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Pharmacy

Today

*Health-System
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Glucose regulation with
second-generation
antipsychotics 18

Counseling patients
with depression 20

Identifying payers for
MTM services 28

FDA approval does not
preclude manufacturer
liability HSE 5

◀ RoseMarie Babbitt makes
corporate compliance her
specialty HSE 6



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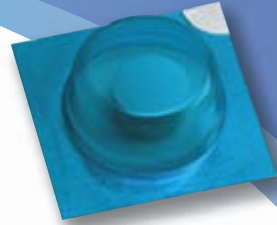
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Avoiding cookbook pharmacy

Evidence-based medicine (EBM) has been criticized by more than a few practitioners who continue to prefer “the way we’ve always done it” over what the data show. A recent editorial in the *Archives of Internal Medicine* (April 13, pages 649–50) gives a name to this phenomenon. Playing off the title of Leonard Mlodinow’s recently published book, Wayne B. Jonas, MD, wrote that this “drunkard’s walk,” with respect to EBM, is further proof that “humans are notoriously bad at, and often even averse to, the straightforward use of data and probability in making daily judgments.”

Within the nation’s hospitals and health systems, pharmacists are emerging as important champions of EBM, defining relevant questions, investigating the best evidence, proposing protocols and algorithms for consideration by pharmacy and therapeutics (P&T) committees, and enforcing adherence to these best practices. The fact that pharmacists are in danger of becoming perceived as the bearers of bad tidings may be one of the things that keeps you awake at night. This situation can be worsened if enforcement is taken to an extreme or interventions are applied in clinically

irrelevant situations.

How can pharmacists effectively bring EBM into patient care each day

Pharmacists are emerging as important champions of evidence-based medicine.

when it comes to supporting anticoagulation, antibiotic therapy, parenteral nutrition, and nutritional support/electrolyte management? Here are few ideas that will enhance your chances of success.

- Be sure that the pharmacy has more than a rubber stamp from the P&T committee and that the affected physicians have had meaningful input into the proposed interventions. These are medical staff decisions; while pharmacy may be the champions, the prescribers need to have real input beforehand.
- Be ready to counter the argument

that interventions are based on price rather than on good medicine. Costs are important and relevant in today’s health care environment, but they are not usually included in discussions about EBM. In fact, sometimes the best medication may be more expensive, but will actually save money for the health system in the long run.

- Before you make the call to the prescriber about a needed change in therapy, have a plan for what you will say and how you will answer any questions you can anticipate. Look up your information and have your facts ready.
- Be flexible. The prescriber may have a legitimate reason for using a medication differently than called for in a protocol. Be sure to document this information so that the prescriber does not get multiple telephone calls about the same issue.
- Don’t call prescribers too quickly; be sure that the prescribed therapy falls outside recommended guidelines before you call.
- If you’re contacting a specialist about medications used routinely in that part of medicine, be doubly certain of your position and your facts beforehand.

—L. Michael Posey, BPharm



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Close monitoring of the blood pressure is required during therapy. CARDENE I.V. is contraindicated in patients with known hypersensitivity to the drug and in patients with advanced aortic stenosis. Reduction of diastolic pressure and reduced afterload may worsen rather than improve myocardial oxygen balance. Caution is advised when administering CARDENE I.V. to patients with impaired renal or hepatic function, in combination with a beta-blocker in patients with congestive heart failure, or portal hypertension. Observe caution in patients with significant left ventricular dysfunction due to possible negative inotropic effect. CARDENE I.V. gives no protection against the dangers of abrupt beta-blocker withdrawal; beta-blocker dosage should be gradually reduced. Levels of cyclosporine should be closely monitored during therapy. The most common side effects of CARDENE I.V. are headache (14.6%), hypotension (5.6%), nausea/vomiting (4.9%), and tachycardia (3.5%). Less frequent adverse effects, in each case occurring at 1.4%, include ECG abnormalities, postural hypotension, ventricular extrasystoles, injection-site reaction, dizziness, sweating and polyuria.

Please see next page for brief summary of prescribing information.

References: 1. Ruble J. Impact safety, efficiency, and the bottom line with premixed IV products. Pharm Purchasing Prod. February 2008. <http://www.pppmag.com>. Accessed August 28, 2008.

For more information, visit: www.cardeneiv.com or e-mail us at cardeneiv@ekrtx.com.

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CARDENE® I.V.

(nicardipine hydrochloride)

Premixed Injection in either 5% Dextrose or 0.83% Sodium Chloride

Brief Summary of Prescribing Information

Cardene® I.V. Premixed Injection in 5% Dextrose

40 mg in 200 mL (0.2 mg/mL)

Each mL contains 0.2 mg nicardipine hydrochloride, 50 mg dextrose hydrate, USP, and 0.0384 mg citric acid, anhydrous, USP. Hydrochloric acid and/or sodium hydroxide may have been added to adjust pH to 3.7 to 4.7.

Cardene® I.V. Premixed Injection in 0.83% Sodium Chloride

40 mg in 200 mL (0.2 mg/mL)

Each mL contains 0.2 mg nicardipine hydrochloride, 8.3 mg sodium chloride, USP, 0.0384 mg citric acid, anhydrous USP, and 3.84 mg sorbitol, NF. Hydrochloric acid and/or sodium hydroxide may have been added to adjust pH to 3.7 to 4.7.

INDICATION AND USAGE: For the short-term treatment of hypertension when oral therapy is not feasible or desirable. For prolonged control of blood pressure, patients should be transferred to oral medication as soon as their clinical condition permits.

CONTRAINDICATIONS: In patients with known hypersensitivity. Cardene® I.V. is also contraindicated in patients with advanced aortic stenosis because part of the effect of Cardene® I.V. is secondary to reduced afterload. Reduction of diastolic pressure in these patients may worsen rather than improve myocardial oxygen balance.

WARNINGS: BETA-BLOCKER WITHDRAWAL: Nicardipine is not a beta-blocker and provides no protection against the dangers of abrupt beta-blocker withdrawal; any such withdrawal should be by gradual reduction of dose of beta-blocker. **RAPID DECREASES IN BLOOD PRESSURE:** No clinical events have been reported suggestive of a too rapid decrease in blood pressure with Cardene® I.V. However, as with any antihypertensive agent, blood pressure lowering should be accomplished over as long a time as is compatible with patient's clinical status.

USE IN PATIENTS WITH ANGINA: Induction or exacerbation of angina has been seen in less than 1% of coronary artery disease patients treated with Cardene® I.V. Increased frequency, duration, or severity of angina has been seen with chronic oral Cardene® therapy.

