THE NEXT FRONTIER FOR RISK-SHARING AGREEMENTS IN THE U.S.: DOES THE CHANGING HEALTH CARE LANDSCAPE BRING NEW PROMISE FOR PARTNERSHIPS BETWEEN MANUFACTURERS AND PAYERS?

ISPOR Issues Panel
June 3, 2014
Montreal, Quebec
Canada

Issues Panelists

- **Moderator: Josh J Carlson, MPH, PhD**, Assistant Professor, Pharmaceutical Outcomes Research and Policy Program, University of Washington, Seattle, WA, USA
- **Panelists: Lou Garrison, PhD**, Professor, Pharmaceutical Outcomes Research & Policy Program, School of Pharmacy, University of Washington, Seattle, WA, USA;
- **Adrian Towse, MA, MPhil**, Director, Office of Health Economics, London, United Kingdom;
- **Peter J. Neumann, ScD**, Professor and Director, The Center for the Evaluation of Value and Risk in Health, The Institute for Clinical Research and Health Policy Studies, Tufts Medical Center, Boston, MA, USA
Collaboration

- Study sponsored by National Pharmaceutical Council
- Other collaborators:
  - Sean Sullivan (UW)
  - Bobby Dubois (NPC)
  - Kimberly Westrich (NPC)
  - Preeti Bajaj (UW)

Performance-based Schemes by Year

Total Schemes: 209

Source: UW PBRSA Database
The Issue

Risk-sharing agreements (RSAs) have been leveraged frequently in Europe, and offer the potential for earlier access to new products by linking coverage and reimbursement levels to real-world performance or utilization of the product.

There are potential advantages for patients, payers, and manufacturers; however, the dearth of schemes in U.S. raises questions as to why their use has been limited and also as to what might become feasible in the rapidly evolving health care system, especially with the new emphasis on accountable care organizations.
NPC Study Components and Session Presentations

Study Components
• UW Database Review
• Interviews
• Literature review of taxonomies
• Brief online survey on barriers

Presentations:
• Lou Garrison—US Perspective
• Adrian Towse—EU Perspective
• Peter Neumann—Barriers and U.S. Health Reforms

Study Findings:
U.S. Focus on Risk-Sharing Agreements

ISPOR 19th International Meeting
Montreal, Canada
June 3, 2014

Lou Garrison, Ph.D.
Professor, Pharmaceutical Outcomes Research and Policy Program,
Department of Pharmacy
Adjunct Professor, Departments of Global Health and Health Services
University of Washington
and VeriTech Corporation
U.S. RSA experience

• 17 arrangements in the U.S. between the years 1997 and 2012.
  – 10—had coverage with evidence development component,
  – 6 had a performance-linked reimbursement component
  – 1 had a conditional treatment continuation component.

• 12 with public payers
• 5 with private payers

Junuvia and Janumet (Merck) and CIGNA for Diabetes

• Scheme has three core components:
  1. CIGNA assesses the blood sugar levels (A1c lab values) for patients 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 uses 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) and CIGNA for Diabetes

• In 2010, CIGNA announced positive outcomes from the diabetes support program:
  – patients’ blood sugar levels were reduced by more than 5%,
  – individuals who participated were more likely to control their blood sugar than those who did not participate in the program, 87% of patients who took Januvia or Janumet took their medications correctly.

• According to Dr. Jeffrey Kang, Cigna’s Chief Medical Officer, ‘what makes this unique approach so successful is that everyone’s incentives line up behind helping customers keep their diabetes under control’

Risedronate (Proctor & Gamble, Sanofi-Aventis) and Health Alliance for Osteoporosis

• 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.

• 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.
Risedronate (Proctor & Gamble, Sanofi-Aventis) and Health Alliance for Osteoporosis

- Reimbursement rate for non-spinal fractures was 79% lower than the maximum outlined in the agreement in the first nine months.

- *Christina Barrington, Health Alliance’s pharmacy director, stated,* “the Fracture Protection Pilot Program was launched to highlight the effectiveness of Actonel through medical outcomes reimbursement. Initially, we had hoped that this program could lower insurance costs not only for Health Alliance, but for our subscribers as well. As a result, Health Alliance independently chose to help our subscribers by lowering their costs. We look forward to continuing and building upon this successful pilot.”

