

The Debate

The following debate between John Golenski, EdD, and Sean Sullivan, PhD, is based on a moderated session held at the annual meeting of the Academy of Managed Care Pharmacy meeting in San Francisco on April 2, 2004. Attendees of this meeting also participated by asking questions of the debaters and by responding to quick-polling questions posed by the moderator.

Moderator: *Dr Golenski's critical point is that specialty pharmaceuticals haven't been on the market long and there's simply not much evidence. Dr Sullivan, if a guideline isn't well grounded in the evidence, why not leave it up to the specialists?*

Dr Sullivan: In fact, guidelines are needed most at that exact moment when a new pharmaceutical is released. That's essentially what the label is—guidance from the FDA [US Food and Drug Administration] review body based on its interpretation of the information made available to them. So, this initial label becomes a guideline, if you will, and then, as more data emerge in phase 3B and phase 4, the broader community sifts through and modifies the initial label guidance. This layered approach makes sense to me.

Moderator: *More than 1000 medical journal articles are published every day. Can we really expect a busy specialist to read all the important studies or to synthesize all those studies that don't agree with each other? Dr Golenski, isn't it likely that a dedicated panel of experts who spend several days combing through the literature and arguing about these issues will have a superior conclusion compared with some poor, overworked community doctor?*

Dr Golenski: Of course they will. But that's not the issue. The issue is whether we should use consensus guidelines that incent and economically curtail the physician's use of

these agents. That's where I think we don't have the basis to act. Do physicians need assistance? Of course they do. And any good specialty physician will use summaries from organizations such as the Cochrane Collaborative or the ISTAHC [International Society for Technology Assessment in Health Care], which sift and analyze and even rank the research quality of the evidence in given specialties. The specialty societies do that analysis themselves. Are consensus panels an advance? Of course they are. But they may not be a basis for management.

Moderator: *So, you're arguing against consensus guidelines as a basis for reimbursement. You're saying enforcement with prior authorization can be expensive, annoying to patients, hard to monitor and justify, and perhaps even immoral. Isn't this true Dr Sullivan? Given that these specialty pharmaceuticals are not drugs that patients are clamoring to take—they're not taking this pill because their stomach is upset and they want to keep eating pepperoni pizza—isn't it true that the guidelines and the accompanying prior authorization requirement just cost the healthcare system a lot of money with questionable benefit?*

Dr Sullivan: "Questionable benefit?" Well, I would agree that prior authorization for specialty pharmaceuticals is different than prior authorization for the PPIs [proton pump inhibitors]. It is also true that prior authori-

zation programs are a hassle and costly to everyone involved, including patients, physicians, and the health plans that have to implement them. But an appropriate authorization process can assure proper use right out of the gate, right after the adoption decision for the specialty pharmaceutical. If the payer's constant assessment shows that the drug is being used consistently in the way that is supported by the evidence, then I think removing prior authorization makes sense.

Moderator: *So what are the criteria for removing a prior authorization?*

Dr Sullivan: The core guides are who the drug works in and how it should be used. If the health plan's clinicians are following those core guidelines, then perhaps the prior authorization has served its purpose.

Dr Golenski: I would argue the opposite. I think the moral ground for prior authorization programs is very, very strong when you have a very solid research base. But when the evidence base is minimal, that's when the moral ground recedes.

Moderator: *We all have heard stories about specialists who own and operate private infusion centers, have a big markup on the injectables, and make a lot of money on the product. We have heard of some specialists who have used the products excessively. Some have even opened vials, split them among patients, then billed the health plan as if each patient were getting the full vial. It's a disturbing reality. Given these financial incentives, can we still say that physician discretion is best for the patients?*

Dr Golenski: The Department of Labor estimates that approximately 20% of employees in all enterprises steal from their employers—for instance, through inappropriate time clock use, reimbursements for expenses, or outright stealing of goods from a manufacturing organization. But does this mean that you should punish the other 80% of the people and have cameras in the workplace? No, that's an inappropriate solution. An

appropriate solution for fraud such as you describe is not a practice guideline but the police or law courts. It's not an inappropriate use of a guideline; it's fraud.

