

Reckoning With The Growing Impact Of CMS

→ On Biopharmaceutical Product
Development and Life Cycle Management

**2nd Annual FDA Regulatory and
Compliance Symposium, Harvard University**
Morning Track 3 – Where the FDA and CMS Meet
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Matthew B. Van Hook
Engel & Novitt, Washington, D.C.

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Payers v. MDs & Patients

- Culmination of transition from model of MD primacy in prescribing treatment
- Medicare Prescription Drug program underscores CMS as biggest payer
- Every expectation CMS will act as other institutional payers, and that cost pressures will force Congress to defer
- Payers, not patients or prescribers, increasing focus of marketing, and drug development

Payers Eclipse Patients

- *Merck has announced “a new marketing strategy that involves focusing more resources on payers, such as health plans that pay for the majority of drugs, rather than on the doctors who prescribe them.”*
 - Wall Street Journal, April 4, 2006, p. A21, “Merck Taps GE Official Loescher To Lead Human Health Division.”

Merck Will Sell Zocor Below Price of Generics

Move May Spur Bidding War Among Drug Makers to Keep Pace in Nonbranded Market

By **HEATHER WON TESORIERO**

June 22, 2006; Page A2

With [Merck & Co.](#)'s Zocor facing generic competition tomorrow, the drug maker has decided to sell its cholesterol-fighting drug to some major managed-care companies at what is expected to be a lower price than what it will be available for in generic form.

Merck's pricing strategy could set off a bidding war among generics manufacturers, which likely will have to slash their prices to maintain a foothold in the market for simvastatin, the generic name for Zocor.

[WellPoint](#) Inc., of Indianapolis, said it has entered into an arrangement with Merck to sell branded Zocor -- and not competing generic versions -- through its mail-order pharmacy service. "Through mail order, we will exclusively use the Merck Zocor and take a generic co-payment," said Robert Seidman, WellPoint's chief pharmacy officer. Members will pay \$10 for 30 days of the drug, the same as they would pay for a generic drug. Mr. Seidman said the company hasn't yet priced the generic versions of the drug, which will be sold by Teva Pharmaceuticals USA, a unit of [Teva Pharmaceutical Industries](#) Ltd., of Israel, and Dr. Reddy's Laboratories Ltd., an Indian generic-drug maker.

Generic Prices Often Fall Later

Typically, the first few generic drugs are initially priced lower than the branded drug they copy. But prices of generics don't usually plunge until a larger number of generic copies enter the market.

With its pricing strategy, Merck is speeding up that price collapse for the generic copiers of its drug. "The Merck price is very aggressive, and its price could set the ceiling for the entry price for the generics," Mr. Seidman said. "All of the maneuvering that's taking place is speeding the decline in the price of the generics."

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Payer Impact Across Product Lines, Even Innovator/Innovator



June 22, 2006

Big Buyers Push For Steep Price Cuts From Drug Makers

By **SCOTT HENSLEY**

June 22, 2006; Page B1

Earlier this year, the U.S. Department of Veterans Affairs made Levitra its preferred impotence pill, toppling Viagra from the spot it had held for years. The VA decision boiled down to cold cash.

“Competition on prices paid by the biggest customers is now heating up in some categories Remarkably, that rivalry is often hot even in cases where generics are either unavailable or not used widely.”

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Implications of Payer Focus

- Less likelihood of proving medicine in marketplace (Lipitor contrasting model)
- Relative efficacy *and cost* an emerging factor, if not overt standard for NDA/BLA review by FDA
 - Note lurking implications of HHS “One Dept. Policy”
- Growing role of post-approval studies – safety, ***and efficacy***
- Less predictability, for innovators and generics alike, from a growing *CMS/Part D Payer Gauntlet*
 - Heightened stakes for drug development
 - Paradoxically, may dis-incent or stifle innovation

Why Payer/CMS Focus?

- Healthcare spending remains a concern
- Still unresolved – assuring universal & adequate coverage (another national healthcare debate on tap?)
- Jury still out on MMA Rx for seniors . . . and the steps CMS is prepared to take.
- CMS provides Congress with the easiest ‘dials’ to turn re coverage/\$\$

HHS 'One Department' Policy?

- Once touted, now inoperative?
- Fading rumors of CMS involvement in FDA product review & approval
 - Prospect of 'parallel reviews' envisioned by Secretary Thompson (as FDA approves NDAs, as CMS makes coverage decisions) have apparently not yet happened
- But . . . does latest CED guidance clarify or further cloud roles of FDA & CMS?

