Representative Waxman urged him not to go forward with this “ill-advised” guidance.

Waxman has two concerns. First, he thinks drug companies should be required to obtain the FDA's permission before they may disseminate medical journal articles promoting the off-label use of approved drugs; the 1997 exception included this. Second, without the FDA's agreement, he thinks that drug companies will have no incentive for conducting clinical trials supporting new uses of their products when they can “short-circuit FDA review,” tilt less-than-rigorous trials to “deliver positive results,” and then use the findings to influence prescribing patterns.

However, the concerns of both Waxman and Grassley (who opposes the off-label overuse of atypical antipsychotic drugs in nursing homes) are focused on the wrong end of the pipeline; that is, the focus should be on information going out to physicians, not on the physicians receiving the information. Off-label use is vital to many patient groups, and the benefits in those cases often outweigh the risks. However, using drugs in an off-label fashion can present dangers to patients, and the effectiveness of any drug or class of drugs used this way is far from ensured. But it is the physician who is the critical link here, not the drug company.

As for the FDA's draft guidance, no one could read it and say that the agency is making life easy for pharmaceutical companies. There are more hurdles to sending out promotional literature than there are on a steeplechase course. For example, a journal or online article cannot be published if the content is “inconsistent with the weight of credible evidence;” it cannot run counter to what has been found in other, similar clinical investigations. If an article contradicts the results of only one other article, that previously published dissenting article would have to be distributed at the same time.

And there is more, much more. If the FDA enforces these requirements, drug companies would probably not be sending around dubious articles based on bogus clinical trials, which is Waxman's concern. The bigger risk is that physicians might not pay close enough attention to the risks of off-label use, which can be substantial. These risks come into play in connection with atypical antipsychotic agents, which are Grassley's concern.

In the October 2007 issue of P&T, David A. Casey, MD, reviewed the blackbox warnings that the FDA requires for the labeling of atypical antipsychotic agents. He stated:

Combined with the lack of an FDA indication, the warnings call for a special focus on documentation, informed consent, and monitoring for all patients with dementia who are taking atypical antipsychotic drugs.

Medical professionals must pay very careful attention to the off-label use of atypical antipsychotic drugs. Peter V. Rabins, MD, MPH, a psychiatry professor at Johns Hopkins School of Medicine, chaired the American Psychiatric Association's work group, which published a practice guideline last fall. In an interview, he emphasized that nonpharmacological interventions should be tried first for agitated or aggressive nursing-home patients with Alzheimer's disease or dementia unless these patients pose a clear danger to themselves or others. If those interventions don't work, antipsychotic agents can be "modestly effective," he said.

Dr. Rabins added that the question of whether antipsychotic agents are being overused in nursing homes is an important one. He explained:

I don't think there is enough scientific evidence to say they are overused. There is
good evidence that even when they are appropriately used, the dose can often be lowered or the drug can be discontinued after several months.

Rather than alter a pretty toughly worded FDA guidance document, Congressmen Waxman, Grassley, and others who are worried about the overuse of off-label drugs might think about requiring physicians to sign off on an authorization before they prescribe them; they could simply check a box on a script. Signing off would commit doctors to seeing how their patients are handling the drug every few days or every few weeks, and it would confirm that the physicians themselves understand the risks of that prescription and have explained these risks to the patient and family. The American Medical Association would go bonkers, of course, but maybe just raising the possibility means that the message would get out: that off-label prescribing is serious business.

REFERENCES

