

# Psychotropic Medications and Informed Consent: A Review

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**Background.** There is increasing concern about the safety of various psychotropic medications within the scientific community, as evidenced by the number of black-box warnings issued by the Food and Drug Administration (FDA), and “Dear Doctor” letters sent by pharmaceutical companies. Health-care providers need to be mindful of the increasing ethical, legal, and financial risks associated with prescribing these medications.

**Methods.** The English language literature was searched using Medline and the Internet using relevant terms such as “black-box warning,” “malpractice,” “off-label prescribing,” “informed consent,” “medications and pregnancy,” and with specific medication names, and appropriate articles and information were selected.

**Results.** Essential elements of obtaining informed consent when prescribing psychotropic medications to patients who are presumed to have capacity to make decisions regarding their health care are reviewed. In addition, specific concerns vis-à-vis use of psychotropics during pregnancy, off-label use, and combining medications are discussed. Finally, ten essentials of informed consent are noted, with a focus on practicing good medicine and avoiding malpractice law suits.

**Conclusions.** There are an ever increasing number of special interest groups and legal firms lining up against psychiatry and psychiatrists, especially when it comes to prescribing “powerful, potentially dangerous, mind-altering, psychotropic medications.” Obtaining informed consent has always been important, but never more so than now.

**Keywords** Psychotropic, Informed consent, Off-label use, Black-box warning, Malpractice

## INTRODUCTION

Every year up to 98,000 people may die in hospitals from medical errors (1) and more than 1.3 million people are injured due to medication errors (2). All such errors do not necessarily equate to malpractice, as only errors that are so egregious as to fall below the “standard of care” constitute malpractice. Total national costs (lost income, lost household production, disability, and health care costs) of preventable medical adverse events are estimated to be between \$17 billion and \$29 billion, of which health care costs represent over one-half (3). An analysis of data from the National Practitioner Data Bank revealed that between 1991 and 2004, there were 276,274 medical malpractice-related payments in the United States (4). A recent Medco national survey of 3,200 Americans, including 2,000 consumers, 300

practicing physicians, 450 retail pharmacists and 450 health benefit administrators, found that 70% of physicians, 55% of consumers, and 62% of pharmacists were more concerned about the safety of pharmaceuticals due to recent issues affecting several prescription drug classes (especially COX-2 inhibitors and antidepressants) currently on the market (5).

As medicine continues its evolution from medical paternalism to patient autonomy, and as patients become more educated about their medical conditions and medications via a variety of sources—especially the Internet—informed consent has become one of the central elements of the provider-patient relationship (6) and malpractice litigation (7).

With more and more concerns about psychotropic medications being raised, both from inside as well as outside the medical community, prescribing clinicians appear to be entering into a psychotropic perfect storm. One attorney described the changing landscape wherein four significant issues have converged to impact and heighten concern about the potential for more malpractice litigation related to psychopharmacology (8):

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1. Psychiatric malpractice lawsuits frequently include allegations of negligence related to the use of psychotropic medications because these drugs have become more and more vital to the treatment of mental disorders;
2. A host of controversies about the safety of psychotropic medications have been widely publicized, debated and considered in various forums (e.g., regulatory, research, clinical, drug industry, litigation, medical profession, patient advocacy);
3. Adverse drug events (ADEs) are a focus of attention by the patient safety movement in an effort to decrease medical errors; and,
4. Historically, advances in medical treatment tend to increase medical malpractice litigation.

Are these concerns having an impact on prescribing patterns, either because of concerns about patient safety or because of fears about litigation? A recent Harris poll found that 43% of physicians surveyed have avoided prescribing a particular drug that was appropriate for a patient, because they were aware that it might be involved in product liability litigation (9). The authors of the study also reported that 40% of the physicians surveyed knew of colleagues who have been sued by patients who experienced side effects from a drug, even when the drug was indicated and properly prescribed in their opinion. Ominously, the authors also found that 38% of the doctors polled knew of patients who had stopped taking a medication that was properly prescribed for them because the patient discovered the drug was involved in product liability litigation.

As of June 2006, drug manufacturers are required by the FDA to provide more concise and better organized patient information package insert sheets (10). The inserts will feature a table of contents, a toll-free number to encourage reporting of adverse drug events, the initial date of FDA product approval, and a section called "Highlights" that will summarize some of the most important drug information including benefits, risks, and usage. Any drug approved within the last 5 years will have new requirements implemented gradually over the next 7 years. New evidence related to the drugs will be updated and available online free of cost to healthcare professionals and consumers at <http://dailymed.nlm.nih.gov>.

