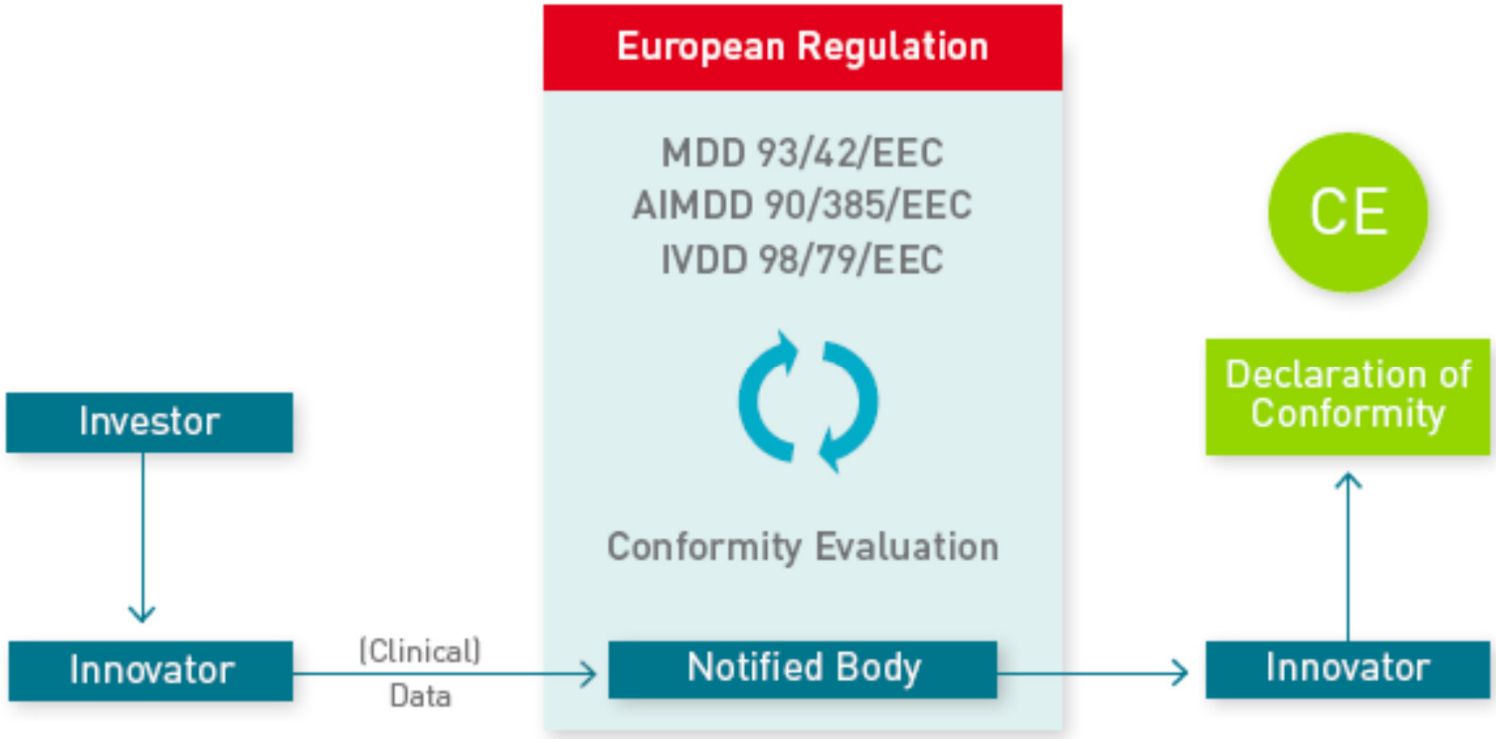
Prerequisite: European Certification

Three Directives

- **Medical Devices**
- **Active Implants**
- ***in vitro* Diagnostics**

Four Risk Classes

I. **Crutches** etc.
II. **a. Syringes** etc.
b. Irradiation Equipment etc.
III. **Cardiac Pacemakers** etc.



Graphic: Germany Trade & Invest, April 2015

Reimbursement by Statutory Health Insurance (SHI *[GKV]*)

Inpatient Market

- **In the past, innovative procedures were generally permitted (*Verbots-vorbehalt* SGB V §137c).**
- **If not explicitly prohibited by the JFC *(G-BA)*, devices could be used, but:**
- **New innovative high-risk products will be subject to an official clinical benefit assessment in the future.**

Outpatient Market

- **Innovative procedures need official approval (*Erlaubnisvorbehalt* SGB V §135,1).**
- **In the absence of a positive assessment by the JFC *(G-BA)*, devices may not be used, but:**
- **A new "coverage with evidence development" pathway has been created.**

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Access Pathways

to the Inpatient (Hospital) Market

for Medicinal Products in Germany

Reimbursement by SHI

1. Inpatient Market: Hospital Financing

- **German Diagnostic Related Group (G-DRG) System**

  DRGs are directly linked to specific transfer payments from SHI to hospitals

- **G-DRGs are defined by a combination of disease and procedure codes**

  ICD-GM: German version of International Classification of Diseases and Related Health Problems (ICD)

  OPS: German version of International Classification of Procedures in Medicine (OPS) [*OPS: Operationen- und Prozedurenschlüssel*]

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Reimbursement by SHI

1. Inpatient Market

- **If an adequate OPS / DRG is already available:**

  => reimbursement √

- **If a new OPS / DRG is required:**

  => OPS / DRG application

- **If additional reimbursement will be required:**

  => NUB application (*Neue Untersuchungs- und Behandlungsverfahren*)

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Reimbursement by SHI

1. Inpatient Market

Stepwise Approach

1. **OPS Code existing?**
   - ¬ if not, involve **national medical association** for => OPS application (=> to DIMDI)

↓

2. **Appropriate DRG existing?**
   - ¬ if not, involve **national medical association** for => DRG application (=> to InEK)

↓

3. **DRG reimbursement adequate?**
   - ¬ if not, **hospitals** need to submit => NUB application (=> to InEK)

↓

4. **Reimbursement**

Reimbursement by SHI

1. Inpatient Market

NUB Application Procedure (SGB V §137h)

- **New regulation for "high-risk" products**
  (Classes IIb, III, active implants; GKV-VSG 2015 / JFC VerfO 2016)

- **Hurdles for manufacturers:**

  1. Centralized assessment

  - NUB rating by InEK (need "status 1"); lack of transparency
  - for "high risk" products, followed by a subsequent **early benefit assessment** by the Joint Federal Committee (JFC; *GBA: Gemeinsamer Bundesausschuss*)

  2. Decentralized reimbursement negotiations

  - SHI: MDS "expert reports" not transparent
  - arbitration possible (but heterogeneous criteria)

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Reimbursement by SHI

1. Inpatient Market

NUB Application Procedure with InEK

- Recommendation to use MEDNOG dossier format for preparation
- **NUB submission to InEK** (KHEntgG §6,2):
  - Method description; evidence supporting clinical benefit; OPS
  - Patient population; existing alternative method(s) / addition or replacement
  - Innovation and impact on length of hospital stay
  - Marketing authorization (for drugs) or launch date
  - Introduction in hospital and patient numbers (past, current, and future)
  - Resource use and cost impact (specified by category)
  - DRG(s) affected by introduction of new method
  - Reasons why German DRG system does not yet cover the new method

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Reimbursement by SHI

1. Inpatient Market

Early Benefit Assessment by JFC *(G-BA)*

- Prior consultation opportunity offered to both hospitals and manufacturers
- High-risk or invasive method
- New ("*neues theoretisch-wissenschaftliches Konzept*") – novel mode of action or new indication
- First application – method neither applied for listing before Dec. 31, 2015, nor under assessment (ongoing or completed)

