Legal Requirements for Managing Potential Drug-Drug Interactions
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Live Activity Handout
2 slides per page
Legal Requirements for Managing Potential Drug-Drug Interactions

ACTIVITY DESCRIPTION
Health care software provides alerts for numerous drug-drug interactions. Health professionals must determine their responsibilities based on a risk stratification of the importance of each potential drug-drug interaction. Legal requirements provide guidance on how risk stratification should be done, and what responses are legally required once a potential drug-drug interaction is identified.

TARGET AUDIENCE
The target audience for this activity is pharmacists, pharmacy technicians, and nurses in hospital, community, and retail pharmacy settings.

LEARNING OBJECTIVES
After completing this activity, the pharmacist will be able to:
- State the characteristics of a "significant" drug-drug interaction
- Illustrate legally appropriate management of potential drug-drug interaction
- Develop a system for detection and resolution of potential drug-drug interactions

After completing this activity, the pharmacy technician will be able to:
- Define the term "drug-drug interaction"
- Recognize legal responsibilities for managing drug-drug interactions
- Discuss the technician's role in managing drug-drug interactions

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What is the difference between a drug interaction (DI) and a drug-drug interaction (DDI)?

DI is a general term referring to interactions of drugs with foods, beverages, dietary supplements, underlying conditions, lab tests, or other drugs. DDI, a narrower term, refers specifically to interactions between two or more drugs.

How frequent are DDIs?

Hard to know. There are no comprehensive studies (outside sponsor studies—hard to access). The available data are case reports. Polypharmacy likely increases the incidence of DDIs.
More Frequently Asked Questions

Are all DDIs harmful?
No, some DDIs are actually beneficial, in that they enhance therapeutic effectiveness or decrease toxicity, or reduce drug costs.

Whose responsibility is it to detect, classify, and manage DDIs?
Usually computer software does the detection and classification. Pharmacists, prescribers, and patients must work together to manage DDIs.

How can I deal with “alert fatigue”?
Do your best to choose battles well, and focus primarily on the really important DDIs. We can all do better with this.

FDA Requirement for the DI Section of the PI

*Drug interactions.* (i) This section must contain a description of clinically significant interactions, either observed or predicted, with other prescription or over-the-counter drugs, classes of drugs, or foods (e.g., dietary supplements, grapefruit juice), and specific practical instructions for preventing or managing them. The mechanism(s) of the interaction, if known, must be briefly described. Interactions that are described in the “Contraindications” or “Warnings and Precautions” sections must be discussed in more detail under this section. Details of drug interaction pharmacokinetic studies that are included in the “Clinical Pharmacology” section that are pertinent to clinical use of the drug must not be repeated in this section.
How FDA Explains DDIs to the Public

Drug-drug interactions occur when two or more drugs react with each other. This drug-drug interaction may cause you to experience an unexpected side effect. For example, mixing a drug you take to help you sleep (a sedative) and a drug you take for allergies (an antihistamine) can slow your reactions and make driving a car or operating machinery dangerous.

The OBRA-90 Mandate

• ProDUR (Point of Sale or Distribution)
  • Patient Records (Reasonable effort)
  • Offer to Discuss (May be waived by patient/agent)
  • Potential Drug Therapy Problems Screen (No waiver by patient/agent)
    • Therapeutic Duplication
    • Drug-Disease Contraindication
    • Adverse Drug-Drug Interaction
    • Incorrect Drug Dosage
    • Incorrect Duration of Treatment
    • Drug-Allergy Interactions
    • Clinical Abuse/Misuse

• Implementation varies by state, pharmacy, pharmacist.
Classic Legal Case, Michigan—1996

- Physician prescribes tranylcypromine (Parnate) for patient & pharmacy processes accurately.
- Second physician prescribes clemastine/phenylpropanolamine (Tavist-D) for patient & pharmacy processes accurately.
- Computer alerts to DDI; pharmacist “did not personally see the interaction on the computer, probably because a technician overrode it.”
- Pharmacy ads said: “How can you avoid unwanted drug interactions? Simple. Get your prescriptions filled at [our pharmacy].”
- Patient dies; survivors sue for negligence.
- Pharmacy defense--no duty beyond accurate order processing.

What Should the Court Do?

- Dismiss the case, because drug-drug interactions cannot be completely prevented due to inadequacies of computer software.
- Dismiss the case, because order processing accuracy is the only reasonable legal expectation of pharmacists.
- Decline to dismiss the case, because the advertisement constituted a voluntary undertaking by the pharmacy to review and appropriately address drug-drug interactions.
- Decline to dismiss the case, because pharmacy standards require that pharmacists prevent all drug-drug interactions.
What the Court Actually Did

- Declined to dismiss the case, adopting the “voluntary undertaking” rule that expands pharmacist responsibilities beyond accuracy in order processing.
- “We hold that the defendant voluntarily assumed a duty to utilize the computer technology with due care.”
- “A reasonable juror could find that defendant’s advertisements were made to induce customers to utilize its pharmacy.”

What We Can Learn from the Case

- Patient expectations are important in determining pharmacist legal responsibilities, and patient expectations can be elevated through claims of professional expertise, such as claims in advertisements.
- Pharmacy technicians must refer drug-drug interactions alerts to pharmacists for evaluation and management.
- Courts no longer allow pharmacists to rely on technical accuracy in order processing as an absolute insurance policy against legal liability.
Legal Case, Indiana—2011

• Patient prescribed lisinopril, processed accurately by pharmacy.
• Prior to colonoscopy, patient prescribed OsmoPrep, processed accurately by pharmacy.
• Computer alert—potential for kidney damage resulting from interaction of OsmoPrep and lisinopril. Pharmacist “dismissed the warning.”
• After unsuccessful prep, second Rx for OsmoPrep. Alert repeated. Patient tells tech, who then tells pharmacist, “experiencing tingling running from her fingers to her elbows,” asks whether it may be OsmoPrep. Pharmacist says no, OsmoPrep doesn’t do that.
• Patient suffers kidney failure. Sues pharmacy for negligence.
• Pharmacy defense—no duty to warn or to decline OsmoPrep Rx.