This is an important step in helping to adequately educate patients about their medicines, and may help limit pharmaceutical product liability. However, as black-box warnings and "Dear Doctor" warning letters are issued, responsibility for giving patients informed consent about their medications shifts from pharmaceutical companies to prescribing clinicians. Ultimately, responsibility for helping patients make informed judgments about their medications rests squarely on the prescribing clinician's shoulders. According to one source (11):

A pharmaceutical manufacturer's primary duty is to physicians. Thus, a manufacturer generally will not be liable for a patient's injuries, as long as it adequately informed the physician of all known risks associated with a particular drug. In most cases, the prescribing physician is considered a "learned intermediary," which means that because of his or her superior medical

knowledge, and assuming he or she has been given adequate information from the manufacturer, he or she is in the best position to determine whether a particular drug or device is appropriate for a patient. Thus, the physician has the primary duty of advising the patient of the risks and side effects of a medication or medical device he or she prescribes."

### *Causes of Medical Malpractice*

Medical malpractice can occur in a large array of settings (3):

1. When a physician fails to properly diagnose the patient's condition, or delays in making the correct diagnosis;
2. When a physician fails to properly treat the patient's condition;
3. When a laboratory technician fails to properly conduct a test;
4. When a physician erroneously interprets an X-ray;
5. When a nurse or the hospital pharmacy gives the patient the wrong drug, or the wrong strength of the right drug;
6. When a physician or the hospital staff fails to take precautions against foreseeable complications;
7. ***When a physician fails to get the patient's informed consent for the medical treatment;***
8. When a physician prescribes a drug to which the patient is allergic, without first checking for such an allergy;
9. When a medical facility fails to provide proper nursing care; or
10. When a clinician fails to adequately monitor the patient, including obtaining appropriate clinical tests.

According to a 2004 analysis by The Psychiatrists' Program, the American Psychiatric Association-endorsed Psychiatrists' Liability Insurance Program, the most commonly cited categories of allegations in malpractice claims against psychiatrists are: incorrect treatment (32%), suicide/attempted suicide (17%), adverse drug reactions (15%), and incorrect diagnosis (nine percent) (12). Inadequate informed consent vis-à-vis medications could involve any of these areas, as many lawsuits against psychiatrists include allegations involving medications (13).

### *Informed Consent*

The American Medical Association (AMA) Code of Medical Ethics establishes informed consent as an ethical obligation of physicians. In addition to being an ethical obligation of physicians, legislation in all 50 states requires that patients be informed of all important aspects of a treatment and/or procedures, although the details of these laws and statutes differ greatly. Failure to obtain adequate informed consent in some settings renders a physician liable for negligence or battery and may constitute medical malpractice (14).

What is informed consent? Informed consent is an interactive process culminating in an agreement between a patient and a healthcare provider on a course of treatment. A signed consent form may help validate that the patient and provider have reached an agreement through this process, although it is not a

substitute for a meaningful discussion between the clinician and patient. Lack of informed consent or battery is often alleged in medical malpractice claims. Battery occurs when a patient is treated or even touched without prior consent. The only negligence that need be shown is not having obtained the consent of the patient (although damages must be proven according to the “reasonable man” standard).

Lack of informed consent occurs when a physician does not provide adequate information to the patient to make an informed decision. The patient must demonstrate that if adequate information had been provided, he or she (or a reasonable man in their stead) would have made a different decision. As in a general negligence claim, a plaintiff in a medical malpractice action must prove the elements of duty, breach of duty, causation and damages (15).

There exists a wide disparity in the degree of informed consent patients receive about their treatment options—from no discussion whatsoever to the use of highly interactive CD-ROM devices (16).

### *Elements of Informed Consent*

While the laws of informed consent vary from state to state, it is generally accepted that it is the healthcare provider’s duty to obtain the informed consent from each patient for each “procedure.” To satisfy this duty, the clinician should disclose sufficient information about the patient’s diagnosis, prognosis, proposed treatment, the risks and benefits associated with the proposed treatment, any alternative treatments, the risks and benefits of the alternatives, and the risks of forgoing treatment, should the patient refuse treatment. The patient should be asked whether all of his or her questions have been satisfactorily answered. If a patient expresses unanswered questions or concerns, he or she should not sign a consent form until the prescribing clinician has addressed all concerns.

