The Future of Medicine

Change is a fact of life—and a fact of medicine. New developments in clinical procedures, technology, reimbursement structures, policy, and demographics will no doubt impact physicians and their careers.

Fast Facts

- *A 2004 survey by the physician-recruiting firm, Merritt, Hawkins & Associates, revealed that about half of doctors between ages 50 and 65 plan to retire or to reduce their patient loads in the next few years. Page 13*
- *Publication of patient satisfaction data is one example of increased transparency in health care. Access to actual prices for healthcare services will likely follow and may change how patients choose their health care. Page 16*
- *A recent study by the Center for Studying Health System Change found that the proportion of physicians in solo and two-physician practices decreased significantly from 41 percent in 1996-97 to more than 32 percent in 2004-05. Page 22*

Physicians who love their careers have created practices that work for them, says Richard Moss, MD, spiritual teacher and author of six books on transformation and healing. "Each physician who is going to find his or her way through medicine has to think in terms not of being obedient to a system, but in service to the principles he or she lives."

Pressures on physicians have been building up over the past decades and will likely continue to mount in the future. Debates about medical business models, reimbursement, universal health coverage, medical ethics, and malpractice reform continue to swirl in medical circles all over the country. The healthcare sys-

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Important Safety Information

Afluria® is indicated for active immunization of persons 18 years of age and older against influenza disease caused by influenza virus subtypes A and type B present in the vaccine. The indication is based on the immune response elicited by Afluria®; no controlled clinical studies have demonstrated a decrease in influenza disease after vaccination with Afluria®.

Afluria® should not be administered to individuals with hypersensitivity to eggs or chicken protein or other components of Afluria,® or to anyone who has had a life-threatening reaction to previous influenza vaccination.

The most common injection-site adverse reactions were tenderness, pain, redness, and swelling. The most common systemic adverse reactions were headache, malaise, and muscle aches.

Vaccination with Afluria® may not protect all individuals. Immunocompromised persons may have a diminished immune response. If Guillain-Barré syndrome has occurred within 6 weeks of receipt of prior influenza vaccine, the decision to give Afluria® should be based on careful consideration of the potential benefits and risks.

Please see brief summary of full prescribing information on adjacent page.

*Afluria® is also available in a latex-free, multidose vial formulation containing thimerosal as a preservative (CPT® code 90658).

†CPT is a registered trademark of the American Medical Association.

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BRIEF SUMMARY OF PRESCRIBING INFORMATION

AFLURIA®
Influenza Virus Vaccine Suspension for Intramuscular Injection

Before prescribing, please consult full prescribing information, a brief summary of which follows. Some text and references refer to full prescribing information.

4 CONTRAINDICATIONS

AFLURIA® is contraindicated in individuals with known hypersensitivity to eggs or chicken protein, neomycin, or polymyxin, or in anyone who has had a life-threatening reaction to previous influenza vaccination.

5 WARNINGS AND PRECAUTIONS

5.1 Guillain-Barré Syndrome (GBS)

If GBS has occurred within 6 weeks of previous influenza vaccination, the decision to give AFLURIA® should be based on careful consideration of the potential benefits and risks.

5.2 Altered Immunocompetence

If AFLURIA® is administered to immunocompromised persons, including those receiving immunosuppressive therapy, the immune response may be diminished.

5.3 Preventing and Managing Allergic Reactions

Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration of the vaccine.

5.4 Limitations of Vaccine Effectiveness

Vaccination with AFLURIA® may not protect all individuals.

6 ADVERSE REACTIONS

6.1 Overall Adverse Reactions

Serious allergic reactions, including anaphylactic shock, have been observed during postmarketing surveillance in individuals receiving AFLURIA®.

The most common local (injection-site) adverse reactions observed in clinical studies with AFLURIA® were tenderness, pain, redness, and swelling. The most common systemic adverse reactions observed were headache, malaise, and muscle aches.

6.2 Safety Experience from Clinical Studies

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a vaccine cannot be directly compared to rates in the clinical studies of another vaccine and may not reflect the rates observed in clinical practice.

Clinical safety data for AFLURIA® have been obtained in two clinical studies (*see Clinical Studies [14]*).

A US study (Study 1) included 1,357 subjects for safety analysis, ages 18 to less than 65 years, randomized to receive AFLURIA®, Influenza Virus Vaccine Suspension for Intramuscular Injection, (1,089 subjects) or placebo (268 subjects) (*see Clinical Studies [14] for study demographics*). There were no deaths or serious adverse events reported in this study.

A UK study (Study 2) included 275 subjects, ages 65 years and older, randomized to receive preservative-free AFLURIA® (206 subjects) or a European-licensed trivalent inactivated influenza vaccine as an active control (69 subjects) (*see Clinical Studies [14]*). There were no deaths or serious adverse events reported in this study.

The safety assessment was identical for the two studies. Local (injection-site) and systemic adverse events were solicited by completion of a symptom diary card for 5 days post-vaccination (Table 1). Unsolicited local and systemic adverse events were collected for 21 days post-vaccination (Table 2). These unsolicited adverse events were reported either spontaneously or when subjects were questioned about any changes in their health post-vaccination. All adverse events are presented regardless of any treatment causality assigned by study investigators.

Table 1: Proportion of Subjects With Solicited Local or Systemic Adverse Events* Within 5 days After Administration of AFLURIA® or Placebo, Irrespective of Causality†

	Study 1 Subjects ≥ 18 to < 65 Years		Study 2 Subjects ≥ 65 Years
Solicited Adverse event	AFLURIA®‡ n=1089	Placebo § n=268	AFLURIA® n=206
Local			
Tenderness‖	60%	18%	34%
Pain¶	40%	9%	9%
Redness	16%	8%	23%
Swelling	9%	1%	11%
Bruising	5%	1%	4%
Systemic			
Headache	26%	26%	15%
Malaise	20%	19%	10%
Muscle aches	13%	9%	14%
Nausea	6%	9%	3%
Chills/ Shivering	3%	2%	7%
Fever ≥ 37.7°C (99.86 °F)	1%	1%	1%
Vomiting	1%	1%	0%

* In Study 1, 87% of solicited local and systemic adverse events were mild, 12% were moderate, and 1% were severe. In Study 2, 76.5% were mild, 20.5% were moderate, and 3% were severe. In both studies, most solicited local and systemic adverse events lasted no longer than 2 days.

† Values rounded to the nearest whole percent.

‡ Includes subjects who received either the single-dose (preservative-free) or multi-dose formulation of AFLURIA®.

§ Thimerosal-containing placebo.

‖ Tenderness defined as pain on touching.

¶ Pain defined as spontaneously painful without touch.

Table 2: Adverse Events* Reported Spontaneously by ≥ 1% of Subjects Within 21 Days After Administration of AFLURIA® or Placebo, Irrespective of Causality†

	Study 1 Subjects ≥ 18 to < 65 years		Study 2 Subjects ≥ 65 years
Adverse Event	AFLURIA® ‡ n=1089	Placebo § n=268	AFLURIA® n=206
Headache	8%	6%	8%
Nasal Congestion	1%	1%	7%
Cough	1%	0.4%	5%
Rhinorrhea	1%	1%	5%
Pharyngolaryngeal Pain	3%	1%	5%
Reactogenicity Event	3%	3%	0%
Diarrhea	2%	3%	1%
Back Pain	2%	0.4%	2%
Upper Respiratory Tract Infection	2%	1%	0.5%
Viral Infection	0.4%	1%	0%
Lower Respiratory Tract Infection	0%	0%	1%
Myalgia	1%	1%	1%
Muscle Spasms	0.4%	1%	0%

* In Study 1, 63% of unsolicited adverse events were mild, 35% were moderate, and 2% were severe. In Study 2, 47% were mild, 51% were moderate, and 3% were severe. In both studies, most unsolicited adverse events lasted no longer than 5 days.

† Values greater than 0.5% rounded to the nearest whole percent.

‡ Includes subjects who received either the single-dose (preservative-free) or multi-dose formulation of AFLURIA®.

§ Thimerosal-containing placebo.

6.3 Postmarketing Experience

Because postmarketing reporting of adverse reactions is voluntary and from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure. The adverse reactions described have been included in this section because they: 1) represent reactions that are known to occur following immunizations generally or influenza immunizations specifically; 2) are potentially serious; or 3) have been reported frequently. The following adverse reactions also include those identified during postapproval use of AFLURIA®, Influenza Virus Vaccine Suspension for Intramuscular Injection, outside the US since 1985.

Blood and lymphatic system disorders
Transient thrombocytopenia

Immune system disorders
Allergic reactions including anaphylactic shock and serum sickness

Nervous system disorders
Neuralgia, paresthesia, and convulsions; encephalopathy, neuritis or neuropathy, transverse myelitis, and GBS

Vascular disorders
Vasculitis with transient renal involvement

Skin and subcutaneous tissue disorders
Pruritus, urticaria, and rash

General disorders and administration site conditions
Influenza-like illness (e.g., pyrexia, chills, headache, malaise, myalgia), injection-site inflammation (e.g., pain, erythema, swelling, warmth), and induration

6.4 Other Adverse Reactions Associated With Influenza Vaccination

Anaphylaxis has been reported after administration of AFLURIA®. Although AFLURIA®, Influenza Virus Vaccine Suspension for Intramuscular Injection, contains only a limited quantity of egg protein, this protein can induce immediate hypersensitivity reactions among persons who have severe egg allergy. Allergic reactions include hives, angioedema, allergic asthma, and systemic anaphylaxis (*see Contraindications [4]*).

The 1976 swine influenza vaccine was associated with an increased frequency of GBS. Evidence for a causal relation of GBS with subsequent vaccines prepared from other influenza viruses is unclear. If influenza vaccine does pose a risk, it is probably slightly more than one additional case per 1 million persons vaccinated.

Neurological disorders temporally associated with influenza vaccination, such as encephalopathy, optic neuritis/neuropathy, partial facial paralysis, and brachial plexus neuropathy, have been reported.

Microscopic polyangiitis (vasculitis) has been reported temporally associated with influenza vaccination.