What Should the Court Do?

• Dismiss the case, because the DDI is obscure and relatively unknown.
• Dismiss the case, because patients cannot rely on pharmacists for information about prescribed medications—that is the prescriber’s job.
• Decline to dismiss the case, because as medicine has become more specialized, patients have come to rely more on pharmacists, and this patient informed the pharmacist of unusual sensations possibly related to the drug.
• Decline to dismiss the case, because OsmoPrep is contraindicated for a patient who is using lisinopril.
What the Court Actually Did

• Declined to dismiss the case.
• “The practice of medicine has become more specialized and consumers have come to rely more and more upon pharmacists and pharmacies—which often have national resources to support their operations—for help in understanding the effects and interactions of various medications.”
• The pharmacist had a duty to the patient “either to warn of the side effects of OsmoPrep or to withhold the medication.”

What We Can Learn From The Case

• When patients raise questions about possible adverse effects of medications they have received and are using, careful listening skills should be employed to determine whether the concerns warrant attention.
• Under some circumstances there may be alternative solutions to potential problems with medication use. One possible solution is to warn the patient of possible adverse effects, and possible another solution is to withhold the medication. The potential outcomes of medication use may determine which solution is more appropriate.
Legal Case, Dist. Of Columbia—2012

• Patient is prescribed duloxetine and lisdexamfetamine by same physician at same time. Pharmacy processed both orders accurately.

• Computer alert warns not to dispense together “without first contacting the prescriber to confirm that the prescriber wants the patient to take both medications at the same time.” This was not done.

• Patient died. Sues pharmacy for negligence.

• Pharmacy defense—Avoiding DDI is the physician’s responsibility when there is a single prescriber.

What Should the Court Do?

• Dismiss the case, because there was a single prescriber and pharmacists can rely on prescribers to avoid problematic DDIs.

• Dismiss the case, because requiring a pharmacist to contact a physician regarding DDIs places the pharmacist in the position of practicing medicine without a license.

• Decline to dismiss the case, because DDI detection is an inherent part of accuracy in processing of any prescription.

• Decline to dismiss the case, because the computer alert placed the pharmacist on notice of a specific risk to the patient.
What the Court Actually Did

• Declined to dismiss the case.
• “The computer system alerted the pharmacist to the serious adverse interaction and of the substantial threat this posed.”
• The pharmacist “had a duty to warn because the patient was at risk of a specific, defined, and foreseeable harm about which the pharmacist knew or should have known.”
• Had the pharmacist “warned the patient or notified the doctor, the pharmacist would not have placed himself between the patient and his physician, and would not have practiced medicine without a license.”

What We Can Learn From the Case

• Although a single physician who prescribes potentially interacting drugs for the same patient at that same time is of less concern than the situation when there are two different physicians at two different times, this factor does not negate the responsibility of a pharmacist to manage a potential DDI.
• Consultation with a prescriber, when conducted in a collaborative matter in the best interest of patient safety, is not a threat to the physician-patient relationship, rather such a consultation supports the physician-patient relationship.
Legal Case, New Mexico—2017

- Patient was prescribed oxycodone and oxymorphone along with alprazolam by a pain management specialist.
- Patient died from “from multiple drug toxicity” related to the three drugs being used together.
- Survivors of patient sued pharmacy for negligence.
- Pharmacy contends that the prescriptions were legal and in the absence of evidence that prescribed drugs are being abused, a pharmacist has a responsibility to honor the prescriptions.

What Should the Court Do?

- Dismiss the case, because pharmacists are in no position to question the appropriateness of pain medications prescribed by a pain specialist.
- Dismiss the case, because it is impossible to predict when patients using pain medications will misuse them and die.
- Decline to dismiss the case, because pharmacist responsibilities extend beyond accurately processing legal prescriptions.
- Decline to dismiss the case because the epidemic of prescription drug abuse expands responsibilities for pharmacists to the public as well as to individual patients.
What the Court Actually Did

• Decline to dismiss the case.
• “The pharmacy’s expert advocates what amounts to a clerical-accuracy standard, requiring only that a pharmacist fill a prescription accurately.”
• “But a standard of care that requires nothing more of pharmacists in the circumstances presented here—involving repeated requests for high dosages of Schedule II opioids taken with Schedule IV benzodiazepines—than that they accurately fill an apparently valid prescription raises other concerns related to the potential harm to patients and the public at large.”

What We Can Learn From the Case

• The backdrop of prescription drug abuse and opioid addiction can expand judicial expectations of pharmacists—the context matters.
• Compliance with rules applicable to controlled substance prescription validity does not necessarily equate with the standard of care for preventing DDIs.
• Questions about medication appropriateness should be addressed prior to dispensing controlled substances, and since these are rarely emergency situations, they can wait for resolution—better safe than sorry.
In Conclusion

• Prioritize DDI management (worst first) by considering factors such as: Two prescribers, High level of risk, First time user. But…. There are no insignificant drug-drug interactions.
• Refer to the PI for authority, perhaps as prompted by computer-based information.
• Listen carefully to patients when they relate concerns about adverse drug effects.
• Consult with the prescriber—They created this problem; let them deal with it; and there is usually no rush.
• Document what you have done, and keep the documentation in a place where it can be found (electronically or physically).