- *Raulo Frear, Pharmacy Director of Regence Health Plan, stated,* “we have reviewed the Fracture Protection Program and are enthusiastic about the opportunity to partner with the makers of Actonel to tie expected outcomes to drug utilization in our patient population. This program is an example of an innovative way plans and pharmaceutical manufacturers can partner and bring value to our plan sponsors.”

U.S. Experience: Take-Home Points

- Most likely to target high cost disease areas and expensive drugs.
- CED is a mechanism to compel additional data generation to resolve existing uncertainty.
- Successful arrangements can provide benefits for payers, manufacturers, and patients. *Example: Januvia/Janumet*
- Arrangements should address an agreed-upon uncertainty. *Example: Actonel and non-spinal fractures*
- Arrangements may link to disease and/or treatment related costs to avoid issues related to drug price. *Example: Actonel*
- Arrangements should use existing data systems when possible. *Example: Januvia/Janumet*
Key Themes from Interviews (1)

• 14 one-hour –semi-structured interviews—manufacturers, payers, experts
  – 5 US Pharma, 2 EU Pharma
  – 4 US Payer, 1 EU Payer
  – 2 Experts

• RSA Types and Trends:
  – There is an increasing interest in financial deals and mixed interest in outcomes-based deals. Outcomes-based agreements are difficult to execute and transaction costs are high, whereas financial agreements are easier to implement. Simple agreements work well.

Key Themes from Interviews (2)

Logistics:

• Payers only have the bandwidth to do a few outcomes-based deals simultaneously due to burden of data collection.

• Payers are willing to have multiple agreements with companies for competing products (more likely to be feasible for bigger plans).

• Medium-term deals (2-4 years) are necessary if making an investment in evidence development.

• Data collection is typically the responsibility of payers.
Key Themes from Interviews (3)

Reasons to Use RSAs:

- Depends on the product, disease area, and data infrastructure.
- Differentiate their product and demonstrate product value.
  - Usually done for newly launched products
  - Maintain market share over generics.
  - Some challenges exist but where there is still evidence of clinical benefit.
  - Draw the link between efficacy and effectiveness, and/or demonstrate comparative effectiveness.

“If somebody can help reduce risk, take some of the variability out of the equation, or can actually help you manage some of those medical costs, then that’s very attractive and that’s more attractive than just getting a discount. It allows us to actually get experience using the medication or our members using the medication but it takes some of the risk off us.” - US Payer

Key Themes from Interviews (4)

What works:

- It may be easier to measure outcomes for drugs that are administered in settings where there are more immediate clinical data available (e.g., hospital settings) or where drugs are administered in person. Complex outcomes might require an active provider (e.g., patient-centered medical home) to measure.
- Clinical outcomes deals are most successful where the infrastructure is robust to collect clinical data (e.g., single payer/closed settings - hospitals, Kaiser, integrated delivery networks).
- Manufacturers should be able to predict the outcomes of the agreement and assess the risk they are taking on. - e.g., what level of compliance is required, to what extent clinical trial population differs from the real-world population.

“There are very few disease areas where these make sense. Need a very severe, acute condition where you can then see response within 3-6 months.” – EU Pharma
Key Themes from Interviews (5)

What doesn’t work:

• Having multiple products as part of a single agreement is a challenge: difficult to track and execute.
• Payers often do not have the systems/data to support agreements in which the manufacturer pays for non-pharmaceutical expenditures.
• Population-based agreements are risky for manufacturers because there are many unknowns around compliance, prescribing, etc. Don’t want to take on risk when you cannot control how the drug is being prescribed/used.
• It is critical that both parties trust the data; if one party tries to poke holes in the data after it is collected, this will affect the ability to have future arrangements

“Setting up individual agreements with all these individual players, and without the benefit of large populations, economics of scale, or large datasets, it is very difficult to enact a financial agreement that makes sense without a straightforward rebate. Or if you try to get into the more complicated clinical outcomes-based agreements, payers just aren’t sophisticated enough at this point to have the kind of databases and track and follow patients with enough time to be able to make those agreements reasonable. It’s a combination of the fragmentation of the market but it’s also a very fluid market as well.” — US Pharma

Key Themes from Interviews (6)

Potential in the U.S.