7 DRUG INTERACTIONS

7.1 Concurrent Use With Other Vaccines

There are no data to assess the concomitant administration of AFLURIA® with other vaccines. If AFLURIA® is to be given at the same time as another injectable vaccine(s), the vaccine(s) should be administered at different injection sites.

AFLURIA® should not be mixed with any other vaccine in the same syringe or vial.

7.2 Concurrent Use With Immunosuppressive Therapies

The immunological response to AFLURIA® may be diminished in individuals receiving corticosteroid or immunosuppressive therapies.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C: Animal reproduction studies have not been conducted with AFLURIA®. It is also not known whether AFLURIA® can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. AFLURIA® should be given to a pregnant woman only if clearly needed.

8.3 Nursing Mothers

AFLURIA® has not been evaluated in nursing mothers. It is not known whether AFLURIA® is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when AFLURIA® is administered to a nursing woman.

8.4 Pediatric Use
Safety and effectiveness in the pediatric population have not been established.

8.5 Geriatric Use
In four clinical studies, 343 subjects ages 65 years and older received AFLURIA®. Hemagglutination-inhibiting (HI) antibody responses in geriatric subjects were lower after administration of AFLURIA® in comparison to younger adult subjects (*see Clinical Studies [14]*). Adverse event rates were generally similar in frequency to those reported in subjects ages 18 to less than 65 years, although some differences were observed (*see Adverse Reactions [6.2]*).

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tem is not likely to get any easier moving forward.

Nevertheless, it is clear that the rewards of practicing medicine can be considerable.

Physicians who thrive in this environment must keep the complexities in perspective. "You can't stop the paperwork, the problems, or the patient who is going to give you a tough time," says Dr. Moss. "You have to try to take charge, and where you can't take charge you need a spiritual connection so you're not a victim of the circumstances. That can be learned."

He says that what helps physicians have satisfying careers despite the changes around them is to "find some higher order of meaning that transcends being a doctor." Physicians who build rewarding careers have "a set of values they've chosen," Dr. Moss says, adding that spirituality is "anything that helps us and those around us be better human beings," and that physicians are "spiritual beings as well as rationally trained scientists."

Both sides of the physician personality—the spiritual and the scientific—determine how each physician will navigate the changes ahead and how medical careers will unfold in the coming years.

Physician Shortages Ahead?

There are about 300 million people in the United States. According to the Kaiser Family Foundation, about 943,000 of those people are physicians; and approximately 370,000 of those physicians work in primary care. Simply looking at the numbers, one would think that there are plenty of physicians to provide care to the population. In some parts of the country, that's true. But in many areas—mostly rural or poor urban areas—there are severe physician shortages. As baby boomers are now reaching the age when they'll require more and more care, many expect physician shortages to become widespread.

The aging of the population is hitting medicine from two sides.The patient population is getting older, needing ongoing care for the chronic conditions that often accompany the aging process. But the physician population is also aging. A 2004 survey by the physician recruiting firm, Merritt,Hawkins & Associates, revealed that about half of doctors between ages 50 and 65 plan to retire or reduce their patient loads in the next few years.

The aging of the population is hitting medicine from two sides. The patient population is getting older, needing ongoing care for the chronic conditions that often accompany the aging process. But the physician population is also aging. A 2004 survey by the physician recruiting firm, Merritt, Hawkins & Associates, revealed that about half of doctors between ages 50 and 65 plan to retire or reduce their patient loads in the next few years.

"Traditionally, physicians in their 50s and early 60s have been the workhorses of medicine," Joseph Hawkins, chief executive officer of Merritt, Hawkins, noted when the report was released. "If these physicians stop seeing patients, millions of patient visits will have to be absorbed by an already limited number of doctors."

Jeff Goldsmith, president of Health Futures, Inc, and a health-care trends analyst, believes the increased stress associated with practicing medicine is driving some physicians out of traditional full-time practice early. "Physicians aren't going to quit working, but they're going to do something that won't be 100 hours a week and beeper driven." And he agrees that, combined with the onslaught of baby-boomer patients, this spells trouble.

At the same time as the physician supply will contract, the demand from baby-boomer patients will grow, Mr. Goldsmith says. "When it begins to grow, there will be a huge problem because newly entitled Medicare beneficiaries won't be able to find physicians to take care of them, particularly primary care physicians. It's really very clear."

A seemingly obvious solution would be to train more physicians. But, as Mr. Goldsmith points out, "just training more people who don't want to go into primary care won't get the job done. . . It's already begun, and it's going to create a tremendous amount of pressure on the physicians who remain."

There are even more layers to this situation. There's a wide perception that newer physicians may have in mind a practice model that differs from the 80-hour workweeks required in some residency programs or that many older physicians put in. "When you place a head-banging baby-boomer doctor with a Gen-Y doc, you're getting about 6/10 of the clinical effort [from the Gen-Y physician]," says Mr. Goldsmith. Younger physicians have different priorities and values, and working 24/7 is not at the top of their list. Although the stereotype is that women physicians are less willing to work long hours, Mr. Goldsmith sees this trend across gender lines. "I don't know a lot of young male resident graduates who want to work constantly as their parents, aunts, and uncles did," says Mr. Goldsmith.

This isn't all bad—by setting boundaries and designing their careers to fit their life priorities, these young physicians may be setting themselves up for a longer, happier professional path. "The human wreckage from the older physicians' model is obvious," says Mr. Goldsmith.

The change is bound to have an effect on the practice of medicine in general. Physicians who take an active role in adapting to that change will be set to thrive despite the change.

Avoiding career burnout, working with purpose, finding a practice style that's in synch with your values, and staying engaged with lifelong learning may be—at least in part—a remedy for an impending physician shortage. Physicians who are engaged in their work and find meaning in their mission are more likely to stay in medicine and add to the overall health of the population.

Roundtable: Practicing Physicians Speak Out on the Future of Medicine

Doctor's Digest asked a panel of practicing physicians about their perspectives on the future of medicine. Their responses to specific questions are presented in sidebars throughout this chapter. Participants included the following:

Peter Moskowitz, MD, *Radiology, Palo Alto, Calif.*

Joseph Ewing, MD, *Family Practice, Las Cruces, N.M.*

Jeffrey Mechanick, MD, *Endocrinology, New York, N.Y.*

Timothy McNichols, MD, *Internal Medicine, Springfield, Mo.*

Question: What makes you optimistic about the future of medicine?

Dr. Moskowitz: I am optimistic that the medical research enterprise will continue to unravel the mysteries of many of mankind's chronic and fatal illnesses. The genetic basis of most diseases will become known, which will eventually lead to more effective and/or permanent cures for many, if not most diseases.

The implications to world economics, the distribution of wealth, the productivity of societies, and the challenges of world health will be explosive. At the same time, there will be massive new strains put upon the world's natural and other resources as a result of rapidly growing populations and a drastic reduction in the death rate among the very young and the very old.

Dr. Ewing: There seems to be some movement toward universal coverage, for example, in Oregon and California.

Dr. Mechanick: The advent of genomic medicine and advances in technology are proceeding at a rapid rate. [That] coupled with advances in informatics to process, organize, and store data [will make] disease prevention, diagnosis and treatment more achievable. Doctors are being educated in a fashion that promotes humanism, which creates a friendlier environment.

Patients Are Different, Too

Physicians aren't the only ones who are changing, says Joe Flower, who lectures and writes about change and the future of health care. The CEO and founder of Imagine What If, Inc., he regularly works with physician groups and healthcare organizations. Grouping himself with what he calls "leading-edge baby

boomers," Mr. Flower says patients in this age group approach how they take care of themselves and how they interact with healthcare providers in a vastly different way from their parents' generation. "We're not terribly compliant," says Mr. Flower. "We're picky, pushy, and we tend to think we know everything. We are much more information conscious than the generation before us. We're not brand loyal."

Gen-X and Gen-Y patients also bring their own expectations to the doctor-patient relationship. They expect their physicians to use high-tech customer service and to put the emphasis on prevention rather than treatment of disease.

These patients are opening doors to new practice models—such as concierge practices, mobile practices that make house calls, and high-tech surgery centers that take the hassle out of hospitalization. But they're also placing new stresses on physicians—especially when combined with a new degree of transparency in medicine.

The publication of patient satisfaction data is just the first of many examples of increased transparency in health care. "Government and business associations are demanding that certain data be up on the Web," says Mr. Flower. Access to actual prices for healthcare services will likely follow. The shift from publishing prices for services as retrospective averages to making prices available in "real time" will likely change how patients choose their health care.

"No other industry has this 'pay what we tell you to pay' pricing system," says Mr. Flower. "We'll see a movement toward actual prices—a single bill for an uncomplicated birth," for example. This will require a fairly dramatic change in structure. "How do you include the anesthesiologist's bill if he's independent?" asks Mr. Flower.

Another shift Mr. Flower sees on the horizon is that consumers and those concerned about (i.e., paying for) their health care will begin to look at quality outcome statistics instead of process statistics. For example, rather than reviewing the percentage of patients who receive perioperative antibiotics for a given procedure, the focus will be on the percentage of patients who acquire postoperative infections. Measuring physicians' outcomes and making that information available to the public are

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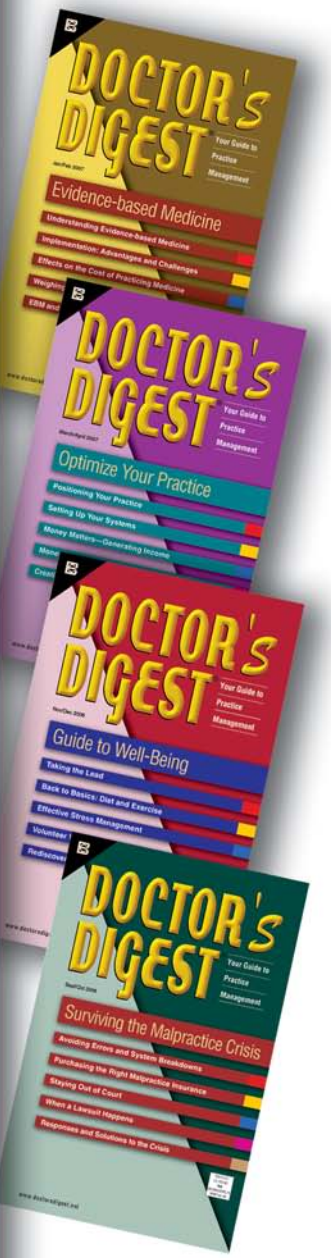

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things we can look forward to in the near future, he says. "If I go to my doctor and she says, 'Joe, you need an arthroscopic operation. Go to Dr. McAnderson. He's pretty good,' how does she know? By his reputation, patients like him, maybe he's written some papers. But she doesn't know, and I don't know [if Dr. McAnderson is good]. And Dr. McAnderson doesn't know, either. Because he's not measured. Most things in health care we don't measure," says Mr. Flower. The demand for new levels of transparency will change that.