Obtaining informed consent is not a onetime event; it is an ongoing process. For example, studies have shown that patients’ understanding of tardive dyskinesia (TD) remains limited, even after initial attempts at informed consent, and that ongoing education is essential (17).

### *Communication*

Communication forms the basis of all human relationships and effective communication is essential in discussing medications and forming strong therapeutic alliances with patients. Levinson and colleagues found that, at least for primary care physicians—but not surgeons—good communicators were sued less frequently than physicians who spent less time with their patients and did not communicate as well (18). Psychiatrists could be vulnerable to malpractice suits for violation of the standard of care where treatment was compromised due to ineffective communication (19). Title VI of the Civil Rights Act of 1964, which prohibits discrimination on the basis of

race, color, or national origin, and state human rights laws impose requirements on healthcare providers to ensure effective communication with patients who cannot fully communicate in English. In addition, healthcare providers are required by the Americans with Disabilities Act (ADA) of 1990 to ensure adequate communication with patients with hearing or vision impairments, irrespective of cost.

### *Documentation of the Informed Consent Process*

The most powerful defense against a meritless malpractice suit is a well-documented chart. It can often prevent a successful malpractice suit by providing evidence that the healthcare provider adequately evaluated the available information and made a good-faith effort, using his or her best judgment. Generally, the amount of documentation provided parallels the amount of protection gained (20).

All informed consent statements should be typed or written legibly, signed, and dated. (When it comes to legal documents, like medical records, dates are critically important.) Patients, and when appropriate, guardians, translators, and family members should also sign and date informed consent statements. It is critically important to have written consent for medication treatment from the parent/guardian when treating a minor.

### *Black Box Warnings*

A prominently displayed boxed warning, the so-called “black box,” is added to the labeling of drugs or drug products by the FDA when serious adverse reactions or special problems occur, particularly those that may lead to death or serious injury. A comprehensive study of black-box warnings by Lasser and colleagues of 548 new chemical entities approved in the United States between 1975 and 1999 revealed that 56 (10.2%) of the agents acquired a new black box warning or were withdrawn during the period of study (21). Forty-five drugs (8.2%) acquired one or more black box warnings and 16 (2.9%) were withdrawn from the market. The authors estimated the probability of acquiring a new black box warning or being withdrawn from the market over 25 years for any agent was 20%. They concluded that serious adverse drug reactions (ADRs) commonly emerge after FDA approval, and that the safety of new agents cannot be known with certainty until a drug has been on the market for many years. If a medication has a black-box warning, it must be discussed with the patient as part of obtaining informed consent.

While most black-box warnings are generally accepted by prescribing clinicians, some recent warnings—such as the warning about antidepressants and suicide risk, and the warning about atypical antipsychotics and the risk of cerebrovascular events in individuals with dementia—have generated much controversy (22, 23).

Although there are sometimes conflicting research studies and opinions about these warnings, prescribing clinicians are, however, obliged to strictly abide by them. Nevertheless, in a

recent analysis of 324,548 outpatients who received a medication in 2002, 2354 patients (0.7%) received a prescription in violation of a black box warning (24).

The consequences of black-box warnings are not insignificant. According to the FDA, at its peak in 2002, nearly 11 million antidepressant prescriptions were written for American children. However, since the FDA-mandated black-box warnings on antidepressants was issued in the spring of 2004, pediatric prescriptions for antidepressants plummeted 20% (25). Table 1 lists medications that have black box warnings.

### Correct Diagnosis

One cannot adequately prescribe and give appropriate informed consent unless one has correctly diagnosed the patient's medical

condition. In psychiatry, this is often not as easy as it sounds. For example, a recent survey of the National Practitioner Data Bank for the period February 1, 2004 through December 31, 2005, found that failure to diagnose was the leading reason for child-related payments (18%), followed by improper performance (9%), delay in diagnosis (9%), and improper management (6%) (26). Never assume diagnoses made by a preceding clinician are correct; always reconsider established diagnoses in new patients. Avoid treating the "chart virus" (i.e., the disease is in the medical record, not in the patient). Ongoing assessment of patients is needed and, as the clinical picture becomes clearer over time, a patient's diagnosis or diagnoses may change. It is, needless to say, imperative that a patient's medications match the patient's current diagnosis or diagnoses.

