Performance-Based Risk-Sharing Arrangements for Drugs and Other Medical Products

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Acknowledgments

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Performance-Based Risk-Sharing Arrangements: A Variety of Names

- managed entry agreements (MEA)
- outcomes-based schemes
- risk-sharing agreements
- coverage with evidence development (CED)
- access with evidence development
- patient access schemes (PAS)
- conditional licensing
- pay-for-performance programs (P4P)
- And others?
Pricing Pills by the Results

Drug companies like to say that their most expensive products are fully worth their breathtaking prices. Now one company is putting its money where its mouth is — by offering a money-back guarantee.

Johnson & Johnson has proposed that Britain’s national health
Why the interest in performance-based risk-sharing?

• **Health care production is complex:**
  Economists think of it as a “Health Production Function”:
  – Output = f(Inputs)
  – Health = f(hospital stays, doctors visits, drugs, OTHER)

• The physician acts as the “patient’s agent” in organizing and advising on this process.

• Historically, either (1) all of these inputs were provided by a system of care or (2) each input is purchased on a fee-for-service basis—or some mix of these.

But the process is so complex that no one has offered guarantees of good outcomes.
Well, that’s not entirely true:

All Headaches Instantly Cured or Money Refunded.

LEGAL GUARANTEE.

D. EMERSON’S BROMO-SELTZER, the most successful American Remedy, is an effervescence Powder, taken in water. If three doses do not Cure any Headache, no matter how caused, send the Bottle to us, saying where obtained, AND WE WILL AT ONCE REFUND THE PRICE. TRIAL BOTTLE, post free, 6d. Larger Sizes 1s. and 2s. Sold by many Chemists or obtained to order by almost all.

EMERSON DRUG CO., LTD.,
46, HOLBORN VIADUCT, LONDON, E.C.

Insist on Full Name—

EMERSON’S BROMO-SELTZER
Greater interest in “pay for performance”

1. In the U.S, for health plan processes and for physician services.
2. Internationally, for branded drugs.

Why the new interest? What has changed?
Bioclinical Health Outcomes Framework: Which Outcomes to Measure?

- Weight Loss

  \[\rightarrow\]

  Improvements in Surrogate Co-Morbidities:
  - Glucose tolerance
  - Cholesterol
  - Blood Pressure

  \[\rightarrow\]

  Long-Term Improved Clinical Outcomes:
  - Cardiovascular/
  - Cerebrovascular Events

  \[\rightarrow\]

  Better Health Outcomes:
  - Length of Life
  - Quality of Life

Example: Obesity Disease-Treatment Model
Basics: The Pervasiveness of Uncertainty

• Drugs are approved, launched, and reimbursed under conditions of uncertainty, affecting many key parameters:
  – Efficacy (heterogeneity)
  – Effectiveness in real world
  – Risks (safety)
  – Models, including links between surrogate markers and long-term outcomes
  – Cost-effectiveness
  – Budget impact.

1. Variability $\rightarrow$ Uncertainty (=Risk)

2. Gathering more evidence to reduce uncertainty is costly.
Some Important Economic Terms and Concepts

- **“Market failure”**—when “free markets” do not provide an “optimal” allocation of resources—often when the conditions for a free market are not met.
  - For example, public goods, externalities, informational asymmetry, uncertainty, etc. —patent protection to incentivize investment and risk-taking

- **“Public good”**—a good for which one person’s usage or consumption does not keep other from using it, e.g., national defense.
  - The free market can be expected to undersupply public goods.
  - We address this with interventions, such as **“intellectual property”** and **public subsidies**.
  - There can be a **“free rider”** problem.

- Information and scientific advances can be public goods—even **“global public goods”**
  - The whole world has a stake in innovative pharmaceutical R&D.
  - Economists agree that **“differential pricing”** would be an improvement: the challenge is how to implement it.
The Historical Risk-Sharing “Equilibrium”

• **Risk to manufacturer:** we operate with a blockbuster financing model for R&D.
  — Intellectual property—patent protection to incentivize investment and risk-taking
  — There is no *ex ante* clause to share innovation cost or to purchase drugs.

• **Risk to payer:** The payer negotiates a price and/or use.
  — The payer bears the risks of making a bad buy (i.e., when incremental health benefits are not worth the additional cost).
  — The payer is free to collect post-launch data. Manufacturers will only do this if it is in their competitive interests.

