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Pharmaceutical Care Across the Continuum

Inside: 2000 reader survey

IN THIS ISSUE

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Caring for an aging America: Pharmacists have a critical role

Help avoid unnecessary hospitalizations

A large segment of the American population, and one that will grow enormously in the coming years, can use a helping hand from pharmacists. The elderly have special needs that pharmacists can help fill.

In 1990, approximately 13% of the U.S. population was older than 65. In the year 2015, 20% of Americans are expected to be part of that population, **Melissa Webb**, PharmD, CGP, assistant professor at the University of Kansas Medical Center's Center on Aging, tells *Drug Utilization Review*. "The over-85 group is the fastest-growing segment of older adults," Web explains. "Our older adults have special needs, the greatest of which is maintaining their independence. Many hospital admissions occur because the patient is on the wrong medication or because of a drug-drug interaction occurring between two of their medications. Pharmacists can make a huge difference in patient care by being alert to potential drug-related reasons for hospitalization upon admission."

> **"Pharmacists can make a huge difference in patient care by being alert to potential drug-related reasons for hospitalization upon admission."**

Throughout the hospital stay, pharmacists can detect and prevent drug-related problems for patients as medications and doses are changed. "Older adults should have their doses adjusted based on calculated creatinine clearance, not simply based on serum creatinine," Webb adds.

When depression occurs in older patients, it often goes untreated, although depression does not have to be a part of older age. Finances enter as another area of need because many older adults lack the funds necessary to support the medications they need. "Finances have become a vogue topic in this election year," Webb notes, "but it remains a very real need for patients."

In addition, she says, pharmacists should ask patients about use of herbal therapies and vitamins. Patients still are not asked about alternative medications routinely, although many patients use them, and the potential for interactions is real.

Webb encourages pharmacists to counsel patients on their medications when possible during a hospital stay, especially when drugs are changed. Upon hospital discharge, pharmacists again can help patients by providing clear written instructions regarding administration of drugs to be taken at home.

"Written instructions are important, as patients will often forget details of the counseling session. It's also important to review the patient's medications with the caregiver present," she says.

Make no bones about it

Among several other diseases, osteoporosis is more prevalent in older people. The Food and Drug Administration recently approved a new drug for treatment of osteoporosis. Actonel (risedronate) is a bisphosphonate that may be used for the treatment and prevention of osteoporosis in postmenopausal women and of glucocorticoid-induced osteoporosis in men and women.

The National Osteoporosis Foundation (NOF) commended the FDA for its approval of Actonel. "With approval of Actonel, women now have another choice of therapy for this disabling disease," says **Sandra C. Raymond**, NOF executive director.

"This therapy for the prevention and treatment of osteoporosis and its associated fractures will help at-risk women remain active, strong, and independent throughout their lives. This can only happen if women past menopause talk to their physicians to evaluate their bone health and, if appropriate, take action," Raymond explains.

At the same time, Lilly has reported tremendous sales growth for the post-menopausal osteoporosis drug Evista (raloxifene HCl) since its launch in 1999.

In May, the NOF launched its "Step On It America!" campaign for a lifetime of bone health. The campaign is a nationwide multiyear program. The first year focuses on the importance of weight-bearing exercises meant to build and maintain bone strength, helping to prevent painful fractures in the future. Weight-bearing exercise, as defined by the NOF, is any type of physical activity in which the bones and muscles work against gravity. It should be performed for 30 minutes at a time, four times a week to promote good bone health.

In the future, the campaign will emphasize other steps to bone health, including:

1. a diet rich in calcium and vitamin D;

2. abstinence from smoking and excessive alcohol consumption;

3. bone-density tests and preventive medications, if appropriate.

"Bone-density tests are not typically a routine part of a physical for older adults," says Webb. "However, they are often performed for patients who, after assessment or by history of a fracture, appear at higher risk for osteoporosis and bone fractures." She adds that bone-density tests are covered by most insurance plans.

Whether pharmacists recommend preventive tests or provide good medication counseling, Webb says, "We owe it to our patients to do everything we can do to help them prolong good quality of life." ■

SOURCES

- **Melissa Webb**, PharmD, CGP, Assistant Professor, University of Kansas Medical Center, Center on Aging, Kansas City, KS. Telephone: (913) 588-5372.

COMING IN FUTURE MONTHS

- Technology's involvement with medication errors
- Evaluating evidence-based medicine
- Occupational allergens
- Preventive medicine
- Pharmacy and gene therapy

Pharmacists play role in fighting breast cancer

Pharmacists play a key role in the fight against breast cancer. Being an integral part of the health care team, providing information necessary to help patients make informed decisions, and assisting in good clinical outcomes are among the goals pharmacists have set for pharmaceutical care.

As regular counselors of patients, pharmacists also are in a prime position to encourage patients to seek and be regular about preventive measures. They also can counsel patients who are on or are considering hormone replacement therapy (HRT) regarding its risks and benefits. Because HRT with estrogen may be associated with an increased risk of breast cancer, patients must weigh that risk against the potential benefits of a reduction of overall mortality based on the use of the drug. A family history of breast cancer also should be factored into counseling and decision making.

