



Reducing Drug Interaction Alerts: Not So Easy

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Recently, the Institute for Safe Medication Practices (ISMP) devoted part of its newsletter to the problem of ignored drug interaction alerts that are generated by computerized screening systems.¹ Readers of this column in *Pharmacy Times* know that this is an issue we have discussed on other occasions over the past several years.² We strongly believe that this is a critically important problem for all pharmacists in all practice settings. Further, it is becoming increasingly significant for other health care providers as the screening systems reach new users; for example, following the initiation of computerized physician order entry.

The ISMP newsletter mentions a couple of ways that pharmacists have dealt with the problem of excessive computer alerts. Perhaps the most common approach is to choose a level of alerts that will be active and shut off the others. This will result in a reduction in sensitivity of the drug-interaction screening system; however, we believe that this is very risky and potentially dangerous for both patients and pharmacist/physician users. The risk to the patient is directly related to the potential severity of the interactions that are no longer being brought to the attention of the practitioner. The risk to the health care provider is the medical-legal exposure that such behavior invites. A patient, injured by a drug interaction that was in the screening system but not seen because it was deemed "unimportant" and excluded from review, will expect full compensation.

Various computerized screening programs sometimes use different severity ratings for the same interaction pairs.³ This is not surprising, because none of the databases use the same criteria to assign severity ratings to the drug interactions. What is more problematic are the differences in the actual interactions that are included in a particular severity class. We reviewed the interactions associated with sirolimus in 2 different computerized screening systems. One system included protease inhibitors, azole antifungals, and macrolide antibiotics as "major" interactions with sirolimus. The other system listed all these drugs as "moderate" interactions with sirolimus, but did list the lipid-lowering statins in the "major" category.

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Within each of the systems, drugs that might be expected to produce similar interactions (eg, various CYP3A4 inhibitors paired with an object drug that is a CYP3A4 substrate) are often divided between 2 or more classes. Protease inhibitors, azole antifungals, macrolide antibiotics, and diltiazem might all be in the same class with one object drug, even though these inhibitors have markedly different inhibitory potencies. For another object drug, one might find the azole antifungals and the protease inhibitors classified at the same severity level, with macrolides and other miscellaneous inhibitors placed in a lower severity level. Sometimes data are available to allow for differentiation based on the measured in vivo magnitude of the interaction, but most often such data are lacking. In the absence of specific data, the rules used to classify the interactions

become even more important.

Another way that interaction alerts may be reduced is by having pharmacists or physicians note interaction alerts that do not result in an adverse event and therefore can be considered overrated or simply incorrect. The interaction pairs so identified are then removed from the system or downgraded in severity. This sounds like a reasonable approach until the variable response to drug interactions is considered. It is common to see a 5- or 6-fold difference in the magnitude of the response between patients in drug interaction studies. Response variability in the real world is probably even greater. Many potentially serious drug interactions appear to produce adverse outcomes in a small subset of patients. If these adverse events occur once in every 100 patients who receive the interacting drugs, they are unlikely to be observed by any one practitioner. Deeming these interactions as unimportant would be in error. With the current emphasis on employing evidence-based decisions, it is remarkable how often decisions regarding potential drug interactions are made based on anecdotal observations. Of course, if we could get practitioners to collect their observations on potential drug interactions, we would be able to discern the frequency with which adverse events occur and make some informed judgments regarding an interaction's relative risk to patients.

Controlling unwanted drug interaction alerts is a uniform goal for all who use these systems. It is a difficult task to accomplish while balancing the needs of patient safety and smooth work flow. Customizing drug interaction lists to limit the number of alerts should be done by those with special knowledge. To do otherwise places both patients and practitioners at risk. **PT**

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