• Individual countries strike different types of deals with manufacturers
  — Range of country environments: negotiated prices < -- > free pricing
  — All of this provides an incentive for manufacturers to seek highest justifiable price at launch. Manufacturers would like to price for future (larger) indications.
1. **There is a program of data collection** agreed between the manufacturer (or provider, in some instances) and the payer.

2. **This data collection is typically initiated during the time period following the regulatory approval** (which may be full, conditional, or adaptive), and linked to post-launch coverage decisions.

3. **The price, reimbursement, and/or revenue for the product are linked to the outcome of this program of data collection** either explicitly by a pre-agreed rule or implicitly through an option to renegotiate coverage, price, and revenue at a later date.

4. **The data collection is intended to address uncertainty about** .... *For example:*
   - efficacy or effectiveness in the tested population as compared to current standard of care;
   - the efficacy or effectiveness in a broader, more heterogeneous population than used in registration trials or in pre-licensing testing;

5. **These arrangements provide a different distribution of risk** between the payer and the manufacturer than the historical manufacturer-payer relationship.

Source: ISPOR PBRSA Task Force Report
Why the “sudden” interest?  
Fad or trend?  

• Understanding the cause should be helpful to predict long-term adoption and impact.  

• Two general explanations:  
  1) Innovation—it’s a new invention.  
  2) Environment has changed.  

• Some “trends” may be fads:  
  – Example: disease management (carve-outs)  
    • Did not fulfill original promise. Why?
Cost Pressures

• Increasing drug expenditures attributed to:
  – Use of high cost biopharmaceuticals for common, chronic conditions (RA, Asthma, Psoriasis, etc)
  – Expensive, combination biopharmaceutical treatments in oncology and infectious disease
  – Prescribing beyond evidence and approved indications
  – Other factors (aging population, fewer resources, etc)

Real cost of new branded drugs is rising—fewer approvals and higher R&D spending.
Co-Payments Soar for Drugs With High Prices

Robin Steinwand had been paying $20 a month for her multiple sclerosis drug, which she keeps in the refrigerator. When she went to pick up her prescription in January, it cost $325.

By GINA KOLATA
Published: April 14, 2008
Payer Response to Increasing Cost Pressures

- Public and private sector payers are facing these challenges with various cost-control instruments and management strategies:
  - Increasing patient co-payments
  - Pre-use authorization (targeting appropriate patients and appropriate use)
  - Quantity and dose limitations
  - Specialty pharmacy vendors
  - Benefit restrictions (e.g. generic-only benefits)
  - Denial of coverage

Working hypothesis: Performance-based agreements are a market response to increasing cost pressures: manufacturers have incentive (esp. in US) to push prices to limit of willingness to pay, and payers are pushing back.
Other Related Developments and Discussions

• Value-based pricing and reimbursement (UK Office of Fair Trading)
• Real-world data (ISPOR Task Force, Netherlands)
• Drug safety and benefit-risk assessment (FDA; EMEA)
• Conditional licensing (MHRA, Cooksey Review)
• Personalized medicine/tailored treatments
• Comparative effectiveness research
• Financing R&D and fostering innovation
Landscape of Performance-Based Arrangements: Taxonomy and Review of Cases

Josh Carlson, Ph.D.
Review of Performance-Based Arrangements: Methods

• Sources:
  – PubMed, Scrip, Embase, and Google
  – Experts and peers
• 25 year time frame
• Included: Health outcomes based agreements: price, level, or nature of reimbursement are tied to measures ultimately related to patient quality or quantity of life.
• Excluded: non-outcomes based models including price volume agreements, market share agreements
• Develop a taxonomy of agreements:
  – Inductive approach
  – Refined using a modified Delphi approach with experts in the area.
Performance-based schemes by year

Performance-based Schemes by Year

Total Schemes: 149
Performance-based schemes between health care payers and manufacturers

Non-outcomes based schemes
- Population level
  - Market share
  - Price volume
- Patient level
  - Utilization caps
  - Manufacturer funded treatment initiation

Health outcomes-based schemes
- Conditional coverage
  - Coverage with evidence development (CED)
    - Only in research
      - [Ex: Cochlear implants in US (CMS)]
    - Only with research
      - [Ex: Risperidone in France]
  - Conditional treatment continuation (CTC)
    - [Ex: Alzheimer's drugs in Italy]
- Performance-linked reimbursement (PLR)
  - Outcomes guarantee
  - Pattern or process of care
    - [Ex: OncotypeDx in US (United Healthcare)]
  - Clinical Endpoint
    - [Ex: Bortezomib in UK]
  - Intermediate Endpoint
    - [Ex: Simvastatin in US]
Taxonomy Definitions: Coverage with Evidence Development

