Prioritizing Safety Versus Budget:
FDA and CMS Adopt Different Stances

By Paul Greenberg and Tammy Sisitsky

The U.S. Food and Drug Administration (FDA) and the Centers for Medicare & Medicaid Services (CMS) are both central to the process by which drug and biologic therapies and devices are made available to the public. FDA oversees the safety and efficacy of medical products, while CMS reimburses these products for Medicare- and Medicaid-covered patients. There is a built-in tension between the two agencies, which are both under the umbrella of U.S. Health and Human Services: FDA's emphasis on safety and efficacy can be at odds with CMS's need for cost containment. Additionally, each agency's decisions must withstand substantial public scrutiny, heightened by the fact that the public has much greater access to safety, efficacy, and financial information than ever before (through a variety of online resources, for example).

Clearly, both agencies are in challenging positions as they attempt to fulfill their duties appropriately. But even if each is successful in this regard, tensions between the two can arise in the presence of their sometimes competing objectives. And how these tensions get resolved has implications for patient access to potentially important medical products. Indeed, two examples that have made recent headlines reveal different ways in which these tensions manifest.

1. Off-label use of the lower-priced Avastin as an alternative to the on-label use of the higher-priced Lucentis to treat wet age-related macular degeneration (WMD); and

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2. Pfizer's request for over-the-counter (OTC) approval of Lipitor, a drug that at one point was the most widely prescribed product in the United States.

Below we take a closer look at these two examples and some key questions they raise concerning FDA's and CMS's optimal paths forward in the midst of regulatory and budgetary challenges.

Treatment of Wet Age-Related Macular Degeneration

Lucentis is a relatively expensive drug that has been approved by FDA for treatment of wet age-related macular degeneration. A collection of evidence, including the early results from a National Institutes of Health study, suggests that Avastin, which has been approved for treatment of certain cancers but not for WMD, may be a cost-effective alternative to Lucentis. Lucentis, it turns out, is a derivative of Avastin, and both of these injectable biologics are manufactured by the same company. However, the price difference between the two drugs for this particular condition is striking. Lucentis costs approximately 50 times more than Avastin for each injection. Avastin's pricing is a function of the much larger quantities typically needed for treating cancer compared with the quantities usually needed to treat WMD. From CMS's perspective, the potential savings associated with using Avastin to treat WMD would be significant. FDA, however, may not want to encourage such off-label use, if it could not vouch for the drug's safety and efficacy in this context without an appropriate showing by the manufacturer.

The tension between the two agencies is unlikely to be resolved with an FDA approval, since the manufacturer has no financial incentive to invest in getting Avastin approved for the treatment of wet AMD, and CMS has an incentive to allow for the reimbursement of off-label use of the drug. Regardless of how the situation unfolds, this example raises critical questions for policymakers, including:

- Should FDA's concerns about safety (that is, its insistence on the traditional drug-label approval process) trump CMS's concerns about cost containment, or should it be the other way around?
- Can a company with two different drugs that can be used to treat the same condition be compelled to seek a label expansion for the less-expensive treatment?
- Should FDA or another government entity (say, the National Institutes of Health) be empowered by FDA, at the request of CMS, to seek a label expansion on behalf of a drug company for a less-expensive but competing treatment?

Over-the-Counter Lipitor

Lipitor is a popular cholesterol-lowering prescription drug that achieved more than $10 billion in annual worldwide sales before losing patent protection in November 2011, at which time generic versions became available. In an effort to retain sales, the manufacturer publicized its intent to seek FDA approval for an over-the-counter (OTC) version of the medication. In addition to evaluating patients' ability to use the drug safely, FDA would need to consider the likely impact of reduced physician oversight and increased patient self-care associated with OTC availability of Lipitor. CMS, on the other hand, would likely welcome this opportunity to manage down the statin budget. By shifting all of the cost of the drug to the patient, it could save even more money than is commonly associated with generic substitution. The Lipitor story, like the Lucentis/Avastin story, has yet to play out in its entirety, but it raises provocative questions including:

- Should self-prescribing of a popular statin be permitted, given the therapeutic area involved?
- How different is this situation from earlier landmark instances of OTC drug approvals in the case of gastrointestinal (Prilosec, Tagamet) and allergy treatments (Claritin, Zyrtec)?
- If FDA is open to Lipitor being sold over the counter—particularly if CMS pushes hard for it as a cost-saving measure—will other sensitive therapeutic classes of chronic-use drugs eventually find their way to drugstore shelves (for instance, antidepressants, antipsychotics, or ADHD treatments)?
- Will a hybrid system evolve in which an OTC prescription will be required (to satisfy FDA concerns) but patients will be responsible for paying 100% of the purchase price (to satisfy CMS concerns)?

These examples illustrate how two government agencies with a shared goal of advancing public health can find themselves taking different positions on the same issue. In the current constrained economic climate, different pressure points—limited tolerance for adverse outcomes on the one hand, and an eagerness for cost containment on the other—may steer FDA and CMS toward different stances. They appear to be attempting to address some of these tensions; they recently initiated a pilot parallel review process for medical devices with the goal of "reduc[ing] regulatory burden and improv[ing] patient outcomes" by creating efficiencies across both agencies. Such a cooperative effort may be a useful step toward resolving their differences and increasing patient access to and affordability of a variety of important medical products.