USE IN PATIENTS WITH CONGESTIVE HEART FAILURE: Cardene® I.V. reduced afterload without impairing myocardial contractility in preliminary hemodynamic studies of CHF patients. However, *in vitro* and in some patients, a negative inotropic effect has been observed. Exercise caution when using Cardene® I.V., particularly in combination with a beta-blocker, in patients with CHF or significant left ventricular dysfunction.

USE IN PATIENTS WITH PHENOCROMOCYTOMA: Limited clinical experience exists in these patients; therefore, exercise caution when administering Cardene® I.V.

PERIPHERAL VEIN INFUSION SITE: To minimize the risk of peripheral vein irritation, it is recommended that the site of infusion of Cardene® I.V. be changed every 12 hours.

PRECAUTIONS: GENERAL: Blood pressure: Because Cardene® I.V. decreases peripheral resistance, monitoring of blood pressure during administration is required. Cardene® I.V., like other calcium channel blockers, may occasionally produce symptomatic hypotension. Caution is advised to avoid systemic hypotension when administering the drug to patients who have sustained an acute cerebral infarction or hemorrhage.

Use in Patients with Impaired Hepatic Function: Nicardipine is metabolized in the liver; exercise caution in patients with impaired liver function or reduced hepatic blood flow; consider use of lower dosages. Nicardipine administered intravenously has been reported to increase hepatic venous pressure gradient by 4 mm Hg in cirrhotic patients at high doses (5 mg/20 min). Use Cardene® I.V. with caution in patients with portal hypertension.

Use in Patients with Impaired Renal Function: When Cardene® I.V. was given to mild to moderate hypertensive patients with moderate renal impairment, a significantly lower systemic clearance and higher AUC was observed. These results are consistent with those seen after oral administration of nicardipine. Careful dose titration is advised when treating renally-impaired patients.

DRUG INTERACTIONS: Since Cardene® I.V. may be administered to patients already being treated with other medications, including other antihypertensive agents, careful monitoring of these patients is necessary to detect and promptly treat any undesired effects from concomitant administration.

Beta-Blockers: In most patients Cardene® I.V. can safely be used with beta-blockers. However, exercise caution when using this combination in CHF patients (see WARNINGS).

Cimetidine: Cimetidine has been shown to increase nicardipine plasma concentrations following Cardene® capsule administration; carefully monitor concomitant use. Data with other histamine-2 antagonists are not available.

Digoxin: Studies have shown that Cardene® capsules usually do not alter digoxin plasma concentrations; however, as a precaution, evaluate digoxin levels when initiating concomitant Cardene® I.V. therapy.

Fentanyl anesthesia: Hypotension has been reported during fentanyl anesthesia with concomitant use of a beta-blocker and a calcium channel blocker. Even though such interactions were not seen during clinical studies with Cardene® I.V. (nicardipine hydrochloride), an increased volume of circulating fluids might be required if such an interaction were to occur.

Cyclosporine: Concomitant use of Cardene® capsules and cyclosporine results in elevated plasma cyclosporine levels. Monitor cyclosporine plasma levels closely and reduce its dose accordingly.

In vitro interaction: The plasma protein binding of nicardipine was not altered when therapeutic concentrations of furosemide, propranolol, dipyrindamole, warfarin, quinidine, or naproxen were added to human plasma *in vitro*.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY: Rats treated with nicardipine in the diet (at doses of 5, 15, or 45 mg/kg/day) for two years showed a dose-dependent increase in thyroid hyperplasia and neoplasia (follicular adenoma/carcinoma). One- and three-month rat studies have suggested that these results are due to a nicardipine-induced reduction in plasma thyroxine (T₄) levels, with resultant increase in plasma levels of thyroid stimulating hormone (TSH). Mice treated with nicardipine in the diet (at concentrations calculated to provide daily dosage levels of up to 100 mg/kg/day) for up to 18 months showed no evidence of neoplasia of any tissue and no evidence of thyroid changes. There was no evidence of nicardipine-induced thyroid effects in dogs (treated with nicardipine at doses up to 25 mg/kg/day for one year) or in man. Nicardipine did not display mutagenic potential in genotoxicity tests conducted in microbes, mice and hamsters. No fertility impairment was seen in male or female rats administered oral nicardipine doses as high as 100 mg/kg/day (50 times the 40 mg TID maximum recommended human dose [MRHD]) in man, assuming a patient weight of 60 kg.

PREGNANCY CATEGORY C: There are no adequate and well-controlled studies in pregnant women; Cardene® I.V. should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Cardene® I.V. administered at doses up to 5 mg/kg/day and up to 0.5 mg/kg/day to pregnant rats and rabbits, respectively, produced no embryotoxicity or teratogenicity. Embryotoxicity, but not teratogenicity, was seen at 10 mg/kg/day in rats and at 1 mg/kg/day in rabbits. Nicardipine was embryocidal at oral doses of 150 mg/kg/day, given during organogenesis, to pregnant white rabbits but not at 50 mg/kg/day (25 times MRHD). No adverse effects on the fetus were observed when albino rabbits were treated, during organogenesis, with up to 100 mg/kg/day of nicardipine. Pregnant rats receiving oral doses up to 100 mg/kg/day (50 times MRHD) showed no evidence of embryolethality or teratogenicity. However, dystocia and reductions in birth weights, neonatal survival, and neonatal weight gain were noted. There are no adequate and well-controlled studies in pregnant women. Cardene® should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus.

NURSING MOTHERS: Studies in rats have shown significant concentrations of nicardipine in maternal milk. Therefore, use in nursing mothers is not recommended.

PEDIATRIC USE: Safety and efficacy in patients under the age of 18 have not been established.

USE IN THE ELDERLY: In clinical studies, no significant difference was observed in the antihypertensive effect of Cardene® I.V. in patients >65 years compared to other adult patients.

ADVERSE EXPERIENCES: 244 patients participated in two multicenter double-blind, placebo-controlled trials of Cardene® I.V. Adverse effects were generally not serious and most were expected effects of vasodilation. Some adverse effects required dosage adjustments. Therapy was discontinued in approx. 12% of patients due mainly to hypotension, headache and tachycardia. The following numbers represent percentage of patients with adverse experiences during the double-blind portion of controlled trials with Cardene® I.V. (n=144) versus Placebo (n=100), respectively.