- **Coverage with evidence development**: coverage is conditioned on collection of additional population level evidence, from pre-specified study, to support continued, expanded, or withdrawal of coverage

  - Only in research: coverage conditional on individual participation in research (i.e. only patients participating in the scientific study are covered)
    - Example: CMS may cover cochlear implantation for treatment of hearing loss when the provider is participating in, and patients are enrolled in, an approved clinical trial

  - Only with research: coverage conditional on agreement to conduct a study that informs the use of the medical product in the payer patient population
    - Example: France's ministry of health agreed to cover Risperidone if J&J performed studies to evaluate whether it helps patients stay on their medications.
Coverage with Evidence Development: What problems are being addressed?

- Insufficient evidence at product launch or time of coverage decision.

- CED: Creates a middle ground between coverage and no coverage for products that appear promising, but may not yet have the evidence base to support full coverage.

- Payer Benefit:
  - Provides access while generating additional evidence to support future coverage decision

- Manufacturer Benefit:
  - Access
  - Reduced cost of data collection
Coverage with Evidence Development

• Seven countries were found to have implemented a total of 65 CED schemes.
  – Netherlands with 22 (34%),
  – Sweden with 16 (25%),
  – U.K. 9 (15%)
  – U.S with 11 (17%),
  – France with 3 (5%)
  – China with 2 (3%)
  – Australia with 1 (2%)

• Majority of CED in the U.S. involved devices.
• Outside the US, CED focused on pharmaceuticals.
  – Increased willingness in the EU, relative to the US, to limit the use of pharmaceuticals in patients and patient subgroups for which the benefits and cost-effectiveness remain questionable.
Performance-based schemes between health care payers and manufacturers

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- Intermediate Endpoint [Ex: Simvastatin in US]
Taxonomy Definitions: Conditional Treatment Continuation

• **Conditional treatment continuation**: continuation of coverage for individual patients is conditioned upon meeting short-term treatment goals.
  
  – A.K.A. Stopping rule
  
  – Example: Alzheimer’s drugs provided free by manufacturer in Italy. If treatment goals are met after 3 months, treatment is continued with drug costs reimbursed by national health service.
Conditional Treatment Continuation: What problems are being addressed?

• Problem: Medical products are used in inappropriate patient populations
• Solution: Conditioning coverage on short-term treatment goals helps ensure that only patients benefiting from treatment remain on treatment.
• Benefit to Payer:
  – Minimizing their long-term cost exposure
  – Improving a product’s cost-effectiveness
  – Replaces need for limits on patient access (e.g. prior authorization)
  – Assuage payers’ concerns over patients receiving continued treatment despite a lack or loss of benefit.
  – Advantages increased when manufacturers cover cost of treatment initiation (E.g. Alzheimer’s drugs in Italy).
• Benefit to Manufacturer
  – Access
Conditional Treatment Continuation

• Eight countries were found to have implemented a total of 20 schemes involving CTC including:
  – Italy (13)
  – Australia, Brazil, Canada, Slovenia, U.K., Spain and U.S. (1 each)

• In multiple schemes, the manufacturer provided funding or discounts during the treatment initiation period.

• Key component: availability of a reliable measure of short-term response, benefit, and/or continued benefit (e.g. tumor response) that is acceptable to both parties.
Performance-based schemes between health care payers and manufacturers

Non-outcomes based schemes
- Population level
  - Market share
  - Price volume
  - Utilization caps
  - Manufacturer funded treatment initiation

Patient level

Health outcomes-based schemes
- Conditional coverage
- Conditional treatment continuation (CTC)
  - Only in research
    - [Ex: Cochlear implants in US (CMS)]
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  - Pattern or process of care
  - Clinical Endpoint
    - [Ex: Bortezomib in UK]
  - Intermediate Endpoint
    - [Ex: Simvastatin in US]
Taxonomy Definitions: Performance-Linked Reimbursement

Performance-linked reimbursement: reimbursement level for covered products is tied, by formula, to the measure of clinical outcomes in the “real world”;

