

# ***Comparative Effectiveness Research: Impact on Pharmaceutical Pricing and Marketing***



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# Structural Changes in Pharmaceutical Industry Stimulating Focus on Comparative Effectiveness Research

- Structural changes in the pharmaceutical industry environment enhance focus on cost-containment mechanisms
- Changes include:
  - **Demographic changes, increasing demand for pharmaceutical products**
    - Expansion of healthcare insurance coverage to approximately 32 million people by the healthcare reform law (Patient Protection and Affordable Care Act)
    - Demographic changes (shift of over 70 million people in baby-boom generation to over 65 beginning in 2011)
  - **Integration of healthcare insurers with providers**
- Resulting pressure from both governmental and private payors to address increased demand through access and/or payment restrictions

# Potential Changes by Healthcare Reform Law Affecting Demand Levels and Prices/Payments

- Stimulating comparative effectiveness research (by both government and private payors)
- Independent Payment Advisory Board (IPAB) activities
- Patient-Centered Outcomes Research Institute (PCORI) activities
- Use of quality of care/service guidelines by healthcare providers
- Use of healthcare information technology to manage/reduce demand
- Use of provider/physician practices/insurer combined entities to manage/reduce demand, e.g., accountable care organizations (ACOs)
- Stimulating use of pharmacoeconomics and personalized medicine
- Creation of biosimilars regulatory approval pathway

# Healthcare Reform Law and Comparative Effectiveness Research

- Healthcare reform law contains provisions supporting the development of comparative effectiveness research (CER) concerning healthcare products and services
- Section 6301 establishes the Patient-Centered Outcomes Research Institute (PCORI) to assist in conducting CER and disseminating research findings
  - PCORI is to identify national priorities, establish a methodology committee, and establish a research project agenda
- PCORI is required to ensure that CER “findings not be construed as mandates for practice guidelines, coverage recommendations, payment, or policy recommendations”
  - Private payers can, however, use such findings as a basis for their product or service approval or reimbursement decisions
  - Head of PCORI has stated PCORI will not do CER, but noted “cost analysis” is undefined, and patients will decide whether PCORI will fund research regarding costs and healthcare outcomes ([Inside CMS](#), Sept. 29, 2011)

# Healthcare Reform Law and Comparative Effectiveness Research

- Healthcare reform law allows CMS to use CER results to make a determination concerning Medicare coverage if such use is (1) through an iterative and transparent process, and (2) a determination to deny coverage is not based solely on CER
  - Agency for Healthcare Research and Quality proposed use of “academic detailing” to disseminate CER to healthcare providers ([Pink Sheet](#), April 26, 2010)
  - Total Therapeutic Management awarded \$11.7 million contract in Sept. 2010 to undertake academic detailing on cost effectiveness research studies ([Pink Sheet](#), June 27, 2011)
  - The American Medical Association remains concerned that PCORI will apply CER using cost analysis, and opposed such activities in its comments to PCORI on definition of outcomes research. ([Pink Sheet](#), Sept. 5, 2011). The National Pharmaceutical Council raised similar concerns to PCORI ([Inside CMS](#), Sept. 15, 2011)
  - By contrast, the American Hospital Association has proposed using CER, including cost analysis, to improve healthcare quality and efficiency, in its presentation to the Congressional deficit super-committee ([Inside CMS](#), Nov. 10, 2011)

# Potential Effects of CER on Biopharma Pricing and Reimbursement

- Significant practical limitations on use of CER including absence of accepted protocols, lack of historical CER studies for comparison, and controversy as to interpretation of results
  - Comparative effectiveness data was available for only about half of new drugs approved by FDA over the past decade (J. of Am. Med. Ass'n, May 4, 2011)
  - Raises concerns regarding utility of CER for pricing/reimbursement decisions
- Potential for controversy – e.g., rejection of 2009 recommendations by U.S. Preventive Services Task Force to end routine mammograms for women in their forties
- Private payors moving to apply CER regardless of status of government activity
  - WellPoint released standardized CER guidelines on May 19, 2010 for use in evaluating drug coverage. (Pharmaceutical Law & Industry Report, May 25, 2010)

# Potential Effects on CER on Biopharma Pricing and Reimbursement

- Potential for significant impact of CER on drugs/biologics access and reimbursement
  - Note study of Australian drug market by Tufts University Center for the Study of Drug Development, concluding that “comparative effectiveness research severely restricts access to drugs not deemed cost-effective” (Life Sciences Law and Industry Report, July 16, 2010)
- Note potential effects on product purchasing of first comparative effectiveness trial of two pioneer drugs by National Institutes of Health
  - Comparative NIH trial of two Genentech drugs (Lucentis - \$2,000/dose and Avastin - \$40/dose) -- results showed both equally effective at treating an eye disease (Pink Sheet, May 9, 2011)
  - Office of Inspector General of HHS subsequently concluded Medicare Part B could have saved \$1.1 billion by substituting Avastin for Lucentis (OIG Report, Sept. 7, 2011)