- **Possible outcomes of assessment** (by JFC)
  - **Acceptance of method**: clinical benefit sufficiently demonstrated ("*hinreichend belegt*")
  - **Coverage with evidence development**: clinical benefit not yet demonstrated, but **potential** for clinical benefit (=> "***Erprobungsstudie***", => SGB V § 137e)
  - **Rejection of method**: either no reason to assume potential for clinical benefit or even harmful to patients

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Reimbursement by SHI

1. Inpatient Market

Early Benefit Assessment: Key Dossier Elements

Hospital submission to JFC (SGB V §137h; VerfO BAnz AT 22.08.2016 B3):

- I **Administrative** (e.g., agreement with manufacturer, NUB application; …)
- II **Procedure** (e.g., indication / disease, prevalence, current standard of care; description of method, mode of action, indication / patient groups; novelty / innovation; replaced alternative methods; impact on length of hospital stay; market introduction in Germany; other indications and prior experience […])
- III **Additional product-related information**; A from hospital; B from manufacturer (clinical experience, adverse events)
- IV **State of the art / current evidence** (e.g., systematic literature search; search in trial registries etc.; full listing of all clinical studies and results)
- V **Cornerstones of an experimental study** (*optional*) – incl. implementation; budget
- VI **References** / complete list of data sources (to be provided electronically)
- VII **Authorization** & signatures

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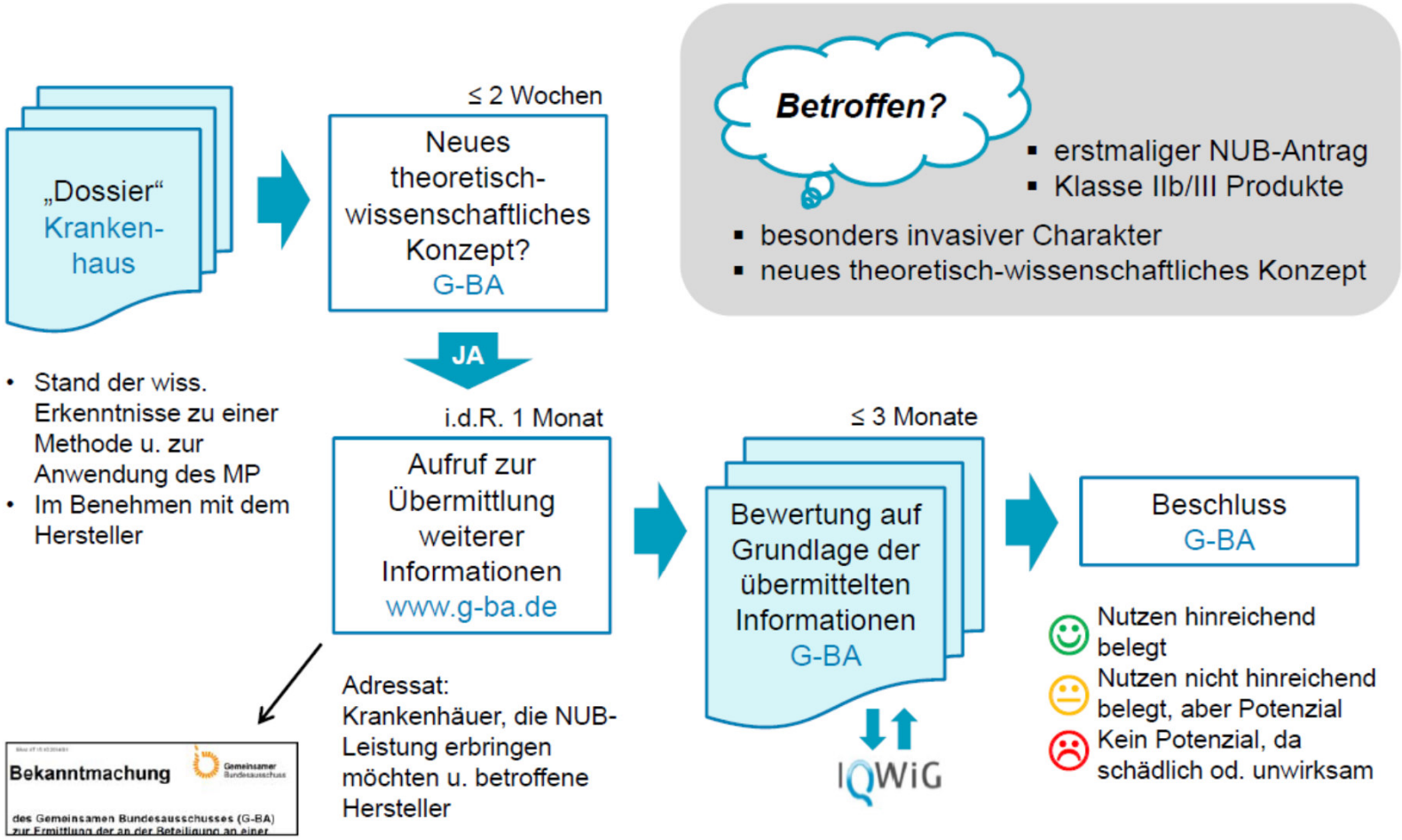
Reimbursement by SHI

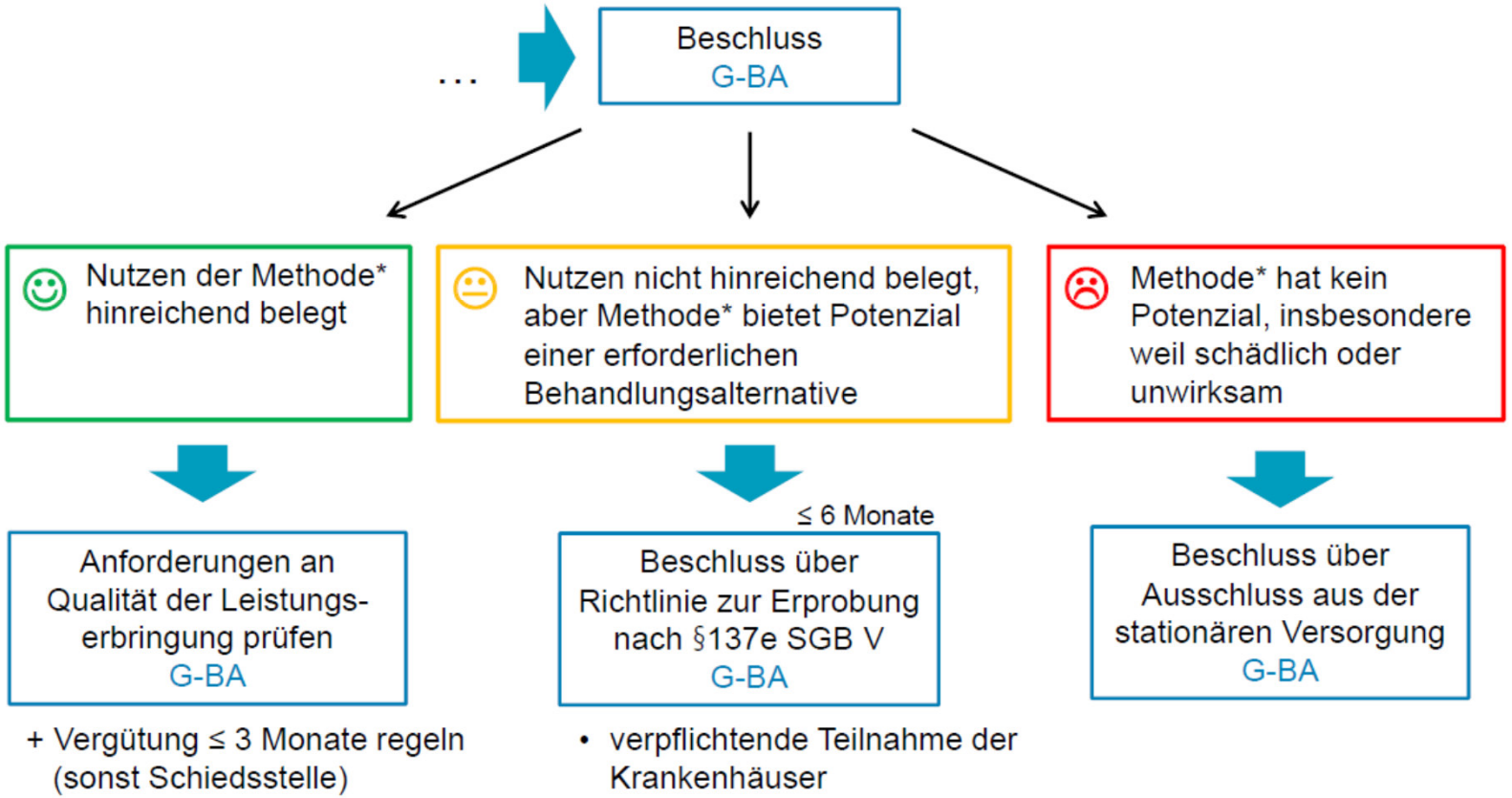
1. Inpatient Market Assessment Process (1)