Moderator: *Another criticism of guidelines is that they're created by groups of academics. Typical community doctors see a different type of patient in a different setting. Isn't a good specialist in the community likely to know more about the reality of treating patients than a bunch of committee members from the ivory tower?*

Dr Sullivan: If it's only academics who don't see a lot of patients putting the guidelines together, that's the wrong process. The guideline process should involve stakeholders beyond the clinical trialists or those academic specialists who spend only half a day per week seeing patients.

Moderator: *So who are these stakeholders that should be on the guideline committee?*

Dr Sullivan: For specialty pharmaceuticals, the committee should have the specialists, including clinical trialists involved in the drug's development as well as practicing physicians and pharmacists. It might also include patient advocacy groups and others who have an interest in the outcome of the guidelines. Guidelines written only by academics need to be viewed critically.

Moderator: *Should a guideline that does not include the proper mix of authors be ignored?*

Dr Sullivan: The mere presence of a guideline doesn't absolve the payer from having to carefully and critically review the data and the guideline itself.

Moderator: *Some specialty pharmaceuticals are now advertised directly to consumers. And so, as with the heavily promoted small-molecule therapies, some patients come into a doctor's office and ask for them. Not surprisingly, some physicians feel pressured or obliged to provide those new drugs even if that therapy isn't the best choice. Does a legitimate*

treatment guideline provide doctors with some cover? Dr Golenski, isn't this an argument in favor of guidelines as opposed to physician discretion?

Dr Golenski: With the common pharmaceuticals, I think that's true. One of the physicians on a national P&T [Pharmacy and Therapeutics] Committee told us a few years ago that a lady in her 80s came into his office with a *Newsweek* full-page ad showing this older couple who appeared very, very happy. This woman said "I want you to give me this drug. These people seem so happy." The drug was Propecia [finasteride]. Most physicians hate direct-to-consumer advertising of medications. Sadly, perhaps, patients, particularly in AARP [American Association of Retired People] surveys, love them. They say they learn a lot about pharmaceuticals from advertising that their physicians don't tell them. So we're not likely to see any reduction in direct-to-consumer advertising. However, in the case of specialty pharmaceuticals, I suspect that advertising is not a major driver of patient use. Certainly the physician can still use the guideline in talking with the patient about what's appropriate.

Moderator: *Dr Sullivan, how can you say that guidelines can be cost effective if the products themselves typically are so expensive?*

Dr Sullivan: There's a difference between cost saving and cost effective. Using generic beta blockers post-myocardial infarction is a cost-saving strategy. The total treatment costs are outweighed by the avoided costs of morbidities. Cost effective is an expression of the willingness of individuals to pay for added outcome. With specialty pharmaceuticals, given the current pricing structures, these agents don't meet traditional cost-effectiveness thresholds. But if they're available on the formulary, then a guideline should be able to describe a cost-effective way to use these agents.

Moderator: *Clearly, one aim of guidelines is to reduce variation in care. But if we rely on specialists' discretion, won't*

we increase the likelihood that 2 patients in similar situations will be treated differently? And won't this impact both the health outcome and the cost outcome? Dr Golenski, are you saying that variation in treatment is a good thing?

Dr Golenski: No. I'm simply suggesting that we don't know if variation increases with specialist discretion. That's an empirical question that should be studied. In the introductory presentation, we saw that most guidelines are, in fact, very similar to the product labeling for specialty pharmaceuticals. Perhaps we should just ask physicians to read the labels.

Dr Sullivan: There is actually plenty of evidence, even with specialty provided care, suggesting tremendous variability in practice.

Dr Golenski: But is that variation connected to negative outcomes?

Dr Sullivan: John Wennberg has shown that in many circumstances—although not with specialty pharmaceuticals—that variation is associated with negative outcomes. He's shown it for surgical interventions.