The idea of being measured may make physicians feel a bit uneasy, but Mr. Flower foresees one potential upside. "As we move into a world of measurement," he says, "malpractice will fade as a problem because we'll have other feedback loops. Lousy doctors will end up out of the business or forced to change." Mr. Flower says that doctors will be measured not only for clinical outcomes and competence, but also for their efficiency and cost-effective patient care.

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To compete in this type of marketplace, physicians will need to restructure how they practice. "Doctors tend not to think of themselves as team members, but as lone operators. It's a heroic model of medicine that we've inherited from the past," says Mr. Flower. That model will likely need to be adjusted.

Growing pains sound inevitable if Mr. Flower's predictions are correct. But he's optimistic about the future of health care. "It's reasonably possible to have health care in ten years in which we cover everyone, that has demonstrably higher quality, and is half the cost." Mr. Flower acknowledges that this would require "large structural changes." For this to come to fruition, physicians will need to work as members of teams, systems will need to become more fully integrated, and evidence-based medicine will need to be more prevalent.

Technology and Research

Evidence of the changes occurring in medicine can be found in the pockets of today's residents. Whereas their attending physicians—back when they were trainees—had lab coat pockets stuffed with note cards and reference books, today's residents have pockets packed with cellphones, PDAs, and iPods. Most of these young doctors grew up at a keyboard. For them, technology is just another tool in their arsenal.

Advances in technology have the potential to radically change the practice of medicine—both positively and negatively. "There are a number of technical advances out there that people have built their careers around," says Mr. Flower. "We often act as if they're permanent. When we bring that assumption to consciousness and think about the history of medicine and the history of technology, that's obviously ludicrous."

New studies come out every year that influence how physicians approach treating patients. For example, look at the recent debates over the utilization of hormone replacement therapy in menopausal women, the indications for and long-term effectiveness of back surgery, and the debate over whether statins or stents are better at preventing second heart attacks. Physicians who have spent many years doing things a certain way may find it difficult to suddenly shift perspective. Sometimes accepting change means talking yourself out of a job—something physicians are understandably reluctant to do. Mr. Flower offers the example of new drugs in the pipeline intended to treat tumors. These drugs, he says, could eliminate the need for certain types of radiation oncology. Will this consideration affect adoption rates among physicians?

Technology, of course, reaches far beyond the clinical side. Electronic medical records (EMRs) are no longer a rarity, even in smaller medical practices. As the systems become more efficient, less expensive, and more widely used, it will be the rare office that uses paper charts five years from now. Still, some doctors are reluctant to jump on the technology bandwagon.

One reason? Uncertainty, Mr. Flower answers. With technology standards unsettled and new advances every day, physicians ask themselves: "If I invest in a system, how do I know that the standards won't change and I'll have to do it all over again," he

says. Well, the fact is, you don't know. In fact, the standards probably will change, and you probably will have to do it all over again. This type of problem may be pushing physicians into joining bigger organizations, where there are more resources for dealing with the cost of this change, Mr. Flower says.

But there's another side to advances on the technology front: the potential to revolutionize patient care.

"There is an emerging cluster of technologies including e-mail, voice response technology, and remote patient monitoring that, combined, may yield a non-visit-based way to connect with and manage patients," says Mr. Goldsmith. It's already being done by cardiologists who continually and remotely monitor patients with rhythm disorders.

"There is something exciting happening here that may yield a different model of the doctor-patient relationship," says Mr. Goldsmith. "Not one that's less personal, but more continuous, more focused. Many things that physicians need to do don't justify an $80-100 office visit charge . . . prescription renewals,

Roundtable: Practicing Physicians Voice Their Concerns

Question: What is your number-one concern about the future of medicine?

Dr. McNichols (Internal Medicine) : My concern about the future is that with diminishing rewards—both financial and personal—and increasing costs of education, there will be fewer and fewer students training in my specialty. This will cause an increasing shortage of internists and further practice stress. Unless efforts are made to narrow the gap between reimbursement for the procedure-based specialties and the cognitive ones, this problem will only worsen. Ultimately the shortage of quality internists will be a tremendous detriment to medical care in this country.

Dr. Ewing (Family Practice): [I am concerned] that medicine will consume more and more of the Gross National Product without getting rid of the many costly layers…that do nothing to actually contribute to health care and at the same time leave millions without adequate access to the care they need.

checking vital signs, looking for adverse drug reactions." These, he says, may be performed remotely, monitored by information technology, and backstopped by physicians' office personnel. The concept of a patient physically showing up at his or her doctor's office as the only way of receiving care may go by the wayside. "Visits that are truly needed—that are not primarily administrative—will be longer and deeper." These longer office visits may be more satisfying to patient and physician alike.

Mr. Goldsmith sees this change happening very quickly, setting up opportunity on one side and challenge on the other. "There is going to be a tremendous struggle with a lot of nontraditional players getting involved, like cellphone, cable, and home security companies," says Mr. Goldsmith. Home security companies, for example, already have infrastructure in homes onto which someone could hook clinical monitoring equipment.

Practice Models

What do all of these predictions and trends mean for practic-

Dr. Mechanick (Endocrinology): [I'm concerned about] being able to provide state-of-the-art medical care to the masses. At present, the trajectory of medical advances is toward "personalized" medicine based on genomics, but it is unlikely with the political and economic layout of the nation and international community that these advances will find their way to all individuals across socio-economic classes. Problems with reimbursement unfortunately sour the enthusiasm that should be pervading the practice of medicine.

Dr. Moskowitz (Radiology): As an academic physician I see medical schools turning out new physicians who are armed with a great deal of factual, scientific knowledge, but very little in the way of clinical decision-making skills, no common sense, and inadequate personal skills to help them relate well to and empathize with their patients. They rely much too heavily on diagnostic imaging tests and laboratory tests to manage patients. As a result, healthcare costs will continue to skyrocket, and patient satisfaction with their care and their physicians will continue to deteriorate.

ing physicians? Mr. Goldsmith says doctors will soon realize—if they haven't already—that the organizational systems that worked for them in the past may not be viable in the future. Even the structure of physician practices may have to change.

"What has inhibited physicians from organizing more effectively is that they've been so busy practicing medicine that they couldn't devote that much attention to the infrastructure of their practices, to exploring the working relationships needed to have some scale and economic leverage," he says. But economic forces may be driving those changes now.

A recent study by the Center for Studying Health System Change (HSC) found that the proportion of physicians in solo and two-physician practices decreased significantly from just over 41 percent in 1996-97 to about 33 percent in 2004-05. Most of the movement towards larger practices was among specialists and surgeons, the report revealed. The proportion of primary care physicians in solo or two-physician practices actually remained stable at about 36 percent during the period, while the proportion of medical specialists in solo or two-physician practices declined from 38 percent to 26 percent. The proportion of surgical specialists in one- or two-person practices declined from 48 percent to 38 percent.

Physicians may be moving to larger practices, the study found, but these larger groups tend to be single-specialty groups of 6 to 50 physicians rather than the multispecialty groups that were touted as the way of the future in the mid-90s. The proportion of physicians in multispecialty groups dropped from 31 percent to 28 percent from 1998-99 to 2004-05, HSC found. The proportion of physicians in single-specialty groups with 6 to 50 physicians grew from 13 percent in 1996-97 to 18 percent in 2004-05.

The survey also found that physicians are giving up their ownership stake in their practices: the proportion of physician-owners fell from just under 62 percent in 1996-97 to a bit more than 54 percent in 2004-05.

"Trends in physician practice setting and ownership likely reflect changes in physician financial incentives over the past decade," says Paul B. Ginsburg, PhD, president of HSC. Multispecialty groups were formed in response to tightly managed

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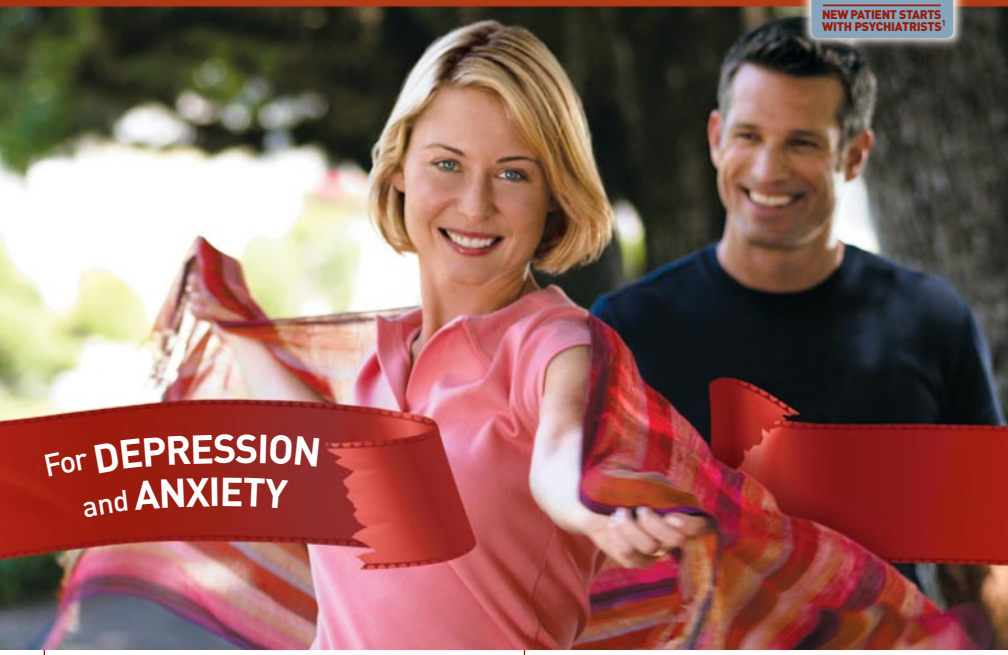

PROVEN EFFICACY for Major Depressive Disorder and Generalized Anxiety Disorder[2]

UP TO 90% of depressed patients present with symptoms of anxiety[3]

Lexapro® escitalopram oxalate

POWER TO ENJOY LIFE™

IMPORTANT SAFETY INFORMATION - Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Antidepressants increased the risk of suicidality (suicidal thinking and behavior) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of antidepressants in children, adolescents or young adults must balance the risk to clinical need. Patients of all ages started on antidepressant therapy should be closely monitored and observed for clinical worsening, suicidality or unusual changes in behavior, especially at the beginning of therapy or at the time of dose changes. This risk may persist until significant remission occurs. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Lexapro is not approved for use in pediatric patients.