Assessing potential risk

Patients may ask their pharmacists about using tamoxifen to help prevent breast cancer. Clinical evidence suggests that tamoxifen reduces the risk of developing breast cancer in women who are at high risk for the disease. As with most clinical decisions, however, one must review the risk/benefit ratio involved. Tamoxifen can put patients at a higher risk for developing endometrial cancer or for experiencing thrombotic vascular events such as stroke, pulmonary embolism, or deep vein thrombosis.[1]

Pharmacists can help patients learn their estimated personal risk of developing breast cancer by using the Breast Cancer Risk Assessment Tool, a computer program developed by scientists at the National Cancer Institute and the National Surgical Adjuvant Breast and Bowel Project. The program assesses patients by asking for information regarding personal history of breast abnormalities, current age, age at first menstrual period, age at first live birth, history of breast cancer among first-degree family members, history of breast biopsy, and race. The program estimates the risk of developing cancer over the next five years and over the patient's lifetime. A diskette containing the assessment tool software is available free by request at http://cancertrials.nci.nih.gov/forms/CtRiskDisk.html.

Patients who ask for informative scientific information on the Internet regarding breast and other types of cancer can be directed to the National Cancer Institute's site at http://cancernet.nci.nih.gov/. Additionally, free publications on the prevention, early detection, diagnosis, and treatment of breast cancer may be obtained from the National Cancer Institute's Cancer Information Service by calling (800) 4-CANCER.

Not only does mammography (MMG) serve to provide early detection of breast cancer, it also appears to provide good outcomes in those cancers that are detected. In a report in the April 24 issue of *Archives of Internal Medicine*, Sandra Y. Moody-Ayers, MD, and colleagues from Yale University School of Medicine share the results of their study.[2]

The team performed a review of medical records of a natural cohort of 233 women who received their first antineoplastic treatment for breast cancer at Yale-New Haven Hospital between Jan. 1 and Dec. 31, 1988, with a median follow-up of 82.4 months. Members of the cohort had a median age of 62 years (range 26 to 87 years); 90% were white; and 93% had private insurance and/or Medicare.

Among the women, 14% had a history of breast cancer among first-degree relatives, and 68% of patients were post-menopausal. Clinically, 78% of patients had TNM **(see box, below)** stages 0, I, or IIA. Cancer was detected in the cohort by MMG screening in 42%, by other screening in 40%, and by symptomatic manifestation in 18%.

TNM Classification of Tumor Stages

T – Characteristics of primary tumor
N – Extent of nodal involvement
M – Presence/absence of metastatic disease

Of 31 patients with carcinoma in situ (CIS; microscopic lesions in the area of the ducts and lobules of the breast), none suffered recurrences or death, despite detection method of the cancer. Of those with stages I and IIA cancer, none of those detected by MMG had cancer deaths; one had a recurrence. In that same group, among those detected by other screening or by symptoms, 11 women suffered cancer death or had a recurrence. Similar results were seen among

those in stage IIB and in the combined stages III and IV groups; those with cancers detected by MMG screening had better outcomes. All patients had surgery, and the MMG-screened group was not treated more aggressively than those detected by other means. Therefore, treatment is not the reason for better outcomes for MMG-screened women, according to the study.

The skinny on prevention

Recently, the question has been raised whether obesity is a barrier to preventive care of both cervical and breast cancer. Because obesity often is accompanied by poor self-esteem and body image, it is thought that poor self-perception may prevent obese women from pursuing Pap smears and mammograms. Christina C. Wee and colleagues addressed that question in recent paper in the *Annals of Internal Medicine*.[3] Wee et al. performed a population-based survey using 11,435 responses from women to the "Year 2000 Supplement" of the 1994 National Health Interview Survey.

Results of the study showed that overweight women (body mass index 25 to < 30 kg / m^2) and obese women (body mass index 30 kg / m^2) "reported significantly lower rates of screening with Pap smears in the previous three years than did normal-weight women." The heavier women also tended to be older, less likely to be white or to have private health insurance, and were lower in socioeconomic status. They reported more illness than their thin counterparts and were more likely to seek care from general internists and family physicians than from gynecologists.

As members of the health care team, pharmacists can remind patients to perform monthly breast self-examinations and report any changes right away to their physicians. Patients also should be reminded to have yearly mammograms upon reaching the age of 40. Because mammography alone does not reveal all cases of breast cancer, the American Cancer Society recommends three methods of detection for asymptomatic women at usual risk for breast cancer:[4]

• Women ages 40 and older should have a screening mammogram every year.

• Between the ages of 20 and 39, women should have a clinical breast examination by a health professional every three years. After age 40, women should have a breast exam by a health professional every year.

• Women ages 20 and older should perform breast self-examination every month. By making that a habit, women become familiar with how their breasts normally feel and can detect changes more readily.

• Women with risk factors for breast cancer should discuss detection methods with their physicians and may decide to start mammography earlier than age 40.

