The role of real world data (RWD) in the decision making for the reimbursement of medicines

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Prepared for:

Prepared by:
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1. Background
   • Product lifecycle and value
   • HTA requirements
   • Pre-approval stage RWD
   • Post approval stage RWD
   • RWD study designs
   • Sources of RWD

2. Examples of RWD use
   • Pre-approval
   • Post-approval
   • Niche segments
Product development till implementation in healthcare

Different goals between stakeholders

Regulators
- Efficacy and safety

Health technology assessment
- Clinical effectiveness, economic impact & patient preference

Payors (healthcare systems)
- Comparative/Relative effectiveness

Pre-clinical research
- Clinical research
- Regulatory approval
- Reimbursement & market access
  - Health Technology Assessment
  - Pricing
  - Reimbursement

Marketing, sales & distribution

Health Technology Assessment
The big picture: Product value

Challenges:

- Bridge gaps among stakeholders
- Align scientific methodology
- Share and link Real World Data (RWD)

- Market access
- Affordability • Value for money
- Efficient delivery of healthcare services • Use of proprietary databases
- Optimal patient care
Value steps in the product life cycle

Preclinical/phases 1-3 studies → Benefit Risk → EMA Approval

Product Safety → Safety Alerts

Pre-approval (controlled experiment conditions)
Primary endpoints: safety/efficacy
Selected population

National healthcare system value → National healthcare HTA/P&R
Regional healthcare value → Local/hospital formulary list
Clinical practice → Patient benefit

Post-approval (real world conditions)
Direct product comparisons (H2H)
Costs collected
Real world population
Long term data data collection

Patient outcomes (disease and treatment)
Health technology assessment (HTA): “a multidisciplinary field of policy analysis, studying: medical, economic, social and ethical implications of development, diffusion and use of health technology”

Regulators: Does the health technology work and is it safe?

Payors: Is the health technology worth it? Can it work in practice?

http://www.inahta.org/HTA/
RWD in reimbursement decisions

What is real world data (RWD) in healthcare?
Data not collected in conventional randomized controlled trials (RCTs), providing an understanding of real life practice circumstances, from non-interventional studies

Outcomes (RWD in healthcare vs RCTs)

<table>
<thead>
<tr>
<th>Endpoints</th>
<th>Comparators</th>
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<tr>
<td>Safety</td>
<td>Long term drug effect</td>
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<td>Patient population</td>
<td>Economic implications</td>
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Research activity to gather RWD:
• Before product approval
• After product regulatory approval and marketing

## HTA/P&R requirements in European countries

### Need for RWD: health technology assessments, pricing & reimbursement

<table>
<thead>
<tr>
<th>Country</th>
<th>Clinical trial</th>
<th>Economic analysis</th>
<th>Observational/epidemiology</th>
<th>Decision models</th>
<th>Post-marketing surveillance</th>
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RWD input to projects that support product value

- Eligible patient population estimation
- Patient-reported outcomes
- Unmet need
- Economic models (QALYs, comparator)
- Pricing and HTA
- Treatment patterns survey
- Burden and cost of illness

Real world data
Pre-approval RWD generation

Pre-approval RWD collection includes:

• Epidemiological data
• Data on current patients’ management
• Identification of unmet medical needs
• Determination of costs associated with a disease or treatment related-events, in terms of longer term outcomes, and in comparison with the current standard of care.
• Inputs for cost-effectiveness and budget impact models

Questions to answer:

• What is the actual incidence of treatment failure in real life?
• What is the burden of the disease to the patient or the wider society?

Post-approval RWD generation

RWD collection after regulatory approval allows:

• Effectiveness to be demonstrated against key competitors

• Generation of evidence on:
  • medication adherence
  • compliance parameters
  • long-term clinical events
  • differentiation in sub-populations
  • potential off-label use
  • evaluation of the changing treatment landscape.

Question to answer:

• What is the actual safety or effectiveness in real-world clinical settings vs observed drug efficacy?

RWD study designs and data collection

Study designs providing evidence for coverage and payment decisions:

Registries:
• Large patient population reflecting RW patients, management practices, and outcomes.