Graphic: Naomi Fujita-Rohwerder, Sept. 24, 2015

Reimbursement by SHI

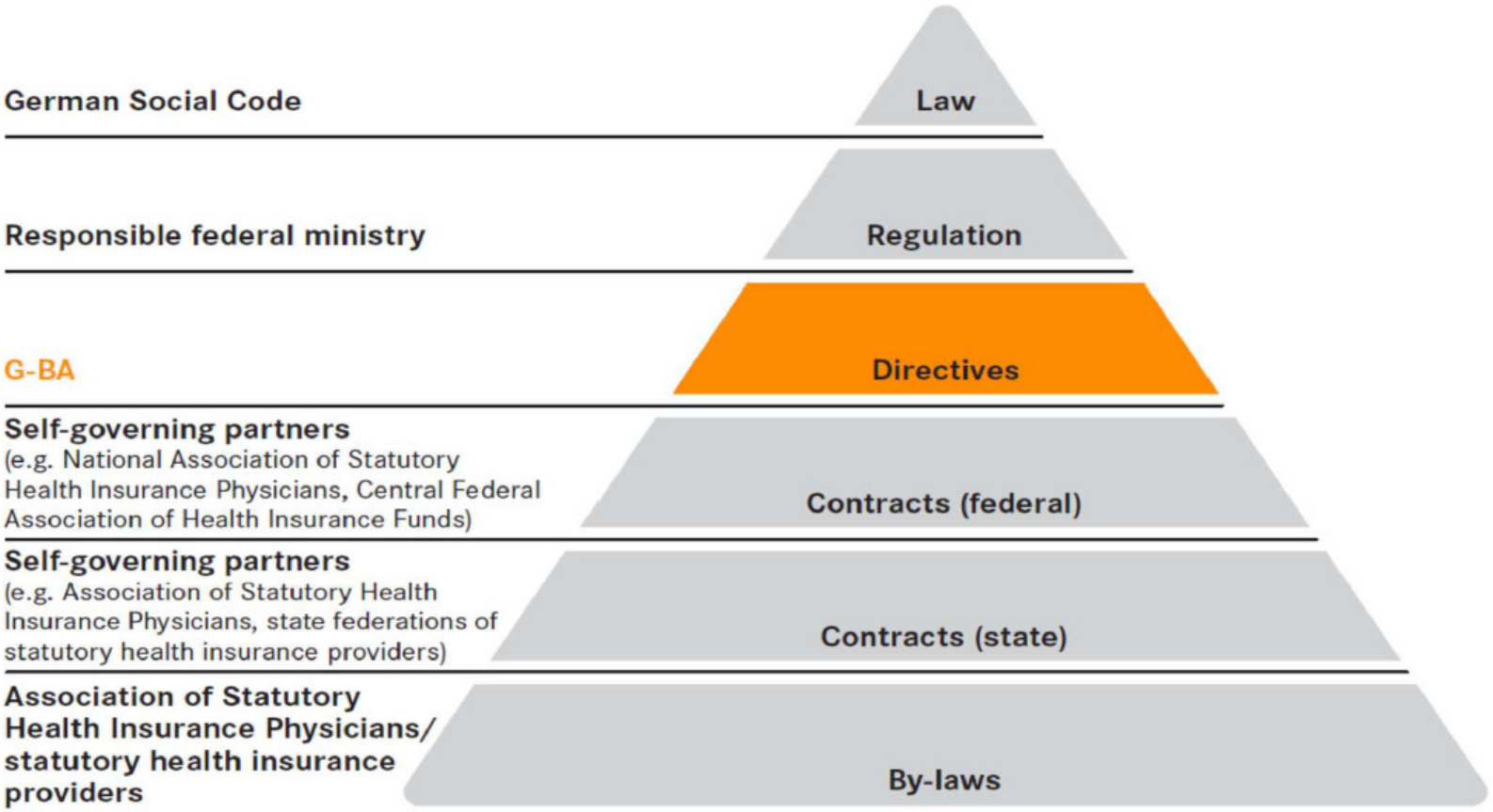
1. Inpatient Market Assessment Process (2)



* unter Anwendung des Medizinprodukts

Graphic: Germany Trade & Invest, April 2015

Legal Status of Joint Federal Committee (JFC; *G-BA*)



Graphic: www.marketaccess-pricingstrategy.de

2

Access Pathways

to the Outpatient (Physician) Market

for Medicinal Products in Germany

Without Reimbursement by SHI:

2. Outpatient Market

- **IGeL** (individual health service; *"individuelle Gesundheitsleistung"*)
  => i.e., out-of-pocket payment of product or procedure by patients
- easiest route to market access
- standard approach:
  applying for inclusion into the => **GOÄ fee schedule**
  (of German private health insurance)
- application to be made by a physician,
  ideally a renowned medical expert,
  to the German Medical Association (BÄK; *Bundesärztekammer*)
- Once the service has been listed in the GOÄ fee schedule,
  all German physicians may offer it to patients

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Reimbursement by SHI

2. Outpatient Market: Product Listing with SHI

- Since **GOÄ inclusion only** gives limited access (excl. SHI)
  =>
- **Filing for inclusion into EBM** (the fee schedule of SHI)
  - **JFC will decide** on coverage by SHI
  - Applications should be filed via
    the *Kassenärztliche Bundesvereinigung*, KBV
    (Association of Physicians registered with SHI)
  - Alternatively, an application may be presented to the JFC
    by any of its other members, including patient representatives
- **Value dossier needs to be submitted to JFC.**
- In the past, this process used to be slow and poorly predictable.

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Reimbursement by SHI

2. Outpatient Market: Selective Contracting

- Since 2012, **national and regional SHI organizations** may enter into selective contracts that allow their members access to innovative outpatient procedures (SGB V §11,6 regulation).
- In order to qualify, procedures must not have been excluded from reimbursement by the JFC (G-BA) on the national level.
- Obviously, a compelling clinical and/or economic argument will have to be presented to the SHI organization.