CMS Role Growing

- CMS role as largest Rx payer a reality, even though MMA structured to avoid raw government monopsony power.
- CMS (and states) will be making decisions about how much to pay, but also:
 - How much to buy of a particular medicine, and
 - Whether to buy at all.

CMS – Formulary Changes for Black Box Warnings

- CMS guidance on allowable formulary changes now contemplates fast track removal of a drug from formularies in the event a “black box” warning is added to labeling (30 days after no hear from CMS; 60 days notice to affected enrollees). April 27, 2006, memorandum of Abby Block, Director, CMS/Center for Beneficiary Choices, re “Formulary Changes During The Plan Year”
- Consistent with the reported “firewall” between FDA & CMS on drug safety issues? Or green light for Part D sponsors to trim coverage?
Michael McCaughan in RPM Report, June 2006 pp.19-22, “Medicare Formulary Rules Add Bite to “Black Box” Warnings”

GAO Examining Part D Plan “Management Techniques”

- Excluding a drug from coverage list
- Charging higher co-pays
- Requiring prior authorization
- Requiring step therapy (switch to cheaper or generic) before filling with ‘preferred’
- Limits on quantity of pills (30 v. 60/90)

Request to GAO in May 12 House Democrats’ letter –
Inside Health Policy June 13, 2006

FDA Role Also Changing

- Historic FDA focus on science (safety & efficacy) increasingly yielding to political pressure on applications/policy issues.
- E.g., is NDA approval standard evolving, to ‘safe, effective, ***and appropriate***’?
 - Andrew von Eschenbach, Acting Commissioner of Food and Drugs, FDLI 4/6/2006
 - ‘Appropriate’ for: individual patient? relative efficacy? cost? administration public policy?

Roche Challenge to Amgen EPO Franchise

- Focus has been on the legal and regulatory aspects of Roche's BLA submitted April 20 for follow-on CERA, and related litigation.
- But CMS role could drive market impact:
“ . . . the U.S. government, as a purchaser for Medicare, could be a natural ally for Roche. To get that type of support, Roche may have to indicate a willingness to use lower pricing in the EPO field.”
 - “A CERA-ous Challenge to Amgen's EPO Franchise?”, The RPM Report, June 2006, p. 45, Cole Werble (citing views of Elise Wang/Citibank)

Factors Driving CMS

1. Different statutory mission
2. Recurring CMS focus on notions of comparative clinical effectiveness and use of outcomes data, re coverage decisions*
3. CMS Coverage with Evidence Determination (CED) policy

* See *Comparable Alternatives, Cost Effectiveness, and Clinical Trial Data: [MMA §1013] Changes The Reimbursement Landscape*, FDLI Update, Sep/Oct 2004, pp. 34-37, by Michael Gaba, Holland & Knight

1. Contrasting CMS Mission

- **FDA:**
 - determines if product is safe and effective as a condition of approval.
 - Must receive FDA clearance for at least one indication to be eligible for Medicare coverage.
 - **CMS:**
 - determines if the product is reasonable and necessary as a condition of coverage.
 - FDA clearance alone does not automatically entitle the product to coverage.
- From CMS website “What is the Difference between FDA and CMS Review?”
 - Social Security Act: “. . . **no payment may be made** under Part A or part B of this subchapter **for any expenses** incurred for items or services - (1)(A) **which . . . are not reasonable and necessary** for the diagnosis or treatment of illness or injury” 42 U.S.C. §1395y(a)(1)(A)

2. Recurring CMS Focus on Comparability & Outcomes

- Cost-Effectiveness (1980's HCFA debate)
- Comparable Alternatives (1997) and Concept of Comparability
- Evidence-Based Medicine (1990's . . .)
- Notion of Practical Clinical Trials (PCTs)
 - Retrospective collection of comp alts data
 - MMA §1013 (review existing data, then PCT option)
- Evolving CED Policy (latest guidance 7/12/06)

2. Comparability & Outcomes

MMA §1013

- HHS/AHRQ authorized to conduct and support outcomes research to help CMS make well-informed coverage and reimbursement decisions.
- *Statute:* research re “the outcomes, comparative clinical effectiveness, and appropriateness of health care items and services (including prescription drugs) . . .”
MMA §1013(a)(1)(A)(i)
- See HHS Agency for Healthcare Research and Quality, <http://www.ahrq.gov/>

MMA §1013-AHRQ Continued

- Inevitable CMS will use AHRQ analyses as a cost-effectiveness tool in making coverage and reimbursement decisions?
- Recent AHRQ draft report found no substantial efficacy difference among second-generation antidepressants; though CMS may not use data to withhold coverage, §1013(d), “results could increase political pressure on CMS.”

