Evidence-Based And Value-Based Formulary Guidelines

The movement toward formulary guidelines reflects the larger trend toward evidence-based decision making in medicine.

by Peter J. Neumann

ABSTRACT: Health plans and hospitals have long used drug formularies, but the processes by which formulary committees made decisions have typically lacked transparency and scientific rigor. A growing number of organizations have begun implementing formulary guidelines issued by the Academy of Managed Care Pharmacy (AMCP). These guidelines call for health plans to request formally that drug companies present a standardized “dossier” that contains detailed information not only on the drug’s effectiveness and safety but also on its economic value relative to alternative therapies. This paper describes the guidelines, reviews progress to date, and analyzes several critical issues for the future.

Health plans and hospitals have long used drug formularies, which list the prescription medications approved for routine use.1 However, the processes by which these organizations have made formulary decisions frequently lacked transparency and scientific rigor. The pharmacy and therapeutics (P&T) committees overseeing the process often based decisions on scattered reports in the medical literature, promotional materials provided by drug manufacturers, anecdotal information from physicians, and the extent to which plans could negotiate discounts. When they did conduct their own reviews and analyses, P&T committees tended to focus narrowly on consequences to pharmacy budgets, rather than on broader health and economic consequences to the health plan or hospital.

In recent years health policymakers have worked to standardize and improve formulary processes, with the goal of grounding decisions in stronger clinical and economic evidence. The trend reflects two broader movements in health care, one toward evidence-based medicine and the other toward explicit consideration of cost-effectiveness or “value for money” arguments.

The United States has trailed other countries in its adoption of formulary guidelines, but a growing number of U.S. health plans and other organizations have begun to implement them. This paper describes the guidelines, reviews progress to date, and analyzes critical issues for the future.

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The Emergence Of Formulary Guidelines

The idea of drug formulary committees' using explicit value-based evidence guidelines took hold abroad beginning in the early 1990s. In 1992 Australia became the first country to require drug companies to submit evidence of their products' cost-effectiveness to national authorities as a condition for consideration on the national formulary. Other countries, including Canada, the United Kingdom, and the Netherlands, followed suit with their own versions.

Some differences exist across guidelines—for example, in the type of information required or in extent to which they impose mandates. Australia requires drug companies to submit evidence of cost-effectiveness. In contrast, the United Kingdom's National Institute for Clinical Excellence (NICE) initiates and conducts evaluations itself and makes nonbinding recommendations to the National Health Service (NHS), although drug manufacturers and other interested parties can and do provide input to the process.

The movement toward formulary guidelines has evolved more slowly in the United States. In the absence of any national payer, local plans in the 1980s and 1990s developed internal processes to manage their pharmacy programs or turned to the growing pharmacy benefit management (PBM) industry for this service. Formularies became a critical benefit design component.

Although formulary committees have used pharmacoeconomic data as an input into their decision-making processes for some time, the information was used informally, and great variation existed across plans. When drug spending began to increase rapidly in the 1990s, plans and PBMs began to employ formularies more aggressively in an attempt to contain costs. This combined with the increase in the availability and acceptance of cost-effectiveness analyses began to change minds. In 1998 the Regence BlueShield health plan in Seattle began asking drug manufacturers to submit standardized packages of clinical and economic evidence as a condition for formulary review.

The AMCP Format. In 2000 the Academy of Managed Care Pharmacy (AMCP), a national professional society of pharmacists in managed care environments, endorsed its own guidelines, based largely on the Regence guidelines, called the AMCP Format for Formulary Submission, and began encouraging health plans nationwide to implement them. The Format represents a paradigm shift for U.S. formulary committees accustomed to being relatively passive recipients of information submitted by drug companies. It urges health plans to request formally that drug companies present a standardized “dossier” that contains detailed information not only on the drug’s effectiveness and safety but also on its economic value relative to alternative therapies. The Format further prescribes the layout for the submission, recommending that companies include unpublished studies, data on off-label indications, information on the drug's place in therapy, related disease management strategies, and an economic model that provides evidence of the product’s value. Although the AMCP guidelines do not represent the first time cost-effectiveness has
been considered in formulary decisions, they do mark an important endorsement of the concept and of the idea that standards are needed.

