ASSESSING THE EVIDENCE FOR BETTER PATIENT CARE:
SYNTHESIZING THE BODY OF EVIDENCE – A TOOL FOR
FORMULARY DECISION MAKING

Symposium: Sunday, May 19th

ISPOR 18th International Meeting, New Orleans LA

Agenda

• Environmental Context
• Collaborative Background
  – Process
  – Tool and Deliverables
• Next Steps
• Implications
• Feedback
Increasing Information and Funding For CER

Interest

Availability and Quality of Data

Funding
Payers Are Expecting Greater Use Of New Information

Current Use of HEOR in Contracting

- Only Exceptionally: 29%
- Yes, Increasingly: 33%
- No: 38%

Expected Future Use

- To a Limited Degree: 40%
- Probably: 32%
- No: 18%
- Certainly: 10%


Payer Approach Evidence in Varying Ways

- Types and sources of evidence considered differ
- Few organizations grade evidence for rigor and quality

Leung MY. J Manag Care Pharm. 2012.
Agenda

• Environmental Context
• **Collaborative Background**
  – Process
  – Tool and Deliverables
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Environmental Context

Staff Resources
• Consolidation
• ACA Requirements

Increased Presence of Real World Data
• Growing Number of Studies
• Evolution in Research Techniques
• Increased Availability of High Quality Observational Data
AMCP-ISPOR-NPC CER Collaborative

- **Objective:** Enhancing usefulness of CER to improve patient health outcomes:
  - Guidance and practical tools to help P&T members critically appraise CER (primarily observational) studies to inform decision making
  - Guidance to industry on what kinds of evidence payers want to see and how evidence will be considered in decision making
  - Provide greater uniformity and transparency in the use and evaluation of CER for coverage and decision making

Evidence Synthesis as One Part of the Critical Appraisal and Coverage Determination Process

- What evidence exists?
- Is an individual piece of evidence good?
- What does the evidence say?
- What is the decision?
Part 1: Evaluate Quality of Individual Studies
- Prospective
- Retrospective
- Modeling
- Indirect Methods

Part 2: Synthesizing the Evidence Across Multiple Study Types
- RCT, Observational studies

Part 3: Assessing the Evidence by Decision Makers: A Toolkit
- Tools
- Educational Materials and Training

Task Force Participants

AMCP
Lisa Cashman, PharmD
Manager, Drug Information
MedImpact Healthcare Systems, Inc.
Helen Sherman, PharmD
Vice President,
Solid Benefit Guidance
Jeff White, PharmD MS
WellPoint NextRx
Bernadette Eichelberger, PharmD
Director of Pharmacy Affairs
AMCP

NPC
Rahul Ganguly MPharm PhD,
Sr. Director, Global Health Outcomes, GlaxoSmithKline
Brian Sweet, BS Pharm, MBA,
Executive Director, Healthcare Alliances, AstraZeneca
Dick Willke, PhD, Sr. Director,
Market Access, Primary Care Business Unit, Pfizer
Jennifer Graff, PharmD
Director CER
National Pharmaceutical Council
Robert Dubois, MD, PhD
Chief Science Officer
National Pharmaceutical Council

ISPOR
Jon Clouse, RPh, MS
Executive Vice President
Economic and Outcomes Research, OptumInsights
Bryan Luce PhD
Chief Science Officer, PCORI
Randa Eldessouki, MBBCH, MSc, MD
Director, Scientific & Health Policy Initiatives, ISPOR
Process

Systematic Lit Review
- Critique
  - Task Force
  - 2 MCO Rx reviewers
- AMCP Focus Group
  - October 21 2011 meeting
- Decision Point
  - Accept existing framework
  - Initiate a de novo process
  - Modify an existing framework