As a crosscheck as treatment progresses, it is often helpful to look first at a patient's medications and then at his or her

**Table 1** Medications with Black Box Warnings

Medications		Black Box Warnings
1	Typical Antipsychotics: haloperidol, fluphenazine, perphenazine, thioridazine, droperidol	1. Droperidol: unexpected cardiovascular deaths may occur at normal therapeutic doses. 2. Thioridazine: contraindicated in patients with a history of cardiac arrhythmia or congenital long QT syndrome.
2	Atypical Antipsychotics: aripiprazole, clozapine, olanzapine, paliperidone, quetiapine, risperidone, ziprasidone; olanzapine-fluoxetine combination (Symbyax)	1. Increased mortality in elderly with dementia-related psychosis.  2. Quetiapine: Suicidality in children, adolescents, and young adults up to age 25. 3. Clozapine: a) agranulocytosis, b) seizures, c) myocarditis, other adverse cardiovascular and respiratory effects, and d) use with benzodiazepines or other psychotropic drugs. Check weekly WBC count for first 6 months and biweekly thereafter. 4. Symbyax: Suicidality in children, adolescents, and young adults up to age 25.
3	Anticonvulsants: carbamazepine, gabapentin, lamotrigine, oxcarbazepine, tiagabine, topiramate, valproic acid	1. Carbamazepine: Aplastic anemia and agranulocytosis (complete pretreatment hematological testing should be obtained as a baseline, including CBC and platelet count, and once per year). 2. Valproic Acid: a) teratogenicity, b) hepatotoxicity, c) pancreatitis. Check baseline liver function tests (LFTs) and periodic monitoring (once per year). 3. Lamotrigine: serious rashes.
4	Lithium	Check serum levels at least every 2 months.
5	Antidepressants (SSRIs & SNRIs): citalopram, duloxetine, escitalopram, fluoxetine, paroxetine, sertraline, venlafaxine	Suicidality in children, adolescents, and young adults up to age 25.
6	Tricyclic & Tetracyclic Antidepressants: amitriptyline, clomipramine, desipramine, doxepine, imipramine, maprotiline, mirtazapine, nortriptyline, protriptyline, trimipramine	Suicidality in children, adolescents, and young adults up to age 25.
7	Monoamine Oxidase Inhibitors (MAOIs): isocarboxazid, phenelzine, tranylcypromine	Suicidality in children, adolescents, and young adults up to age 25.
8	Other Antidepressants: bupropion, nefazodone, selegiline, trazodone,	1. Suicidality in children, adolescents, and young adults up to age 25.  2. Nefazodone: Contraindicated in patients with "active liver disease"; withdraw therapy if AST or ALT levels > 3 times the upper limit of normal.
9	Stimulants: amphetamines, dexamethylphenidate, methylphenidate	Drug dependence
10	Non-Stimulant ADHA Drugs: atomoxetine, guanfacine	Atomoxetine: Suicidality in children, adolescents, and young adults up to age 25.
11	Anti-Alcohol Abuse Drugs: acamprosate, disulfiram, naltrexone	Naltrexone is contraindicated in acute hepatitis or liver failure, and its use in patients with active liver disease must be carefully considered in light of its hepatotoxic effects. Patients should be warned of the risk of hepatic injury and advised to stop the use of naltrexone and seek medical attention if they experience symptoms of acute hepatitis.

diagnosis or diagnoses to ensure that there is a clear reason why the patient is taking the medication in question. In the legal system, almost all situations are seen as black and white, not gray. When push comes to shove, the jurors, judges—and especially the plaintiff's attorney—want to know *exactly* what the plaintiff's diagnosis is, and why the prescribing clinician decided to treat their condition with a particular “powerful, potentially dangerous, mind-altering, psychotropic medication.” Under such circumstances, the prescribing clinician must be able to clearly explain their rationale for prescribing the medication—especially if the medication is prescribed off-label.

