such report should be investigated to see if something was done incorrectly and was the real reason for the reaction. If given incorrectly, all drugs, including fosphenytoin, can have adverse effects.

As with other pharmaceutical sales efforts, Parke-Davis has done a fine job of detailing fosphenytoin to my neurologists. Many of them tell me that the hospital should buy fosphenytoin regardless of its price. I do not necessarily agree. Yes, fosphenytoin has a place in medicine, but I am not sure that my opinion of this drug is the same as that now held by many of my neurologists. And now, thanks to AJHP, my neurologists can simply look at one of my peer-reviewed journals and read just how good fosphenytoin is and how bad i.v. phenytoin is. This really makes me look good.

Practicing pharmacists need timely, accurate, unbiased information in review articles and editorials. If AJHP cannot provide this, then I believe we would be better served without the information.

I challenge AJHP, in publishing drug information, to change its stance on potential conflicts of interest in clinical review articles and editorials. Otherwise, the journal will become just another of the throwaway journals I receive.


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W e were concerned and disappointed to see that ASHP allows drug company representatives to report on their products’ safety in AJHP’s clinical reviews.¹ Now that AJHP allows the fox to guard the hen house, maybe other businesses will take advantage of the precedent.

Think of it. Car manufacturers could write standards for their own emissions tests and bypass the Environmental Protection Agency; airlines could publish their own safety standards (and records) and avoid hassles from the Federal Aviation Administration; i.v. product manufacturers could set their own sterility recommendations and advise the Food and Drug Administration on how to do its job.

One of the first skills we teach pharmacy students from Auburn University and residents is how to critically evaluate the literature. No matter how green the student or resident, he or she can usually spot the potential for bias in an article, such as a study funded by an organization with a financial stake in the study’s results. The AJHP clinical review authored by Parke-Davis representatives is another such example.

We think a clinical review should be developed and authored by pharmacy practitioners, who can approach the topic more objectively than industry employees can. If the industry must be involved either as sponsor or author (as AJHP states is sometimes the case²), we recommend that clinical practitioners be included as coauthors to help balance the focus.

We are certain that all the other drug research and manufacturing companies will want to write their own clinical reviews for a publication that reaches more than 30,000 pharmacists, many of whom have influence over their institution’s drug product selection process. Maybe next time AJHP will save pharmaceutical manufacturing representatives a great deal of time by simply changing the lettering in the package insert to match the journal’s type style and then adding the company’s opinions to round out the article.

Today’s clinical drug literature is flawed enough by bias from multiple sources—bias that is often unintended or difficult to eliminate. We should never deliberately create a situation in which bias is inherent. Prudent farmers are wary of the fox; they do not put it in charge of the henhouse security.

In preparing this letter, we were torn between expressing our concerns over AJHP’s printing this potentially biased review and expressing our opinion (shared by many clinicians) that fosphenytoin offers little real advantage over phenytoin but will increase revenues for Warner-Lambert stockholders.

We hope someone else will step up and challenge the manufacturer on this issue. Any takers?


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F ierro et al.¹ accomplished their task in informing us that, compared with phenytoin, fosphenytoin causes fewer injection-site reactions and can be administered intramuscularly. This information is useful to practicing pharmacists, and there is no doubt that fosphenytoin has an important role in anticonvulsant therapy.

I am more concerned about the information not covered in the article. Fiero et al. stated: “It is expected that Dilantin injection will no longer be available after January 1997.” The authors, employees of Parke-Davis, obviously know this as fact. Does this mean, however, that phenytoin injection will no longer be available? Of course not. Did the authors mention the continued availability of phenytoin injection? No. I believe that this is part of the marketing strategy for fosphenytoin injection—mislead people into thinking that the new product will soon be the only form of injectable phenytoin available.

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Correction

New trends in the drug therapy of localized and disseminated Mycobacterium avium complex infection (November 1, 1996, Therapy Update). On page 2585, the author identification section should have listed Shannon French Manzi’s title as Staff Pharmacist in Pediatrics.
Check out the large, colorful, multiple-page advertisements in the December 1996 issues of pharmacy journals. "Urgent! On January 1, 1997, Parke-Davis will replace IV Dilantin with Cerebyx." This misleading marketing has also been presented by company representatives at my hospital. Again, I believe it is part of a corporate policy for selling the drug.