**Outcomes guarantees:** manufacturer provides rebates, refunds, or price adjustments if their product fails to meet the agreed upon outcome targets

Example: J & J agreed to reimburse the NHS in either cash or product for patients who do not respond (Response measure: 50% decrease in serum M protein) after 4 cycles of treatment with Velcade. Responding patients receive additional 4 cycles.
Performance-Based Schemes for Oncology Drugs

- **Treatment Initiation**
  - Manufacturer discount

- **Conditional Treatment Continuation**
  - Response (Y/N)

- **Outcomes Guarantee**
  - Rebate for Non Responders
AIFA Risk Sharing procedure

Initial cycles of treatment for new patients

Treatment ex-post evaluation

- NON-RESPONDERS
  - Treatment is stopped
  - Discount on price paid by Marketing Authorisation Holder

- RESPONDERS
  - Treatment is continued
  - Treatment is reimbursed by NHS

Source: Paolo Siviero, AIFA
Performance-Linked Reimbursement: What problems are being addressed?

• Problem 1: Payers may desire more evidence to support manufacturer’s claims
  – Expensive: Direct costs & lost revenues due to delays in market access.

• Solution: Manufacturers provide payers a guarantee for certain outcomes linked by formula to the reimbursement level in place of additional product research.

• Problem 2: External reference pricing doesn’t allow for price discrimination for individual markets

• Solution: Alternative mechanism to provide discounts without changing list prices.
  – Example: List price for 3.5 mg vial of Velcade is £760 in U.K., after rebate for non responders the effective price paid is closer to £300 per vial—yet the list price remains the same.

• Benefit to Payer:
  – Provide access to patients at a discounted net price

• Benefit to Manufacturer
  – Access at or near launch
  – Can be used to provide a discount
Performance-Linked Reimbursement

- Overall, six countries were found to have implemented a total of 54 PLR schemes:
  - Italy with 25 (46%)
  - U.K. with 9 (17%)
  - U.S. with 6 (11%)
  - Australia, Canada, and Spain with 3 (6%)
  - France with 2 (4%)
  - Germany, Slovenia, Brazil (1 each)
- Most (53 of 54) involved pharmaceuticals
- Majority utilized rebates or refunds as opposed to price adjustments
  - Reluctance of manufacturers to adjust list prices → external reference pricing
Performance-Based Agreements: Overall Summary

- Fourteen countries had performance-based arrangements.
- Most (88%) outside of the US, (77%) in the European Union.
  - Increased negotiating power of national payers vs. U.S. payers.
    - Mandates to consider costs in coverage and reimbursement decisions
    - Greater power to deny coverage for medical products even if they have received marketing approval by regulatory authorities.
  - Better and more integrated administrative and information systems.
  - Require evidence of cost-effectiveness and economic modeling.
    - Adds another layer of uncertainty for payers
      - May feel comfortable that a product is efficacious based on the available clinical data
      - Remain unsure of the product’s cost-effectiveness due to the uncertainty in the modeled long-term outcomes, e.g. life expectancy.
Junuvia and Janumet (Merck) for Diabetes and CIGNA

- Scheme has three core components:
  1. CIGNA will assess the blood sugar levels (A1c lab values) for pts on any oral antidiabetic medications.
     - If the A1c values, in aggregate, improve by the end of the agreement period, the discounts will increase by a pre-agreed amount.
  2. CIGNA will use claims data to determine if patients are taking Januvia and Janumet as prescribed
     - Merck will further increase the discounts
  3. Better placement on CIGNA’s formulary + lower copayment versus that for other branded drugs.
Junuvia and Janumet (Merck) for Diabetes and CIGNA

• Different from other schemes → deeper discount when patients improve their A1c lab values.
• Benefit all the key parties—payers, manufacturers, and patients.
  – Diabetes patients who are more adherent tend to have better outcomes.
  – Pts with better adherence and outcomes utilize fewer resources → cost savings
  – Manufacturers can improve sales volumes with better patient adherence
    • Offset the lost revenues related to the per unit discount offered by Merck.