**The Format’s impact to date.** To date more than fifty health plans, PBMs, hospitals, Medicaid programs, and other public agencies (for example, the Department of Defense), covering well over 100 million lives, have adopted the Format or a Format-like process. To date more than fifty health plans, PBMs, hospitals, Medicaid programs, and other public agencies (for example, the Department of Defense), covering well over 100 million lives, have adopted the Format or a Format-like process.11 (Exhibit 1). The Foundation of Managed Care Pharmacy (FMCP), which oversees research, educational, and other activities for the AMCP, has undertaken a series of initiatives to educate pharmacists, drug company executives, and other interested professionals about the guidelines.12

**Critical Questions**

The advent of formulary guidelines represents a potentially powerful shift for consumers and producers of evidence, and for regulators overseeing the dissemination of promotional material from drug companies to health plans. For health plans and PBMs, guidelines mean more formal internal processes for judging evidence. For pharmaceutical companies, the change underscores the importance of differentiating a product's enhanced value relative to alternative therapies. For regulatory authorities, it could signal a profound change in the way they oversee information disseminated by drug companies to health plans. This section considers eight critical questions for the future.

**Are formal guidelines better than informal ones?** In theory, one might expect formal guidelines to improve upon informal ones because they promote the use of broader economic and health outcomes to inform decisions, and promise to foster a more careful deliberation about a drug's overall value. Standardized guidelines might enable plans to streamline processes and lower administrative costs.

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**EXHIBIT 1**
Selected Organizations Adopting Evidence-Based Formulary Guidelines, 2002

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<thead>
<tr>
<th>Health plans</th>
<th>PBMs</th>
<th>Other</th>
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<td>ACS State Healthcare</td>
<td>Department of Defense</td>
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<td>Blue Shield of California</td>
<td>AdvancePCS</td>
<td>State Medicaid programs:</td>
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<td>Anthem Rx Management</td>
<td>Alabama</td>
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SOURCE: S. Avey, “AMCP Format for Formulary Submissions”  (Presentation at the Fourteenth Annual Meeting of the Academy for Managed Care Pharmacy, Salt Lake City, 3–6 April 2002); and Steve Avey, executive director, Foundation for Managed Care Pharmacy, personal communication, February 2003.

NOTE: PBM is pharmacy benefit manager.
“The challenge will be to convince health plans that the guidelines are a vehicle to enhance value, not to lower drug spending.”

However, these are not foregone conclusions. Whether plans prefer formal guidelines and standards will depend on their costs and benefits above existing practices. Whether and to what extent explicit guidelines will enhance efficiencies and improve patient care remains unclear and should be subject to further evaluation.

Limited empirical evidence is available. Awareness of the AMCP Format among health plan managers appears high, although small studies suggest wide variation in plans’ adherence to the guidelines’ recommendations, as well as poor quality in submitted materials. Data on the guidelines’ actual impact on patient outcomes are lacking.

Will formulary guidelines impose an undue burden on health plans and drug companies? One concern, expressed by health plan and drug company officials anecdotally and in response to small-scale surveys, pertains to the potential burden imposed by new guidelines. Such fears are not without foundation. As Mark Sculpher and colleagues note in commenting on the NICE process, evidence costs money. The AMCP Format asks for resource commitments on the part of both health plans and manufacturers. On the plan side, the Format requires human, technical, and financial resources to support the review process. For manufacturers, the Format means shoring up internal health economics and outcomes research capabilities or contracting out for preparation of dossiers, which can run up to 100 pages each.