Pilot Testing & Evaluation

Evidence Synthesis Frameworks Reviewed
- AAOS (Am Academy of Orthopaedic Surgeons)
- AAP (Am Academy of Pediatrics)
- ACCF/AHA (Am College of Cardiology Foundation/Am Heart Assoc)
- ACP (Am College of Physicians)
- AHRQ (Agency for Healthcare Research & Quality)
- Bandolier
- CEBM (Oxford Centre for Evidence-based Medicine)
- DELFINI
- FORM (Australian)
- GRADE (Grades of Recommendation, Assessment, Development, & Evaluation)
- ICER (Integrated Comparative Evidence Rating Matrix)
- IDSA-USPHS (Infectious Diseases)
- LEGEND (Let Evidence Guide Every New Decision)
- NCCN (National Comprehensive Cancer Networks)
- NSF-LTC (UK National Service Framework for Long-term Conditions)
- SIGN (Scottish Intercollegiate Guidelines Network)
- SORT (Strength of Recommendation Taxonomy)
- SURE (UK Support Unit for Research Evidence)
- USPSTF (US Preventive Services Task Force)
Factors Considered in Selecting a Synthesis Framework

- Objectivity
- Transparency
- Reliability/validity
- Ease of application
- Experience in P&T decision making

Health Evidence for Decision Making: Synthesizing A Body of Evidence

ICER Evidence Rating Matrix

<table>
<thead>
<tr>
<th>Certainty of Evidence</th>
<th>High Certainty</th>
<th>Moderate Certainty</th>
<th>Low Certainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>Comparable</td>
<td>Small</td>
<td>Substantial</td>
</tr>
<tr>
<td>Net Benefit</td>
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Comparative Net Health Benefit
Frame the Decision Making Question

- **P** = Population
- **I** = Intervention(s) of interest
- **C** = Comparator intervention(s)
  - May be active or standard of care
- **O** = Key Outcomes

Optional:
- **T** = Time Horizon
- **S** = Setting of Interest

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Step 1: The Magnitude of Comparative Net Health Benefit

- Evaluate the evidence on benefits for both drugs
- Evaluate the evidence on risks for both drugs
- Weigh the comparative balance of evidence on both benefits and harms
- Select a “point estimate” for the best estimate of comparative net health benefit in one of the following categories:
  - Negative (-)
  - Comparable (=)
  - Small (+)
  - Substantial (++)
Step 2: The Level of Certainty

- **Key domains**
  - **Amount** of evidence
  - **Potential bias** due to the design and conduct of included studies
  - **Directness**
    - Outcomes (e.g., surrogate outcomes)
    - Comparisons (e.g., head-to-head studies vs. indirect comparisons)
  - **Duration** of studies given the time needed to capture important benefits and harms
  - **Precision** of results
  - **Consistency** of results
  - **Applicability** of results (e.g., generalizability to the “real world”)

### Guidelines On Certainty

<table>
<thead>
<tr>
<th>High</th>
<th>Moderate</th>
<th>Low</th>
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<tbody>
<tr>
<td>Mostly high-quality, larger studies</td>
<td>Mix of study quality</td>
<td>Mostly poor-quality, smaller studies</td>
</tr>
<tr>
<td>Conducted in representative patient populations</td>
<td>Cannot estimate net benefit with good precision, due to:</td>
<td>Evidence insufficient to estimate net benefit at all</td>
</tr>
<tr>
<td>Direct comparisons available</td>
<td>o Weak study design or conduct</td>
<td>Flaws in evidence base make it impossible to make comparison</td>
</tr>
<tr>
<td>Address important outcomes or validated surrogate outcomes</td>
<td>o Inconsistent findings</td>
<td>High likelihood that new evidence would substantially change</td>
</tr>
<tr>
<td>Long-term data on benefits/risks available</td>
<td>o Indirect evidence only</td>
<td>conclusions regarding net benefit</td>
</tr>
<tr>
<td>Consistent results</td>
<td>o Limited applicability of results</td>
<td></td>
</tr>
<tr>
<td>Future studies unlikely to change</td>
<td>o Evidence of reporting bias</td>
<td></td>
</tr>
<tr>
<td></td>
<td>o Future studies may shift net benefit</td>
<td></td>
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Step 2: The Level of Certainty