Dr Golenski: I agree with you, but we don't have evidence about the use of specialty pharmaceuticals.

Moderator: *Do any of the current specialty pharmaceutical guidelines actually rank the evidence?*

Dr Sullivan: From what I've seen, at least explicitly in the written guidance, there really isn't an evidence-grading approach. It may have been done internally, but it's not in print. That's different from the NIH [National Institutes of Health] or Cochrane approach where the evidence grades are shown to support the recommendations.

Moderator: *Is it possible that properly implemented guidelines would provide payers with good risk management? For example, if the state insurance commissioner asks, "Why are you managing this*

specialty pharmaceutical in this way?" can the payer turn around and say, "We are following national guidelines?"

Dr Golenski: I've had direct experience with that. Several years ago, when Viagra [sildenafil citrate] was first introduced, Kaiser Permanente decided to convene a national ad hoc body to review the reasonableness of simply opening that up for provider discretion to prescribe. Kaiser eventually developed a guideline calling for primary care doctors to follow certain criteria, at least by patient report, in identifying individuals with erectile dysfunction. After patient advocacy organizations objected to the guideline, the attorney general of the State of California also took great umbrage and took Kaiser to court and lost. I still believe it was a very good, evidence-based guideline.

Moderator: *If the published data don't guide us in terms of how long to use a biologic or when to stop, how can a guideline be any help?*

Dr Sullivan: Typically, a guideline group would simply state the fact that there is no evidence to inform a recommendation on stopping therapy. This doesn't help, of course, so frequently the payers will ask the manufacturers for guidance. They will ask if the data have been analyzed in a way that will help us understand when to stop therapy for people who are responding, or also to determine that a patient is a nonresponder to therapy. That's a very important question: "Do you have evidence about who is a nonresponder?" Unfortunately, we often lack satisfying answers to these common questions. As drug developers make increasing use of genomic information, we should move closer to identifying responders versus nonresponders and knowing when to stop therapy.

Moderator: *Are guidelines unethical in specialty pharmacy when multiple products exist in the same therapeutic class with the same target, such as the anti-tumor necrosis factor products and when a clear physician-profit motive exists between the products?*

Dr Golenski: We often lack good evidence about physician involvement and motives at the national level. But I do know that Caremark takes an enormous amount of care to separate the clinical decision around formulary inclusion from the trade decisions about contracts. When we get requests from trade, for example, about a ranking of a particular pharmaceutical, we usually have no idea what trade relationships they've crafted. Because there are no trade people in the room, clinicians on the committee often actually say no from a clinical perspective based on evidence. If the clinical decisions and trade issues get conflated in the same room, you have a very dicey situation. And, frankly, an indefensible one.

Moderator: *As specialty medicines such as omalizumab and etanercept become the standard of practice, primary care physicians may become prescribers. Doesn't it make sense for us to be ahead of the curve with guidelines to manage this?*

Dr Golenski: What bedevils me greatly about this potential situation is our difficulty figuring out when a person is a nonresponder. Normally, we recognize a nonresponder by an adverse drug report, not by a lack of improvement. In other words, most people stop a pharmaceutical that's been prescribed because they have an adverse reaction, not because they're not responding. And even when patients have adverse drug reactions, sometimes we can't get providers to change. This will be a problem with primary care doctors prescribing specialty pharmaceuticals.

Dr Sullivan: In general, primary care physicians should not encourage the use of these pharmaceuticals. Geography and rurality might make it necessary on occasion, but the predominance of the prescribing and management of the patient in those 2 specific cases cited needs to be undertaken by the specialists—the allergists and pediatric allergists for omalizumab, and the rheumatologists for etanercept. It's an issue of managing the patients, not the drug therapies. That's my opinion.

Dr Golenski: Many injectable medications that should not be used by primary care physicians are already being used routinely. And it's a continuing difficulty, particularly in medical practices that are not organized into large, integrated groups where physician managers would look at the behavior of rank and file physicians. Limiting use of these agents to specialists is, in itself, a kind of guideline for use.