However, there is no reason to believe that guidelines will impose an excessive burden. Over time efficiencies should develop as plans tinker with the formula and tailor it to their own needs. The Format’s creators emphasize that it represents a template rather than a mandate and that it can be adaptable to individual plans. Plans will likely focus their guideline efforts on big-ticket items or controversial products—for example, medications for certain chronic conditions, or expensive innovations such as biotechnology injectibles. Because they standardize processes, formulary guidelines might actually reduce the time and resources now devoted to formulary decision making. As AMCP officials note, the costs of implementing guidelines will also decline if there are clear expectations and lines of communications between health plans and pharmaceutical companies. Ultimately, formulary guidelines will likely have their greatest impact not on decisions to accept or reject a drug for a formulary but on decisions to guide questions about its place in therapy: Is it on the preferred drug list? To which patient subgroups is it targeted? To which formulary tier does it belong?

For their part, drug companies may view guidelines darkly as yet one more hurdle thrown in their path or more neutrally as a structural change in the market-
place to which they must adapt. They will also likely see opportunities for showcasing products and for arguing for products on the company’s own terms—that is, on the basis of a drug’s overall value rather than acquisition price and negotiated rebates. The changes will likely accelerate the growth and prominence of health economic and outcomes research divisions. In many ways, formulary guidelines represent a continuation of practices to which they have grown accustomed overseas, although with a bigger marketplace and more players.

**Do plans have the expertise?** A concern expressed by drug company officials and some plan managers is that health plans do not possess the expertise necessary to judge the information in dossiers, particularly evidence contained in the economic models featured prominently in the guidelines. U.S. health plans, however, are a diverse lot with a varied ability to conduct dossier reviews. Some large organizations, such as the Blue Cross and Blue Shield or Kaiser plans, have strong in-house capabilities. Increasingly, Medicaid programs and other payers such as the Department of Defense (DOD) are developing the expertise or contracting out these services. Over time other arrangements will undoubtedly evolve. Small plans with insufficient resources will contract with PBMs for formulary management.

Training efforts also will help. Observers of the process note the steep learning curve—as much as one to two years—associated with ramping up capabilities to fully implement the guidelines. The AMCP has launched a national effort to educate managed care pharmacy staff in interpreting and integrating data for the formulary review.

**Are guidelines a smokescreen for cost containment?** A greater fear among manufacturers is that plans will employ formulary guidelines as a means to contain costs under the banner of quality improvement. Although manufacturers might complain that guidelines impose bureaucratic hurdles, impede access to important new drugs, and dampen incentives for innovation, experience suggests that explicit consideration of evidence tends to increase rather than decrease spending, because it sheds more light on under- rather than overtreatment. Drug spending in Australia grew after the country implemented its pharmacoeconomic guidelines, for example. The NICE process has tended to “level up” access to pharmaceuticals. After Oregon implemented its prioritization scheme, its Medicaid spending rose faster than other states’ Medicaid spending.

Drug companies may not like the hassle and uncertainty that come with new guidelines, but they should not expect a negative impact on overall sales. The larger challenge for champions of formulary guidelines will be to handle the expectations of health plan executives and to convince them that the guidelines are a vehicle to enhance value and not to lower drug spending.

**Do plans have the clout to force drug companies to comply?** A possible obstacle is that drug manufacturers will refuse to comply with plan requests for information. Potentially, drug firms will repudiate demands and instead accelerate traditional promotions aimed at physicians and consumers.
Early experience with the AMCP Format suggests that some companies have balked at providing dossiers, although in the end most have made submissions. Most likely, drug companies will find obstructionist tactics difficult to sustain. Health plans and PBMs, particularly those with sizable market shares, can and will play hardball by insisting on dossiers and even refusing to review drugs for a formulary if companies do not comply.

Undoubtedly, problems will persist. Some companies might submit incomplete dossiers—for example, omitting the pharmacoeconomic model or submitting poor-quality evidence, as has happened abroad. It could be difficult for plans, particularly small plans, to force companies to comply with all of the provisions of the Format.

The implementation of formulary guidelines could turn into something of a struggle between big pharma versus big managed care, with both sides scoring some early points. However, the AMCP Format gives plans a useful tool for leveling the playing field, which traditionally favored drug manufacturers. Moreover, plans can always threaten to compile dossiers and conduct reviews themselves, or contract out for reviews, if companies refuse to play. They can also put the drug on prior-authorization status until a dossier is submitted. In the end, drug companies will likely have no choice but to comply with their customers’ requests.