• There are opportunities for RSAs in the U.S.
• The ACO setting could be appealing for risk-sharing. But maybe timing is not right for ACOs; it is too early as they are still being established.
• Medicaid best price is a limiting factor.
• In the U.S., the decentralized system poses a challenge: requires individual agreements with many payers. Agreements may be most likely with large, national payers and ACOs.

“They could evolve in an interesting way. If in fact systems of care and payment reform change, if the ACO concept catches on, if there are more and more integrated delivery networks, risk-bearing entities could change the landscape and make risk-sharing a much more appealing proposition, particularly if we are able to get past some of the constraints from both the compliance side of things as well as the best price issues.” — US Pharma
Summary: U.S. Perspective

• There is continued and even growing interest on the part of both manufacturers and payers.
• Yet, the number of new agreements is still small—mostly exceptional situations.
• There is a lot of talk, but improved data systems and changed incentives (via health reform and ACOs) may generate more action.

An EU Perspective on U.S. Risk-Sharing Agreements

Adrian Towse

19th Annual Meeting of the International Society for Pharmacoeconomics and Outcomes Research
Montreal, Canada
When is a PBRSA worthwhile?

- a payer has four major options:
  - (i) Adopt
  - (ii) Refuse to adopt
  - (iii) Mandate a lower price
  - (iv) Enter into a PBRSA that either
    - (a) manages utilisation/outcome at the patient level
    - (b) is a form of CED where evidence is collected across patients for review.
Key Dimensions of Taxonomies

<table>
<thead>
<tr>
<th>Patient-Level</th>
<th>Non-Outcome-Based</th>
<th>Outcome-Based</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Utilization capitations</td>
<td>Price linked to per patient outcome</td>
</tr>
<tr>
<td></td>
<td>Discounted treatment initiation</td>
<td>Conditional treatment continuation</td>
</tr>
<tr>
<td></td>
<td>Fixed cost per patient</td>
<td>Money-back guarantee</td>
</tr>
<tr>
<td>Population-Level</td>
<td>Market share</td>
<td>Only with research (coverage with evidence development) using observational study or RCT</td>
</tr>
<tr>
<td></td>
<td>Price share</td>
<td>Only in research (patients only get access if they agree to participate in a study)</td>
</tr>
<tr>
<td></td>
<td>Expenditure/budget cap</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Price change/discount</td>
<td></td>
</tr>
</tbody>
</table>
Example: 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
**Votrient (pazopanib) for Renal Cell Carcinoma in UK**

- **12.5% discount on Votrient’s list price**
  - Price parity with Sutent (a monthly cost of just under GBP2,000 (US$3,085) per patient).

- Future financial rebate if Votrient proves inferior to Sutent with regards to its efficacy, in ongoing head-to-head trials.

- Exact scale of the potential rebate not disclosed

- The results of the COMPARZ study reported in October 2012 and showed non-inferiority in PFS
Database Review: UK

- The National Institute for Health and Care Excellence (NICE) employs a variety of methods to manage uncertainty and financial risks for new interventions.
- These include ‘patient access arrangements’, which they define as agreements made between the National Health Service (NHS) with input from NICE and the pharmaceutical company in order to improve the cost-effectiveness of a drug and enable patients to receive access to cost-effective, innovative medicines.
- We identified 29 arrangements between the years 2000 and 2011 with oncology arrangements making up more than half of all arrangements. Among these, 10 had a CED component, 13 had a financial utilization (FU) component, 9 had a PLR component, and 1 had a CTC component.