Percent of Patients with Adverse Experiences
During the Double-Blind Portion of Controlled Trials

Adverse Experience	Cardene® (n=144)	Placebo (n=100)
Body as a Whole		
Headache	14.6	2.0
Asthenia	0.7	0.0
Abdominal pain	0.7	0.0
Chest pain	0.7	0.0
Cardiovascular		
Hypotension	5.6	1.0
Tachycardia	3.5	0.0
ECG abnormality	1.4	0.0
Postural hypotension	1.4	0.0
Ventricular extrasystoles	1.4	0.0
Extrasystoles	0.7	0.0
Hemopericardium	0.7	0.0
Hypertension	0.7	0.0
Supraventricular tachycardia	0.7	0.0
Syncope	0.7	0.0
Vasodilation	0.7	0.0
Ventricular tachycardia	0.7	0.0
Digestive		
Nausea/vomiting	4.9	1.0
Injection Site		
Injection site reaction	1.4	0.0
Injection site pain	0.7	0.0
Metabolic and Nutritional		
Hypokalemia	0.7	0.0
Nervous		
Dizziness	1.4	0.0
Hypesthesia	0.7	0.0
Intracranial hemorrhage	0.7	0.0
Paresthesia	0.7	0.0
Respiratory		
Dyspnea	0.7	0.0
Skin and Appendages		
Sweating	1.4	0.0
Urogenital		
Polyuria	1.4	0.0
Hematuria	0.7	0.0

RARE EVENTS: The following events have been reported in clinical trials or in the literature with intravenous use of nicardipine. **Body as a Whole:** fever, neck pain. **Cardiovascular:** angina pectoris, atrioventricular block, ST segment depression, inverted T wave, deep vein thrombophlebitis. **Digestive:** dyspepsia. **Hemic and Lymphatic:** thrombocytopenia. **Metabolic and Nutritional:** hypophosphatemia, peripheral edema. **Nervous:** confusion, hypertonias. **Respiratory:** respiratory disorder. **Special Senses:** conjunctivitis, ear disorder, tinnitus. **Urogenital:** urinary frequency. **Sinus node dysfunction and myocardial infarction,** possibly due to disease progression, have been seen in patients on chronic oral nicardipine therapy.

OVERDOSAGE: Several overdoses with orally administered nicardipine have been reported. One adult patient allegedly ingested 600 mg of nicardipine (standard [immediate release] capsules), and another patient, 2160 mg of the sustained release formulation of nicardipine. Symptoms included marked hypotension, bradycardia, palpitations, flushing, drowsiness, confusion and slurred speech. All symptoms resolved without sequelae. An overdose occurred in a one year old child who ingested half of the powder in a 30 mg nicardipine standard capsule. The child remained asymptomatic. Based on results obtained in laboratory animals, lethal overdose may cause systemic hypotension, bradycardia (following initial tachycardia) and progressive atrioventricular conduction block. Reversible hepatic function abnormalities and sporadic focal hepatic necrosis were noted in some animal species receiving very large doses of nicardipine. For treatment of overdose, standard measures including monitoring of cardiac and respiratory functions should be implemented. The patient should be positioned so as to avoid cerebral anoxia.

Frequent blood pressure determinations are essential. Vasopressors are clinically indicated for patients exhibiting profound hypotension. Intravenous calcium gluconate may help reverse the effects of calcium entry blockade.

DOSAGE AND ADMINISTRATION: DOSAGE MUST BE INDIVIDUALIZED depending on severity of hypertension and patient response. Monitor blood pressure during and after the infusion; avoid too rapid or excessive reductions in systolic or diastolic blood pressure.

Cardene® I.V. premixed injection is available as a single-use, ready-to-use, iso-osmotic solution for intravenous administration in a 200 mL GALAXY container with 40 mg (0.2 mg/mL) nicardipine hydrochloride in either dextrose or sodium chloride. No further dilution is required. Cardene® I.V. premixed injection should not be combined with any product in the same intravenous line or premixed container. Protect from light until ready to use.

See package insert for full prescribing information.

To report an adverse event or for questions of a medical nature, please call 1-877-207-5002

Cardene® I.V. is a registered trademark of EKR Therapeutics, Inc.

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Baxter Healthcare Corporation
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THERAPEUTICS

U.S. Supreme Court affirms manufacturers' liability

FDA approval not a shield in Vermont case

In a ruling handed down on March 4, 2009, the U.S. Supreme Court restored the status quo in terms of manufacturers' responsibilities under state law for the provision of information concerning the drugs they market. This dispels manufacturers' reliance on "preemption"—a legal notion, advanced by the George W. Bush administration, that would have given drug manufacturers blanket immunity from lawsuits when their product has been approved by FDA—as a defense in such cases. While noting that "compounding pharmacies may be treated under state law as manufacturers," Washington State University law professor William Hassett, BPharm, told **Today** that this verdict only obliquely affects the profession of pharmacy. "The specific verdict ... is relevant ... only to manufacturers, since it eliminates or restricts one kind of defense to product liability suits against them," Hassett said. Levine's suit against the Vermont clinic for negligence, Hassett continued, "illustrates how a pharmacist could have had a positive input on the patient outcome by educating the physician and physician assistant concerning the known dangers of I.V. push of promethazine."

The 6-3 verdict upheld a ruling made by the Vermont Supreme Court concerning *Wyeth v Levine*, in which plaintiff Diana Levine, a musician and teacher, was awarded \$6.7 million in damages from the drug manufacturer. The lower half of Levine's right arm was amputated after she was injected with Wyeth's promethazine (Phenergan) via I.V. push injection.

The case

On April 7, 2000, Levine went to her local clinic for treatment of a severe migraine. As with the past migraines, she was given meperidine hydrochloride (Demerol—sanofi-aventis) and promethazine for nausea; however, on this occasion, the drugs were given via push I.V. rather than

intramuscularly. Then, according to the Supreme Court opinion, promethazine "entered Levine's artery, either because the needle penetrated an artery directly or because the drug escaped from the vein into surrounding tissue (a phenomenon called 'perivascular extravasation') where it came in contact with arterial blood."

A gangrene infection developed, necessitating two emergency procedures, with physicians amputating Levine's right hand and then her right forearm. Before filing the claim against Wyeth, Levine was awarded \$700,000 in a malpractice settlement with the Vermont clinic.

While promethazine's product labeling complied with FDA regulation and warned against arterial injection, it did not specifically warn against I.V. push administration. Wyeth had submitted a request to add such a warning, but this request was denied by FDA. Levine argued that even if promethazine's labeling technically complied with FDA requirements as they stood, the adequacy of the warning was still not established, and Wyeth had a responsibility to warn against adverse events about which it had data.

At stake besides restitution for a lost career and pain and suffering was the principle of "preemption," defined as the legal notion that FDA approval of a drug supersedes state law claims challenging safety, efficacy, or labeling and makes the agency the final word on safety and effectiveness. Wyeth appealed the Vermont court's decision and maintained that compliance with both state law and FDA labeling requirements was impossible, as the requirement to comply with state law to preclude the I.V. push method would "obstruct the purposes and objectives" of the Federal Food, Drug, and Cosmetic Act and its implementation by FDA. The Supreme Court agreed to review the case. Levine, in response, filed her own appeal with the Supreme Court.