### ***Pregnancy Warning***

Half of all pregnancies in the United States are unplanned (27). Zing and colleagues recently reviewed the use of antidepressants during pregnancy and concluded the following (assuming pregnancy is discovered at six or more weeks of gestation in a woman already taking antidepressants) (28):

1. As many as 70% of women present with depressive symptoms during pregnancy and up to 16% fulfill criteria for major depression;
2. Antidepressants appear to be generally safe during pregnancy (although paroxetine was switched to Category D in December 2005 by the FDA);
3. Discontinuing antidepressant treatment during pregnancy dramatically increases the likelihood of recurrent depression; abruptly stopping treatment is unwise, as is gradual tapering;
4. Switching to an agent with more extensive reproductive safety is also inadvisable, as it exposes the fetus to yet another medication and inadvertently increases the likelihood of fetal exposure to maternal depression, since there is no certainty that the second agent will be effective;
5. Inquiring routinely about birth control at all visits when treating women during the reproductive years reduces the risks for mother and child, as some antidepressants (e.g., fluoxetine, sertraline, citalopram, bupropion, and venlafaxine) seem to carry fewer risks and could be chosen proactively prior to pregnancy; and
6. There is no risk-free alternative when advising women with histories of depression regarding treatment during pregnancy.

In each clinical encounter, the likelihood and risks of untreated prenatal depression must be weighed against the risks of fetal exposure to antidepressant medication.

Because many medications are excreted into the milk of nursing mothers, nursing is not recommended while on medications unless specifically recommended by the prescribing clinician.

Up to 30% of neonates exposed to SSRIs late in the third trimester may develop features of an abstinence syndrome, characterized by lack of crying, increased muscle tone, irritability, abnormal breathing, and disrupted sleep (29). Complications requiring prolonged hospitalization, respiratory support and tube feeding sometimes occur. Nevertheless, the existence of

this syndrome is insufficient reason to withhold antidepressant treatment in mothers at high risk for intrapartum or postpartum major depression (30).

Chambers and colleagues recently found a worrisome association between intrauterine exposure with SSRIs and an elevated risk of persistent pulmonary hypertension of the newborn (PPHN), a condition with significant morbidity and mortality (31). Other potential problems with SSRI intrauterine exposure include low birth weight and long-term neurodevelopment complications, but data are weak.

The FDA use-in-pregnancy rating system is as follows:

- Category A: controlled studies show no risk;
- Category B: no evidence of risk in humans;
- Category C: risk cannot be ruled out (There is a chance of fetal harm if the drug is administered during pregnancy; but the potential benefits may outweigh the potential risk);
- Category D: Positive evidence of risk;
- Category X: contraindicated in pregnancy.

Most psychotropic medications fall into Category C, while lithium, benzodiazepines, amitriptyline, depakote, and paroxetine fall into Category D.

McKenna and colleagues prospectively studied 151 pregnancy outcomes that included exposure to olanzapine (N = 60), risperidone (N = 49), quetiapine (N = 36), and clozapine (N = 6), and concluded that atypical antipsychotics do not appear to be associated with an increased risk for major malformations (32).

The evidence that led the FDA to warn that paroxetine taken during the first weeks of pregnancy increases the risk of birth defects, including serious heart defects, was recently disputed by German researchers (33). However, this has not stopped a wave of new litigation surrounding this issue (34).

### ***Off-Label Use***

Off-label use of a medication is the use of an FDA-approved medication for non-FDA-approved indications, use in doses higher than approved, or use for periods longer than approved. A recent study found that off-label use of antidepressant, anticonvulsant, and antipsychotic medications is highly prevalent (35). Because of this, some have suggested that more vigorous efforts should be made to scrutinize under-evaluated off-label prescribing that may compromise patient safety (36). However, in general, courts have ruled that off-label use is an accepted practice, that off-label use does not mean “experimental,” and in and of itself is not a risk (37). Nevertheless, in some jurisdictions, practitioners who go outside guidelines established by Physicians' Desk Reference (PDR) may be liable; for example, a practitioner in Illinois who goes outside PDR guidelines is presumed to be guilty of malpractice and must prove why he or she was not negligent (as opposed to a plaintiff proving that the practitioner was negligent) (38).