Claims databases/electronic medical records:
• Billing codes from health care providers (physicians, pharmacies, hospitals) submitted to payors (insurance companies, public healthcare system)

Practical or pragmatic clinical trials (PCTs) observational studies:
• Longitudinal care, drugs, devices, and diagnostic (biological or imaging) used.
• Developed to answer the questions faced by decision makers
### RWD sources and types

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<tr>
<th>Data source</th>
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<tr>
<td>Clinical</td>
<td>• Clinical outcomes (morbidity and mortality)</td>
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<td>• Safety data</td>
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<td>• Natural history of the disease</td>
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<td>• Epidemiology</td>
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<td>• Utility data for economic modelling</td>
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<td>• Prescribing patterns</td>
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<td>• Treatment pathways</td>
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<td>• Health care resource use</td>
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<td>• Health related quality of life</td>
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<td>• Treatment preference/satisfaction</td>
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Supply of RWD (international examples)

**National payor systems database size**

- National Health Service’s *Clinical Practice Research Datalink* (20% UK population; anonymized patient records in primary care)
- *Nationella Kvalitetsregister* (nationwide; 80 national registries covering diagnosis, treatment, outcome measures in various therapeutic areas)
- *BARMER GEK* statutory health insurance (13% German population; records outpatient physician and pharmaceutical claims)

**Private payors and integrated systems examples**

Studies have linked inpatient and outpatient electronic medical records with claims among the following datasets:

- *Wellpoint’s HealthCore* (34 million lives across 14 states)
- *Kaiser Permanente* health plan (9 million patients across 8 states)

**Clinical IT systems providers examples**

Allscripts and GE both offer access to de-identified clinical datasets on millions of patients via electronic health records systems (although limited longitudinally).

Clinical information systems in the US cover about 65% of hospitals and 35% of physicians’ offices.

Science-based information in the real world setting

Scientifically valuable information that meets real world needs

Observational studies provide an opportunity for the science to yield commercial value at pre- and post-approval phases:

- Ethics approval when necessary
- Use of pre-defined statistical analysis plan
- Validation of instruments or questionnaires from experts (clinical, health economics)
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1. **Extrapolation of survival data based on RWD (cost-effectiveness models)**

   • Cost-effectiveness models can incorporate RWD (survival) (e.g., US SEER registry database, >60,000 patient records, for long term survival)

2. **Costs of adverse events**

   • Primary research with clinicians: identifying the resource use for the management of SAEs (inpatient, outpatient)

   • To be used for budget impact and cost-effectiveness analyses
3. Treatment pattern surveys in oncology

Practicing clinicians in individual markets globally are surveyed in order to collect RWD on:

- current use of different treatments and standard of care (comparators)
- factors that influence treatment decisions (guidelines, biomarkers, line of treatment)
- treatment setting (hospitals, private office, residential)
- patient selection and definitions, including subpopulations
- adherence to treatment guidelines
Examples in P&R (pre-approval) Treatment patterns survey
Examples in P&R (post-approval/market)

1. **Maintain preferred formulary status (osteoporosis):**

   - **Actonel** (P&G/Sanofi)
   - **Fosamax** (MSD)
   - **Boniva/generic**

   **RWD:**
   - Pharmacy use & drug adherence
   - Compliance & efficacy
   - Few fractures
   - Risk-sharing agreement to cover for costs for non-spinal bone fractures

2. **Challenge and defend efficacy of product class (insulin analogues):**

   In 2010 long-acting insulin analogues were excluded from reimbursement list

   - **Lantus** (Sanofi)
   - **Levemir** (Novo Nordisk)
   - **Human insulin**

   **RWD:**
   - Studies in medical databases
   - Improved outcomes: lower blood glucose level, patient satisfaction & economic benefit (lower healthcare cost)

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Elery T, Hansen N 2012 *Pharmaceutical lifecycle management: Making the most of each and every brand*, Wiley, New York
**AstraZeneca PATHOS retrospective observational registry study in moderate to severe COPD:**

- Swedish national hospitals

**Results:** Budesonide/formoterol more effective than fluticasone/salmeterol in preventing COPD exacerbations. Use of former appears to reduce hospitalization, emergency visits, and use of oral steroids and antibiotics.

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Larsson K et al. Intern Med 2013; 273: 584–594
Niche market segments

**Orphan drugs: limited clinical data lead to reliance on RWD**

Example: ZonMW (the Netherlands) funds hospital care based on the conduct of outcomes research studies, and re-evaluation after 4 years by CVZ

**Companion diagnostics: different reimbursement models**

(e.g., Payment for Tx/Dx provided there is RWE on clinical benefit)

Example: PBAC (Australia) has developed a clear set of guidelines to assess Dx:

- prevalence of a true positive biomarker in the population likely to receive the test
- linked evidence available of the test's impact on patient health outcomes

Simoens S. Orphanet Journal of Rare Diseases (2011),42
Summary of presentation

• RWD are widely used for pricing and reimbursement decisions

• Clinical, economic and PRO RWD are essential for decision-making

• Pre- and post-approval RWD oriented projects support value claims throughout the product lifecycle
Contact details

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