Results of a recent survey by Caredata.com show that women are more likely to re-enroll in their health plans when either the plan or the physician encourages them to receive preventive tests and services that apply to them, including Pap smears and mammograms.

"Health plans have a real opportunity to keep female members healthier as well as more satisfied and loyal to their plan by encouraging more preventative services," says **Tony Morgan**, vice president of Research for Caredata.com's Consumer Research Group.

References

1. Wickerham DL, Cronin W, et al. The NSABP Breast Cancer Prevention Trial (BCPT): A progress report. *Proceedings of the American Society of Clinical Oncology* 1993; 12:A-76, 69.

2. Moody-Ayers SY, Wells CK, Feinstein AR. "Benign" tumors and "early detection" in mammography-screened patients of a natural cohort with breast cancer. *Arch Intern Med* 2000; 160:1,109-1,115.

3. Wee CC, McCarthy EP, Davis RB, Phillips RS. Screening for cervical and breast cancer: Is obesity an unrecognized barrier to preventive care? *Ann Intern Med* 2000; 132:697-704.

4. www3.cancer.org / cancerinfo / load_cont.asp?st= ds&ct=5&language=english. ■

Core measures identified by Joint Commission

The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) is launching the ORYX performance assessment system to provide a continuous, data-driven accreditation process. Pharmacists can help their hospitals by anticipating the core measures to be used at those institutions, then becoming better acquainted with health outcomes measures used and the interpretation of the data.

Collection of core data will commence in hospitals and long-term care facilities as early as 2002. Be prepared to anticipate and capture data at your institution, based on the health care services your hospital provides. JCAHO expects that data will

be collected monthly by health care organizations, then transmitted quarterly to JCAHO. However, what is sent to the Joint Commission will not be raw data as collected by the organization. Rather, the data will be in summary form, in a specified format. The Joint Commission says implementation of the ORYX performance assessment system will improve clinical outcomes for patients. By improving health outcomes, health care organizations should then be able to decrease their costs of providing care to patients.

JCAHO states that these measures:[1]

• have precisely defined specifications;

• can be uniformly embedded in multiple performance measurement systems;

• have standardized data collection protocols based on a uniform medical language so they can be implemented uniformly across accredited organizations;

• meet established evaluation criteria;

• can be implemented in stages within and across accreditation programs;

• permit comparisons of organizational performance over time;

• foster the use of national performance benchmarks.

ORYX integrates measurable outcomes and other performance measurement data into the accreditation system. The next phase in implementing the system is the identification of 25 core measures in five focus area as tools for the evaluation of hospital performance. Those core measures are:[1]

1. Acute myocardial infarction (AMI).

• the number of AMI patients with a history of smoking who are given smoking cessation advice or counseling during hospitalization;

• the number of AMI patients who are given aspirin within 24 hours of arrival or within 24 hours prior to arrival at the hospital;

• the timely reperfusion (opening blocked arteries) of eligible AMI patients; time from arrival to initiation of thrombolysis medication administration or primary percutaneous transluminal coronary angioplasty procedure;

• the number of AMI patients who are prescribed aspirin at discharge from the hospital;

• the number of AMI patients who receive ß-blocker medication within the first 24 hours of arrival to the hospital;

• the number of AMI patients with low left ventricular ejection fraction (index of how well the heart functions) who are prescribed an angiotensin converting enzyme inhibitor (ACEI) medication at discharge from the hospital;

• the number of AMI patients who are ideal candidates for ß-blocker medication who are given a prescription for ß-blocker at discharge;

• the number of patients with a primary diagnosis of AMI who die during hospitalization.

2. Heart failure (HF).

• the number of HF patients with atrial fibrillation who are given a prescription for oral anticoagulation therapy (warfarin) at discharge from the hospital;

• the number of HF patients who receive patient education (as documented on their written discharge instructions) regarding all of the following: all discharge medications, weight monitoring, diet, activity level, follow-up appointment, and what to do if symptoms worsen;

• the number of HF patients not admitted on ACEIs or angiotensin receptor blocking agents who have left ventricular ejection fraction (LVEF) evaluated before or during admission;

• the number of patients with low LVEF who are prescribed an ACEI medication at discharge;

• the number of HF patients with a history of smoking who are given smoking cessation advice or counseling during hospitalization.

3. Community-acquired pneumonia.

• the number of patients ages 65 or older who are screened for or given pneumococcal vaccination during hospitalization;

• the number of pneumonia patients with a history of smoking, who are given smoking cessation advice or counseling during hospitalization, or advice or counseling is given to pediatric caregiver about effects of secondhand smoke;

• the number of patients who receive oxygenation assessment (determine amount of oxygen in blood) within 24 hours of hospital arrival;

• of patients who had blood cultures collected, the number who had them drawn prior to the first dose of antibiotic administration in the hospital;

• the time in hours from initial presentation at hospital to first dose of antibiotics;

• the number of pneumonia patients *not admitted* to an intensive care unit for whom the antibiotic given is consistent with current consensus guidelines (e.g., the American Thoracic Society, Infectious Disease Society of America, and the Centers for Disease Control and Prevention);

• the number of pneumonia patients admitted to an intensive care unit for whom the antibiotic

given is consistent with current consensus guidelines (e.g., the American Thoracic Society, Infectious Disease Society of America, and the Centers for Disease Control and Prevention).