Reimbursement by SHI

2. [In- and] Outpatient Market:

Coverage with Evidence Development Scheme

- A new **Coverage with Evidence Development (CED)** scheme was enacted with the VStG in 2012 (SGB V §137e):
- **Premise**:
  A new procedure must hold promise (i.e., show **potential**), but there remains an **evidence gap**, which may be closed by one well-conducted randomized controlled clinical trial (RCT)
- **Consequence**:
  Testing of hypothesis in an appropriate RCT; product will be reimbursed while RCT will have to be paid for by manufacturer (a cost-sharing policy is in place for KMUs and orphan indications)

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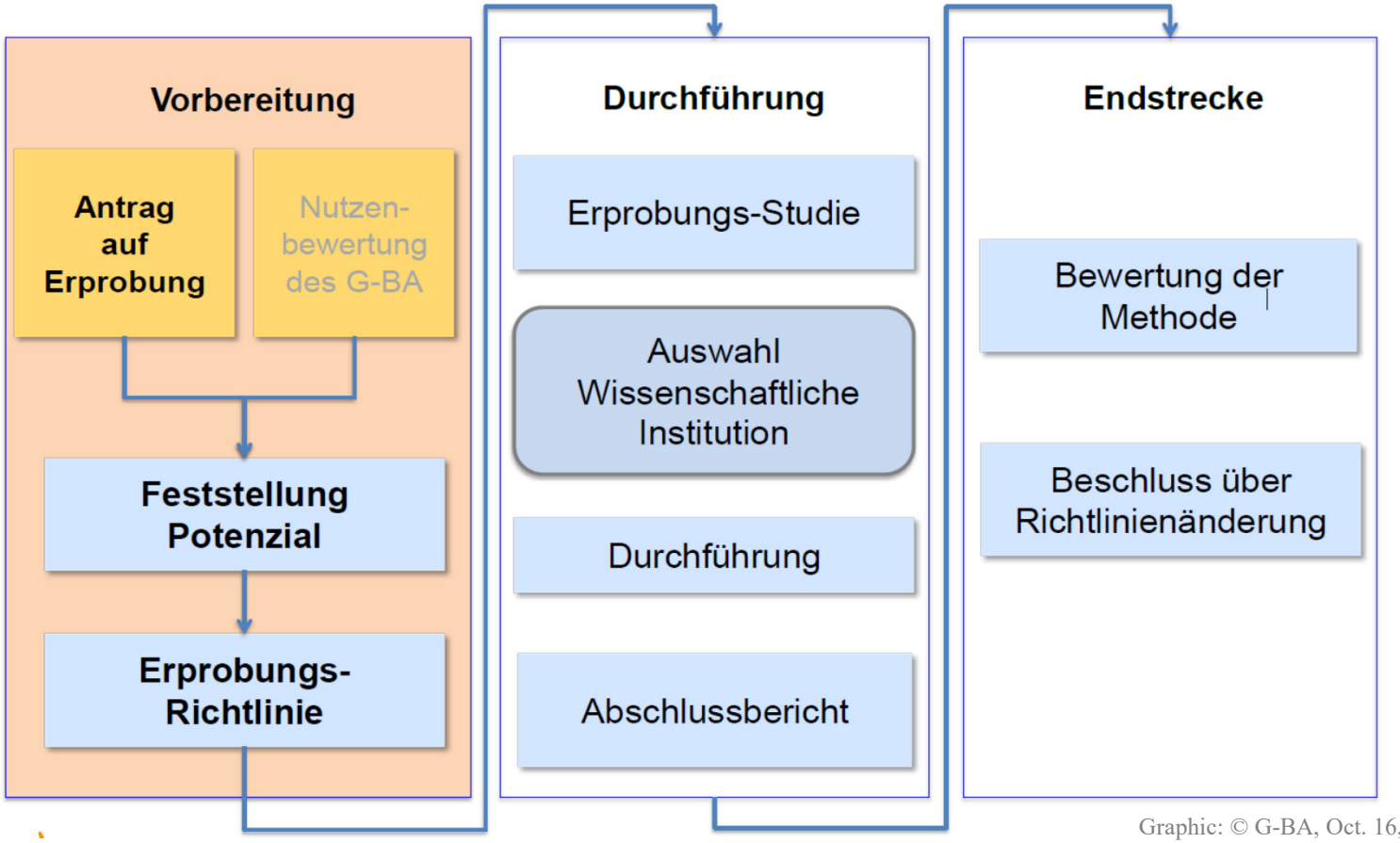
Reimbursement by SHI

2. [In- and] Outpatient Market:

Coverage with Evidence Development Scheme

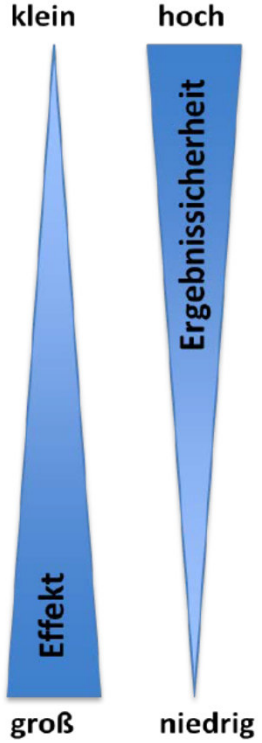


Graphic: © G-BA, Oct. 16, 2015

Reimbursement by SHI

2. [In- and] Outpatient Market:

Coverage with Evidence Development Scheme



Graphic:
© G-BA,
Oct. 16, 2015

Potenzialbeleg	Nutzenbeleg
Evidenzlücke	• RCTs oder systematische Übersichtsarbeiten von RCTs (LoE I)
• mindestens kleine Effekte bei geringer Ergebnissicherheit (LoE II: prospektive vergleichende Kohortenstudie mit Confounder-Kontrolle)	• niedrigere Evidenzstufen bei seltenen Erkrankungen, bei Methoden ohne vorhandene Alternative oder aus anderen Gründen (z. B. medizinische Notwendigkeit)
• mindestens mittlere Effekte bei sehr geringer Ergebnissicherheit (LoE III: sonstige Vergleichsstudien)	
• große Effekte bei minimaler Ergebnissicherheit (LoE IV: nicht-vergleichende Studien, z. B. Fallserien)	
• Surrogatendpunkte (RR, BZ, Lungenfunktion) und/oder patientenrelevante Endpunkte (Morbidität, Mortalität, Lebensqualität)	• grundsätzlich patientenrelevante Endpunkte

Reimbursement by SHI

2. Outpatient Market:

Coverage with Evidence Development Scheme

- Opportunity for early consultation offered by JFC

Elements of manufacturer submission to JFC (SGB V §137e):

- I **Administrative** (manufacturer, applicant[s]; …)
- II **Summary** (general description; indication / target disease; mode of action; anticipated patient-relevant benefits, incl. reasoning and evidence; indication / target patent population; current standard of care; anticipated market uptake)
- III **Product-related information** (class, CE registration, market launch, international marketing authorizations, clinical experience, adverse events [MPSV §3], clinical evidence summary; provisions for use; emergency measures, if any)
- IV **State of the art / current evidence** (for each indication [and patient group]; appropriate comparator and clinical benefit: systematic bibliographic literature search [minimum Pubmed/Medline and Cochrane; trial registries; internal databases; transparent presentation: PRISMA statement, in- and exclusion criteria]; complete detailed listing of all clinical studies and results); summary evaluation
- V **Cornerstones of an experimental study** (*optional*) – incl. implementation; budget

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Reimbursement by SHI

2. Outpatient Market:

Coverage with Evidence Development Scheme

- As a standard, study costs will be borne by JFC (*G-BA*)
- Exception: procedure relies on use of medicinal product
  [Methoden, die „maßgeblich auf der Anwendung eines Medizinprodukts“ beruhen]
  - Study costs (RCT) to be borne by manufacturer
  - Financial support possible by way of cost sharing:
    - Discounts (/cost-sharing) for KMUs (25-50%)
    - Discount (/cost sharing) for orphan indications (20%)
- During *Erprobung*, procedure will be reimbursed by sick funds