Court's opinion

Writing for the majority, Justice John Paul Stevens emphasized that Congress did not intend FDA oversight to be the exclusive means of ensuring drug safety and effectiveness. Stevens also pointed out that FDA's limited resources place the responsibility on manufacturers to alter their drug labeling when needed, and noted that an FDA regulation allows manufacturers to add contraindications, warnings, precautions, and adverse reactions without prior agency approval. In dissent, Justice Samuel Alito wrote, "The physician assistant ... disregarded at least six separate warnings that are already on Phenergan's labeling, so [Levine] would be hard pressed to prove that a seventh would have made a difference."

Implications for pharmacy

An opinion piece in the *Chicago Tribune* cautioned against "overwarning," which the author felt might deter physicians from prescribing necessary drugs for fear of liability or deter patients from taking them for fear of adverse effects. David Brushwood, BPharm, JD, disagreed that the Wyeth verdict would result in increased instances of overwarning, telling **Today**, "Manufacturers have been labeling products based on the assumption that there is no federal preemption. Perhaps this [in itself] is overwarning. The balance between too much information and too little information in the package insert is best resolved by consideration of both state and federal standards, and not just federal standards."

The decision in Levine's favor may have implications outside pharmacy. According to FindLaw.com, some 27,000 lawsuits are pending over Merck's rofecoxib (Vioxx), and this is just one of several drugs withdrawn in recent years. The Levine verdict also strikes a blow against the Bush administration's efforts to create federal preemption of a wide range of state laws, including environmental regulations, consumer safety protections, and antitrust laws. States are pushing for a reversal of this policy.

—Beth Farnstrom



ROSEMARIE
BABBITT
DIRECTOR
CORPORATE COMPLIANCE

From patient care to corporate compliance

RoseMarie Smith Babbitt is always putting patients first

WHILE MOST PHARMACISTS view reimbursement challenges as one of the most frustrating parts of the job, RoseMarie Smith Babbitt, BPharm, MA, CHC, Director of Corporate Compliance at Parkland Health and Hospital System in Dallas, considers them opportunities to help patients. “I am never satisfied hearing, ‘We just do not get paid for that,’” Babbitt recently told *Pharmacy Today*. Throughout her career in pharmacy, Babbitt has always been a champion for the uninsured and the less fortunate. “There are a lot of services out there to help patients, such as indigent services, hospital programs, pharmaceutical companies’ patient assistance programs, and so on. It just takes a little effort to find them and to make sure that those in need are aware of the programs available to assist them,” she explained.

Babbitt is charged with ensuring that business is conducted legally and ethically at her 900-bed hospital. “Money must come in to our institution for us to be able to keep our doors open and to take care of patients,” she explained, “I make sure that we manage conflicts of interests, and that all relationships between Parkland and outside sources are appropriate.”

Early influences

This year marks Babbitt’s 39th working in health care. She told *Today*, “You could say that I have been in health care forever.” Babbitt is quick to mention that her teenage years working at a local independent pharmacy in Chicago really shaped her career. “The gentleman that I worked for, William Warner, loved pharmacy, took much pride in the profession and, most important, conducted business ethically and legally. Basically, he gave me the right start in pharmacy.” This experience, along with her strong aptitude in chemistry, influenced Babbitt to pursue a career in pharmacy.

Family loss also played a role in shaping Babbitt’s career. In 1987, her mother was diagnosed with pancreatic cancer, which later took her life. Babbitt noted, “My mother worked her entire life, but she was not fortunate enough to have health insurance when she was diagnosed with cancer.” During her mother’s illness, Babbitt learned about patient assistance programs. She explained, “The patient assistance programs that helped my mother and the generosity of her surgeon who extended his services as an act of charity during her final days—these made the experience of my mother not having health insurance a positive rather than a negative one for our family.” Babbitt said that, because of her experience, she is humbled and will always have a soft spot in her heart for people who do not have health insurance and for those who are less fortunate.



Nancy Merritt, Vice President and Chief Compliance Officer, reviews the Office of the Inspector General 2009 workplan with Babbitt.

Diverse career

Babbitt has worked in many areas of the profession, including community, hospital, ambulatory care, and long-term care. “I have basically done everything but industry,” she noted. After graduating from pharmacy school, she began working at the Owen Company in Jasper, TX, an organization that managed hospital pharmacies. Her primary responsibilities in this role were I.V. admixtures, unit dose distribution, supervision of supportive personnel,

drug inventory and acquisition, narcotic distribution, and inventory. While in this position, Babbitt realized that many of the visiting emergency department physicians were not using emergency medications correctly in children, so she took the initiative to develop guidelines for these circumstances.

Less than a year after starting her job with the Owen Company, Babbitt’s sister was diagnosed with metastatic cervical cancer. Babbitt resigned and moved to New Orleans so she could

help take care of her sister. Babbitt explained, "I will do anything [in pharmacy] as long as it allows me to be near my family."

In New Orleans, Babbitt worked as a pharmacist at Tulane Medical Center. After only 1 year at Tulane, she was promoted to a supervisory position, overseeing unit dose distribution. In addition to the distributive parts of her position, she was able to get involved clinically. "There was a huge cystic fibrosis population at Tulane. Those children were on so many medications and really needed pharmacists to monitor their medications," she said. While at Tulane, she also worked with the Code Blue Team and was on the renal transplant committee.

From Tulane, Babbitt went into long-term care with Abbey Pharmaceutical Services. In this role, she directed and supervised the activities of the staff consultant pharmacists in 14 long-term care facilities. She also organized and obtained grants for annual nursing educational meetings.

Medication therapy management (MTM) played a part in her duties, although she didn't call it MTM at the time. Babbitt said, "I was doing MTM in long-term care before it was called MTM. I reviewed each patient's chart every month, I monitored for adverse drug reactions, and I attended Pharmacy and Therapeutics meetings, along with a whole host of other clinical tasks." Wanting to do everything ethically and legally, she also became familiar with state and federal regulations pertaining to drug distribution in long-term care facilities.

Parkland Health and Hospital System

After she returned to Texas, Babbitt began working at Parkland Health and Hospital System and has been there for almost 16 years. She was originally hired as Coordinator of Inpatient Pharmacy Services. In less than a year, she was promoted to Assistant Director of Pharmacy Services. In this role, she managed the Parkland Prescription Center, a 6,000-square foot ambulatory pharmacy. Under her leadership, ambulatory services at Parkland have expanded greatly.

One of Babbitt's favorite parts of her job was her involvement with patient assistance and manufacturer drug replacement programs. She also worked with patient financial services to educate qualified patients about programs for which they were eligible for assistance. She worked closely with the Director of Pharmacy to ensure that the pharmacy department followed procurement guidelines as a 340B hospital.