4. **Surgical procedures and complications.**
- the number of patients undergoing selected surgical procedures who develop a surgical site infection within 30 days of the procedure;
- the timing of when patients were given prophylactic intravenous antibiotic administration for selected surgical procedures.

5. **Pregnancy and related conditions.**
- the number of patients who have had a cesarean who have a vaginal delivery;
- the number of patients who have vaginal deliveries with third- or fourth-degree laceration;
- the number of infants who die within 28 days of birth.

Reference

1. www.jcaho.org/perfmeas/perfmeas_frm.html. ■

NEWS BRIEFS

FDA warning: TriCitrasol may cause death

The Food and Drug Administration has issued an urgent warning to all hospital pharmacies and hemodialysis units that triCitrasol (Cytosol Laboratories), an unapproved product that is used to keep bloodlines open, may cause death when infused into patients. One patient died of cardiac arrest shortly after triCitrasol, a 46.7% concentration of sodium citrate anticoagulant, was injected full strength into the hemodialysis permanent blood access catheter that had just been implanted.

The FDA is reviewing other incidents that may involve triCitrasol in the hemodialysis setting and is recommending that alternative 4% solutions of citrate be used in that and other medical settings. More information on this issue can be viewed in an FDA Talk Paper on-line at www.fda.gov/bbs/topics/ANSWERS/ANS01009.html. ▼

Class action suit filed over Rezulin

Was this drug on the market too long?

A nationwide class action lawsuit was filed April 17 in federal court against Warner-Lambert and Parke-Davis over harmful effects suffered by patients taking Rezulin prior to its March 21 withdrawal from the market. Damages are expected to exceed $1 billion.

It is estimated that more than 1.9 million Americans took Rezulin for the treatment of type 2 diabetes during the past three years. Currently, 90 cases of hepatic failure and 63 deaths have been associated with the use of Rezulin. The lawsuit claims that the drug remained on the market too long, even after deaths and liver failure were reported.

Attorneys for the plaintiffs note that the drug was withdrawn from the European market more than a year ago. Additionally, the lawsuit claims improprieties leading to the fast-track approval of the Food and Drug Administration. Because of the allegations of conflicts of interest and contrived data from a clinical trial, the consumer group Public Citizen has called for both a criminal investigation and congressional hearings on the decision by the FDA to give Rezulin a six-month priority review. ▼

Date set for alcohol, drug dependency school

The 49th session of the University of Utah School on Alcoholism and Other Drug Dependencies is scheduled for June 18-23 in Salt Lake City. The pharmacy section is geared toward those who are working or who desire to work in state-level programs to assist chemically dependent pharmacists and pharmacy students.

The program covers information on chemical dependency; the identification, referral, treatment, and aftercare of recovering pharmacists and pharmacy students; relapse prevention and treatment; federal and regulatory issues affecting recovering individuals; and discussion sessions for networking and exchange of information. ▼

New Pyxis MedStation SN focuses on patient safety

Pyxis Corp. has launched a new product, MedStation SN (SafetyNet), designed to provide advanced technology, customer service, and support programs to enhance patient safety and clinical care. MedStation SN was developed to set a new standard for safe medication management by offering control, access, flexibility, and clinical information for health care providers. It integrates the Pyxis Computerized Unit-Based Inventory Exchange (Cubie); Pyxis Biometric ID; unlimited pharmacy profile interfaces; Pyxis Automated Replenishment; Cardinal Information Companies' ALERxT Clinical Safety System; and Lexi-Comp's On-Line Drug Reference. The station is also Cardinal ASSIST ready and is backed by on-site or Internet-based training and education programs. ■

New FDA Approvals

These drugs have received final approval from the Food and Drug Administration:

✔ Bisphosphonate **Actonel** (risedronate sodium) by Procter & Gamble Pharmaceuticals and Aventis Pharmaceuticals. Actonel is indicated for treatment and prevention of osteoporosis in postmenopausal women; for the prevention and treatment of glucocorticoid-induced osteoporosis in men and women who are either initiating or continuing systemic glucocorticoid treatment (daily dosage equivalent to 7.5 mg or greater of prednisone) for chronic diseases; and for treatment of Paget's disease of the bone (osteitis deformans). Actonel is available as a 5 mg or 30 mg tablet. Recommended doses are 5 mg daily for post-menopausal or glucocorticoid-induced osteoporosis and 30 mg daily for two months for Paget's disease.

✔ Anesthetic **Chirocaine** (levobupivacaine injection) by Purdue Pharma. Chirocaine is now available in the United States for the production of local or regional anesthesia for surgery and obstetrics and for postoperative pain management. It is available preservative-free in 10 mL and 30 mL single-dose vials.