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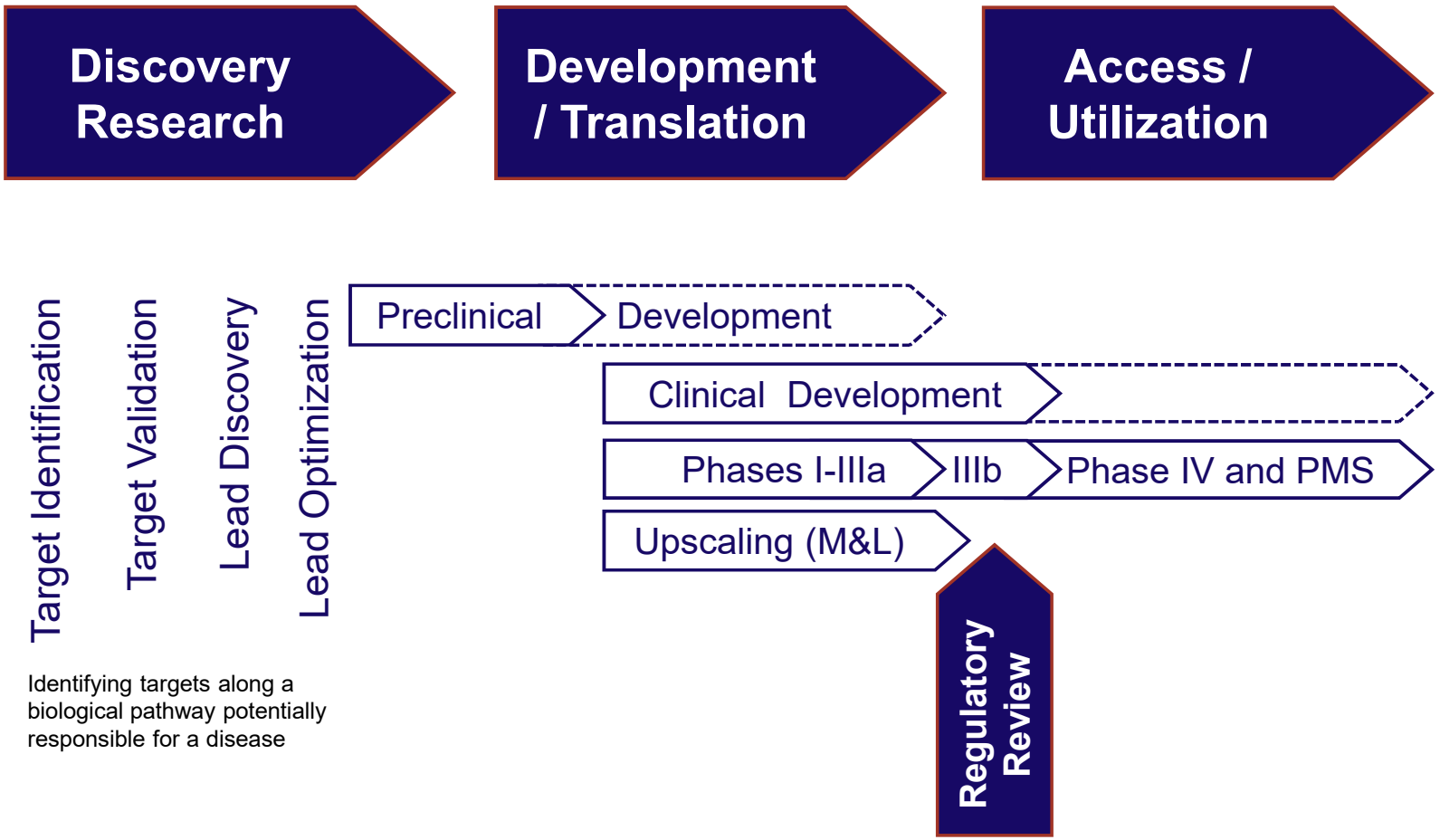
The Growing Role of Health Technology Assessments for Medicinal Products in Germany

Biopharmaceutical Industry:
The Old Market Access Paradigm



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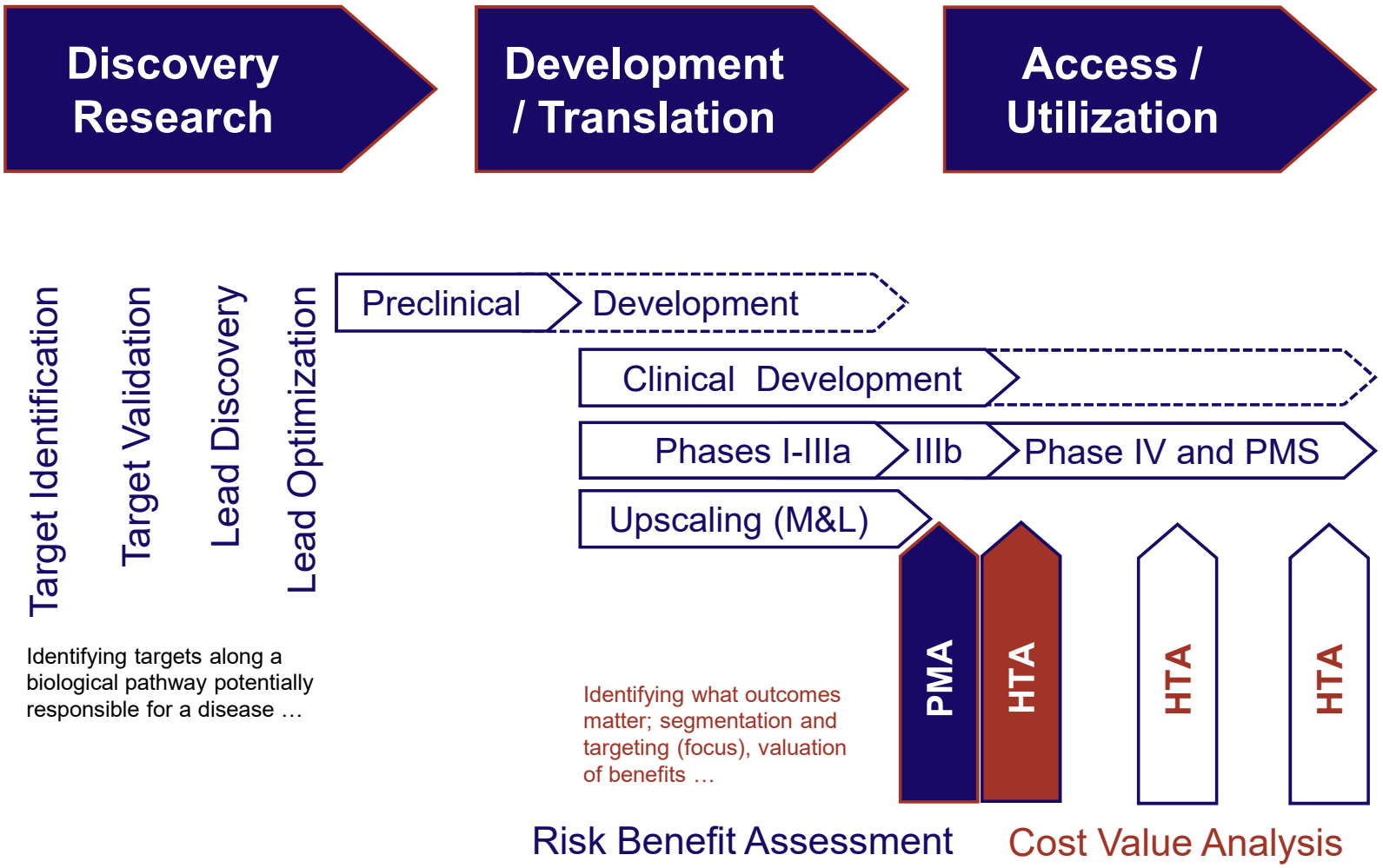
Biopharmaceutical Industry:
The New Market Access Paradigm



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Health Technology Assessment (HTA)

Typology and Key Elements

Early / Rapid HTAs

- **Horizon Scanning**
- **Early Consultation**
- [Assessment /] **Dossier**
- **Assessment** [/ Review]
- **Appraisal**
- **Decision**

Comprehensive HTAs

- **Topic Selection**
- **Assignment**
- **Scoping**
- **Assessment**
- **Appraisal**
- **Decision**

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Health Economic Evaluation Principles

The Logic of Cost-Effectiveness – Questions Asked:

1. Safety

- **Does it harm?**
  (controlled conditions)

↓

2. Efficacy

- ***Can*** **it work?**[1]
  (controlled conditions)

↓

3. Effectiveness

- ***Does*** **it work and is it safe?**[1]
  (normal practice)

↓

4. Efficiency

- **Do its benefits outweigh its costs?**
  (*frequently*: "Is it cost-effective"?)