Lexapro is contraindicated in patients taking monoamine oxidase inhibitors (MAOIs), pimozide (see DRUG INTERACTIONS – Pimozide and Celexa), or in patients with hypersensitivity to escitalopram oxalate. As with other SSRIs, caution is indicated in the coadministration of tricyclic antidepressants (TCAs) with Lexapro. As with other psychotropic drugs that interfere with serotonin reuptake, patients should be cautioned regarding the risk of bleeding associated with the concomitant use of Lexapro with NSAIDs, aspirin, or other drugs that affect coagulation. The most common adverse events with Lexapro versus placebo (approximately 5% or greater and approximately 2x placebo) were nausea, insomnia, ejaculation disorder, somnolence, increased sweating, fatigue, decreased libido, and anorgasmia.

References: 1. Verispan Weekly VONA Data (Retail Only). Twenty-four-week rolling average. September 2006. **2.** LEXAPRO [package insert]. St. Louis, Mo: Forest Pharmaceuticals, Inc.; 2007. **3.** Sadock BJ, Sadock VA. *Kaplan and Sadock's Synopsis of Psychiatry: Behavioral Sciences/Clinical Psychiatry.* 9th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2003:552.

Please see brief summary of prescribing information for LEXAPRO on following page.

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LEXAPRO® (escitalopram oxalate) TABLETS/ORAL SOLUTION

Rx Only

Brief Summary: For complete details, please see full prescribing information for Lexapro.

Suicidality and Antidepressant Drugs Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of Lexapro or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Lexapro is not approved for use in pediatric patients. (See WARNINGS: Clinical Worsening and Suicide Risk, PRECAUTIONS: Information for Patients, and PRECAUTIONS: Pediatric Use)

CONTRAINDICATIONS Concomitant use in patients taking monoamine oxidase inhibitors (MAOIs) is contraindicated (see **WARNINGS**). Concomitant use in patients taking pimozide is contraindicated (see **Drug Interactions – Pimozide and Celexa**). Lexapro is contraindicated in patients with a hypersensitivity to escitalopram or citalopram or any of the inactive ingredients in Lexapro. **WARNINGS WARNINGS-Clinical Worsening and Suicide Risk Clinical Worsening and Suicide Risk** Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Suicide is a known risk of depression and certain other psychiatric disorders, and these disorders themselves are the strongest predictors of suicide. There has been a long-standing concern, however, that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients during the early phases of treatment. Pooled analyses of short-term placebo-controlled trials of antidepressant drugs (SSRIs and others) showed that these drugs increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults (ages 18-24) with major depressive disorder (MDD) and other psychiatric disorders. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction with antidepressants compared to placebo in adults aged 65 and older. The pooled analyses of placebo-controlled trials in children and adolescents with MDD, obsessive compulsive disorder (OCD), or other psychiatric disorders included a total of 24 short-term trials of 9 antidepressant drugs in over 4400 patients. The pooled analyses of placebo-controlled trials in adults with MDD or other psychiatric disorders included a total of 295 short-term trials (median duration of 2 months) of 11 antidepressant drugs in over 77,000 patients. There was considerable variation in risk of suicidality among drugs, but a tendency toward an increase in the younger patients for almost all drugs studied. There were differences in absolute risk of suicidality across the different indications, with the highest incidence in MDD. The risk differences (drug vs. placebo), however, were relatively stable within age strata and across indications. These risk differences (drug-placebo difference in the number of cases of suicidality per 1000 patients treated) are provided in **Table 1. TABLE 1: Age Range and Drug-Placebo Difference in Number of Cases of Suicidality per 1000 Patients Treated:** Increases Compared to Placebo; <18 (14 additional cases); 18-24 (5 additional cases); Decreases Compared to Placebo; 25-64 (1 fewer case); ≥65 (6 fewer cases). No suicides occurred in any of the pediatric trials. There were suicides in the adult trials, but the number was not sufficient to reach any conclusion about drug effect on suicide. It is unknown whether the suicidality risk extends to longer-term use, i.e., beyond several months. However, there is substantial evidence from placebo-controlled maintenance trials in adults with depression that the use of antidepressants can delay the recurrence of depression. **All patients being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases.** The following symptoms, anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and nonpsychiatric. Although a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, there is concern that such symptoms may represent precursors to emerging suicidality. Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse, or who are experiencing emergent suicidality or symptoms that might be precursors to worsening depression or suicidality, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms. If the decision has been made to discontinue treatment, medication should be tapered, as rapidly as is feasible, but with recognition that abrupt discontinuation can be associated with certain symptoms (see PRECAUTIONS and DOSAGE AND ADMINISTRATION—Discontinuation of Treatment with Lexapro, for a description of the risks of discontinuation of Lexapro). **Families and caregivers of patients being treated with antidepressants for major depressive disorder or other indications, both psychiatric and nonpsychiatric, should be alerted about the need to monitor patients for the emergence of agitation, irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to health care providers. Such monitoring should include daily observation by families and caregivers.** Prescriptions for Lexapro should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose. **Screening Patients for Bipolar Disorder:** A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled trials) that treating such an episode with an antidepressant alone may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. Whether any of the symptoms described above represent such a conversion is unknown. However, prior to initiating treatment with an antidepressant, patients with depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. It should be noted that Lexapro is not approved for use in treating bipolar depression. **Potential for Interaction with Monoamine Oxidase Inhibitors In patients receiving serotonin reuptake inhibitor drugs in combination with a monoamine oxidase inhibitor (MAOI), there have been reports of serious, sometimes fatal, reactions including hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, and mental status changes that include extreme agitation progressing to delirium and coma. These reactions have also been reported in patients who have recently discontinued SSRI treatment and have been started on an MAOI. Some cases presented with features resembling neuroleptic malignant syndrome. Furthermore, limited animal data on the effects of combined use of SSRIs and MAOIs suggest that these drugs may act synergistically to elevate blood pressure and evoke behavioral excitation. Therefore, it is recommended that Lexapro should not be used in combination with an MAOI, or within 14 days of discontinuing treatment with an MAOI. Similarly, at least 14 days should be allowed after stopping Lexapro before starting an MAOI. Serotonin syndrome has been reported in two patients who were concomitantly receiving linezolid, an antibiotic which is a reversible non-selective MAOI.** ***Serotonin Syndrome:*** The development of a potentially life-threatening serotonin syndrome may occur with SNRIs and SSRIs, including Lexapro treatment, particularly with concomitant use of serotonergic drugs (including triptans) and with drugs which impair metabolism of serotonin (including MAOIs). Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (e.g., hyperreflexia, incoordination) and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). The concomitant use of Lexapro with MAOIs intended to treat depression is contraindicated (see **CONTRAINDICATIONS** and **WARNINGS - Potential for Interaction with Monoamine Oxidase Inhibitors.**) If concomitant treatment of Lexapro with a 5-hydroxytryptamine receptor agonist (triptan) is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases (see **PRECAUTIONS - Drug Interactions**).The concomitant use of Lexapro with serotonin precursors (such as tryptophan) is not recommended (see **PRECAUTIONS - Drug Interactions**). **PRECAUTIONS General** Discontinuation of Treatment with Lexapro During marketing of Lexapro and other SSRIs and SNRIs (serotonin and norepinephrine reuptake inhibitors), there have been spontaneous reports of adverse events occurring upon discontinuation of these drugs, particularly when abrupt, including the following: dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesias such as electric shock sensations), anxiety, confusion, headache, lethargy, emotional lability, insomnia, and hypomania. While these events are generally self-limiting, there have been reports of serious discontinuation symptoms. Patients should be monitored for these symptoms when discontinuing treatment with Lexapro. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose but at a more gradual rate (see **DOSAGE AND ADMINISTRATION**). Abnormal Bleeding Published case reports have documented the occurrence of bleeding episodes in patients treated with psychotropic drugs that interfere with serotonin reuptake. Subsequent epidemiological studies, both of the case-control and cohort design, have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. In two studies, concurrent use of a nonsteroidal anti-inflammatory drug (NSAID) or aspirin potentiated the risk of bleeding (see **Drug Interactions**). Although these studies focused on upper gastrointestinal bleeding, there is reason to believe that bleeding at other sites may be similarly potentiated. Patients should be cautioned regarding the risk of bleeding associated with the concomitant use of Lexapro with NSAIDs, aspirin, or other drugs that affect coagulation. Hyponatremia Cases of hyponatremia and SIADH (syndrome of inappropriate antidiuretic hormone secretion) have been reported in association with Lexapro treatment. All patients with these events have recovered with discontinuation of escitalopram and/or medical intervention. Hyponatremia and SIADH have also been reported in association with other marketed drugs effective in the treatment of major depressive disorder. Activation of Mania/Hypomania In placebo-controlled trials of Lexapro in major depressive disorder, activation of mania/hypomania was reported in one (0.1%) of 715 patients treated with Lexapro and in none of the 592 patients treated with placebo. One additional case of hypomania has been reported in association with Lexapro treatment. Activation of mania/hypomania has also been reported in a small proportion of patients with major affective disorders treated with racemic citalopram and other marketed drugs effective in the treatment of major depressive disorder. As with all drugs effective in the treatment of major depressive disorder, Lexapro should be used cautiously in patients with a history of mania. Seizures Although anticonvulsant effects of racemic citalopram have been observed in animal studies, Lexapro has not been systematically evaluated in patients with a seizure disorder. These patients were excluded from clinical studies during the product's premarketing testing. In clinical trials of Lexapro, cases of convulsion have been reported in association with Lexapro treatment. Like other drugs effective in the treatment of major depressive disorder, Lexapro should be introduced with care in patients with a history of seizure disorder. Interference with Cognitive and Motor Performance In a study in normal volunteers, Lexapro 10 mg/day did not produce impairment of intellectual function or psychomotor performance. Because any psychoactive drug may impair judgment, thinking, or motor skills, however, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that Lexapro therapy does not affect their ability to engage in such activities. Use in Patients with Concomitant Illness Clinical experience with Lexapro in patients with certain concomitant systemic illnesses is limited. Caution is advisable in using Lexapro in patients with diseases or conditions that produce altered metabolism or hemodynamic responses. Lexapro has not been systematically evaluated in patients with a recent history of myocardial infarction or unstable heart disease. Patients with these diagnoses were generally excluded from clinical studies during the product's premarketing testing. In subjects with hepatic impairment, clearance of racemic citalopram was decreased and plasma concentrations were increased. The recommended dose of Lexapro in hepatically impaired patients is 10 mg/day (see **DOSAGE AND ADMINISTRATION**). Because escitalopram is extensively metabolized, excretion of unchanged drug in urine is a minor route of elimination. Until adequate numbers of patients with severe renal impairment have been evaluated during chronic treatment with Lexapro, however, it should be used with caution in such patients (see **DOSAGE AND ADMINISTRATION**). **Information for Patients** Physicians are advised to discuss the following issues with patients for whom they prescribe Lexapro. Patients should be cautioned about the risk of serotonin syndrome with the concomitant use of Lexapro and triptans, tramadol or other serotonergic agents. In a study in normal volunteers, Lexapro 10 mg/day did not impair psychomotor performance. The effect of Lexapro on psychomotor coordination, judgment, or thinking has not been systematically examined in controlled studies. Because psychoactive drugs may impair judgment, thinking, or motor skills, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that Lexapro therapy does not affect their ability to engage in such activities. Patients should be told that, although Lexapro has not been shown in experiments with normal subjects to increase the mental and motor skill impairments caused by alcohol, the concomitant use of Lexapro and alcohol in depressed patients is not advised. Patients should be made aware that escitalopram is the active isomer of Celexa (citalopram hydrobromide) and that the two medications should not be taken concomitantly. Patients should be advised to inform their physician if they are taking, or plan to take, any prescription or over-the-counter drugs, as there is a potential for interactions. Patients should be cautioned about the concomitant use of Lexapro and NSAIDs, aspirin, or other drugs that affect coagulation since the combined use of psychotropic drugs that interfere with serotonin reuptake and these agents has been associated with an increased risk of bleeding. Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during therapy. Patients should be advised to notify their physician if they are breastfeeding an infant. While patients may notice improvement with Lexapro therapy in 1 to 4 weeks, they should be advised to continue therapy as directed. Prescribers or other health professionals should inform patients, their families, and their caregivers about the benefits and risks associated with treatment with Lexapro and should counsel them in its appropriate use. A patient Medication Guide about "Antidepressant Medicines, Depression and other Serious Mental Illness, and Suicidal Thoughts or Actions" is available for Lexapro. The prescriber or health professional should instruct patients, their families, and their caregivers to read the Medication Guide and should assist them in understanding its contents. Patients should be given the opportunity to discuss the contents of the Medication Guide and to obtain answers