✔ Recombinant human insulin analog **Lantus** (insulin glargine [rDNA origin] injection) by Aventis Pharmaceuticals. Lantus has FDA approval for once-daily subcutaneous administration at bedtime in the treatment of adult and pediatric patients with type 1 diabetes mellitus or adult patients with type 2 diabetes mellitus who require basal (long-acting) insulin for the control of hyperglycemia. The approval also provides for the OptiPen One Insulin Delivery Device for use with Lantus cartridges. Lantus, at 100 U per mL, is supplied in 5 and 10 mL vials and in 3 mL cartridges (packages of 5).

✔ Nonsteroidal anti-inflammatory drug (enolic acid group) **Mobic** (meloxicam) by Boehringer Ingelheim Pharmaceuticals. Mobic is indicated for relief of the signs and symptoms of osteoarthritis, is dosed once daily, and is available in 7.5 mg tablets.

✔ Photodynamic agent **Visudyne** (verteporfin for injection) by QLT Phototherapeutics. Visudyne has received FDA approval for the treatment of age-related macular degeneration in patients with predominantly classic subfoveal choroidal neovascularization. A course of Visudyne is a two-step process requiring administration of both drug and light. The first step is the intravenous infusion of Visudyne. The second step is the activation of Visudyne with light from a nonthermal diode laser.

✔ Oxazolidinone antibiotic **Zyvox** (linezolid) by Pharmacia & Upjohn. Zyvox is indicated for the treatment of adult patients with vancomycin-resistant *Enterococcus faecium* infections, nosocomial pneumonia, complicated and uncomplicated skin and skin structure infections, and community-acquired pneumonia caused by strains of designated microorganisms. Zyvox is dosed twice daily and is available in IV form in single-use infusion bags (200 mg/100 mL, 400 mg/200 mL, 600 mg/300 mL), 400 and 600 mg tablets, and a 150 mL oral suspension (equivalent to 100 mg/5 mL).

✔ Antiretroviral agent **Viracept** (nelfinavir mesylate) by Agouron Pharmaceuticals Inc. Viracept has received approval for a new dosage form, as a film-coated tablet. The new formulation is intended to preserve the tablet integrity and thereby diminish the possibility of premature tablet dissolution and tablet breakage. The dosage strength remains the same. ■

IN THE PIPELINE

The following drugs are still in clinical trials:

- ✔ The Food and Drug Administration's arthritis advisory committee has unanimously recommended approval of Immunex's **Enbrel** (etanercept) for use to delay radiographic progression of joint damage in patients with early rheumatoid arthritis and voted in favor of approval of Enbrel for use to improve signs and symptoms of patients with early stage disease.

- ✔ Genelabs Technologies Inc. reports statistically significant results from its phase III clinical trial of **GL701** (prasterone, dehydroepiandrosterone) in treating systemic lupus erythematosus (SLE). Patients treated with GL701 had a significantly greater rate of response than those receiving placebo. Response to treatment was defined as improvement or stabilization of SLE disease activity and symptoms. ■

From the Editor

Feed your 'pocket brain'

Here is this month's recommendation for your growing pocket brain. Readers are encouraged to send suggestions for future items to the editor at ruthnoland@hotmail.com.

Temperature Conversion
Celsius to Fahrenheit = (°C x 9/5) + 32 = °F
Fahrenheit to Celsius = (°F - 32) x 5/9 = °C

°C	=	°F	°C	=	°F	°C	=	°F
100.0		212.0	39.0		102.2	36.8		98.2
50.0		122.0	38.8		101.8	36.6		97.9
41.0		105.8	38.6		101.5	36.4		97.5
40.8		105.4	38.4		101.1	36.2		97.2
40.6		105.1	38.2		100.8	36.0		96.8
40.4		104.7	38.0		100.4	35.8		96.4
40.2		104.4	37.8		100.1	35.6		96.1
40.0		104.0	37.6		99.7	35.4		95.7
39.8		103.6	37.4		99.3	35.2		95.4
39.6		103.3	37.2		99.0	35.0		95.0
39.4		102.9	37.0		98.6	00.0		032.0
39.2		102.6						

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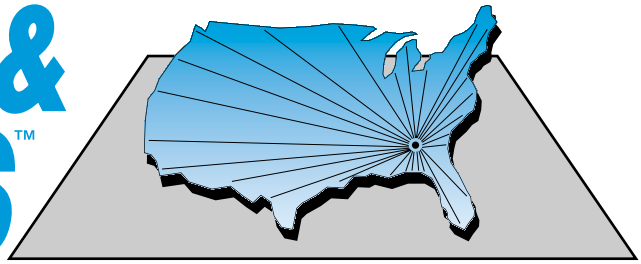

Gatifloxacin (Tequin): Observations on its use

By **Claire Merinar**, PharmD
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Charleston, SC

❑ **Indications:** Gatifloxacin, manufactured by Bristol-Myers Squibb Co., is indicated for the treatment of adults (over 18 years of age) with infections caused by certain susceptible microorganisms in certain conditions **(see table I, below)**.[1]