EBM[2]: How sure can we be?

[1]cf. D. Schwartz and J. Lellouch (1967); [2]EBM: "evidence-based medicine"

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Early Benefit Assessments in Germany

The Logic of Comparative Effectiveness – AMNOG:

1. **Safety**
   - **Does it harm?** (controlled conditions)

↓

2. **Efficacy**
   - ***Can* it work?**[1] (controlled conditions)

↓

3. **Effectiveness**
   - ***Does* it work and is it safe?**[1] (normal practice)

↓

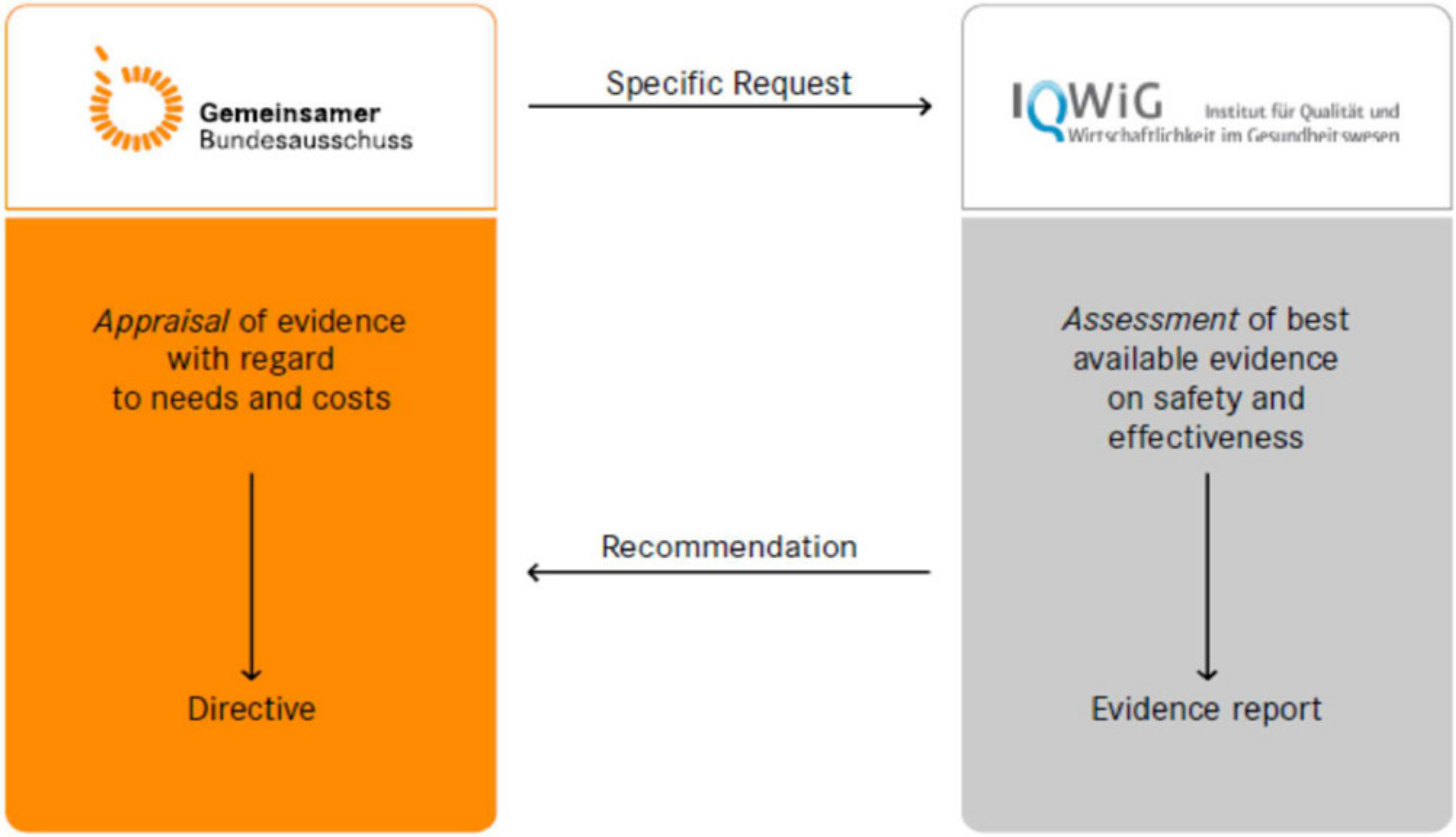
4. **Comparative Effectiveness**
   - **Does it outperform current standard therapy?** (***Germany*: "Is it more effective"?)**

[1] cf. D. Schwartz and J. Lellouch (1967)

Reference Case

AMNOG: Early Benefit Assessment

Mode of Cooperation between JFC *(G-BA)* and IQWiG



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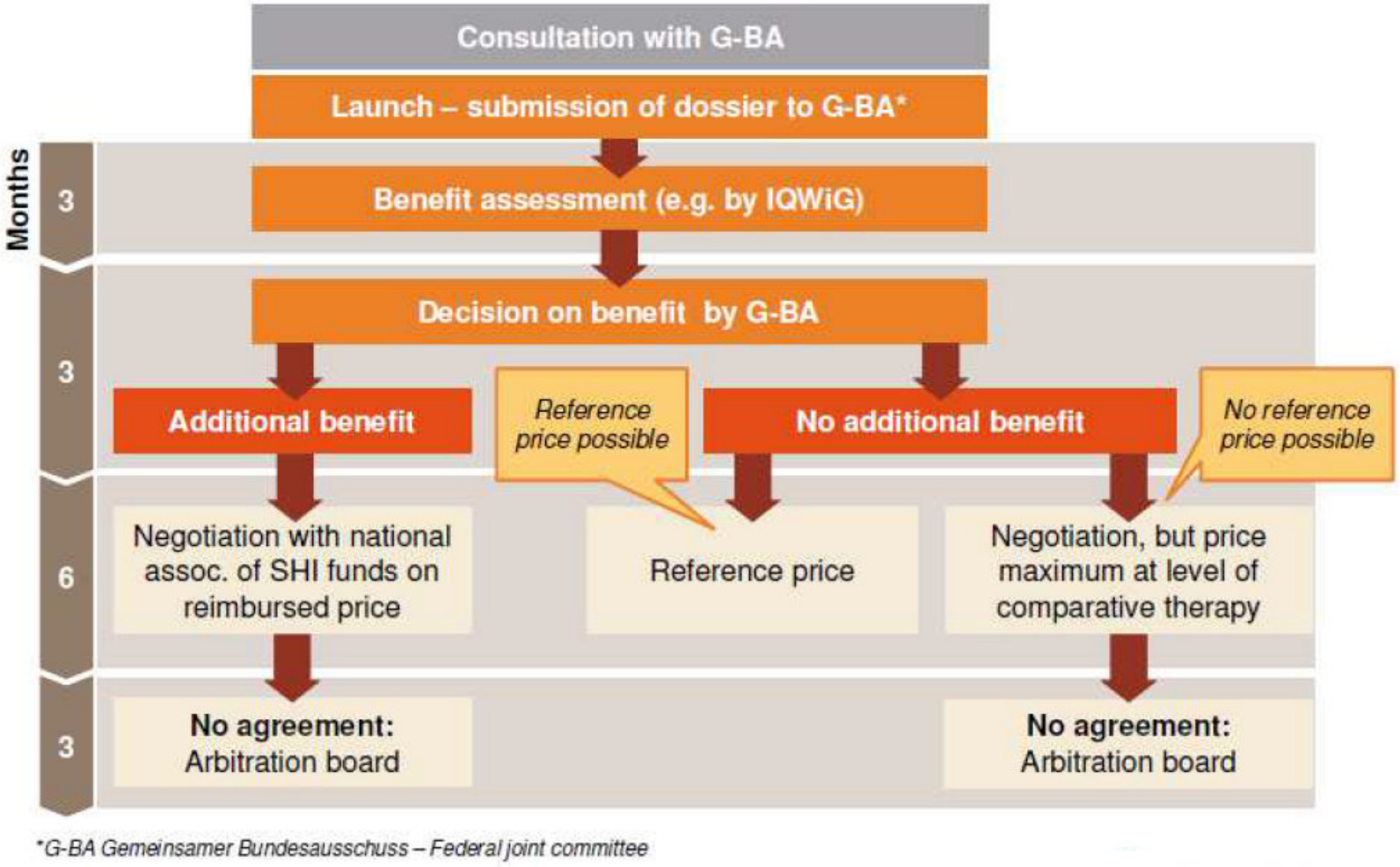
AMNOG: Early Benefit Assessment & Pricing