Moderator: *What should be done with physicians who refuse to cooperate with PBM [pharmacy benefit management] guidelines on very costly medications?*

Dr Golenski: Physician adherence is a continuing difficulty. As I said before, I believe that when we have a strong evidentiary base and when we have long experience using a pharmaceutical or intervention, we have every moral right to intervene aggressively and to incent physicians financially.

Moderator: *Do you think we'll see more guidelines on therapies that have not yet been FDA-approved, such as the omalizumab consensus guidelines?*

Dr Sullivan: Yes, because there's a demand in managed care for that type of early guidance. They need to know: What am I going to do with this biologic? How am I going to manage it? And so organizations will increasingly try to develop guidelines similar to what Genentech did with Xolair [omalizumab].

Moderator: *Will specific guidelines or reimbursement criteria increase risk in the case of a lawsuit against the health plan?*

Dr Golenski: The health consequences of any inappropriate use of a pharmaceutical always produce a legal risk in terms of the potential for a significant claim against the organization. My experience, which is, unfortunately, pretty extensive around this in MCOs [managed care organizations], is that the use of scientific evidence is almost never protective in an individual case litigation.

Moderator: *Because the target population that gets specialty pharmaceuticals is typically small and because the therapies are quite costly, aren't they ideal for a guideline-driven case management approach?*

Dr Golenski: Case management is, of course, a wonderful way to address the issues. Friendly Hills Medical Group in Southern California significantly reduced morbidity and mortality in people taking Coumadin [warfarin] with a case management, actually a case-finding, approach. But that is very different from managing the utilization decision of individual physicians.

Moderator: *The FDA labeling may be a general guideline, but because it doesn't offer comparative information on best practices, isn't the specialist best in finding the up-to-the-minute information on which specific patient should get a specific therapy?*

Dr Sullivan: I agree with the premise of the question, but not the suggested solution. It's true that most product labeling does not include data on comparative efficacy or comparative safety—although that is changing very fast in Europe. The European FDA equivalent is now proactively telling the pharmaceutical industry that comparative studies will be the standard, not the exception. And this may hint at changes ahead in the United States, which is a good thing. But in the meantime, I'm not sure the specialist has up-to-date information. This is a false assumption. I'm just not sure that specialists can find the answers any better than a panel of folks who sat down and thought through the label and the data, which includes the committee who sat and weighed the evidence for the FDA.

Moderator: *Aren't comparative trials rare? If Manufacturer A has the standard of care and Manufacturer B is coming out with another therapy, then Manufacturer A certainly doesn't want Manufacturer B to design the comparative trial.*

Dr Sullivan: Well, it depends. We had an experience this last month with the PROVE-

IT [Pravastatin or Atorvastatin Evaluation and Infection Therapy] trial comparing 2 cholesterol-lowering drugs where one manufacturer was quite excited that the other manufacturer paid for the trial.

Dr Golenski: Only after the fact!

Moderator: *Dr Golenski, you mentioned that guidelines are reasonable approaches in disease states where there's a wealth of data available, such as hypertension. As biologics begin to be approved for diseases where there's a lot more baseline evidence, and as the evidence mounts—for example, for omalizumab in asthma—wouldn't you then suggest the integration of these biologics into guidelines?*

Dr Golenski: That seems perfectly reasonable to me. But this doesn't mean we forget to devote resources to 2 other key areas that have been mentioned already, and the first is comparative studies. When I was running RxHealthValue, a Washington advocacy group for prescription drug policy, we were strongly advising the FDA to require comparative studies as they do now in Europe. Some PBMs and MCOs in the United States are even now looking at the European data to guide their decisions. But more importantly, we also need to invest in a systematic gathering and analysis of evidence from phase 4. Here is where you need to engage the experienced specialty physicians and make it easier for them to report phase-4 evidence. This will give us the information needed to figure out the most effective way to use these specialty pharmaceuticals in the first place.