to any questions they may have. Patients should be advised of the following issues and asked to alert their prescriber if these occur while taking Lexapro. **Clinical Worsening and Suicide Risk:** Patients, their families, and their caregivers should be encouraged to be alert to the emergence of anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, mania, other unusual changes in behavior, worsening of depression, and suicidal ideation, especially early during anti-depressant treatment and when the dose is adjusted up or down. Families and caregivers of patients should be advised to look for the emergence of such symptoms on a day-to-day basis, since changes may be abrupt. Such symptoms should be reported to the patient's prescriber or health professional, especially if they are severe, abrupt in onset, or were not part of the patient's presenting symptoms. Symptoms such as these may be associated with an increased risk for suicidal thinking and behavior and indicate a need for very close monitoring and possibly changes in the medication. **Laboratory Tests** There are no specific laboratory tests recommended. **Concomitant Administration with Racemic Citalopram** Citalopram - Since escitalopram is the active isomer of racemic citalopram (Celexa), the two agents should not be coadministered. **Drug Interactions Serotonergic Drugs:** Based on the mechanism of action of SNRIs and SSRIs including Lexapro, and the potential for serotonin syndrome, caution is advised when Lexapro is coadministered with other drugs that may affect the serotonergic neurotransmitter systems, such as triptans, linezolid (an antibiotic which is a reversible non-selective MAOI), lithium, tramadol, or St. John's Wort (see **WARNINGS-Serotonin Syndrome**). The concomitant use of Lexapro with other SSRIs, SNRIs or tryptophan is not recommended (see **PRECAUTIONS - Drug Interactions**). **Triptans:** There have been rare postmarketing reports of serotonin syndrome with use of an SSRI and a triptan. If concomitant treatment of Lexapro with a triptan is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases (see **WARNINGS - Serotonin Syndrome**). CNS Drugs - Given the primary CNS effects of escitalopram, caution should be used when it is taken in combination with other centrally acting drugs. Alcohol - Although Lexapro did not potentiate the cognitive and motor effects of alcohol in a clinical trial, as with other psychotropic medications, the use of alcohol by patients taking Lexapro is not recommended. Monoamine Oxidase Inhibitors (MAOIs) - See **CONTRAINDICATIONS** and **WARNINGS**. **Drugs That Interfere With Hemostasis (NSAIDs, Aspirin, Warfarin, etc.)** Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies of the case-control and cohort design that have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding have also shown that concurrent use of an NSAID or aspirin potentiated the risk of bleeding. Thus, patients should be cautioned about the use of such drugs concurrently with Lexapro. Cimetidine - In subjects who had received 21 days of 40 mg/day racemic citalopram, combined administration of 400 mg/day cimetidine for 8 days resulted in an increase in citalopram AUC and C_{max} of 43% and 39%, respectively. The clinical significance of these findings is unknown. Digoxin - In subjects who had received 21 days of 40 mg/day racemic citalopram, combined administration of citalopram and digoxin (single dose of 1 mg) did not significantly affect the pharmacokinetics of either citalopram or digoxin. Lithium - Coadministration of racemic citalopram (40 mg/day for 10 days) and lithium (30 mmol/day for 5 days) had no significant effect on the pharmacokinetics of citalopram or lithium. Nevertheless, plasma lithium levels should be monitored with appropriate adjustment to the lithium dose in accordance with standard clinical practice. Because lithium may enhance the serotonergic effects of escitalopram, caution should be exercised when Lexapro and lithium are coadministered. Pimozide and Celexa - In a controlled study, a single dose of pimozide 2 mg co-administered with racemic citalopram 40 mg given once daily for 11 days was associated with a mean increase in QTc values of approximately 10 msec compared to pimozide given alone. Racemic citalopram did not alter the mean AUC or C_{max} of pimozide. The mechanism of this pharmacodynamic interaction is not known. Sumatriptan - There have been rare postmarketing reports describing patients with weakness, hyperreflexia, and incoordination following the use of an SSRI and sumatriptan. If concomitant treatment with sumatriptan and an SSRI (e.g., fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram, escitalopram) is clinically warranted, appropriate observation of the patient is advised. Theophylline - Combined administration of racemic citalopram (40 mg/day for 21 days) and the CYP1A2 substrate theophylline (single dose of 300 mg) did not affect the pharmacokinetics of theophylline. The effect of theophylline on the pharmacokinetics of citalopram was not evaluated. Warfarin - Administration of 40 mg/day racemic citalopram for 21 days did not affect the pharmacokinetics of warfarin, a CYP3A4 substrate. Prothrombin time was increased by 5%, the clinical significance of which is unknown. Carbamazepine - Combined administration of racemic citalopram (40 mg/day for 14 days) and carbamazepine (titrated to 400 mg/day for 35 days) did not significantly affect the pharmacokinetics of carbamazepine, a CYP3A4 substrate. Although trough citalopram plasma levels were unaffected, given the enzyme-inducing properties of carbamazepine, the possibility that carbamazepine might increase the clearance of escitalopram should be considered if the two drugs are coadministered. Triazolam - Combined administration of racemic citalopram (titrated to 40 mg/day for 28 days) and the CYP3A4 substrate triazolam (single dose of 0.25 mg) did not significantly affect the pharmacokinetics of either citalopram or triazolam. Ketoconazole - Combined administration of racemic citalopram (40 mg) and ketoconazole (200 mg), a potent CYP3A4 inhibitor, decreased the C_{max} and AUC of ketoconazole by 21% and 10%, respectively, and did not significantly affect the pharmacokinetics of citalopram. Ritonavir - Combined administration of a single dose of ritonavir (600 mg), both a CYP3A4 substrate and a potent inhibitor of CYP3A4, and escitalopram (20 mg) did not affect the pharmacokinetics of either ritonavir or escitalopram. CYP3A4 and -2C19 Inhibitors - *In vitro* studies indicated that CYP3A4 and -2C19 are the primary enzymes involved in the metabolism of escitalopram. However, coadministration of escitalopram (20 mg) and ritonavir (600 mg), a potent inhibitor of CYP3A4, did not significantly affect the pharmacokinetics of escitalopram. Because escitalopram is metabolized by multiple enzyme systems, inhibition of a single enzyme may not appreciably decrease escitalopram clearance. Drugs Metabolized by Cytochrome P4502D6 - *In vitro* studies did not reveal an inhibitory effect of escitalopram on CYP2D6. In addition, steady state levels of racemic citalopram were not significantly different in poor metabolizers and extensive CYP2D6 metabolizers after multiple-dose administration of citalopram, suggesting that coadministration, with escitalopram, of a drug that inhibits CYP2D6, is unlikely to have clinically significant effects on escitalopram metabolism. However, there are limited *in vivo* data suggesting a modest CYP2D6 inhibitory effect for escitalopram, i.e., coadministration of escitalopram (20 mg/day for 21 days) with the tricyclic antidepressant desipramine (single dose of 50 mg), a substrate for CYP2D6, resulted in a 40% increase in C_{max} and a 100% increase in AUC of desipramine. The clinical significance of this finding is unknown. Nevertheless, caution is indicated in the coadministration of escitalopram and drugs metabolized by CYP2D6. Metoprolol - Administration of 20 mg/day Lexapro for 21 days in healthy volunteers resulted in a 50% increase in C_{max} and 82% increase in AUC of the beta-adrenergic blocker metoprolol (given in a single dose of 100 mg). Increased metoprolol plasma levels have been associated with decreased cardioselectivity. Coadministration of Lexapro and metoprolol had no clinically significant effects on blood pressure or heart rate. Electroconvulsive Therapy (ECT) - There are no clinical studies of the combined use of ECT and escitalopram. **Carcinogenesis, Mutagenesis, Impairment of Fertility** Carcinogenesis Racemic citalopram was administered in the diet to NMRI/BOM strain mice and COBS WI strain rats for 18 and 24 months, respectively. There was no evidence for carcinogenicity of racemic citalopram in mice receiving up to 240 mg/kg/day. There was an increased incidence of small intestine carcinoma in rats receiving 8 or 24 mg/kg/day racemic citalopram. A no-effect dose for this finding was not established. The relevance of these findings to humans is unknown. Mutagenesis Racemic citalopram was mutagenic in the *in vitro* bacterial reverse mutation assay (Ames test) in 2 of 5 bacterial strains (Salmonella TA98 and TA1537) in the absence of metabolic activation. It was clastogenic in the *in vitro* Chinese hamster lung cell assay for chromosomal aberrations in the presence and absence of metabolic activation. Racemic citalopram was not mutagenic in the *in vitro* mammalian forward gene mutation assay (HPRT) in mouse lymphoma cells or in a coupled *in vitro*/*in vivo* unscheduled DNA synthesis (UDS) assay in rat liver. It was not clastogenic in the *in vitro* chromosomal aberration assay in human lymphocytes or in two *in vivo* mouse micronucleus assays. Impairment of Fertility When racemic citalopram was administered orally to 16 male and 24 female rats prior to and throughout mating and gestation at doses of 32, 48, and 72 mg/kg/day, mating was decreased at all doses, and fertility was decreased at doses ≥ 32 mg/kg/day. Gestation duration was increased at 48 mg/kg/day. **Pregnancy** Pregnancy Category C In a rat embryo/fetal development study, oral administration of escitalopram (56, 112, or 150 mg/kg/day) to pregnant animals during the period of organogenesis resulted in decreased fetal body weight and associated delays in ossification at the two higher doses (approximately ≥ 56 times the maximum recommended human dose [MRHD] of 20 mg/day on a body surface area [mg/m^2] basis). Maternal toxicity (clinical signs and decreased body weight gain and food consumption), mild at 56 mg/kg/day, was present at all dose levels. The developmental no-effect dose of 56 mg/kg/day is approximately 28 times the MRHD on a mg/m^2 basis. No teratogenicity was observed at any of the doses tested (as high as 75 times the MRHD on a mg/m^2 basis). When female rats were treated with escitalopram (6, 12, 24, or 48 mg/kg/day) during pregnancy and through weaning, slightly increased offspring mortality and growth retardation were noted at 48 mg/kg/day which is approximately 24 times the MRHD on a mg/m^2 basis. Slight maternal toxicity (clinical signs and decreased body weight gain and food consumption) was seen at this dose. Slightly increased offspring mortality was seen at 24 mg/kg/day. The no-effect dose was 12 mg/kg/day which is approximately 6 times the MRHD on a mg/m^2 basis. In animal reproduction studies, racemic citalopram has been shown to have adverse effects on embryo/fetal and postnatal development, including teratogenic effects, when administered at doses greater than human therapeutic doses. In two rat embryo/fetal development studies, oral administration of racemic citalopram (32, 56, or 112 mg/kg/day) to pregnant animals during the period of organogenesis resulted in decreased embryo/fetal growth and survival and an increased incidence of fetal abnormalities (including cardiovascular and skeletal defects) at the high dose. This dose was also associated with maternal toxicity (clinical signs, decreased body weight gain). The developmental no-effect dose was 56 mg/kg/day. In a rabbit study, no adverse effects on embryo/fetal development were observed at doses of racemic citalopram of up to 16 mg/kg/day. Thus, teratogenic effects of racemic citalopram were observed at a maternally toxic dose in the rat and were not observed in the rabbit. When female rats were treated with racemic citalopram (4.8, 12.8, or 32 mg/kg/day) from late gestation through weaning, increased offspring mortality during the first 4 days after birth and persistent offspring growth retardation were observed at the highest dose. The no-effect dose was 12.8 mg/kg/day. Similar effects on offspring mortality and growth were seen when dams were treated throughout gestation and early lactation at doses ≥ 24 mg/kg/day. A no-effect dose was not determined in that study. There are no adequate and well-controlled studies in pregnant women; therefore, escitalopram should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Pregnancy-Nonteratogenic Effects** Neonates exposed to Lexapro and other SSRIs or SNRIs, late in the third trimester, have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. Such complications can arise immediately upon delivery. Reported clinical findings have included respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying. These features are consistent with either a direct toxic effect of SSRIs and SNRIs or, possibly, a drug discontinuation syndrome. It should be noted that, in some cases, the clinical picture is consistent with serotonin syndrome (see **WARNINGS**). Infants exposed to SSRIs in late pregnancy may have an increased risk for persistent pulmonary hypertension of the newborn (PPHN). PPHN occurs in 1–2 per 1000 live births in the general population and is associated with substantial neonatal morbidity and mortality. In a retrospective, case-control study of 377 women whose infants were born with PPHN and 836 women whose infants were born healthy, the risk for developing PPHN was approximately six-fold higher for infants exposed to SSRIs after the 20th week of gestation compared to infants who had not been exposed to antidepressants during pregnancy. There is currently no corroborative evidence regarding the risk for PPHN following exposure to SSRIs in pregnancy; this is the first study that has investigated the potential risk. The study did not include enough cases with exposure to individual SSRIs to determine if all SSRIs posed similar levels of PPHN risk. When treating a pregnant woman with Lexapro during the third trimester, the physician should carefully consider both the potential risks and benefits of treatment (see **DOSAGE AND ADMINISTRATION**). Physicians should note that in a prospective longitudinal study of 201 women with a history of major depression who were euthymic at the beginning of pregnancy, women who discontinued antidepressant medication during pregnancy were more likely to experience a relapse of major depression than women who continued antidepressant medication. **Labor and Delivery** The effect of Lexapro on labor and delivery in humans is unknown. **Nursing Mothers** Racemic citalopram, like many other drugs, is excreted in human breast milk. There have been two reports of infants experiencing excessive somnolence, decreased feeding, and weight loss in association with breastfeeding from a citalopram-treated mother; in one case, the infant was reported to recover completely upon discontinuation of citalopram by its mother and, in the second case, no follow-up information was available. The decision whether to continue or discontinue either nursing or Lexapro therapy should take into account the risks of citalopram exposure for the infant and the benefits of Lexapro treatment for the mother. **Pediatric Use** Safety and effectiveness in the pediatric population have not been established (see **BOX WARNING** and **WARNINGS—Clinical Worsening and Suicide Risk**). One placebo-controlled trial in 264 pediatric patients with MDD has been conducted with Lexapro, and the data were not sufficient to support a claim for use in pediatric patients. Anyone considering the use of Lexapro in a child or adolescent must balance the potential risks with the clinical need. **Geriatric Use** Approximately 6% of the 1144 patients receiving escitalopram in controlled trials of Lexapro in major depressive disorder and GAD were 60 years of age or older; elderly patients in these trials received daily doses of Lexapro between 10 and 20 mg. The number of elderly patients in these trials was insufficient to adequately assess for possible differential efficacy and safety measures on the basis of age. Nevertheless, greater sensitivity of some elderly individuals to effects of Lexapro cannot be ruled out. In two pharmacokinetic studies, escitalopram half-life was increased by approximately 50% in elderly subjects as compared to young subjects and C_{max} was unchanged (see **CLINICAL PHARMACOLOGY**). 10 mg/day is the recommended dose for elderly patients (see **DOSAGE AND ADMINISTRATION**). Of 4422 patients in clinical studies of racemic citalopram, 1357 were 60 and over, 1034 were 65 and over, and 457 were 75 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but again, greater sensitivity of some elderly individuals cannot be ruled out. **ADVERSE REACTIONS** Adverse event information for Lexapro was collected from 715 patients with major depressive disorder who were exposed to escitalopram and from 592 patients who were exposed to placebo in double-blind, placebo-controlled trials. An additional 284 patients with major depressive disorder were newly exposed to escitalopram in open-label trials. The adverse event information for Lexapro in patients with