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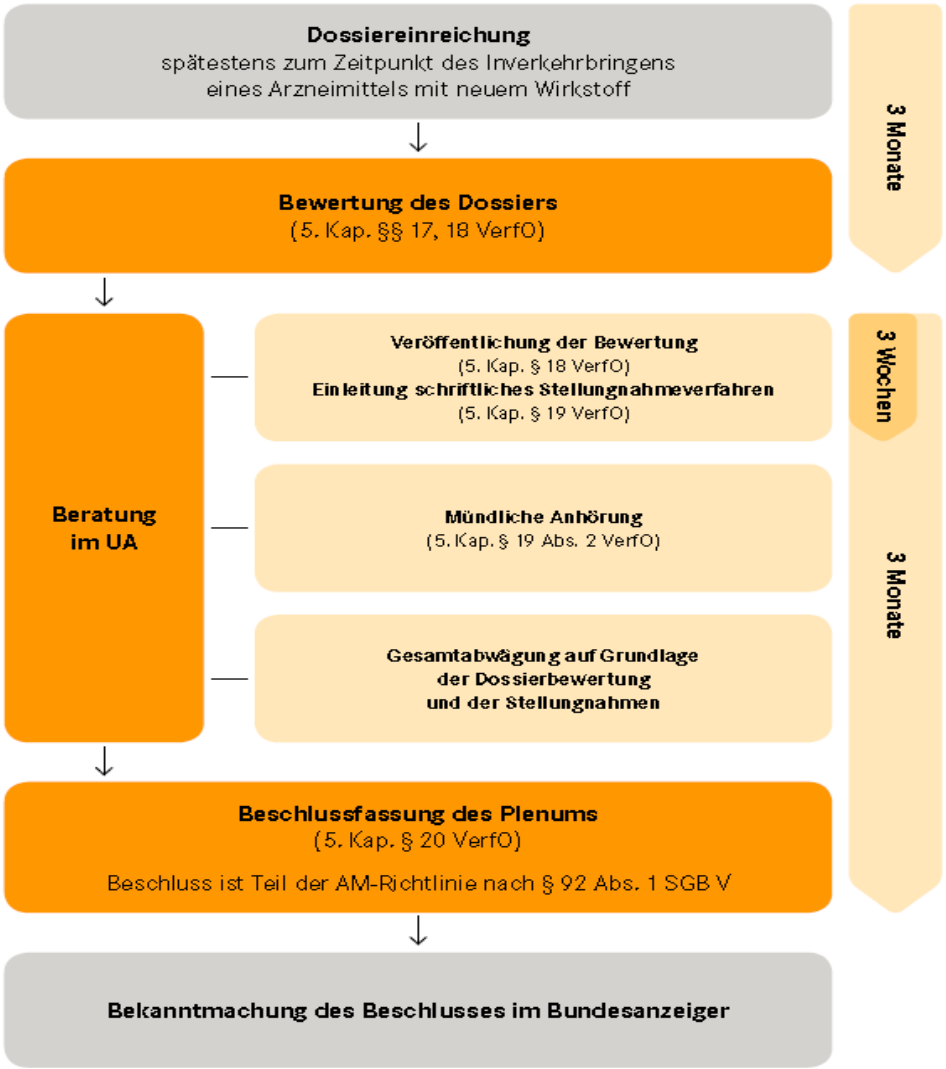
AMNOG: Early Benefit Assessment Process



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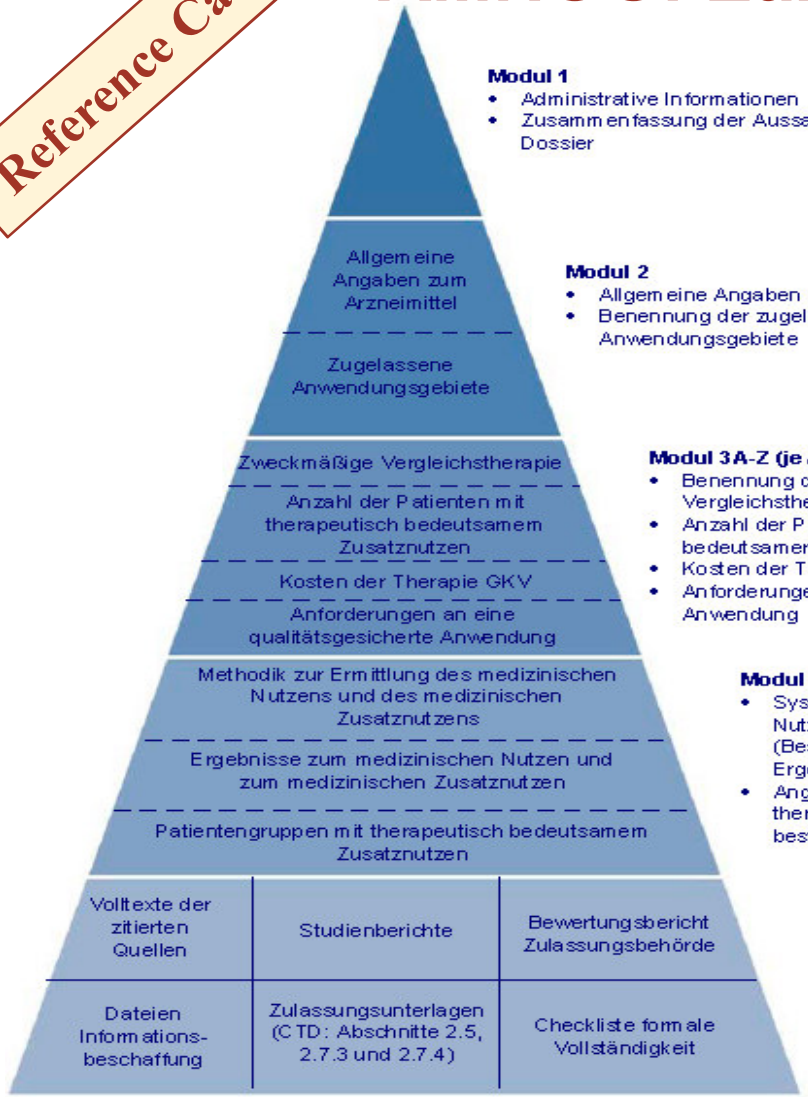
AMNOG: Early Benefit Assessment Dossiers



Module 1
- Administrative information
- Summary of the statements in the dossier

Module 2
- General information about the medicinal product
- List of the approved indications