• As a recent New York Times article stated,

  “Merck is betting not only that its drugs prove superior but that CIGNA’s incentives to reap the benefits of the deeper discounts will prompt the insurer to try to keep patients on those drugs.”
Risedronate (Proctor & Gamble, Sanofi-Aventis) for Osteoporosis and Health Alliance

- Two companies agree to reimburse the insurer for the costs of treating non-spinal fractures suffered by patients who consistently take their medications.
- First published example of a manufacturer agreeing to cover the cost of disease-related sequelae as opposed to discounting or refunding the cost of their product.
- Hip and wrist fractures cost approximately $30,000 and $6,000, respectively.
- The benefit to the manufacturers:
  - Keeps patients from switching to generic version
  - Maintains a lower copayment level than their competitor, ibandronate.
Risedronate (Proctor & Gamble, Sanofi-Aventis) for Osteoporosis and Health Alliance

• Clinical trials of risedronate failed to show a statistically significant reduction in non-spinal fractures, whereas some competitors have demonstrated this benefit in their trials.

• Benefit to payer:
  – Outcome guarantee on uncertain clinical endpoint

• Makers of risedronate are betting:
  – Product will reduce non-spinal fractures in actual practice and/or,
  – The cost of treating them will be offset by maintaining or even expanding their market share in a highly competitive market in which it may not be the market leader.
Performance-based schemes by country

Performance-based Schemes by Country

Total Schemes: 149
Performance-based scheme types by country

Performance-based Scheme Components by Country

Total Schemes: 149

CED: Coverage with evidence development; CTC: Conditional treatment continuation; PLR: Performance linked reimbursement; FU: Financial or utilization based agreements

*Note: Multiple schemes had multiple performance-based components
**Cases by Country**

**Canada**
- Province level
- Lack of transparency

**USA**
- A few outcomes guarantees
- CED at CMS

**Netherlands/Sweden**
- CED schemes for expensive medicines

**Germany**
- Agreements have been made in the past with the G-BA in relation to conditional reimbursement

**UK**
- National level
- PPRS changes may affect innovative agreements?

**Italy**
- National authorities proactive
- Uniform model

**France**
- CEPS prefer traditional price-volume agreements

**Australia**
- Agreements on national level
- PBAC has risk-sharing guidelines
- Lack of transparency
Cases by Manufacturer

![Bar chart showing cases by manufacturer]

- Novartis
- Roche
- Multiple
- Pfizer
- Johnson and Johnson
- GlaxoSmithKline
- Bristol-Myers Squibb
- Merck
- Sanofi-Aventis
- Eli Lilly
- AstraZeneca
- Genzyme
- Bayer Schering Pharma AG
- Celgene
- Amgen

Number of Cases
Cases by Therapeutic Area

- Oncology
- Neurology
- Immunology
- Psychiatry
- Nephrology/Urology
- Musculoskeletal
- Hematology
- Cardiovascular Disease
- Otology
- Hormonal Treatment

Number of Cases
Results of Implemented Schemes

• Difficult: Very little published, and even less on the results
• Arrangements used to gain or expand coverage → existence = successful access

• Cigna and Januvia/Janumet:
  – Blood glucose levels improved by more than 5 percent
  – Adherence was 87 percent for patients taking Januvia or Janumet

• NHS and drugs for treating multiple sclerosis (UK)
  – Delays publishing scheduled 3-year cost-effectiveness report.
    • “it is too early to reach any conclusion about the cost-effectiveness of disease modifying treatments.”

• CMS and CED:
  – Data used to inform two policy decisions
  – Other studies failed to be designed, funded, or implemented due to costs, measurement issues, and legal challenges.
Results of Implemented Schemes

• Updated coverage status after additional CED studies:
  – Subsequent approval
    • Bosentan in Australia,
    • Docetaxel, irinotecan, and oxaliplatin in U.K.
    • Insulin detemir, pimecrolimus, Duodopa in Sweden
  – Not subsequently approved for general coverage.
    • Paclitaxel in the U.K. and rasagiline in Sweden
• Schemes have been rejected (e.g. lapatinib and bevacizumab for RCC in the U.K.).
  – Didn’t meet payers needs: effectiveness, cost-effectiveness, budget impact
  – The needs of the manufacturer in terms of pricing, access, and revenues.
Results of Implemented Schemes

• French CED for Risperidone.
  – The requested study, which followed 1600 patients for 1 year, found that patients treated with risperidone had a lower relative risk of hospitalization than those on other antipsychotics and the premium list price was maintained.