GAD was collected from 429 patients exposed to escitalopram and from 427 patients exposed to placebo in double-blind, placebo-controlled trials. Adverse events during exposure were obtained primarily by general inquiry and recorded by clinical investigators using terminology of their own choosing. Consequently, it is not possible to provide a meaningful estimate of the proportion of individuals experiencing adverse events without first grouping similar types of events into a smaller number of standardized event categories. In the tables and tabulations that follow, standard World Health Organization (WHO) terminology has been used to classify reported adverse events. The stated frequencies of adverse events represent the proportion of individuals who experienced, at least once, a treatment-emergent adverse event of the type listed. An event was considered treatment-emergent if it occurred for the first time or worsened while receiving therapy following baseline evaluation. **Adverse Events Associated with Discontinuation of Treatment Major Depressive Disorder** Among the 715 depressed patients who received Lexapro in placebo-controlled trials, 6% discontinued treatment due to an adverse event, as compared to 2% of 592 patients receiving placebo. In two fixed-dose studies, the rate of discontinuation for adverse events in patients receiving 10 mg/day Lexapro was not significantly different from the rate of discontinuation for adverse events in patients receiving placebo. The rate of discontinuation for adverse events in patients assigned to a fixed dose of 20 mg/day Lexapro was 10%, which was significantly different from the rate of discontinuation for adverse events in patients receiving 10 mg/day Lexapro (4%) and placebo (3%). Adverse events that were associated with the discontinuation of at least 1% of patients treated with Lexapro, and for which the rate was at least twice that of placebo, were nausea (2%) and ejaculation disorder (2% of male patients). **Generalized Anxiety Disorder** Among the 429 GAD patients who received Lexapro 10-20 mg/day in placebo-controlled trials, 8% discontinued treatment due to an adverse event, as compared to 4% of 427 patients receiving placebo. Adverse events that were associated with the discontinuation of at least 1% of patients treated with Lexapro, and for which the rate was at least twice the placebo rate, were nausea (2%), insomnia (1%), and fatigue (1%). **Incidence of Adverse Events in Placebo-Controlled Clinical Trials Major Depressive Disorder Table 2** enumerates the incidence, rounded to the nearest percent, of treatment-emergent adverse events that occurred among 715 depressed patients who received Lexapro at doses ranging from 10 to 20 mg/day in placebo-controlled trials. Events included are those occurring in 2% or more of patients treated with Lexapro and for which the incidence in patients treated with Lexapro was greater than the incidence in placebo-treated patients. The prescriber should be aware that these figures cannot be used to predict the incidence of adverse events in the course of usual medical practice where patient characteristics and other factors differ from those which prevailed in the clinical trials. Similarly, the cited frequencies cannot be compared with figures obtained from other clinical investigations involving different treatments, uses, and investigators. The cited figures, however, do provide the prescribing physician with some basis for estimating the relative contribution of drug and non-drug factors to the adverse event incidence rate in the population studied. The most commonly observed adverse events in Lexapro patients (incidence of approximately 5% or greater and approximately twice the incidence in placebo patients) were insomnia, ejaculation disorder (primarily ejaculatory delay), nausea, sweating increased, fatigue, and somnolence (see **TABLE 2**). **TABLE 2: Treatment-Emergent Adverse Events: Incidence in Placebo-Controlled Clinical Trials for Major Depressive Disorder* [Lexapro (N=715) and Placebo (N=592)]: Autonomic Nervous System Disorders:** Dry Mouth (6% and 5%); Sweating Increased (5% and 2%). **Central & Peripheral Nervous System Disorders:** Dizziness (5% and 3%). **Gastrointestinal Disorders:** Nausea (15% and 7%); Diarrhea (8% and 5%); Constipation (3% and 1%); Indigestion (3% and 1%); Abdominal Pain (2% and 1%). **General:** Influenza-like Symptoms (5% and 4%); Fatigue (5% and 2%). **Psychiatric Disorders:** Insomnia (9% and 4%); Somnolence (6% and 2%); Appetite Decreased (3% and 1 %); Libido Decreased (3% and 1%). **Respiratory System Disorders:** Rhinitis (5% and 4%); Sinusitis (3% and 2%). **Urogenital:** Ejaculation Disorder[1,2] (9% and <1%); Impotence[2] (3% and <1%); Anorgasmia[3] (2% and <1%). *Events reported by at least 2% of patients treated with Lexapro are reported, except for the following events which had an incidence on placebo ≥ Lexapro: headache, upper respiratory tract infection, back pain, pharyngitis, inflicted injury, anxiety. [1]Primarily ejaculatory delay. [2]Denominator used was for males only (N=225 Lexapro; N=188 placebo). [3]Denominator used was for females only (N=490 Lexapro; N=404 placebo). **Generalized Anxiety Disorder Table 3** enumerates the incidence, rounded to the nearest percent of treatment-emergent adverse events that occurred among 429 GAD patients who received Lexapro 10 to 20 mg/day in placebo-controlled trials. Events included are those occurring in 2% or more of patients treated with Lexapro and for which the incidence in patients treated with Lexapro was greater than the incidence in placebo-treated patients. The most commonly observed adverse events in Lexapro patients (incidence of approximately 5% or greater and approximately twice the incidence in placebo patients) were nausea, ejaculation disorder (primarily ejaculatory delay), insomnia, fatigue, decreased libido, and anorgasmia (see **TABLE 3**). **TABLE 3: Treatment-Emergent Adverse Events: Incidence in Placebo-Controlled Clinical Trials for Generalized Anxiety Disorder* [Lexapro (N=429) and Placebo (N=427)]: Autonomic Nervous System Disorders:** Dry Mouth (9% and 5%); Sweating Increased (4% and 1%). **Central & Peripheral Nervous System Disorders:** Headache (24% and 17%); Paresthesia (2% and 1%). **Gastrointestinal Disorders:** Nausea (18% and 8%); Diarrhea (8% and 6%); Constipation (5% and 4%); Indigestion (3% and 2%); Vomiting (3% and 1%); Abdominal Pain (2% and 1%); Flatulence (2% and 1%); Toothache (2% and 0%). **General:** Fatigue (8% and 2%); Influenza-like symptoms (5% and 4%). **Musculoskeletal:** Neck/Shoulder Pain (3% and 1%). **Psychiatric Disorders:** Somnolence (13% and 7%); Insomnia (12% and 6%); Libido Decreased (7% and 2%); Dreaming Abnormal (3% and 2%); Appetite Decreased (3% and 1%); Lethargy (3% and 1%); Yawning (2% and 1%). **Urogenital:** Ejaculation Disorder[1,2] (14% and 2%); Anorgasmia[3] (6% and <1%); Menstrual Disorder (2% and 1%). *Events reported by at least 2% of patients treated with Lexapro are reported, except for the following events which had an incidence on placebo ≥ Lexapro: inflicted injury, dizziness, back pain, upper respiratory tract infection, rhinitis, pharyngitis. [1]Primarily ejaculatory delay. [2]Denominator used was for males only (N=182 Lexapro; N=195 placebo). [3]Denominator used was for females only (N=247 Lexapro; N=232 placebo). **Dose Dependency of Adverse Events** The potential dose dependency of common adverse events (defined as an incidence rate of ≥5% in either the 10 mg or 20 mg Lexapro groups) was examined on the basis of the combined incidence of adverse events in two fixed-dose trials. The overall incidence rates of adverse events in 10 mg Lexapro-treated patients (66%) was similar to that of the placebo-treated patients (61%), while the incidence rate in 20 mg/day Lexapro-treated patients was greater (86%). **Table 4** shows common adverse events that occurred in the 20 mg/day Lexapro group with an incidence that was approximately twice that of the 10 mg/day Lexapro group and approximately twice that of the placebo group. **TABLE 4: Incidence of Common Adverse Events* in Patients with Major Depressive Disorder Receiving Placebo (N=311), 10 mg/day Lexapro (N=310), 20 mg/day Lexapro (N=125)]: Insomnia** (4%, 7%, 14%); **Diarrhea** (5%, 6%, 14%); **Dry Mouth** (3%, 4%, 9%); **Somnolence** (1%, 4%, 9%); **Dizziness** (2%, 4%, 7%); **Sweating Increased** (<1%, 3%, 8%); **Constipation** (1%, 3%, 6%); **Fatigue** (2%, 2%, 6%); **Indigestion** (1%, 2%, 6%). *Adverse events with an incidence rate of at least 5% in either of the Lexapro groups and with an incidence rate in the 20 mg/day Lexapro group that was approximately twice that