Pink Sheet, May 22, 2006

2. Comparability & Outcomes

CMS leveraging data/role

- CMS Chief McClellan has proposed to assess cost-effectiveness by conditioning payments on companies paying for studies (and patients participating). *NYTimes*, 11/5/04, “Medicare Covers New Treatments With a Catch”
 - “Medicare has decided to use its 41 million beneficiaries to get some answers.”
 - “Patients can only have them [new more expensive drugs] if they enter into studies that evaluate how well they work.”
 - “Medicare holds a powerful hand – its beneficiaries are the biggest users of drugs . . . and private insurance companies often follow Medicare’s lead on coverage decisions.”

3. CMS Coverage with Evidence Determination (CED) Policy

- Updated CED Guidance Issued July 12
- Coverage with Appropriateness Determination – **CAD**
- Coverage with Study Participation – **CSP**
 - CMS cites 1862(a)(1)(E) authority, re extending Medicare coverage only to patients enrolled in ‘reasonable and necessary’ clinical research studies that provide added safety and patient protections.

CMS Principles Governing CED

- National Coverage Decisions involving CED will involve transparent process
- CED “will in general” be used to expand access to technologies and treatments
- Expected to be used infrequently
- CED will not duplicate or replace FDA’s authority re safety, efficacy or security

Meanwhile, Over There . . .

- **NICE urges British health service not buy Pfizer's new inhaled insulin Exubera: "could not be proven to be more clinically or cost effective than existing treatments."**

Wall Street Journal, April 18, 2006, quoting National Institute for Health and Clinical Excellence

- **British health service finds benefit of drugs to delay onset of Alzheimer's disease not worth cost, citing economists' cost/benefit analyses.**

Wall Street Journal, November 22, 2005, p. A1

Industry Signs Of The Times

- Pfizer: New drugs not improving on generics should not get reimbursed; In light of the current reimbursement environment, novel agents with unprecedented targets must be shown early in development to hit the molecular target.*
- MedImmune: Manufacturers cannot afford to invest as much money in high-risk products as in the past; the old days of unlimited upside in the biotech business model “are not over, but are amped down a bit because of the upper hand of payers and the pressures on our healthcare system gaining over the value that will be paid for innovation.”**

* Sr. VP Peter Corr, ** CEO David Mott
Pink Sheet, May 22, 2006

Industry Signs Of The Times

- Amgen: Due to increasingly challenging reimbursement environment, Amgen has begun conducting pre-approval head-to-head trials of its investigational compounds with marketed therapies.*
- Genentech: In the current reimbursement environment, it is becoming more critical to have labeled uses to allow discussion of survival advantages and dosing, instead of less useful off-label listings in compendia.**

**Pink Sheet*, May 22, 2006 **ExVP Ian Clark, *Pink Sheet*, July 17, 2006

Implications for Drug Development Strategies #1

1. Define & sharpen story of your medicine, re benefits for payers and patients alike
2. Examine all potential forms of exclusivity; patents just first of an array of tools
3. Consider all means for expediting FDA review; don't overlook FD&C/PDUFA deadlines (*Omnitrope* case), and role of patients/press
4. Early in development, proactively plan post-approval studies (re efficacy? indications? competitors?)

Implications for Drug Development Strategies #2

5. Anticipate issues re *registry requirements* and *clinical trial design*.
6. Relative efficacy likely to continue to emerge, for some as a shield, for others as a sword (and to be applied by FDA?).
7. CMS scrutiny may particularly focus on biotechnology products, which have so far effectively enjoyed open-ended exclusivity
 - see Omnitrope approval; potential role for substitutable non-generic biosimilars – re-emergence of ‘functional equivalence’; Kate Rawson, RPM Report, *Welcome to the P&T committee: Reining in Biotech Prices*, July/August 2006)

Contact Information

Matthew B. Van Hook

Partner

Engel & Novitt, LLP

801 Pennsylvania Ave., N.W.

Suite 620

Washington, D.C. 20004

Direct phone: 202.207.3302

E-mail: mvanhook@engelnovitt.com

Firm web site: www.engelnovitt.com

Engel & Novitt, LLP