UK Patient Access Schemes

<table>
<thead>
<tr>
<th>TA Ref</th>
<th>Treatment</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>TA185</td>
<td>Trabectedin (Yondelis)</td>
<td>Dose cap</td>
</tr>
<tr>
<td>TA155</td>
<td>Ranibizumab (Lucentis)</td>
<td>Simple discount</td>
</tr>
<tr>
<td>TA171</td>
<td>Lenalidomide (Revlimid)</td>
<td>Dose cap</td>
</tr>
<tr>
<td>TA162</td>
<td>Erlotinib (Tarceva)</td>
<td>Simple discount</td>
</tr>
<tr>
<td>TA129</td>
<td>Bortezomib (Velcade)</td>
<td>Response scheme</td>
</tr>
<tr>
<td>TA180</td>
<td>Ustekinumab (Stelera)</td>
<td>Free stock</td>
</tr>
<tr>
<td>TA179</td>
<td>Sunitinib (Sutent)</td>
<td>Free stock</td>
</tr>
<tr>
<td>TA176</td>
<td>Cetuximab (Erbitux)</td>
<td>Rebate</td>
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<tr>
<td>TA169</td>
<td>Sunitinib (Sutent)</td>
<td>Free stock</td>
</tr>
<tr>
<td>TA186</td>
<td>Certolizumab pegol (Cimzia)</td>
<td>Free initial stock</td>
</tr>
<tr>
<td>TA192</td>
<td>Gefitinib (Iressa)</td>
<td>Single fixed price</td>
</tr>
<tr>
<td>TA215</td>
<td>Pazopanib (Votrient)</td>
<td>Discount+ poss rebate</td>
</tr>
<tr>
<td>TA218</td>
<td>Azacitidine (Vidaza)</td>
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</tr>
<tr>
<td>TA220</td>
<td>Golimumab (Simponi)</td>
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<td>Romiplostim (Nplate)</td>
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</tr>
<tr>
<td>TA225</td>
<td>Golimumab (Simponi)</td>
<td>Free stock</td>
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<tr>
<td>TA233</td>
<td>Golimumab (Simponi)</td>
<td>Free stock</td>
</tr>
<tr>
<td>TA235</td>
<td>Mifamurtide (Mepact)</td>
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<td>TA238</td>
<td>Tocilizumab (RoActemra)</td>
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<td>TA241</td>
<td>Nilotinib (Tasigna)</td>
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<td>TA276</td>
<td>Colistimethate (Colobreathe)</td>
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<td>TA276</td>
<td>Tobramycin (TOBI Podhaler)</td>
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<tr>
<td>TA278</td>
<td>Omalizumab (Xolair)</td>
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<tr>
<td>TA280</td>
<td>Abatacept (Orencia)</td>
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<td>TA282</td>
<td>Pirfenidone (Esbriet)</td>
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<tr>
<td>TA283</td>
<td>Ranibizumab (Lucentis)</td>
<td>Simple Discount</td>
</tr>
<tr>
<td>TA293</td>
<td>Eltrombopag (Revolade)</td>
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<td>Aflibercept (Eylea)</td>
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<td>Fluocinolone (Iluvien)</td>
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<td>Teriflunomide (Aubagio)</td>
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<tr>
<td>TA305</td>
<td>Aflibercept (Eylea)</td>
<td>Simple Discount</td>
</tr>
<tr>
<td>TA306</td>
<td>Pixantrone (Pixuvri)</td>
<td>Simple Discount</td>
</tr>
</tbody>
</table>

Last 25 Patient Access Schemes have been simple discounts
Database Review: UK—Take-home Messages

- Arrangements can be used to secure early access for new products.
- Arrangements can resolve residual uncertainty about relative effectiveness vs. relevant comparator.
- Arrangements should leverage existing data generating programs when possible. Example: Votrient
- Arrangements can be used to estimate key value metrics in real world settings—ensuring good value and informing future negotiations.
- Data generated during initial arrangements can inform future coverage and reimbursement decisions including simple discounts.
- Administrative burden is a large impediment to long-term viability for PBRSAs.
- CED can be risky for manufacturers in terms of lost time in market and potential negative findings.

Performance-Based Schemes for Oncology Drugs

Source: Paolo Siviero, AIFA
Database Review: Italy

- The major healthcare payer is the National Health Service (Servizio Sanitario Nazionale/SSN), which provides universal coverage for citizens and residents.
- The SSN reimburses pharmaceuticals listed on a national drug formulary managed by the Italian Medicines Agency (AIFA).
- The AIFA assesses the value of interventions based on scientific, clinical, and economic data and negotiates with pharmaceutical manufacturers to establish drug prices and risk-sharing arrangements.
- Identified 40 arrangements spanning the years 2007 and 2012.
  - 21 had a FU component,
  - 25 had a PLR component,
  - 14 had a CTC component.
  - 35 of the 40 arrangements were in the therapeutic area of oncology. A large number of hybrid arrangements, combining PLR, CTC, and FU components.
  - Shift in recent years towards stand-alone PLR or FU arrangements