❑ **Pharmacology:** Gatifloxacin is a synthetic 8-methoxy fluoroquinolone, which is a member of the newer fluoroquinolones. These are distinguished by their enhanced spectrum of activity, including activity against gram-positive bacteria, gram-negative bacteria, anaerobes, and atypical pathogens. All fluoroquinolones act by inhibiting the activity of DNA gyrase, which inhibits bacterial DNA replication and transcription and results in cell death. However, the newer fluoroquinolones, including gatifloxacin, also have been shown to inhibit topoisomerase IV, resulting in increased gram-positive spectrum activity.[2]

❑ **Pharmacokinetics:** Gatifloxacin is well-absorbed and achieves steady-state plasma levels after approximately three days of therapy. Gatifloxacin is dosed once daily. Peak and trough concentrations were consistent with both oral and intravenous routes of administration and can be considered interchangeable. Patients receiving 400 mg of oral gatifloxacin once daily achieved approximate peaks of 4.2 g / mL and troughs of 0.4 g / mL; intravenous administration of 400 mg of gatifloxacin once daily resulted in peaks of approximately 4.2 g / mL and troughs of 0.4 g / mL. The elimination half-life of gatifloxacin ranges from seven to 14 hours, and the volume of distribution for gatifloxacin is approximately 1.5-2.0 L / kg.

Gatifloxacin also exhibits 20% binding to serum proteins. Gatifloxacin undergoes limited metabolism (< 1%) in humans, and it is not metabolized by the cytochrome P450 enzyme system. It is therefore unlikely to interact with other medications that may influence the P450 system. Elimination by the kidney accounts for about 70% of

Table I: Indications for Gatifloxacin

Condition	Bacterial Organisms
Acute bacterial exacerbation of chronic bronchitis	*S. pneumonia, H. influenzae, H. parainfluenzae, M. catarrhalis, S. aureus*
Acute sinusitis	*S. pneumoniae, H. influenzae*
Community-acquired pneumonia	*S. pneumoniae, H. influenzae, H. parainfluenzae, M. catarrhalis, S. aureus, M. pneumoniae, C. pneumoniae, L. pneumophila*
Uncomplicated urinary tract infections	*E. coli, K. pneumoniae, P. mirabilis*
Complicated urinary tract infections	*E. coli, K. pneumoniae, P. mirabilis*
Pyleonephritis	*E. coli*
Uncomplicated urethral and cervical gonorrhea	*N. gonorrhea*
Acute, uncomplicated rectal gonorrhea (women only)	*N. gonorrhea*

elimination; therefore, dosage should be adjusted in renal dysfunction **(see dosage details, p. 3)**. About 5% is eliminated by the biliary route.[1,3]

❑ **Microbiology:** Gatifloxacin has shown to be active against most strains of the following organisms:[1-2]

• **Aerobic gram-positive organisms**

— *Staphylococcus aureus* (methicillin-susceptible strains only)

— *Streptococcus pneumoniae* (penicillin-susceptible strains)

• **Aerobic gram-negative organisms**

— *Escherichia coli*

— *Haemophilus influenzae*

— *Haemophilus parainfluenzae*

— *Klebsiella pneumoniae*

— *Moraxella catarrhalis*

— *Neisseria gonorrhoeae*

— *Proteus mirabilis*

• **Other microorganisms**

— *Chlamydia pneumoniae*

— *Legionella pneumophila*

— *Mycoplasma pneumoniae*

Against Enterobacteriaceae species, gatifloxacin is approximately twofold less active than ciprofloxacin. Against gram-positive organisms, gatifloxacin exhibits two- to fourfold more activity than ciprofloxacin. Methicillin-resistant staphylococcus also is resistant to gatifloxacin. Gatifloxacin has only moderate activity against anaerobic organisms. Because of its large volume of distribution and its intracellular penetration, gatifloxacin is active against intracellular and extracellular pathogens.[1-2] Gatifloxacin exhibits a post-antibiotic-effect against *S. pneumoniae, S. aureus, E. faecalis, E. coli,* and *P. aeruginosa.* Resistance to gatifloxacin is chromosomally mediated, and there may be cross-resistance with other fluoroquinolones.[4]

The minimum inhibitory concentration (MIC) breakpoints for gatifloxacin as established and approved by the National Committee on Clinical Laboratory Standards (NCCLS) are in **table II (tables II-IV are inserted in this issue)**.[1]

❑ **Selected clinical trials:**

• **Acute bacterial exacerbation of chronic bronchitis:** Ramirez et al. conducted a double-blind, randomized, multicenter trial comparing the safety and efficacy of oral gatifloxacin 400 mg administered once daily, oral cefuroxime axetil 250 mg twice daily, or levofloxacin 500 mg once daily in the treatment of acute bacterial exacerbation of chronic bronchitis. A total of 924 patients were enrolled and treated for seven to 10 days.