On page 2678 of the November 15 issue of AJHP, Of Special Interest In This Issue... for Managed Care Pharmacists stated: "Be sure to read Safety of fosphenytoin sodium and the editorial Fosphenytoin safety and economics. Learn more about the phenytoin prodrug that will replace Dilantin injection." Again, this wrongly implies that phenytoin injection will not be available.

I have a big problem with employees of drug companies writing clinical review articles for peer-reviewed journals. I believe there is no way such authors can provide a completely unbiased review of a topic, particularly a review of an expensive new drug like fosphenytoin. Even the AJHP editorialist who commented on fosphenytoin is paid by the manufacturer to lecture about this product. I have lost a lot of respect for AJHP because of those editorial decisions.

A few years ago, my hospital instituted the policy that phenytoin injection would not be administered into small veins of the hands or feet. If those veins were the only venous access available, phenytoin would have to be administered by another route. Guidelines for dilution of i.v. phenytoin were delineated. Since the implementation of these policies, we have had no reports of moderate or serious injection-site reactions to i.v. phenytoin.

Phenytoin sodium injection 100 mg costs my hospital less than $0.25; fosphenytoin sodium injection 150 mg (100 mg of phenytoin equivalents) costs $14.62. To maximize the benefits of fosphenytoin injection while minimizing our expense, our pharmacy and therapeutics committee has restricted the drug's use to (1) patients whose only venous access is a small vein in a hand or foot or (2) patients who could benefit from intramuscular injection of phenytoin. We believe that this restriction will control the use of a drug that is as effective as another drug but very expensive in comparison. This policy allows for fosphenytoin to be used in patients who are at high risk for injection-site reactions to i.v. phenytoin.

I hope that pharmacists will continue to analyze with a critical eye review articles and original research. Who pays the reviewer or researcher can make a big difference in what is written or reported.


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The editorial by Paloucek1 deserves comment on several points, particularly in view of the cost of fosphenytoin, a phenytoin prodrug.

Unlike Paloucek, I am not sure there will be "large economic benefits" from the use of fosphenytoin because of fewer admissions to emergency departments (EDs) or acute care settings. Patients with new-onset seizures will still need workups in the ED or acute care setting. Seizures in patients stabilized on anticonvulsant therapy can often be managed without admission. We should not forget that serum phenytoin concentrations can be adjusted and that many patients who receive a loading dose of phenytoin receive it orally. Oral loading doses of phenytoin are probably best given as prompt-release capsules of generic phenytoin sodium or an oral suspension of phenytoin; oral Dilantin products by Parke-Davis were used before generic formulations were available.

Cost savings from the use of fosphenytoin in the hospital are unlikely unless the shortened infusion times, compared with phenytoin, save so much nursing time that nursing positions are eliminated. As for "fewer adverse effects," fosphenytoin seems to be associated only with lower rates of headache, nausea, vomiting, nystagmus, ataxia, hyposthesia, and amblyopia,2 all of which can be caused by excess levels of phenytoin. Proper use of phenytoin should lower the rate of these adverse effects; even if they occur, they probably do not add greatly to the cost of care.

The mythical pharmacoeconomic advantages of fosphenytoin should not be accepted as real until we see published data. We all have heard arguments about pharmacoeconomic advantages of expensive new drugs, but the supporting studies never seem to materialize.

I am a little disturbed by Paloucek's suggestion that fosphenytoin be used as a sort of tolerance test for intramuscular injection volume in patients. I do not think counseling will do much to alleviate patient discomfort from injected volumes of >5 mL i.m. We should remember that the results of tolerance tests in selected patient populations3 may not be similar to the results in patients seen in everyday practice. The i.m. use of antiepileptic drugs should be small, since patients have fared well without this route of administration for more than 20 years.

I think pharmacists should view the introduction of fosphenytoin with a healthy skepticism. Fosphenytoin is a very expensive prodrug unlikely to yield pharmacoeconomic advantages for health systems. Its safety advantages over phenytoin, if any, are marginal. Proper use of generic phenytoin injection would take care of this issue.

Let us hope for a steady supply of generic phenytoin injection. Part of pharmacy's role is to promote the proper use of older drugs that, in most cases, are still effective.


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Letters