According to Humphrey Taylor, chairman of The Harris Poll at Harris Interactive, “There is a massive public ignorance

of 'off-label prescribing,' the widespread practice of prescribing drugs to treat diseases where the FDA has not approved this use of the drug. There are several strong arguments in favor of off-label prescribing, but these data [from a poll of 2,148 adults] suggest that it is a potentially risky issue for both physicians and the pharmaceutical industry (39)." The nationwide poll found that 51% of respondents believe that a doctor can prescribe drugs only for the diseases for which they have been approved by the FDA, 48% believe that doctors "should not be allowed" to prescribe a drug for diseases for which that drug has not been approved, and only half of Americans think that this practice actually happens "very often" (23%) or "often" (33%)—signifying that the reality of off-label prescribing has not penetrated the consciousness of most health consumers.

Failure to use appropriate medication is often claimed when complications result from off-label prescribing. To protect yourself from such a claim, carefully document:

1. The rationale for using off-label medication;
2. Reasons that FDA-approved medications were not selected; and
3. The fact that you informed the patient about the off-label medication's side effects, risks, and benefits.

Prescribing medications in doses higher than FDA-approved doses is considered off-label prescribing. When prescribing off-label, it is important to make sure that there is scientific support for such prescribing. For example, based on available data, high dose antidepressant treatment of patients refractory to medium-dose treatment is recommended for tricyclic compounds, but not for SSRIs (40).

Gabapentin off-label prescribing increased from \$23 million in 1993 to \$2.7 billion in 2004, becoming one of Pfizer's best-selling products (41). In 2004, a class-action lawsuit was filed against Pfizer on behalf of patients who allegedly suffered adverse effects when the medication was prescribed for off-label uses (42). The law firm filing the suit claims to have collected the names of 160 people who committed suicide and 2,000 more who attempted suicide while taking gabapentin.

### ***Driving a Motor Vehicle or Use of Machinery***

In any particular patient, any medication may impair attention span, judgement, thinking, concentration, memory, reaction time, or motor skills. According to one source, injured motorists and pedestrians increasingly are attempting to impose liability on physicians who prescribed medications that may have affected a patient's driving ability (43). Authors of one study of lorazepam and driving impairment determined that lorazepam is capable of causing significant impairment to driving and psychomotor abilities, independent of the concentration detected (44). Patients should be cautioned about using potentially hazardous machinery, including motor vehicles, until they are certain that the medication in question does not affect their ability to safely engage in such activities. This warning should be given for all medications.

### ***Alcohol***

Drugs, including alcohol, are detected commonly among those involved in motor vehicle accidents, with studies reporting up to 33% of accident-involved drivers positive for drugs. Cannabis is generally the most common drug detected in accident-involved drivers, followed by benzodiazepines, cocaine, amphetamines and opioids (45). One study of 322 motor vehicle accident victims found that, after alcohol, marijuana and benzodiazepines were the most frequently detected drugs. (46) Patients should be warned to avoid drinking alcohol when taking prescription medications, because alcohol can potentiate adverse effects.

### ***Combining Medications***

According to the data from the 1989 National Ambulatory Medical Care Survey, patients seen by a psychiatrist were six times more likely to receive multiple psychotropic medications, as compared with those seen by a primary care physician, and a recent pharmacoepidemiology study found Veterans Affairs Administration outpatients on antidepressants were on more medications than age-matched and gender controls not on antidepressants (47).

Although pharmacies cross-check for potentially dangerous interactions when filling a new prescription, that is not enough. Pharmacies may not know all of a patient's medical conditions nor may they be aware of other drugs the patient is taking. A recent study by Medco found that older patients are most at risk because they typically have more medicines and more doctors (48). The analysis found that nearly one-fourth of the seniors filled prescriptions at three or more pharmacies, and that the number of doctors seen by a patient also plays a role in medication errors. Having multiple doctors is not unusual—almost a quarter of seniors get prescriptions from five or more doctors, according to Medco's analysis of drug insurance claims from 2.4 million adults in 2004. Seniors who got prescriptions from two doctors got an average of 27 prescriptions a year and were at risk of 10 errors on average; those with five doctors got an average of 42 prescriptions annually and were at risk for 16 errors, the analysis found.

Opioid-based prescription painkillers have surpassed cocaine and heroin as the cause of accidental drug overdose deaths in the United States, according to a team of CDC researchers (49).

When taking multiple medications, there is always a chance that the side effects of any of the medications may be increased. This may be especially true when combining several medicines that can cause dizziness, drowsiness, or sedation. Patients should be warned about such adverse effects when medications are combined, and this goes for over-the-counter (OTC) medications and herbal preparations as well.

