Real World Evidence and Implications to Value-based Contracting

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Panel Introductions

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Real World Evidence: Defined

Terminology	• Real World Evidence (RWE)/Real World Data (RWD) • Health Economics Outcomes Research (HEOR/HECOR) • Healthcare Economic Information (HCEI) • Comparative Effectiveness
Sources of Data	• Data generated by routine medical care, e.g., administrative claims, electronic medical records, pharmacy data, laboratory data, etc. • Information and communication technologies (ICTs) that enable continuous monitoring of the patient's physiology and experience • Other user-generated data (e.g. social media, survey reports)

Healthcare Economic Information (HCEI)

Any analysis that identifies, measures, or compares the economic consequences, including the costs of the represented health outcomes, of the use of a drug to the use of another drug, to another health care intervention, or to no intervention.

Definition from FDAMA 114

Example Working Definition

Real World Evidence

Information derived from real life experience for disease states, drugs, or therapies

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A Note on the FDAMA 114 Definition…

"This provision is not intended to provide a path for promoting new off-label indications or claiming clinical advantages of one drug over another when these claims do not satisfy FDA's evidentiary standards for the claims being made."

Robert Temple, MD
Deputy Center Director for Clinical Science, FDA CDER
February 9, 2012

Real World Evidence: The Opportunity

- **Unprecedented Data Creation** – global information footprint is doubling every two years
- **Unprecedented Data Analysis** – novel analytics approaches and technologies enable processing
- Real world evidence and novel analytics **together underpin the shift to a value-based healthcare system** focused on health outcomes, quality, and cost-effectiveness
  - Novel data assets and technologies enhance R&D, enabling better characterization of disease, unmet needs, and target populations, enhanced product development, and improved trial design and performance
  - Evidence Based Medicine (EBM) is moving from the population (mean/median) to the individual level, increasing precision in identifying optimal care
  - Improved measurement of effectiveness and value in healthcare decisions

Real World Evidence: The Challenge

- **The bar has been raised**… New and higher hurdles exist to demonstrate economic value of new product candidates; RWE has been cited as the major factor in recent decisions by retailers and PBMs related to:
  - Reimbursement status and level
  - Product utilization decisions
- **…and not just by commercial payers:** While CMS does not explicitly consider cost in coverage decisions, cost has been cited as an impetus for why Medicare will open a national coverage analysis (e.g. Provenge, a treatment for advanced prostate cancer, two months post approval – with a price tag of $93k)
- **Compliance risks abound**: safe harbors exist for communication of data (FDAMA 114), but guidance lags (19 years and counting…)
  - Anti-Kickback concerns
  - Government Pricing concerns

It all comes together...

…in the contract.

Examples of Value-Based Arrangements

- Performance-Based Pricing
  - Upside Model: up-front price with manufacturer sharing in any subsequent savings realized
  - Downside Model: up-front price with manufacturer sharing in any subsequent losses realized
  - Cohort Performance: price tied to patient population performance compared to control group
  - Money-Back Guarantee: up-front price with refund where product not/less than effective
  - Try-Before-You-Buy: free product up-front with price charged only where product effective
- Course of Therapy Pricing
  - Flat Pricing: single price per course of therapy regardless of amount of product needed
  - Pricing Cap: per unit price up to certain volume with remainder free where additional product needed
- Indication-Based Pricing
  - Same product has different pricing depending on indication for which it is used
- Annuity Pricing
  - Product price/cost shared across payers that cover patient across his/her lifetime

Areas of Uncertainty for Manufacturers

- Misalignment between goals of value-based arrangements (e.g., to pay for performance) and the underlying regulatory environment creates significant uncertainty for manufacturers
  - Government price reporting
  - Anti-kickback statute
  - Medicare Part B and Part D requirements
  - Patient privacy
  - Off-label promotion/unsubstantiated claims
- Value-based arrangements raise practical concerns (e.g., data analytics, contracting complexity, financial accounting)

Areas of Uncertainty for Manufacturers (cont'd)

CMS also completely fails to acknowledge or address various regulatory requirements with which manufacturers must comply that stand in tension with the Model – many of which CMS and other agencies are actively working to enforce. CMS's failure to recognize – let alone, attempt to resolve, the following regulatory conflicts is additional evidence that this Model has not been well-conceived and should be fully withdrawn.

Public Comment on the Part B Demo

In order to facilitate the use of value-based contracting in the private sector, CMS and other agencies in the Department of Health and Human Services (HHS) must address the significant regulatory hurdles that currently impede use of this tool. These include legal impediments such as best price reporting requirements, privacy constraints on payer/provider information-sharing with manufacturers, FDA restrictions on the promotion of off-label drug usage, and Anti-Kickback Statute (AKS) requirements.

Another critical area that CMS does not discuss in the Proposed Rule relates to FDA's limitations on promotion of off-label indications by manufacturers—which is another key regulatory consideration, and one that CMS should work with FDA to address.