Babbitt was eventually promoted to Associate Director of Government Programs and Logistical Support for pharmacy services at Parkland. She described her role as "legislative liaison between the pharmacy department and the rest of the hospital." She worked on contracting and negotiating for pharmaceuticals and management of the 340B program for disproportionate share hospitals. She explained, "340B hospitals take care of a large percentage of Medicare patients and are allowed to obtain pharmaceuticals at a lower price."

Babbitt also worked to expand the hospital's patient assistance programs and outside assistance programs, including the Texas HIV/AIDS Medication Program, which provides medica-

tions approved by FDA for the treatment of illnesses caused by HIV. "By assisting the physicians and patients with the paperwork for the Texas HIV/AIDS Medication Program, we [the pharmacy department] were able to decrease the hospitals' financial liability for providing these lifesaving medications to patients," Babbitt told *Today*. Babbitt noted that her efforts in this role resulted in a \$20 million cost avoidance for pharmaceuticals in 2006.

Babbitt acted as liaison between the hospital's Corporate Compliance Office and Clinical Support Services (including respiratory care, laboratory, dietary, pharmacy and radiology), assumed responsibility for two large outpatient pharmacies and the Investigational Drug Services Department, and became involved with Medicare Durable Medical Equipment reimbursement and the implementation of the hospital's Medicare Part D plans.

While in this position, Babbitt accomplished what fewer than 10 pharmacists in the United States have done when she became Certified in Healthcare Compliance (CHC).

Babbitt left the pharmacy department a few months ago when she was promoted to Director of Corporate Compliance. When asked about leaving pharmacy, Babbitt said, "I love the profession of pharmacy and will always love pharmacy. But this role allows me to do something else. I really, really like my new job." While the responsibilities of this new position are still unfolding, Babbitt deals a lot with compliance law, ensuring that conflicts of interest for the hospital and medical staff are managed. She explained, "I review and update the hospital's compliance policies and procedures, including the Code of Conduct and Ethics. I also oversee the Integrity HOTLINE [corporate compliance line] for Parkland and make sure that all staff compliance issues and concerns are investigated."

In her new role, Babbitt hearkens back to her beginning experiences as a teen. "As Director of Corporate Compliance, I oversee the activities of the entire institution, ensuring that business is conducted ethically and legally, just as William Warner conducted his business," she explained.

After hours

Throughout her professional career, Babbitt has been very involved in her profession. She has presented at three American Society of Health-System Pharmacists Midyear Clinical Meetings, precepted for pharmacy schools, and served as a reviewer for *Update to Joint Commission Hospital Accreditation Standards*, 3rd edition.

In her spare time, Babbitt is a PharmTA for the Health Resources and Services Administration's (HRSA) Pharmacy Services Support Center (PSSC). PSSC is a resource established in 2002 to assist HRSA grantees and eligible health care sites optimize the value of the 340B program and provide clinically and cost effective pharmacy services that improve medication use and advance patient care. PSSC operates under a contract between APhA and the Office of Pharmacy Affairs in the HRSA Healthcare Systems Bureau.

—Ellen Whipple Guthrie, PharmD
Contributing writer

Babbitt ensures that business is conducted ethically and legally.