Following are several examples of fatal drug-drug interaction and successful lawsuits (50):

1. A 26-year-old woman, prescribed amitriptyline, alprazolam (unknown dosage, nightly), quetiapine (400 mg bid), extended-release venlafaxine (225 mg bid), and promethazine (100 mg bid), was found dead in her home. An autopsy revealed amitriptyline toxicity as the cause of death. The medical examiner noted "a much larger concentration of the metabolite nortriptyline in the liver versus the parent drug," suggesting a metabolism problem, rather than an overdose, caused the toxic build-up. The patient's estate claimed that amitriptyline was cardiotoxic at the prescribed dosage and combined with the other medications used and that the patient was not properly monitored. A \$2.3 million settlement was reached.
2. A 40-year-old woman was under a psychiatrist's care for anxiety and depression. The psychiatrist continued sertraline, which the woman had been taking, and added nortriptyline. Several weeks after the patient began taking the medications together, she had a fatal cardiac arrest. The patient's estate argued that: (A) toxic levels of the antidepressants caused her death, (B) sertraline and nortriptyline should not be taken concurrently because one drug inhibits clearance of the other, and (C) the psychiatrist should have monitored the patient to make sure sertraline and nortriptyline levels remained normal. The defendant was awarded \$3 million. A statutory capitation reduced the award to \$1.65 million.

### *Ten Essentials of Informed Consent*

1. Document the patient's current diagnosis. (Informed consent begins with a correct diagnosis and rationale for treatment, and the diagnosis may change over time.)
2. Comply with the recommendations provided in medication product inserts (PI), FDA warnings, and "Dear Doctor" letters.
3. Comply with treatment guidelines, and consider taking a risk-management program provided by your malpractice insurance carrier.
4. Periodically review the patient's medical history—including but not limited to allergies to medications, alcohol and/or drug abuse, history of seizures, heart disease, COPD, liver, kidney or thyroid disease, syncope, diabetes, hypertension, pregnancy and possibility of becoming pregnant—and act accordingly.
5. Review all other medications, OTC preparations, and herbs the patient may be taking, and look for possible drug-drug and herb-drug interactions; review this periodically.
6. Be mindful of the patient's family psychiatric and medical history, especially histories of obesity, diabetes, hypertension, hyperlipidemia, heart disease and sudden death.
7. Rule out organic illness; obtain baseline and monitoring bloodwork and other laboratory tests as necessary; obtain height, weight, blood pressure, and girth circumference as warranted; monitor for signs of TD (using AIMS, for example) as warranted.
8. Develop a strong therapeutic alliance with the patient and communicate effectively. Obtain informed consent with the patient (and, hopefully, with his or her significant other and/or family members) frequently (obtaining informed consent is not a one-time process).
9. Review possible drug-drug interactions (including use of other "medical" medications—especially opioids), use of alcohol while taking medications, risks of driving and/or use of machinery while on medications, risks of stopping medications, and any other relevant factors.
10. Document the informed consent process in the chart through use of a form and/or a progress note. (Remember, if it's not in the chart, it didn't happen!)

Finally, it is important to report adverse drug reactions to the FDA and drug manufacturers when they occur; doing so will accelerate the dissemination of information about adverse reactions and help us all make better decisions about the use of psychotropic medications.

### *CONCLUSIONS*

The ultimate choice of a particular psychotropic medication for any individual patient should depend on evidence of efficacy and effectiveness along with other variables such as safety and tolerability, pharmacokinetic properties, formulations, possible drug-drug interactions, and expense. Whenever possible, medications with FDA-approved indications should be selected, and when this is not possible, off-label use should be discussed with the patient.

Pertinent information available in psychotropic product inserts (PIs), FDA warnings, and pharmaceutical "Dear Doctor" letters, form the basis for appropriate informed consent.

A malpractice suit can have a devastating effect on the prescribing clinician, but can be avoided by practicing good medicine, developing a strong therapeutic alliance, and engaging in an ongoing process of informed consent and good documentation.

Disclaimer: The information provided in this article should not be construed as all encompassing. For example, drug-drug interactions and use of medications in patients with impaired renal or hepatic function have not been discussed in detail. It is not intended to be legal advice. It is meant to assist the prescribing clinician in practicing good medicine, especially with regard to informed consent vis-a-vis psychotropic medications. To ensure a full understanding of a particular medication, review the package insert.

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