Federal Food, Drug, and Cosmetic Act

- The Federal Food, Drug, and Cosmetic Act (FDCA) and FDA's implementing regulations prohibit "misbranding" a drug.
- Misbranding can occur in many ways:
  - *Example*: Claims that broaden the approved indication or create new uses of the drug
  - *Example*: Encouraging use in unapproved patient populations (e.g., pediatrics)
  - *Example*: Discussing use of multiple drugs that are not approved for use together
  - *Example:* Comparative claims not supported by substantial evidence
- Generally, the substantial evidence standard applies to efficacy or safety claims
- The FDCA allows comparative health care economic claims to be presented to a formulary committee based on competent and reliable scientific evidence
  - Must "directly relate" to an approved indication
  - FDA has never issued regulations or guidance to clarify key aspects of this statutory provision
- Real-world evidence is, by definition, not substantial evidence

Tension with Value-Based Contracting

- Because off-label prescribing is permissible, **any arrangement that measures performance based on actual use, which can include off-label uses**—whether as a baseline for payments or as a metric to assess future payments—carries a risk that it could be viewed as creating inappropriate incentives for that use

  – *Example*: A drug is approved for combination use with a steroid, but steroids are no longer commonly used in the disease state. Does the manufacturer encourage use without a steroid when it enters a risk share agreement in which none of the plan's patients is receiving the steroid?

  – *Example*: A manufacturer sells a drug approved based on a surrogate endpoint, such as LDL-C lowering. Can its contracts with payors measure quality outcomes based on a treatment outcome, e.g., lower cardiovascular morbidity and mortality?

Potential Solution

- FDA has promised to provide guidance on permissible value claims this year
- CMS could encourage FDA to issue guidance sufficient to reassure manufacturers seeking to develop innovative payment models
- After *Amarin*, manufacturers can develop claims that are truthful and non-misleading (e.g., by using disclaimers)
  - It may be possible to describe value-based agreements under such a construct to lessen the risk that the arrangement is viewed as incentivizing inappropriate use
  - But, it is unclear whether entering into a value-based payment arrangement would be considered speech or conduct

Discussion

Scenario #1

For the drug ONCO-WONDER that was approved based on its effect on overall survival, payor proposes a value-based contract based on levels of circulating tumor markers at 3 and 6 months after treatment. There are no data from the pivotal trials of the drug regarding these tumor markers, but 3 published epidemiological studies conducted after the drug was approved have suggested an association between levels of these markers and overall survival. One other epidemiological study showed no association between the levels of these markers and overall survival.

Scenario #2

For the drug INFECTION-STOPPER that was approved for use in patients aged 18-64, payor proposes a value-based contract that would adjust the payment rate based on the number of days a patient remained in the hospital with the infection. The manufacturer's most comprehensive data source on the number of days a patient remained in the hospital while on therapy is claims data from the Medicare Premier database—i.e., in patients 65 and older.

Session Attendee Survey

- How would you rate your knowledge of your company's current pricing arrangements? (H-M-L)
- How would you rate your knowledge of your company's planned/future pricing arrangements? (H-M-L)
- If you rated either as High or Medium, how did you gain this understanding?
- Do you know who you'd go to within your company to learn about these arrangements?
  - If so, how often have you met with this individual(s) in the past 12 months? 24 months?
- Do you currently monitor compliance with the pricing terms and conditions of your existing agreements?

Take Home!

Take-Home: RWE/VBC "Cheat Sheet" #1

Anti-Kickback Considerations

When reviewing a value-based contract, make sure you're asking whether the pricing arrangements may be characterized by any of the following facts & circumstances:

- ✓Potential to interfere with, or skew, clinical decision-making
- ✓Potential to increase costs to the federal healthcare programs (FHCPs) or beneficiaries
  - FHCP "carve-outs" may not be determinative (OIG is concerned with "seeding" the market)
  - The closer costs are to product competitors, the lower the risk of harm to a federal health care program payer
  - Do contract provisions mitigate risk of billing for "free" product
- ✓Potential to be a disguised discount to circumvent GP calculations
- ✓Potential to increase the risk of overutilization or inappropriate utilization
  - The lower the barriers are to clinical "switching" to competitive therapy, the lower the risk of harm is to FHCP payer
- ✓Patient safety or quality of care concerns
- ✓Can payments be properly accounted for by the recipient? (e.g., Medicare Part D TrOOP, DIR reporting)

Take-Home: RWE/VBC "Cheat Sheet" #2

Government Pricing Considerations

- ✓ Can discounts be adequately accounted for in government price calculations?
  - – Are there multiple products and/or services and/or reporting periods involved in offer?
  - – Restatements/smoothing
- ✓ Will the arrangement result in a $0 or "nominal" Medicaid Best Price?
  - – Certain entities (e.g., 340B) can get nominal prices w/o BP/ASP impact
- ✓ Will the arrangement result in an unduly low base date AMP?
- ✓ If applicable, will the discount unduly lower Medicare Average Sales Price (generally used for Part B drug reimbursement to providers)?
- ✓ Will arrangement increase 340B discounts/refunds?
- ✓ Impact of arrangement on FSS Pricing?

GP should analyze proposed contract terms **sooner**, rather than **later**.