or more of patients treated with venlafaxine hydrochloride extended-release capsules where the incidence in patients treated with venlafaxine hydrochloride extended-release capsules (n=357) was greater than the incidence for the respective placebo-treated patients (n=285). For each adverse reaction, the incidence of reactions in the drug-treated patients is listed before the incidence in placebo-treated patients. **Body as a Whole:** Asthenia (8% and 7%). **Cardiovascular System:** Vasodilation (4% and 2%); Hypertension (4% and 1%). **Digestive System:** Nausea (31% and 7%); Constipation (8% and 5%); Anorexia (8% and 4%); Vomiting (4% and 2%); Flatulence (4% and 3%). **Metabolic/Nutritional:** Weight Loss (3% and 0%). **Nervous System:** Dizziness (20% and 9%); Somnolence (17% and 8%); Insomnia (17% and 11%); Dry mouth (12% and 6%); Nervousness (10% and 5%); Abnormal Dreams (7% and 2%); Tremor (5% and 2%); Depression (3% and <1%); Paresthesia (3% and 1%); Libido Decreased (3% and <1%); Agitation (3% and 1%). **Respiratory System:** Pharyngitis (7% and 6%); Yawn (3% and 0%). **Skin:** Sweating (14% and 3%). **Special Senses:** Abnormal vision (4% and <1%). **Urogenital System:** Abnormal ejaculation (16% and <1%); Impotence (4% and <1%); Female anorgasmia (3% and <1%). [See TABLE 7 in full Prescribing Information]. **TABLE 7: Treatment Emergent Adverse Reaction Incidence in Short-Term Placebo-Controlled Clinical Trials with Venlafaxine Hydrochloride Extended-Release Capsules in Patients with Social Anxiety Disorder.** This table reports adverse events that occurred in 2% or more of patients treated with venlafaxine hydrochloride extended-release capsules where the incidence in patients treated with venlafaxine hydrochloride extended-release capsules (n=277) was greater than the incidence for the respective placebo-treated patients (n=274). For each adverse reaction, the incidence of reactions in the drug-treated patients is listed before the incidence in placebo-treated patients. **Body as a Whole:** Headache (34% and 33%); Asthenia (17% and 8%); Flu Syndrome (6% and 5%); Accidental Injury (5% and 3%); Abdominal Pain (4% and 3%). **Cardiovascular System:** Hypertension (5% and 4%); Vasodilation (3% and 1%); Palpitation (3% and 1%). **Digestive System:** Nausea (29% and 9%); Anorexia (20% and 1%); Constipation (8% and 4%); Diarrhea (6% and 5%); Vomiting (3% and 2%); Eructation (2% and 0%). **Metabolic/Nutritional:** Weight Loss (4% and 0%). **Nervous System:** Insomnia (23% and 7%); Dry mouth (17% and 4%); Dizziness (16% and 8%); Somnolence (16% and 8%); Nervousness (11% and 3%); Libido Decreased (3% and <1%); Anxiety (5% and 3%); Agitation (4% and 1%); Tremor (4% and <1%); Abnormal Dreams (4% and <1%); Paresthesia (3% and <1%); Twitching (2% and 0%). **Respiratory System:** Yawn (5% and <1%); Sinusitis (2% and 1%) **Skin:** Sweating (13% and 2%). **Special Senses:** Abnormal vision (6% and 3%). **Urogenital System:** Abnormal ejaculation (16% and 1%); Impotence (10% and 1%); Female Orgasmic Dysfunction (8% and 0%). **Vital Sign Changes:** Venlafaxine hydrochloride was associated with a mean increase in pulse rate of 4 beats/min in SAD trials. In premarketing trials, the mean change from baseline heart rate for patients treated with extended-release venlafaxine hydrochloride in MDD and SAD trials was 4 beats-per-minute and 5 beats-per-minute, respectively. In a flexible-dose study with doses ranging from 200 mg to 375 mg/day, patients receiving extended-release venlafaxine hydrochloride had a mean increase in heart rate of 8.5 beats-per-minute [see WARNINGS AND PRECAUTIONS in full Prescribing Information for effects on heart rate and blood pressure]. **Laboratory Changes:** Clinically relevant increases in serum cholesterol were noted in venlafaxine hydrochloride clinical trials. Increases were duration dependent over the study period and tended to be greater with higher doses. **ECG Changes:** In a flexible-dose MDD study with doses of venlafaxine hydrochloride immediate-release tablets in the range of 200 to 375 mg/day and mean dose greater than 300 mg/day, the mean change in heart rate was 8.5 beats per minute compared with 1.7 beats per minute for placebo. [See Warnings and Precautions (5.17)]. **POSTMARKETING EXPERIENCE:** Voluntary reports of other adverse reactions temporally associated with the use of venlafaxine have been received since market introduction. Because these reactions have been reported from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. These reports include the following reactions: agranulocytosis, anaphylaxis, aplastic anemia, catatonias, congenital anomalies, impaired coordination and balance, CPK increased, deep vein thrombophlebitis, delirium, EKG abnormalities such as QT prolongation; cardiac arrhythmias including atrial fibrillation, supraventricular tachycardia, ventricular extrasystoles, and rare reports of ventricular fibrillation and ventricular tachycardia, including torsade de pointes; epidermal necrolysis/Stevens-Johnson syndrome, erythema multiforme, extrapyramidal symptoms (including dyskinesia and tardive dyskinesia), angle-closure glaucoma, hemorrhage (including eye and gastrointestinal bleeding), hepatic reactions (including GGT elevation; abnormalities of unspecified liver function tests; liver damage, necrosis, or failure; and fatty liver), interstitial lung disease, involuntary movements, LDH increased, neutropenia, night sweats, pancreatitis, pancytopenia, panic, prolactin increased, renal failure, rhabdomyolysis, serotonin syndrome, shock-like electrical sensations or tinnitus (in some cases, subsequent to the discontinuation of venlafaxine or tapering of dose), and syndrome of inappropriate antidiuretic hormone secretion (usually in the elderly). **DRUG INTERACTIONS: Alcohol:** The effect of alcohol on plasma levels of Venlafaxine Extended Release Tablets is not known. **Cimetidine:** Use caution when administering venlafaxine hydrochloride with cimetidine to patients with preexisting hypertension or hepatic dysfunction, and the elderly. **Diazepam:** A single dose of diazepam did not appear to affect the PK of either venlafaxine hydrochloride (150 mg/day) or its major active metabolite, O-desmethylvenlafaxine (ODV). Venlafaxine hydrochloride did not have any effect on the PK of diazepam or its active metabolite, desmethyldiazepam, or affect the psychomotor and psychometric effects induced by diazepam. **Haloperidol:** Venlafaxine hydrochloride (150 mg/day) decreased total oral-dose clearance of haloperidol, resulting in a 70% increase in haloperidol AUC. The haloperidol C_{max} increased 88%, but the haloperidol elimination $t_{1/2}$ was unchanged. **Lithium:** A single dose of lithium (600 mg) did not appear to affect the PK of either venlafaxine hydrochloride (150 mg/day) or ODV. Venlafaxine hydrochloride had no effect on the PK of lithium. **Drugs Highly Bound to Plasma Proteins:** Venlafaxine hydrochloride is not highly bound to plasma proteins; coadministration of Venlafaxine Extended Release Tablets and a highly protein-bound drug should not cause increased free concentrations of the other drug. **Drugs That Inhibit Cytochrome P450 Isoenzymes:** CYP2D6 and CYP3A4 Inhibitors: Venlafaxine hydrochloride is metabolized to ODV by CYP2D6. Drugs inhibiting this isoenzyme have the potential to increase plasma concentrations of venlafaxine hydrochloride and decrease those of ODV. Because venlafaxine hydrochloride and ODV are approximately equiactive and equipotent, no dosage adjustment is required when venlafaxine hydrochloride is coadministered with a CYP2D6 inhibitor. Pharmacokinetic studies with ketoconazole in both poor and extensive metabolizers of CYP2D6 resulted in higher plasma concentrations and AUCs of both venlafaxine hydrochloride and ODV in most subjects following administration of ketoconazole. Concomitant use of CYP3A4 inhibitors and venlafaxine hydrochloride may increase levels of both venlafaxine hydrochloride and ODV. Use caution if therapy includes venlafaxine hydrochloride and any CYP3A4 inhibitor. **Drugs Metabolized by Cytochrome P450 Isoenzymes:** Venlafaxine hydrochloride is a relatively weak inhibitor of CYP2D6 in vitro. Imipramine: Venlafaxine hydrochloride did not affect the PK of imipramine or 2-OH-imipramine. However, desipramine AUC, C_{max} , and C_{min} increased by about 35% in the presence of venlafaxine hydrochloride. The 2-OH-desipramine AUCs increased by 2.5 to 4.5 fold (with venlafaxine hydrochloride doses of up to 75 mg q 12h). The clinical significance of elevated 2-OH-desipramine is unknown. Imipramine did not affect the PK of venlafaxine hydrochloride and ODV. Metoprolol: Venlafaxine hydrochloride (50 mg q 8h for 5 days) appeared to reduce the blood-lowering effect of metoprolol (100 mg q 24h for 5 days) in one study. Caution should be exercised when these drugs are given together. Risperidone: Venlafaxine hydrochloride (150 mg/day) slightly inhibited metabolism of a single 1-mg dose of risperidone, resulting in an about 32% increase in risperidone AUC. Venlafaxine hydrochloride coadministration did not significantly alter the PK profile of the total active moiety (risperidone plus its metabolite 9-hydroxyrisperidone). CYP3A4: Venlafaxine hydrochloride did not inhibit CYP3A4 in vitro or in vivo. Indinavir: In healthy volunteers, venlafaxine hydrochloride (150 mg/day) resulted in a 28% decrease in the AUC of a single dose of a single 800-mg dose of indinavir and a 36% decrease in indinavir C_{max} . Indinavir did not affect the PK of venlafaxine hydrochloride and ODV. CYP1A2: Venlafaxine hydrochloride did not inhibit CYP1A2 in vitro or in vivo. CYP2C9: Venlafaxine hydrochloride did not inhibit CYP2C9 in vitro. In vivo, venlafaxine hydrochloride 75 mg (75 mg q 12h) did not alter the PK of a single 550-mg dose of tolbutamide or the CYP2C9-mediated formation of 4-OH-tolbutamide. CYP2C19: Venlafaxine hydrochloride did not inhibit the metabolism of diazepam, which is partially metabolized by CYP2C19 (see Diazepam above). **MAOIs:** [See CONTRAINDICATIONS and WARNINGS AND PRECAUTIONS in full Prescribing Information.] **Other CNS-Active Drugs:** Caution is advised if there is concomitant use of venlafaxine and other CNS-active drugs. Serotonergic Drugs and Triptans: Based on the mechanism of action of Venlafaxine Extended Release Tablets and the potential for serotonin syndrome, caution is advised when Venlafaxine Extended Release Tablets are coadministered with other drugs that may affect the serotonergic neurotransmitter systems, such as triptans, SSRIs, other SNRIs, linezolid, lithium, tramadol, or St. John's Wort. If concomitant treatment of Venlafaxine Extended Release Tablets with these drugs is warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases. Concomitant use of Venlafaxine Extended Release Tablets with tryptophan supplements is not recommended [see WARNINGS AND PRECAUTIONS in full Prescribing Information]. There have been rare postmarketing reports of serotonin syndrome with use of an SSRI and a triptan. If concomitant use of Venlafaxine Hydrochloride Extended Release tablets with a triptan is warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases [see WARNINGS AND PRECAUTIONS in full Prescribing Information]. **Drugs That Interfere With Hemostasis:** Interference with serotonin reuptake may affect platelet function and result in bleeding. Concurrent use of NSAIDs or aspirin may increase this risk. Increases in prothrombin time (PT), partial thromboplastin time (PTT), or INR have been reported when venlafaxine hydrochloride was given to patients on warfarin therapy. Patients on warfarin should be carefully monitored when Venlafaxine Extended Release Tablets are begun or discontinued. **Electroconvulsive Therapy:** There is no clinical data establishing the benefit of electroconvulsive therapy combined with Venlafaxine