Won’t all information submitted by companies be “biased”? Another concern is that drug company submissions will amount to thinly veiled promotional pieces. The fear extends in particular to economic models, whose assumptions are seen as easily manipulated by drug firms. Such concerns are probably overblown. Companies now submit information that might be biased. The relevant question is whether the AMCP guidelines will change the potential for bias.

Health plans will naturally expect companies to put their data in the best light possible. They should display a healthy dose of skepticism toward submitted data. Their best defense involves training formulary decisionmakers about the process and forcing a more honest dialogue. Moreover, some other safeguards exist. For one, health plans can, as the Format suggests, request full disclosure of funding arrangements between investigators of studies submitted as part of dossiers and the drug companies. For another, dossier submissions must still comply with U.S. Food and Drug Administration (FDA) rules against false or misleading promotion, although how the FDA will regulate such information is a murky issue.

How will the FDA regulate “unsolicited requests”? Demands by formulary committees to drug manufacturers for product dossiers register on the FDA’s radar as formal and wide-ranging “unsolicited requests.” That is, in principle, they constitute unprompted requests for information and thus liberate drug companies from
strict agency rules stipulating that all information disseminated must be consistent with FDA-approved product labeling, as long as certain conditions are met.

A key question involves whether the request for information is genuinely unprompted and not triggered or influenced by a drug company. Even if the request is unprompted, a question arises about whether it is specific or general in nature (the FDA calls for targeted requests rather than open-ended petitions, which could open the floodgates to misleading promotions). With respect to drug company responses to unsolicited requests, the FDA concern relates to whether the information is false or misleading. But what constitutes “false and misleading” information when material is distributed in response to an unsolicited request? What if the requestor asks explicitly for off-label information or economic models, as the AMCP Format recommends?

How the FDA will view such matters remains unclear. The agency has announced that it will issue guidance on unsolicited requests, which will presumably cover such questions, although none has been issued to date. The FDA’s long-standing trepidation over inappropriate promotion stems from two concerns. One is that it risks opening the door to unsupported claims, thereby potentially misleading the marketplace. Conceivably, drug companies could use the cover of unsolicited requests to promote unreliable or deceptive information—that is, information not studied in adequate and well-controlled trials. The second concern is that a permissive regulatory stance creates a disincentive for companies to conduct rigorous studies in the first place. That is, allowing companies to make promotional claims more freely could undermine the protections enjoyed by drug manufacturers that have undertaken efforts to collect substantial evidence. If a company can use an economic model to project a drug’s effect on long-term economic outcomes, then why should it incur the expense involved in collecting long-term economic data and the risk of an unfavorable outcome? A better strategy would be to obtain approval for a narrow indication and promote freely on other indications, under the cover of formulary guidelines. The counterargument is that such concerns give little credit to health plans’ ability to decipher the merits of evidence underlying promotional information. Drug companies retain incentives to do long-term studies because consumers reward them for it.

Widespread use of formulary guidelines threatens the status quo and puts such abstract arguments to the test of the marketplace. However, the FDA is not empowered to stop unsolicited requests even if it wanted to. Moreover, the FDA will not be aware of information disseminated through such channels, because unlike other promotional materials, drug companies are not required to submit the information to the agency (although the FDA may find out to some extent if complaints arise from health plans or other drug companies). Thus, the FDA will most likely watch the situation closely but take a hands-off stance on grounds that information provided in response to formulary guidelines occupies the traditional safe harbor for unsolicited requests. The agency would still require that requests be
unprompted and that information not be untruthful. For example, a company could disseminate information from a legitimate study of an off-label indication but could not fabricate the data.

In turn, drug companies will keep a close eye on the FDA, particularly with respect to the inclusion of off-label information and data about relevant unpublished information. Health plans can help by implementing mechanisms to delineate more clearly the nature of requests. As an example, the AMCP Format already advises health systems to make explicit the information they desire and to submit signed requests letter to accompany the Format.36

Are dossiers confidential? The confidentiality of dossiers has emerged as a prime concern for drug manufacturers.37 Drug firms fear that proprietary information submitted in a dossier—for example, pharmacoeconomic models, unpublished studies, or off-label information—will become publicly available, thus exposing sensitive data to competitors and potentially alarming regulatory authorities worried about misleading promotion.