Module 3A-Z (for each indication)
- Indication of the appropriate comparative therapy
- Number of patients for whom there is a therapeutically meaningful additional benefit
- Cost of therapy for statutory health insurance
- Requirements for quality-assured application

Module 4A-Z (for each indication)
- Systematic overview regarding the medical benefit and additional medical benefit (description of the methodology and the results)
- Indication of the patient groups for whom where is a therapeutically meaningful additional benefit

Module 5 (Attachments)
- Full text of the quoted sources
- Files documenting the procurement of information
- Reports on all studies of the pharmaceutical entrepreneur
- Essential common technical documents (CTD)
- Assessment report of the regulatory agency
- Checklist for verification of formal completeness

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AMNOG: Early Benefit Assessment Dossiers

Modules 1 & 2

- **Module 1**
  - Summary
    - Checklist for formal completeness (dossier)
    - Checklist for formal completeness (appendices)

  => important input for price negotiation process

- **Module 2**
  - Active agent, ATC code, PZN, packaging size, etc.
  - Mode of action
  - Authorized indication(s)
  - Other authorized indications in Germany
  - Status of international authorizations

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Reference Case

AMNOG: Early Benefit Assessment Dossiers

Module 3

- Appropriate Comparator Therapy (EBM; GBA advice)
- Epidemiology (unmet therapeutic need; including subgroups)
- Budget Impact Model
  - Costs in pharmacy sales prices
  - Costs of additional SHI payments according to SPC
  - Calculation of the annual costs of therapy
  - No cost effectiveness model
- Provisions for Appropriate Use

=> important input for price negotiation process

=> no impact on additional benefit assessment

- will be formally reviewed by IQWiG

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Reference Case

AMNOG: Early Benefit Assessment Dossiers

Module 4

- **(Clinical) Benefit and Additional Benefit**
  - Systematic review
    (bibliographical literature search, study register search, industry sources, …)
  - Assessment of the evidence
    (methodological quality of studies; potential for bias…)
  - Patient relevant endpoints
    (operationalization; validation; potential for bias…)
  - Reviews and meta-analyses, if applicable
  - Identification of relevant subgroups
  - Effect modifying variables

    => basis for benefit evaluation by GBA

    => crucial input for price negotiation process

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Reference Case

AMNOG: Early Benefit Assessment Dossiers

Module 5

- Electronic submission of dossier
  - highly formalized
  - fully referenced
    - Clinical Study Reports (…)
    - Common Technical Documents (…)
      (CTD 2.5, 2.7.3, 2.7.4)
    - EPAR (…)
- Modules 1-4: not confidential
- Module 5: confidential parts may be flagged

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Reference Case

AMNOG: Early Benefit Assessment Methods

		Outcome Category			
		Survival time (mortality)	**Serious (or severe) symptoms (or late complications) and adverse effects**	**Quality of life**	**Non-serious (or non-severe) symptoms (or late complications) and adverse effects**
Added Benefit	**Major** **Sustained and great improvement** in the therapy-relevant benefit, which has not previously been achieved versus the appropriate comparator	Major increase in survival time **CI_s: 0.85** (RR_1=0.50)	Long-term freedom or extensive avoidance **CI_s: 0.75** (RR_1=0.17) **and risk ≥5%**	*Major improvement* **CI_s: 0.75** (RR_1=0.17) **and risk ≥5%**	Not applicable
	Considerable **Marked improvement** in the therapy-relevant benefit, which has not previously been achieved versus the appropriate comparator	Moderate increase in survival time **CI_s: 0.95** (RR_1=0.83)	Alleviation or relevant avoidance **CI_s: 0.90** (RR_1=0.67)	*Significant improvement* **CI_s: 0.90** (RR_1=0.67)	Significant avoidance **CI_s: 0.80** (RR_1=0.33)
	Minor **Moderate and not only marginal improvement** in the therapy-relevant benefit, which has not previously been achieved versus the appropriate comparator	*Any (statistically significant) increase in survival time* **CI_s: 1.00**	*Any (statistically significant) reduction* **CI_s: 1.00**	*Relevant improvement* **CI_s: 1.00**	Relevant avoidance **CI_s: 0.90** (RR_1=0.67)

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Reference Case

AMNOG: Early Benefit Assessment Methods

Differentiation of Subgroups

Test for Interaction using Meta-Regression
(Random Effects Model, REML)

$0.05 < p \leq 0.20$	$p \leq 0.05$	$p > 0.20$
Indication of subgroup effect:	**Proof** of subgroup effect	**No hint** of subgroup effect:
Presentation:	**Presentation:**	**Presentation:**
1. overall results 2. subgroup results	subgroup results	n.a.

Special case:
3 subgroups
=> pair-wise
interaction testing

Reference Case

AMNOG: Appraisal Outcome Categories

Classification (AM-NutzenV)		Description (AM-NutzenV)	Examples (AM-NutzenV)
Level I	Major or extensive additional benefit [*erheblich*]	¬ A sustained improvement of the therapeutically relevant benefit that was previously unattained by the appropriate comparative therapy	¬ Cure or extensive extension of life span ¬ Long lasting suppression of heavy symptoms ¬ Avoidance of severe side effects
Level II	Important or significant additional benefit [*beträchtlich*]	¬ A significant improvement of the therapeutically relevant benefit that was previously unattained by the appropriate comparative therapy	¬ Soothing of severe symptoms ¬ Moderate extension of life span ¬ Perceptible relief ¬ Other significant
Level III	Slight or marginal additional benefit [*gering*]	¬ A moderate and not just small improvement of the therapeutically relevant benefit that was previously unattained by the appropriate comparative therapy	¬ Soothing of mild symptoms
Level IV	Additional benefit not quantifiable	¬ Scientific data do not allow quantification of additional benefit	¬ Not detailed in AM-NutzenV
Level V	No additional benefit	¬ Not detailed in AM-NutzenV	¬ Not detailed in AM-NutzenV
Level VI	Smaller benefit than ACT	¬ Not detailed in AM-NutzenV	¬ Not detailed in AM-NutzenV

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Reference Case

AMNOG: Appraisal Outcome Certainty

- **Proof** *(Beleg)*:
  - At least two well conducted RCTs with significant result
- **Indication** *(Hinweis)*:
  - One well conducted RCT
  - Several studies with modest certainty
- **Hint** *(Anhaltspunkt)*:
  - One study with modest certainty
  - Several studies and ad-justed indirect comparison

- **Head-to-Head Trials**

  are always expected

- **Downgrading**:
  - Adjusted indirect comparisons and MTC are a fall back option
  - Study and / or endpoint scrutinization concerning potential sources of bias may lead to downgrading

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Some Conclusions

- **Health Technology Assessment (HTA)**
  - substantial international heterogeneity
  - national situation represents a “moving target” (sometimes described as a “learning system”), formal approach currently softer for medicinal products – **but**:
- Continuing Trend towards **Increasing Clinical Evidence Requirements**
  - need data on patient-relevant outcomes
  - need data on patient subpopulations
  - need data on resource use and cost
  - need data on cost effectiveness and budget impact
- **Coverage with Evidence Development** (SGB V §137e)
  - representing new opportunities to create win-win situations

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Some Recommendations

for successful applications:

- **Implement Early Strategic Value Assessments**
- **Learn from Biopharmaceutical Industry**
  - Identifying value drivers
  - Early planning of value demonstration
  - Patient-relevant outcomes and health economic evaluation(s)
  - Core Value Dossier and [international] pricing & reimbursement strategy
- **Cooperate with Regulators / HTA Agencies**
  - Never (!) confuse levels of interaction: policy debate versus product evaluation
  - Build trust & use opportunities for early consultation
  - Follow instructions meticulously and pay attention to detail
  - Interact in a spirit of partnership, being aware of different perspectives

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Thank You for Your Attention!

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