Database Review: Italy—Take-home Messages

- Common consistent process facilitates adoption of arrangements.
- Arrangements are most likely to target high cost disease areas and expensive drugs.
- Arrangements can be used to gain earlier access—especially relevant in countries with substantial access and lag time issues.
- National arrangements can decrease regional variation in access to drugs.
- Existence of an arrangement mechanism does not ensure that it will be used (provider burden).
- Conditional treatment continuation arrangements are useful when there are few good alternatives for non-responding patients.
Lessons for U.S. Private Sector from European Experience

• U.S. private sector schemes will face many of the same issues at EU public payer schemes: definition of endpoints and study design, negotiation costs, EHR infrastructure, monitoring costs, arrangements for evaluation, etc.
• UK experience is often on confidential price discounts or de facto price discounts, with only a few pay-for-performance (e.g. Velcade) or CED schemes (e.g. Votrient). Scarred by experience of MS Risk-sharing scheme.
• Italy and Sweden have invested in EHRs and, in Italy, have working pay-for-performance type arrangements tracking patients for most new oncology drugs and for other drugs in high areas of uncertainty.
• In Sweden they are used more to assess effectiveness in the patient groups who receive the treatment leading to a review.
• Netherlands hospital schemes seen as a failure – evidence not collected
• Arguably, what we see is experimentation and then either (i) retreat (UK and Netherlands) or (ii) an established pattern of use (Italy and Sweden).

Risk-sharing arrangements in the US: barriers and developments

Peter J. Neumann, ScD
Director, CEVR, Tufts Medical Center
Health Affairs

By Peter J. Neumann, James D. Chambers, Françoise Simon, and Lisa M. Meckley

Risk-Sharing Arrangements That Link Payment for Drugs To Health Outcomes Are Proving Hard To Implement

ABSTRACT Risk-sharing agreements, under which payers and pharmaceutical manufacturers agree to link payment for drugs to health outcomes achieved, rather than the volume of products used, offer an appealing payment model for pharmaceuticals. Although such agreements have been widely touted, the experience to date mainly demonstrates how hard they are to implement. Barriers include high implementation costs, measurement challenges, and the absence of a suitable data infrastructure. Risk-sharing arrangements could gain traction in the United States as payers and product manufacturers acquire experience with the concept and as measurement techniques and information systems improve. For the foreseeable future, they are likely to remain the exception as drug companies pursue payment models unconnected to data collection or performance assessment.

Insights from the update

• Barriers still exist
• US environment remains challenging
• New landscape (ACOs) present opportunities but major change unlikely
Study Results: Potential Barriers (1)

A. Significant additional effort required to establish/execute RSAs (e.g., compared to traditional rebates/discounts)

B. Challenges in identifying/defining meaningful outcomes

C. Challenges in measuring relevant real-world outcomes

D. Data infrastructure inadequate for measuring/monitoring relevant outcomes

E. Difficulty in reaching contractual agreement (e.g., on the selection of outcomes, patients, data collection methods)

F. Implications for Medicaid best price

Study Results: Potential Barriers (2)

G. Payer concerns about adverse patient selection

H. Fragmented multpayer insurance market with and significant patient switching among plans

I. Challenges in assessing risk upfront due to uncertainties in real-world performance

J. Lack of control over how product will be used

K. Significant resources and/or costs associated with ongoing adjudication
Impact of ACOs

• Potential for ACOs to engage in RSAs, but down the road.
• Will depend on:
  (1) whether they take Rx risk vs. medical risk;
  (2) financial relationship between payer and ACO.
    – Will value get passed back to ACO?
    – Will ACO know contract terms between pharma and payers?
      (Manufacturers won’t know payment relationship between payer and ACO.)
    – Will ACO single out individual product or focus on class or disease
Risk-Sharing Arrangements?

“The idea of the future... and always will be?”

Thanks! Questions?

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• Adrian Towse (atowse@ohe.org)
• Peter Neumann (pneumann@tuftsmedicalcenter.org)
Discussion

Comments and Questions?