Bacterial eradication and clinical cure were the primary endpoints of this trial. Bacterial eradication was defined as absence of the original pathogen in a post-treatment sputum culture. Bacterial eradication rates were considered similar for gatifloxacin (93%), levofloxacin (94%), and cefuroxime (77%). Clinical cure rates were equivalent between gatifloxacin (91%) and comparative (88%) groups. There were no clinically significant differences in adverse side effects; diarrhea was the most common, reported in 4% of patients taking gatifloxacin vs. 7% for levofloxacin or cefuroxime. This study suggests gatifloxacin at a dose of 400 mg once daily may be safe and effective for acute exacerbation of chronic bronchitis.[5]

• **Acute sinusitis:** Gatifloxacin 400 mg once daily for 10 days was compared to clarithromycin 500 mg twice daily for 14 days in a randomized, double-blind, multicenter study of 421 adult patients. The primary outcome of this trial was clinical cure, which was defined as an improvement or resolution of three signs and symptoms of acute infection (purulent discharge, sinus pain, and sinus tenderness). The treatment group results were not statistically different with 90% of patients taking gatifloxacin and 90% of patients treated with clarithromycin responding. Most adverse drug reactions were mild and did not require additional treatment. The most common side effects were nausea (gatifloxacin 13%, clarithromycin 11%) and diarrhea (gatifloxacin 5%, clarithromycin 9%). The data support the use of gatifloxacin in patients with acute sinusitis.[6]

• **Community-acquired pneumonia:** Sullivan et al. conducted a randomized, double-blind, multicenter trial in 418 patients comparing gatifloxacin 400 mg once daily and levofloxacin 400 mg once daily. Clinical cure rate was the primary endpoint, and bacteriologic eradication was the secondary outcome. Clinical cure was defined as resolution or improvement of all signs and symptoms to a level that no further antimicrobial therapy was needed and an improved or stable chest X-ray. Clinical cure rates were 96% for gatifloxacin and 94% for levofloxacin.

Bacteriologic response was defined as eradication of the original pathogen from an adequate sputum sample. Bacterial cure rates were 98% for gatifloxacin and 93% for levofloxacin. The authors did not report a statistically significant difference between treatment groups. Drug-related adverse effects occurred in 28% of gatifloxacin-treated patients and 32% of levofloxacin-treated patients. The most common side effects were nausea, diarrhea, and insomnia, all of which occurred more

frequently in patients treated with levofloxacin. This study demonstrates the effective use of gatifloxacin in community-acquired pneumonia.[7]

• **Uncomplicated urinary tract infections:** Gatifloxacin 400 mg as a single dose was compared to gatifloxacin 200 mg twice daily for three days, or ciprofloxacin 100 mg twice daily for three days. This randomized, double-blind, multicenter trial enrolled 1,323 women. This information is available from data on file with Bristol-Myers Squibb and has not been published. The primary endpoints of this study were clinical cure and microbiologic eradication.

Clinical cure rates were 93% for gatifloxacin (400 mg once daily), 95% for gatifloxacin (200 mg twice daily), and 93% for ciprofloxacin. Bacterial eradication rates were 90% for gatifloxacin 400 mg, 88% for gatifloxacin 200 mg, and 92% for ciprofloxacin. Neither clinical cure nor microbiological cure rates were statistically significant. Adverse reactions were similar for all three treatment groups, with the most common side effects being nausea, vomiting, diarrhea, headache, and dizziness. This study suggests that gatifloxacin may be useful in the treatment of uncomplicated urinary tract infections.[8]

• **Uncomplicated urethral and cervical gonorrhea:** A double-blind, randomized trial was conducted with 728 male and female patients having uncomplicated gonorrhea. Patients received either a one-time dose of gatifloxacin 400 mg, gatifloxacin 600 mg, or ofloxacin 400 mg. This information is taken from data on file at Bristol-Myers Squibb and has been presented in abstract form. Bacteriologic eradication rates and clinical cure rates were the primary efficacy endpoints for this study. There were no statistically significant differences between treatment groups for either clinical or bacteriologic cure rates. Adverse drug effects were similar in all three groups and included nausea, vomiting, headache, and diarrhea. The study supports the use of gatifloxacin in the treatment of uncomplicated gonorrhea.[9]

❑ **Adverse reactions:** Among patients receiving gatifloxacin, 2.9% discontinued due to adverse drug reactions. The most common adverse effects reported during clinical trials included nausea (8%), vaginitis (6%), diarrhea (4%), headache (3%), and dizziness (3%). Additional adverse events that occurred in 0.1% to 3% of study populations included allergic reaction, chills, fever, back pain, chest pain, palpitation, abdominal pain, constipation, mouth ulcer, vomiting, peripheral edema, rash, sweating, hematuria, taste alterations, abnormal vision, tinnitus, dyspnea, and pharyngitis.[1,10]

❑ **Pregnancy/lactation:** Gatifloxacin is classified as pregnancy category C, which means studies in animals have revealed adverse effects on the fetus but there are no controlled studies in women. Therefore, gatifloxacin should be used only if the benefits to the patient outweigh the risks to the fetus. There are currently no data available on whether gatifloxacin is excreted into human milk, but it has been shown to be excreted in the breast milk of rats. Therefore, gatifloxacin is not recommended for use in lactating women.[1,2]

❑ **Contraindications:** Gatifloxacin is contraindicated in patients with a history of hypersensitivity to gatifloxacin, any of the alternative fluoroquinolones products, or any other components of the product.