Hydrochloride Extended Release Tablets. **Postmarketing Spontaneous Drug Interaction Reports:** There have been reports of elevated clozapine levels temporally associated with adverse reactions, including seizures, following the addition of venlafaxine. There have been reports of increases in PT, PTT, or INR when venlafaxine was given to patients also receiving warfarin. **USE IN SPECIFIC POPULATIONS: Pregnancy: Teratogenic Effects: Pregnancy Category C:** There are no adequate and well-controlled studies of venlafaxine in pregnant women. Venlafaxine Extended Release Tablets should be used during pregnancy only if clearly needed. **Non-Teratogenic Effects:** Neonates exposed to venlafaxine hydrochloride late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. Complications can arise immediately upon delivery. Reports include respiratory distress, cyanosis, apnea, seizures, unstable temperature, feeding difficulty, vomiting, hypoglycemia, hypo- and hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying. This is consistent with a toxic effect of SSRIs or SNRIs or a drug discontinuation syndrome. In some cases, it is consistent with serotonin syndrome. When treating a pregnant woman with Venlafaxine Extended Release Tablets during the third trimester, carefully consider the potential risks and benefits of treatment. **Labor and Delivery:** The effect of venlafaxine hydrochloride on labor and delivery in humans is unknown. **Nursing Mothers:** Venlafaxine hydrochloride and ODV, its active metabolite, are excreted in human milk. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue Venlafaxine Extended Release Tablets, taking into account the importance of the drug to the mother. **Pediatric Use:** Safety and effectiveness in the pediatric population have not been established [see BOXED WARNING and Warnings and Precautions: Clinical Worsening and Suicide Risk]. Anyone considering using Venlafaxine Extended Release Tablets in a child or adolescent must balance the potential risks with the clinical need. While no studies have adequately assessed the impact of venlafaxine hydrochloride on growth, development, and maturation of children and adolescents, studies suggest it may adversely affect weight and height [see WARNINGS AND PRECAUTIONS: General: Changes in Height and Changes in Weight in full Prescribing Information]. Should the decision be made to treat a pediatric patient with Venlafaxine Extended Release Tablets, regular monitoring of weight and height is recommended during treatment, particularly if long term. The safety of venlafaxine hydrochloride in pediatric patients has not been assessed for treatment beyond 6 months. In patients aged 6-17, clinically relevant blood pressure and cholesterol increases were similar to those observed in adult patients. The precautions for adults apply to pediatric patients. **Geriatric Use:** While no overall differences in effectiveness or safety were observed between geriatric and younger patients, greater sensitivity of some older individuals cannot be ruled out. The elderly may be at greater risk for significant hyponatremia. No dose adjustment is recommended based on age alone. **Patients With Hepatic Impairment:** Decreased clearance was noted in patients with cirrhosis. A lower dose may be necessary in these patients; extra caution should be used in these patients. **Patients With Renal Impairment:** In patients with GFR = 10 to 70 mL/min, clearance of venlafaxine hydrochloride and its metabolites were decreased. It is recommended that total daily dose of Venlafaxine Extended Release Tablets be reduced by 25% to 50% in these patients. Individualization of dosage may be desirable in some patients. In hemodialysis patients, it is recommended that total daily dose be reduced by 50%. Venlafaxine Extended Release Tablets should be used with caution in such patients. **DRUG ABUSE AND DEPENDENCE:** Venlafaxine Extended Release Tablets are not a controlled substance. Carefully evaluate patients for history of drug abuse and observe such patients closely for signs of misuse or abuse of venlafaxine hydrochloride. Discontinuation effects have been reported in patients receiving venlafaxine hydrochloride [see WARNINGS AND PRECAUTIONS; and DOSAGE AND ADMINISTRATION in full Prescribing Information]. **OVERDOSAGE:** In postmarketing experience, overdose has occurred predominantly in combination with alcohol and/or other drugs. The most commonly reported reactions include tachycardia, changes in consciousness, mydriasis, seizures, and vomiting. Electrocardiogram changes (eg, prolongation of QT interval, bundle branch block, QRS prolongation), ventricular tachycardia, bradycardia, hypotension, rhabdomyolysis, vertigo, liver necrosis, serotonin syndrome, and death have been reported. Ensure an adequate airway, oxygenation, and ventilation. Monitor cardiac rhythm and vital signs. General supportive and symptomatic measures are also recommended. Induction of emesis is not recommended. Gastric lavage with a large-bore orogastric tube with appropriate airway protection, if needed, may be indicated if performed soon after ingestion or in symptomatic patients. Activated charcoal should be administered. Due to the large volume of distribution of this drug, forced diuresis, dialysis, hemoperfusion, and exchange transfusion are unlikely to be of benefit. No specific antidotes for venlafaxine hydrochloride are known. In managing overdose, consider the possibility of multiple drug involvement. Consider contacting a poison control center for additional information on treatment. Telephone numbers for certified poison control centers are listed in the Physicians' Desk Reference® (PDR®). **DOSAGE AND ADMINISTRATION:** Consult full prescribing information for dosing instructions. **Switching Patients to or from an MAOI: At least 14 days should elapse between discontinuation of an MAOI and initiation of therapy with Venlafaxine Extended Release Tablets. At least 7 days should be allowed after stopping Venlafaxine Extended Release Tablets before starting an MAOI [see WARNINGS AND PRECAUTIONS in full Prescribing Information].**