of the 10 mg/day Lexapro group and the placebo group. **Male and Female Sexual Dysfunction with SSRIs** Although changes in sexual desire, sexual performance, and sexual satisfaction often occur as manifestations of a psychiatric disorder, they may also be a consequence of pharmacologic treatment. In particular, some evidence suggests that SSRIs can cause such untoward sexual experiences. Reliable estimates of the incidence and severity of untoward experiences involving sexual desire, performance, and satisfaction are difficult to obtain, however, in part because patients and physicians may be reluctant to discuss them. Accordingly, estimates of the incidence of untoward sexual experience and performance cited in product labeling are likely to underestimate their actual incidence. **Table 5** shows the incidence rates of sexual side effects in patients with major depressive disorder and GAD in placebo-controlled trials. **TABLE 5: Incidence of Sexual Side Effects in Placebo-Controlled Clinical Trials [**In Males Only: **Lexapro** (N=407) **and Placebo** (N=383)**]:** Ejaculation Disorder (primarily ejaculatory delay) (12% and 1%); Libido Decreased (6% and 2%); Impotence (2% and <1%). **[**In Females Only**: Lexapro** (N=737) **and Placebo** (N=636)**]:** Libido Decreased (3% and 1%); Anorgasmia (3% and <1%) There are no adequately designed studies examining sexual dysfunction with escitalopram treatment. Priapism has been reported with all SSRIs. While it is difficult to know the precise risk of sexual dysfunction associated with the use of SSRIs, physicians should routinely inquire about such possible side effects. **Vital Sign Changes** Lexapro and placebo groups were compared with respect to (1) mean change from baseline in vital signs (pulse, systolic blood pressure, and diastolic blood pressure) and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses did not reveal any clinically important changes in vital signs associated with Lexapro treatment. In addition, a comparison of supine and standing vital sign measures in subjects receiving Lexapro indicated that Lexapro treatment is not associated with orthostatic changes. **Weight Changes** Patients treated with Lexapro in controlled trials did not differ from placebo-treated patients with regard to clinically important change in body weight. **Laboratory Changes** Lexapro and placebo groups were compared with respect to (1) mean change from baseline in various serum chemistry, hematology, and urinalysis variables, and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed no clinically important changes in laboratory test parameters associated with Lexapro treatment. **ECG Changes** Electrocardiograms from Lexapro (N=625), racemic citalopram (N=351), and placebo (N=527) groups were compared with respect to (1) mean change from baseline in various ECG parameters and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed (1) a decrease in heart rate of 2.2 bpm for Lexapro and 2.7 bpm for racemic citalopram, compared to an increase of 0.3 bpm for placebo and (2) an increase in QTc interval of 3.9 msec for Lexapro and 3.7 msec for racemic citalopram, compared to 0.5 msec for placebo. Neither Lexapro nor racemic citalopram were associated with the development of clinically significant ECG abnormalities. **Other Events Observed During the Premarketing Evaluation of Lexapro** Following is a list of WHO terms that reflect treatment-emergent adverse events, as defined in the introduction to the **ADVERSE REACTIONS** section, reported by the 1428 patients treated with Lexapro for periods of up to one year in double-blind or open-label clinical trials during its premarketing evaluation. All reported events are included except those already listed in **Tables 2 & 3**, those occurring in only one patient, event terms that are so general as to be uninformative, and those that are unlikely to be drug related. It is important to emphasize that, although the events reported occurred during treatment with Lexapro, they were not necessarily caused by it. Events are further categorized by body system and listed in order of decreasing frequency according to the following definitions: frequent adverse events are those occurring on one or more occasions in at least 1/100 patients; infrequent adverse events are those occurring in less than 1/100 patients but at least 1/1000 patients. Cardiovascular - *Frequent:* palpitation, hypertension. *Infrequent:* bradycardia, tachycardia, ECG abnormal, flushing, varicose vein. Central and Peripheral Nervous System Disorders - *Frequent:* light-headed feeling, migraine. *Infrequent:* tremor, vertigo, restless legs, shaking, twitching, dysequilibrium, tics, carpal tunnel syndrome, muscle contractions involuntary, sluggishness, coordination abnormal, faintness, hyperreflexia, muscular tone increased. Gastrointestinal Disorders - *Frequent:* heartburn, abdominal cramp, gastroenteritis. *Infrequent:* gastroesophageal reflux, bloating, abdominal discomfort, dyspepsia, increased stool frequency, belching, gastritis, hemorrhoids, gagging, polyposis gastric, swallowing difficult. General - *Frequent:* allergy, pain in limb, fever, hot flushes, chest pain. *Infrequent:* edema of extremities, chills, tightness of chest, leg pain, asthenia, syncope, malaise, anaphylaxis, fall. Hemic and Lymphatic Disorders - *Infrequent:* bruise, anemia, nosebleed, hematoma, lymphadenopathy cervical. Metabolic and Nutritional Disorders - *Frequent:* increased weight. *Infrequent:* decreased weight, hyperglycemia, thirst, bilirubin increased, hepatic enzymes increased, gout, hypercholesterolemia. Musculoskeletal System Disorders - *Frequent:* arthralgia, myalgia. *Infrequent:* jaw stiffness, muscle cramp, muscle stiffness, arthritis, muscle weakness, back discomfort, arthropathy, jaw pain, joint stiffness. Psychiatric Disorders - *Frequent:* appetite increased, lethargy, irritability, concentration impaired. *Infrequent:* jitteriness, panic reaction, agitation, apathy, forgetfulness, depression aggravated, nervousness, restlessness aggravated, suicide attempt, amnesia, anxiety attack, bruxism, carbohydrate craving, confusion, depersonalization, disorientation, emotional lability, feeling unreal, tremulousness nervous, crying abnormal, depression, excitability, auditory hallucination, suicidal tendency. Reproductive Disorders/Female* - *Frequent:* menstrual cramps, menstrual disorder. *Infrequent:* menorrhagia, breast neoplasm, pelvic inflammation, premenstrual syndrome, spotting between menses. *% based on female subjects only: N= 905 Respiratory System Disorders - *Frequent:* bronchitis, sinus congestion, coughing, nasal congestion, sinus headache. *Infrequent:* asthma, breath shortness, laryngitis, pneumonia, tracheitis. Skin and Appendages Disorders - *Frequent:* rash. *Infrequent:* pruritus, acne, alopecia, eczema, dermatitis, dry skin, folliculitis, lipoma, furunculosis, dry lips, skin nodule. Special Senses - *Frequent:* vision blurred, tinnitus. *Infrequent:* taste alteration, earache, conjunctivitis, vision abnormal, dry eyes, eye irritation, visual disturbance, eye infection, pupils dilated, metallic taste. Urinary System Disorders - *Frequent:* urinary frequency, urinary tract infection. *Infrequent:* urinary urgency, kidney stone, dysuria, blood in urine. **Events Reported Subsequent to the Marketing of Escitalopram** - Although no causal relationship to escitalopram treatment has been found, the following adverse events have been reported to have occurred in patients and to be temporally associated with escitalopram treatment during post marketing experience and were not observed during the premarketing evaluation of escitalopram: abnormal gait, acute renal failure, aggression, akathisia, allergic reaction, anger, angioedema, atrial fibrillation, choreoathetosis, delirium, delusion, diplopia, dysarthria, dyskinesia, dystonia, ecchymosis, erythema multiforme, extrapyramidal disorders, fulminant hepatitis, hepatic failure, hypoaesthesia, hypoglycemia, hypokalemia, INR increased, gastrointestinal hemorrhage, glaucoma, grand mal seizures (or convulsions), hemolytic anemia, hepatic necrosis, hepatitis, hypotension, leucopenia, myocardial infarction, myoclonus, neuroleptic malignant syndrome, nightmare, nystagmus, orthostatic hypotension, pancreatitis, paranoia, photosensitivity reaction, priapism, prolactinemia, prothrombin decreased, pulmonary embolism, QT prolongation, rhabdomyolysis, seizures, serotonin syndrome, SIADH, spontaneous abortion, Stevens Johnson Syndrome, tardive dyskinesia, thrombocytopenia, thrombosis, torsade de pointes, toxic epidermal necrolysis, ventricular arrhythmia, ventricular tachycardia and visual hallucinations.