Dr Sullivan: That's right. But we don't have that easy process right now.

Moderator: *Do the guidelines for medications used by a fairly small population, such as those with pulmonary hypertension, differ from those for drugs used in larger populations, such as asthma patients?*

Dr Golenski: Yes. One big difference involves the heavy participation of stake-

holder groups in the creation of the guidelines for the major diseases. Breast cancer patient advocacy groups, for example, often have their own medical experts. Kaiser tried to implement its first national practice guideline around the use of BRCA 1 and 2 and had great difficulty because they had not initially included some of these advocacy groups. After we brought their experts in and changed the guideline, Kaiser got their support. That's very important to do. However, getting stakeholder input from patient advocates with the orphan diseases is difficult. It's hard to organize, especially as it relates to the specialty pharmaceuticals.

Moderator: *Many biologics are approved for one disease and used for another, even without adequate information. Should specialists be in charge of this type of off-label use?*

Dr Golenski: That's a tough question. My mother was treated for metastatic breast cancer in the early 1970s, eventually died of bone cancer, but she was one of the first people on whom they discovered the benefits of methotrexate for rheumatoid arthritis. Her arthritis symptoms disappeared when she took methotrexate. So, sometimes the off-label use helps patients in the long run. On the other hand, sometimes it can seriously harm patients.

Moderator: *Given that many medical policies are based, to some degree, on guidelines, is there a role for a pharmaceutical manufacturer in the implementation of these accepted guidelines? Perhaps, for example, a sales representative educating physicians.*

Dr Sullivan: It's possible. Each health plan and PBM has their own approach and their own policies around interacting with industry. Although industry has resources that can be deployed on behalf of a health plan and its policies, this has to be done very carefully. The objectives need to be set very clearly and there needs to be full disclosure. In the right situation, with the appropriate caveats, it could work.

After the Debate—The Vote

At the conclusion of the formal presentations and the debate, Academy of Managed Care Pharmacy participants at this session were asked to cast their votes via instant polling on 2 key questions.

| | Strongly Disagree 1 | Disagree 2 | Neutral/ No Opinion 3 | Agree 4 | Strongly Agree 5 |
|--|---------------------------|---------------|-----------------------------|------------|------------------------|
| 1. I believe that a managed care organization or pharmacy benefit manager is better off using credible treatment guidelines as a basis for specialty pharmaceutical reimbursement than relying primarily on specialist discretion (n = 65) | 12% | 15% | 8% | 48% | 17% |
| 2. As a basis for specialty pharmaceutical reimbursement, my organization should (n = 48): | | | | | |
| Substantially increase reliance on treatment guidelines | | | 8% | | |
| Somewhat increase reliance on treatment guidelines | | | 17% | | |
| Maintain current practices | | | 44% | | |
| Somewhat increase specialist discretion | | | 29% | | |
| Substantially increase specialist discretion | | | 2% | | |

Dr Golenski: At one of our large PBM clients, they've been encouraging manufacturers to develop patient registries so that we can track the implications of these specialty pharmaceuticals over time. In a way, this is a proactive phase 4 development. Industry financing for this may be a good way to go. It's helpful to patients.

Dr Sullivan: That postmarketing approach does help in the accumulation of science about what works. I know that Genentech is the sponsor of this session, but I have to say Genentech has been doing these registries for quite some time and they've made contributions to what we know about their particular products and those disease states. That's a good thing.

Dr Golenski: The tissue plasminogen acti-

vator registry is still one of the largest patient registries in the world.

Moderator: *Thank you both for your spirited debate. In conclusion, it's probably fair to say that the majority of medical breakthroughs coming over the next decade will involve specialty pharmaceuticals—the large molecules instead of the small ones. One job of managed care pharmacists is to figure out how to balance the health needs of members with the economic needs of employers and health systems. We hope this debate has provided some useful insights into figuring out the proper balance between treatment guidelines and specialist discretion. We thank Genentech and Novartis for their support of this debate.*