# CER – Monitor Potential Applications

- Monitor potential for parallel reviews by FDA and CMS that may include consideration of CER
  - Request for comments on proposed pilot program by FDA and CMS to conduct overlapping FDA premarket reviews and CMS national coverage determinations for certain innovative products when sponsors agree. See 75 Fed. Reg. 57045 (Sept. 17, 2010)
  - The Agencies suggest, in their Notice, that the proposed parallel review process “could also create incentives for venture capitalists and companies to increase their investment in innovative products by reducing the time to return on investment for those products eligible for parallel review”
- Note FDA intends to begin a pilot clinical trial data depository for CER in 2012, to disseminate CER data (Gray Sheet, May 30, 2011)

# CER – Monitor Potential Applications

- Monitor assessments by the U.K.’s National Institute for Healthcare and Clinical Excellence and application of CER
  - e.g., NICE decision not to recommend use of Takeda’s bone cancer drug Mepact, based on its cost-effectiveness criteria, even though it stated that the drug “might represent a potentially valuable new therapy.” (Scrip, Oct. 15, 2010).
  - e.g., NICE rejection of Bristol-Myers Squibb’s Yervoy melanoma drug as not cost-effective. (Scrip, Oct. 21, 2011)
- Monitor potential uses of CER in determinations by other governmental/scientific entities affecting product use
  - e.g., decision by Centers for Disease Control’s Advisory Committee on Immunization Practices to limit recommendation for vaccinating adults against hepatitis B to those under age 60 based on cost effectiveness considerations. (Pink Sheet, October 31, 2011)

# Potential Effects of CER on Biopharma Pricing and Reimbursement

- Independent Payment Advisory Board (IPAB)
  - Significant new 15-member IPAB that will present Congress with proposals to reduce costs and improve quality for entire Medicare program
  - May address both products and services
  - IPAB cannot make proposals to ration care, raise taxes or Part B premiums, or change Medicare benefit, eligibility, or cost-sharing standards
- Use by managed care payors to affect drug selection
  - United Healthcare has suggested that CER will foster broader use of co-pays that discourage use of lower-cost drugs. ([Pink Sheet](#), October 25, 2010)
  - Use by payors for formulary selection determinations

# Incorporation of CER in Lifecycle Management

- CER raises several issues regarding product lifecycle management
  - Incorporate outcomes research into clinical trials to provide bases for marketing and promotion of product to government and managed care payors
    - Potential use of discussions with payors concerning CER at clinical development stage
  - Potential for reduction in return on product investment by use of CER
    - Increased costs for clinical CER trials
    - Adverse effects on R&D budget for potential other new products
  - Development of non-clinical trials-based CER to support payment and reimbursement
  - Partnerships with drug companies and managed care entities to support coverage/payment decisions
    - e.g., Pfizer/Medco and AstraZeneca/WellPoint data development partnerships ([Pink Sheet](#), November 14, 2011)

# Incorporation of CER in Lifecycle Management

- Development of integrated market access cross-functional operations by drug companies to effectively generate, manage, and apply CER from drug development stage, through reimbursement and market access negotiations, to marketing and promotion
- Potential focus on development of personalized medicines to enhance likelihood of payor acceptance of proposed pricing
  - e.g., AstraZeneca focus on personalized medicines for cooperation with managed care payors ([Scrip](#), October 21, 2011)
- Potential use of CER in later stages of product lifecycle to support new indications and to defend product from competing products or therapies

# Incorporation of CER into Product Marketing and Promotion

- Incorporation of CER into drug marketing and promotion raises difficult issues concerning FDA regulation
  - CER-based claims (pharmacoeconomics claims) are regulated under FDA's general labeling and advertising provisions
  - Historically, FDA has required two "adequate and well-controlled studies," ordinarily head-to-head trials, to support comparative effectiveness claims
  - Federal Trade Commission (FTC) has similarly focused on scientific evidence supporting comparative drug claims
  - Pharmacoeconomics claims unlikely to be solely clinical trials-based
- In response to likely increased use of pharmacoeconomics claims based on CER, FDA recently requested public comment on a proposed study of comparative advertising of prescription drugs. See 76 Fed. Reg. 36663 (July 1, 2011)
- Need to incorporate claims based on CER in marketing and promotion, and on pricing, reimbursement, and market access to payors, in the absence of clear guidelines
- Potential litigation challenges based on CER (e.g., Utah's action against GlaxoSmithKline in 2010 for allegedly marketing Avandia as a significant advance where several CER studies suggested no superiority over competing products)
- Issues relating to potential to include CER data in drug package insert/labeling

# Consequences of CER for Biopharma Growth and Investment

- Cost effectiveness research presents significant challenges for biopharma product selection, investment, and M&A
  - Potential for restrictions on Medicare or Medicaid coverage and reimbursement from comparative effectiveness research
  - Potential for adoption of similar or independent restrictions on coverage and reimbursement by private payors
  - Consequent uncertainty regarding product and company valuation for investment, licensing, and M&A
- Need to closely monitor and quickly adapt to regulatory and market changes concerning use of CER, and payment and market access expectations or performance, concerning drugs of interest in making investment and acquisition decisions

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