care in order to facilitate risk-sharing arrangements and specialty referrals. According to HSC, the organizational structure of the multispecialty group—with primary care physicians and a range of specialists—may offer patients the best chance at consistently high-quality care.

However, managed care did not grow to the extent expected. With mounting expenses and dwindling reimbursement, multispeciality groups hit hard financial times. Many physicians are now looking at practice models that increase efficiency and maximize income. Single-specialty groups offer a way to share resources and develop ancillary services that boost income. But does this change come at the patients' expense? That remains to be seen.

With mounting expenses and dwindling reimbursement, multispeciality groups hit hard financial times. Many physicians are now looking at practice models that increase efficiency and maximize income. Single-specialty groups offer a way to share resources and develop ancillary services that boost income. But does this change come at the patients' expense?

Another reason physicians are scrutinizing their practice models, says Mr. Goldsmith, is the continuing consolidation of health plans. "In many metro areas there are three plans that control 70 percent of the patients. But physicians continue to be scattered, fragmented. Unless that changes, they'll continue to be at a disadvantage," he says.

While physicians may be moving away from practice ownership, hospitals are heading back into the business of owning or managing medical practices, which could be an option for some physicians who predict that their solo or small practices will struggle in years to come. With luck, it won't be a repeat of the situation from the 1990s, when hospitals mostly fumbled the practice management ball. "They didn't invest in the infrastructure or the people to meaningfully change physician productivity or quality," says Mr. Goldsmith. But while hospitals are stepping back into the practice arena, Mr. Goldsmith says there won't be a repeat of the bidding wars and huge paydays for physicians that were common the first time around.

Mr. Goldsmith also sees the growing trend of separating office-based and hospital-based patient care as something that

will change the way physicians practice on a daily basis. He says that adult services will begin to look more like what pediatrics has looked like for many years, with some physicians based at the clinic and others at the hospital. This, of course, is already happening on a widespread basis with many physicians working as hospitalists. "I would have expected a huge controversy," says Mr. Goldsmith of the hospitalist movement, "but it hasn't occurred. Physicians are too time-famished to manage both a hospital-based and an office-based practice." In fact, the hospitalist movement may offer new opportunities for physicians who want to design a practice that fits their lives more closely.

Tightly managed practices with highly qualified administrators will be the ones that succeed in the future, predicts Jim Higgins, vice president with Applied Management Systems, Inc., an accounts-receivable, health-information, and systems-engineering management consulting company in Burlington, Mass. "The practices I see moving in a positive direction really have a handle on technology, whether it be EMR or the ability to have a

Roundtable: Practicing Physicians Speak Out on the Future of Medicine

Question: If you were put in charge of the healthcare system today, what would it look like ten years from now?

Dr. Ewing (Family Practice): I see a leaner, more effective system that has cut out many middlemen. [I see] universal coverage and a healthier populace at one-half to two-thirds of the current cost.

Dr. Mechanick (Endocrinology): Medical centers would have expanded roles in the community and take more of a lead in promoting healthy lifestyles to prevent disease, as well as improving the social climate. Satellite hospitals and smaller medical arts centers and clinical practices would be better linked to the centralized medical center for dissemination of state-of-the-art care. Reimbursements for practitioners would need to be reformed in a way that provides proper high-level reimbursement commensurate with the expertise of the medical profession, which at the same time would be cost efficient through the elimination of waste, redundancy, corruption, profiteering, and inappropriate decision making.

quick turnaround time with transcription," says Mr. Higgins. "Practices that are oriented toward numbers and quantifying and monitoring different aspects of the business—patient satisfaction, workflow, and throughput" are more likely to be financially viable, says Mr. Higgins. Attention to detail can make the difference between being profitable and not being around five years from now. It pays to pay attention. Mr. Higgins encourages physicians to make use of the statistics available from the Medical Group Management Association (*www.mgma.org*) to compare themselves with other practices.

Looking Ahead

Shrugging off all of the speculation with an 'it doesn't apply to me' or 'no one really knows the future' may be tempting, especially if the situation is not having a direct impact on how you practice today. But physicians who take the time to consider their own futures in the practice of medicine will be better prepared to handle whatever changes come.

Dr. Moskowitz (Radiology): I would provide basic health care to all peoples as a human right rather than as a privilege. The private medicine sector would survive, but be totally financed from patients directly, not insurance. At the same time, to help finance such widespread access to free care, I would drastically reduce the utilization of very expensive technology by placing tighter restrictions on the indications for such technology. Reimbursement for all healthcare services would be controlled and financed at a national level, taking control from third-party payors and insurance companies. Patient care would be based strictly on evidence-based outcomes. I would reduce the financial incentives for procedure-based specialty and sub-specialty practice and find ways to incentivize young physicians to enter and remain in primary care fields. Educational grant support from the federal government would be widely available to encourage young people to enter healthcare careers without incurring financially crippling debt. Clinical training and federally mandated practice guidelines would put practical limits on the work hours of all healthcare workers, eliminating the problems of professional burnout.