To a large extent, the concerns should be addressed through compliance with FDA rules on unsolicited requests and with appropriate confidentiality agreements. A special problem arises with public payers, such as state Medicaid programs, which maintain sunshine laws requiring them to make information gathered for consideration of payment publicly available.38 Oregon’s Medicaid agency has made dossiers available upon request, for example.39 A related concern pertains to dossiers submitted to the DOD, which could be obtained under a Freedom of Information Act request.40 The DOD now has a committee review the dossiers and prepare a brief report summarizing the key points contained therein. It is the summary reports that become public, while the dossiers, with their proprietary cost-effectiveness models, will presumably remain confidential.

The AMCP has strongly recommended that private plans using the Format work diligently to find ways to keep dossiers confidential and that public providers explore all opportunities for assuring confidentiality within their legal constraints.41 They also stress the importance of holding presubmission meetings to disclose the level of confidentiality possible and manage expectations about data to be submitted.42

In the future, drug companies could maintain different dossiers for public and private authorities. But the distinctions could well be blurred over time. As the AMCP notes, dossiers submitted to authorities in the United Kingdom and certain other countries are made available to the public.43

Lessons For A Medicare Drug Benefit

The debate over a Medicare drug benefit has thus far focused primarily on the structure, scope, and financing of proposed plans, as well as the respective roles of the federal government and private sector. Critical questions about the process for considering evidence are left for future deliberations, possibly with the help of a
new Medicare Prescription Drug Advisory Committee. Conceivably, PBMs administering the program will adopt the AMCP Format as a national model for formulary decision making, which could move the United States toward the centralized formulary models used abroad.

One key question involves how much geographic variation in drug coverage will be tolerated for Medicare. Regional P&T committees could come to different conclusions about the value of similar drugs, leading to different formularies and coverage. Another question is whether Medicare will be able to use cost-effectiveness analysis explicitly. Medicare has tried repeatedly to incorporate cost-effectiveness as a criterion for covering new medical technologies in the past but abandoned the pursuit because of political barriers. In recent years Medicare has avoided cost-effectiveness, even as it has restructured its entire apparatus for covering new technologies to make its process more transparent, consistent, and evidence based. The history of Medicare suggests that it will be difficult for the program to use cost-effectiveness analysis explicitly in this process on the national level. Such analysis might be incorporated at a local level by competing plans or PBMs who employ AMCP-like processes.

The movement toward formulary guidelines reflects the larger ongoing movement toward evidence-based decision making in medicine, with economic evaluation as part of the evidence base. The AMCP Format has the potential to serve as a national unifying template for P&T committees to consider clinical and economic information in a systematic and rigorous fashion. The Format in many ways mirrors the national formulary guidelines used by payers abroad, although in a decentralized, uniquely American fashion. The standardized layout and the call for clinical and economic data allow plans to consider evidence of value while avoiding more politically unpalatable forms of centralized priority setting. The Format is a welcome development for a health system in need of more rigorous evaluation of evidence. Many questions remain about its implementation and impact and whether Medicare will adopt the process in a new drug benefit.

The author is grateful to Sean Sullivan, Pete Fullerton, Natalia Olchanski, Steve Avey, Richard Fry, and two anonymous reviewers for helpful comments on earlier drafts of this manuscript.
NOTES


4. Ibid.


18. Jstreetdata, “Attitudes towards Adoption of the AMCP Formulary Guidelines.”


32. Ibid.


37. Robinson, “AMCP’s Format for Formulary Submissions.”

38. AMCP, “Responses to Comments.”


41. The recently revised AMCP Format states: “By submitting this request, the health system recognizes that confidential information may be provided. The health system recognizes the need to respect and honor commercial-in-confidence information and may be willing to sign necessary confidentiality agreements under agreed circumstances” (AMCP, 2002).

42. AMCP, “Responses to Comments.”

43. Ibid.