To report SUSPECTED ADVERSE REACTIONS, contact Upstate Pharma, LLC Pharmaceutical Corp. at 1-888-299-1053 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

This brief summary is based on Venlafaxine Extended Release Tablets Prescribing Information, January 2009. Osmotica Pharmaceutical Corp.

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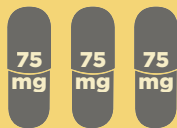
Venlafaxine Extended Release Tablets, a branded alternative for patients with Major Depressive Disorder (MDD)*

A

SINGLE DAILY 225 MG TABLET IS ONE-OF-A-KIND

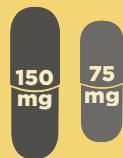
Options for patients with MDD receiving 225 mg of extended-release venlafaxine HCl

3 capsules



OR

2 capsules and potentially 2 copays



OR

Just one 225 mg Venlafaxine Extended Release Tablet



Must be taken with food; capsules may be opened and sprinkled.

Must be taken with food and swallowed whole.

Patients with MDD should start treatment with 75 mg/day (in some patients, 37.5 mg/day for 4 to 7 days then increased to 75 mg/day); daily dose can be increased by 75 mg/day at intervals of ≥4 days (maximum 225 mg/day).

Copays and coverage will vary; some patients may pay 1 or 2 copays per filled prescription; some patients will qualify for copay assistance.

Capsules and tablets not shown actual size.

*Venlafaxine Extended Release Tablets are not indicated for the treatment of generalized anxiety disorder or panic disorder.

Many of your customers may be able to save money on their prescription for Venlafaxine Extended Release Tablets. For more information, call 1.888.299.1053 or visit www.VERTablets.com

Venlafaxine Extended Release Tablets (VENLAFAXINE HYDROCHLORIDE)

37.5 mg 75 mg 150 mg 225 mg

INDICATIONS AND IMPORTANT SAFETY INFORMATION

WARNING: Suicidality and Antidepressants

See full Prescribing Information for complete boxed warning.

Increased risk of suicidal thinking and behavior has been reported in children, adolescents and young adults taking antidepressants for major depressive disorder (MDD) and other psychiatric disorders. Venlafaxine Extended Release Tablets are not approved for use in pediatric patients.

Venlafaxine Extended Release Tablets (venlafaxine hydrochloride) are indicated for the treatment of Major Depressive Disorder (MDD) and Social Anxiety Disorder (SAD). Efficacy of venlafaxine HCl was shown in both short-term trials and a longer-term trial in MDD, and in short-term SAD trials. Venlafaxine Extended Release Tablets are contraindicated in patients taking monoamine oxidase inhibitors (MAOIs).

All patients should be monitored appropriately and observed closely for clinical worsening and suicidality, especially at the beginning of drug therapy, or at the time of increases or decreases in dose. Such monitoring should include daily observation by families and caregivers for emergence of agitation, irritability, unusual changes in behavior, or emergence of suicidality.

Venlafaxine Extended Release Tablets should not be used in combination with an MAOI, or within at least 14 days of discontinuing treatment with an MAOI. At least 7 days should be allowed after stopping Venlafaxine Extended Release Tablets before starting an MAOI.

The development of a potentially life-threatening serotonin syndrome or Neuroleptic Malignant Syndrome (NMS)-like reactions have been reported with SSRIs and SNRIs (including Venlafaxine Extended Release Tablets) alone, but particularly if used concomitantly with serotonergic drugs (including triptans), MAO inhibitors, or with antipsychotics or other dopamine antagonists. Severe serotonin syndrome can resemble NMS, and patients should be monitored for symptoms of these disorders. If symptoms develop, Venlafaxine Extended Release Tablets and any serotonergic or antidopaminergic agents, including antipsychotics, should be discontinued immediately.

Treatment with venlafaxine hydrochloride is associated with sustained hypertension in some patients. Regular blood pressure monitoring is recommended. Mydriasis has been reported in association with venlafaxine; therefore, patients with raised intraocular pressure or those at risk of acute narrow-angle glaucoma should be monitored.

Dosing must be individualized according to the patient's hepatic and renal function status. Abrupt discontinuation or dose reduction has been associated with discontinuation symptoms (generally self-limiting; serious symptoms possible). A gradual reduction in the dose rather than abrupt cessation is recommended.

After treatment with venlafaxine hydrochloride, insomnia and nervousness, activation of mania/hypomania, symptomatic hyponatremia, seizures, abnormal bleeding (most commonly ecchymosis), clinically relevant increases in serum cholesterol, interstitial lung disease and eosinophilic pneumonia have been reported. Venlafaxine Extended Release Tablets should be used cautiously in patients with a history of seizures. Measurement of serum cholesterol should be considered during long-term treatment. Patients should be cautioned about the risk of bleeding associated with concomitant use of Venlafaxine Extended Release Tablets and NSAIDs, aspirin, or other drugs that affect coagulation.

Venlafaxine Extended Release Tablets should be used during pregnancy and nursing only if clearly needed due to the potential for serious adverse reactions.

Adverse reactions occurring in short-term studies of major depressive disorder* were abnormal ejaculation, gastrointestinal complaints (nausea, dry mouth, anorexia), CNS complaints (dizziness, somnolence, abnormal dreams) and sweating. Adverse reactions occurring in short-term studies of social anxiety disorder* were asthenia, gastrointestinal complaints (anorexia, dry mouth, nausea), CNS complaints (anxiety, insomnia, libido decreased, nervousness, somnolence, dizziness), abnormalities of sexual function (abnormal ejaculation, orgasmic dysfunction, impotence), yawn, sweating, and abnormal vision.

*Occurring in at least 5% of patients receiving venlafaxine extended release capsules and at a rate at least twice that of placebo.

Please see brief summary of full Prescribing Information, including complete boxed warning, on adjacent pages.

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