• French CED for pioglitizone:
  – In the AVANCE observational study for rosiglitazone (AVANCE) the data did not support manufacturers’ claims of a superior real-life effectiveness. This resulted in the pricing committee CEPS cutting the drug’s price by 30%, requesting rebates for the drug already purchased and altering the reimbursement level from 65% to 35.
Duodopa in Sweden

Table 1. Duodopa® submission timeline

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003 Nov</td>
<td>Neopharma applies to TLV for reimbursement at a price of SEK6910 (ex factory)</td>
</tr>
<tr>
<td>2004 Jan</td>
<td>TLV grants temporary reimbursement until 31 January 2005 with continued reimbursement contingent upon submission of health economic data</td>
</tr>
<tr>
<td>2004 Nov</td>
<td>Neopharma re-submits for reimbursement at a price of SEK6910 (ex factory), including an economic analysis¹¹</td>
</tr>
<tr>
<td>2005 Jan</td>
<td>TLV extends reimbursement until 31 August 2007 with continued reimbursement contingent upon submission of new evidence of the health economic benefits and costs</td>
</tr>
<tr>
<td></td>
<td>Neopharma acquired by Solvay Pharmaceuticals</td>
</tr>
<tr>
<td></td>
<td>Solvay Pharmaceuticals begins DAPHNE study</td>
</tr>
<tr>
<td>2006 Jan</td>
<td>First patient recruited to DAPHNE study</td>
</tr>
<tr>
<td>2007 May</td>
<td>First interim analysis of DAPHNE</td>
</tr>
<tr>
<td>2007 Jun</td>
<td>Solvay Pharmaceuticals re-submits for reimbursement at a price of SEK6910 (ex factory), including a new economic model partly populated with data from the first interim analysis of DAPHNE</td>
</tr>
<tr>
<td>2007 Sep</td>
<td>TLV halts reimbursement for all new patients</td>
</tr>
<tr>
<td>2007 Dec</td>
<td>Second interim analysis of DAPHNE</td>
</tr>
<tr>
<td>2008 Feb</td>
<td>Solvay Pharmaceuticals re-submits for reimbursement at a price of SEK6688 (ex factory), including a revised model populated more heavily with DAPHNE data (and additional patients and follow-up)</td>
</tr>
<tr>
<td>2008 Jun</td>
<td>TLV grants reimbursement</td>
</tr>
</tbody>
</table>

SEK = Swedish kronor; TLV = Dental and Pharmaceutical Benefits Agency.

Willis et al. 2010
Italy: Time to Patient Access

A mean shortening of 256 days

Ann. Oncol. 2010;21(10):2081-7
Barriers

1. Associated transaction and administration costs;
2. Limitations of current information systems in terms of tracking performance;
3. Agreeing on the scheme details (e.g., the appropriate outcome measure or the financial adjudication process);
4. Physician push-back;
5. “Free-rider” problem—other manufacturer or payer competitors may benefit from the information or schemes developed; and
6. Lack of trust between payers and developers.
Performance-based Schemes in Italy: Lag time

Stakeholder Perspectives

• Increased interest by both developers and payers
  – More experience outside the U.S.

• Developers:
  – Improved market access
    • Secure coverage at or near launch for new products or new indications
    • Better formulary position
  – Provide a means to give discounts without changing list prices
  – Support brand message about product benefits

• Payer: Basis for covering promising technologies that may benefit its members under conditions that ensure:
  – Limits costs and cost exposure
  – Products deliver sufficient value
  – Products are being used in the appropriate patient populations
  – Sufficient quantity of high quality evidence is gathered regarding the benefits and risks of the technologies
Conclusions

• Performance-based agreements in line with healthcare trends
• They are intrinsically appealing
  – Align incentives toward realized value
• Substantial barriers to implementation that will limit both the short-term and long-term impact
  – Especially in the US.
• They will not apply to all medical products, but rather to a select group where the payer and manufacturer can find common ground
• Performance-based schemes are becoming a viable option for the coverage and reimbursement of new medical products.
Case Examples and Evaluation
What problems are being addressed?

1. Impact of uncertainty: substantial residual uncertainty about a product’s expected effectiveness, budget impact, and value at the time of product launch or coverage/reimbursement decision. Performance-based arrangements can help:
   - Resolve residual uncertainty:
     • Coverage with Evidence Development
   - Mitigate the negative consequences of uncertainty:
     • Payers – bad buy if product under delivers relative to expectation
       - Sub optimal patient health, financial losses, inefficient resource allocation.
     • Manufacturers—no or limited market access.
       - Performance-linked reimbursement, conditional treatment continuation.