- Level of certainty is related to the strength of the entire body of evidence:
  - **High:**
    - Confidence interval limited to 1 category of comparative net benefit
  - **Moderate:**
    - Confidence interval extends for 2-3 categories on the matrix
  - **Low:**
    - Confidence interval extends across all 4 categories on the matrix
    - Evidence is inadequate to frame a reasonable estimate of comparative net benefit

Step 1 + Step 2: The Joint Rating

- **High certainty** - allows a precise rating category
  - A = superior
  - B = incremental
  - C = comparable
  - D = inferior

- **Moderate certainty** - reasonable chance that the true net benefit may change
  - B+ = Incremental or better
  - C+ = Comparable or Better
  - P/I = “promising but inconclusive”

- **Low certainty in any point estimate**
  - I = insufficient
Health Evidence for Decision Making: Synthesizing A Body of Evidence

ICER Evidence Rating Matrix

Certainty of Evidence
- High Certainty
- Moderate Certainty
- Low Certainty

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Comparative Net Health Benefit

An Example
Overview of Formulary Evaluation

Outcomes of interest include: Normal Sinus Rhythm Stroke UV mortality non-UV Morality

Name of interest include:
- Mortality
- ICH
- Non-ICH bleeding
- Side effects

Other outcomes of interest:
- Quality of life
- Potential drug interactions

Step 1: Magnitude of Comparative Net Effects

A. Summary of Key Differences in Clinical Benefits

Limited head-to-head data exist with which to judge the differential impact on all-cause mortality for abelimumab vs. revlimid. In the single head-to-head ICT that has been conducted, the ICT trial, all-cause mortality was 3.6% for abelimumab vs. 1.4% for revlimid. On an as-treated basis, a difference that was not statistically significant (Castro, 2010). Revlimid was found to have a significantly lower rate of cardiovascular death vs. placebo in the ASPC, placebo-controlled ALCOR trial (1.4% vs. 2.1%)

B. Summary of Key Differences in Risk: Adverse Effects

Pulmonary Toxicity
As measured in ICTs and comparative studies, the rate of pulmonary toxicity with abelimumab is relatively low, ranging from 0 - 1.4% on an as-treated basis. Long-term follow-up studies and other evidence-based reviews have reported a much wider range of pulmonary toxicity (1.8-17%). However, many of the higher estimates were for abelimumab at higher doses levels (i.e., >500 mg).

C. Summary of Key Differences in Other Potential Adverse Events/Discontinuations

Presence is limited regarding abelimumab’s impact on hospitalization rates when compared to placebo, with data available from a single ICT in our sample (Buchdunger, 2009). The comparison to placebo is highly problematic, however, given that the hospitalization rate is used as a primary outcome in the ASPC, placebo-controlled ALCOR trial as well as in most non-comparative studies (Buchdunger, 2009). Funding supported a lower rate of

Based on above information, what is your point estimate of comparative net health benefits:

- Negative: the drug produces a net health benefit inferior to that of comparator
- Comparative: the drug produces a net health benefit comparable to that of comparator
- Individual: the drug produces a small net health benefit relative to comparator
- Positive: the drug produces a moderate to significant benefit to comparator

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AMCP/ISOR/NPC CER-CI Part 2: ISPOR Forum
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Training and Educational Materials

- Webpage
- CPE and Slides for real-time training
- Training Events (resources)
- Communications
Future Collaborative Opportunities

Other Users

Drive Deeper Use

Education

Enhance Tools

Research

Future

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Rahul Ganguly, PharmD PhD
Senior Director,
Global Health Outcomes
GlaxoSmithKline

Pharmaceutical Perspective

• Overall view
• How does it help the industry?
• My experience from the task force?
SYNTHESIZING THE BODY OF EVIDENCE – A TOOL FOR FORMULARY DECISION MAKING

Helen Sherman, PharmD
Co-Chair, CER-Collaborative
Vice President, Solid Benefit Guidance

Decision Maker Perspective

• Overall view
• How does it help decision-makers?
• My experience from the task force?
Want to Learn More?

Join the ISPOR Plenary Session

“Assessing the Evidence for the Health Care Decision Maker”
Wednesday 9:45am-11:00am