2. Inefficient pricing due to external reference pricing and parallel trade
   - External reference pricing limits differential pricing by county/payer
Understanding and Developing Performance-based Arrangements

• **Product factors:**
  - Effectiveness
    • E.g., amount of evidence, trial endpoints, and comparators (standard of care or placebo)
  - Budget impact/usage:
    • E.g., target population, treatment duration, and potential off-label use
  - Cost-effectiveness/value

• **Market factors:**
  - Payer attributes
    • Reimbursement focus (e.g., cost-effectiveness)
    • Public versus private
  - Unmet need
  - Competitive landscape
Example 1: Velcade for Multiple Myeloma in UK

- **Efficacy/Effectiveness:**
  - Limited data on overall survival: Secondary endpoint, trial stopped early.

- **Budget impact/patient population considerations:**
  - High cost: Cost per cycle, £3,000
  - Variable treatment duration—treat until tumor progression

- **Value:** Not cost-effective at 1st submission (£35,000/QALY, substantial uncertainty).

- **Market factors:**
  - First-in-class, no good alternatives at 1st relapse
  - Public payer, market access based on cost-effectiveness
Velcade for Multiple Myeloma in UK

• Performance-based scheme development:
  – Resubmission to NICE with performance-based scheme
  – Conditional treatment continuation (stopping rule after 4 cycles) and outcomes guarantee (rebate for non-responders)
  – ICER with rebate, stopping rule: £20,700/QALY → NICE approval

• Handling uncertainty: Mitigate negative consequences of uncertainty about value
VELCADE® Response Scheme (VRS) for patients with Multiple Myeloma at 1st relapse within the NHS in England, Wales and N.Ireland - Process Flow

**Customer**

1. Signs VRS agreement with JC
2. Orders VELCADE
   - Evaluate response after a maximum of 4 cycles (≤16 vials)
     - Response Y/N
     - Yes → Order further vials of VELCADE
     - No → JC advises and discusses with customer

**Janssen-Cilag/Ortho Biotech**

1. VRS claim forms are sent to Customer upon receipt of signed VRS agreement
2. Hospital completes VRS claim form for replacement stock, credit or full cash refund for ≤16 vials. Fax/Post to JC
3. VRS Claim Form copied to JC Drug Safety Dept.
4. Drug Safety allocates a specific UK/DS Number and writes to clinician requesting more details on the non-response event

**JC Drug Safety**

1. Claim validated Y/N
   - Yes → JC advises and discusses with customer
   - No → JC advises and discusses with customer

**Notes:**

1. **Response** defined as a patient, at first relapse, with a 50% or greater reduction in serum M-protein, within 4 cycles of treatment, compared to baseline level immediately prior to VELCADE treatment.

2. **Non-response or minor response** defined as a patient, at first relapse, having less than a 50% reduction in serum M-protein, within 4 cycles of treatment, compared to baseline level immediately prior to VELCADE treatment.

   NB: 15% - 20% of patients do not have measurable serum M-protein levels, and for this group Bence-Jones urine protein (urine free light chains) could be used. Response defined according to the standard EBMT (European Group for Blood and Marrow Transplantation) criteria, i.e. at least a 90% reduction, compared to baseline immediately prior to VELCADE treatment (and within 4 cycles).

3. **Claim Validation to check:**
   - VRS claim form completed in full and signed
Understanding and Developing Performance-Based Arrangements

• Understanding the asset
  – Nature of uncertainty
  – What innovative schemes might address the uncertainty

• Understanding the market factors
  – External market factors that may impact the approach
    • Unmet need
    • Competitive landscape
    • Country/payer type

• When might additional investment into evidence generation studies be needed?
  – Expanding into new indication—Colon cancer treatments in US (clinical trials)
  – Long term outcomes—Bosentan in Australia
  – Support manufacturer’s claims—Risperdal Consta in Sweden
  – Cost-effectiveness—Duodopa in Sweden

• Explore impact of schemes using cost-effectiveness and revenue models
• Develop and validate treatment response biomarkers
COMMENTARY

Paying for Outcomes: Innovative Coverage and Reimbursement Schemes for Pharmaceuticals

Josh J. Carlson, PhD; Louis P. Garrison, Jr., PhD; and Sean D. Sullivan, PhD

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Review

Linking payment to health outcomes: A taxonomy and examination of performance-based reimbursement schemes between healthcare payers and manufacturers

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Thanks!
Questions?

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