❑ **Warnings:** The safety and efficacy of gatifloxacin has not been established in pediatric patients less than 18 years of age or in pregnant or lactating women.[1] Quinolones, including gatifloxacin, can stimulate the central nervous system and may cause side effects such as confusion, hallucinations, restlessness, insomnia, and paranoia. Gatifloxacin also should be used with caution in patients who have a seizure history.[1] Phototoxicity is another common side effect of the fluoroquinolones.

Gatifloxacin has been shown to have equivalent or less phototoxic potential than ciprofloxacin.[1,11] Prolongation of the QT interval also has been associated with gatifloxacin. The manufacturers recommend that gatifloxacin be avoided in patients with a known prolonged QT interval, uncorrected hypokalemia, in combination with other agents that prolong the QT interval, or with class IA or class III antiarrhythmic agents.[1]

Pseudomembranous colitis has been reported with gatifloxacin. Treatment with gatifloxacin may disrupt the patients natural intestinal flora, resulting in overgrowth of clostridia, which produces a diarrhea-inducing toxin. Gatifloxacin should be discontinued in patients who develop antibiotic-associated pseudomembranous colitis.[1]

Tendon rupture also has been associated with gatifloxacin. If this occurs, gatifloxacin should be discontinued.[1,2] Stevens-Johnson syndrome and toxic epidermal necrolysis have occurred in patients treated with gatifloxacin, and it is therefore recommended to discontinue the agent if a skin rash develops.[1,11]

❑ **Dosage and administration:** The recommended dose of gatifloxacin is based on the

type of infection **(see table III, insert)**.[1] Dosage adjustment of gatifloxacin is necessary in renal impairment to avoid accumulation **(see table IV, insert)**.[1]

❑ **Drug interaction:** As with other fluoroquinolones, gatifloxacin interacts with ferrous sulfate or antacids containing aluminum or magnesium salts. Bioavailability of gatifloxacin is reduced by 54% when combined with ferrous sulfate. The manufacturers recommend separating administration of gatifloxacin from these products by four hours. Concomitant administration of probenecid results in a 42% increase in area under the curve of gatifloxacin. Concomitant administration of digoxin and gatifloxacin results in increased levels of digoxin. However, this interaction was not considered significant enough to warrant dosage adjustment. Gatifloxacin appears to have minimal effect on the levels of cimetidine, midazolam, theophylline, warfarin, or glyburide.[1,10]

❑ **Drug-food interactions:** No significant drug-food interactions have been reported.[1]

❑ **Dosage forms available:** Gatifloxacin is available in oral and intravenous forms. Tablets are available as white 200 mg and 400 mg biconvex, film-coated tablets. Gatifloxacin intravenous solution is available as single-use vials and premixed bags. The single-use vials contain a pale yellow solution of gatifloxacin at a concentration of 10 mg/mL. These single-use vials are available in 20 mL and 40 mL volumes. Gatifloxacin also is available as 200 mg or 400 mg premixed bags at a concentration of 2 mg/mL. These flexible bags supply gatifloxacin mixed with 5 % dextrose solution and are available in 100 mL or 200 mL volumes.[1]

❑ **Discussion:** Fluoroquinolones on many hospital formularies include ciprofloxacin (Cipro) and levofloxacin (Levaquin). Ciprofloxacin, levofloxacin, and gatifloxacin are FDA-approved for the treatment of acute bacterial exacerbation of chronic bronchitis, community-acquired pneumonia, acute sinusitis, and complicated urinary tract infections. Ciprofloxacin also is approved for the treatment of skin/soft tissue and bone infections. Gatifloxacin does not offer any additional FDA-approved indications for treatment other than those offered by ciprofloxacin and levofloxacin.

Although ciprofloxacin is dosed twice daily, both levofloxacin and gatifloxacin are dosed once daily. All three quinolones are available in oral and intravenous formulations. All three are well-tolerated, and dose adjustment in renal dysfunction is required for each. Ciprofloxacin, levofloxacin, and gatifloxacin bind cation-containing antacids and ferrous sulfate, resulting in reduced absorption of the quinolones.

The order of potency of inhibitory effects on the cytochrome P450 system are as follows: ciprofloxacin > levofloxacin > gatifloxacin. Based on outpatient costs, gatifloxacin is more expensive than ciprofloxacin, but comparable to levofloxacin. For inpatient cost, gatifloxacin is less expensive than ciprofloxacin and comparable to levofloxacin.

For those reasons, gatifloxacin is now being considered for formulary approval over some of the older fluoroquinolones in many institutions.

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Tables II, III, and IV for Gatifloxacin Use Evaluation

The following tables accompany the medication use evaluation of gatifoxacin in this month's issue of *Drug Criteria and Outcomes.* The drug is manufactured by Bristol-Myers Squibb and is used for treating adults infected with a variety of microorganisms, including *Escherichia coli* and methicillin-susceptible strains of *Staphylococcus aureus.* For discussion of the tables, see pages two and four of *Drug Criteria and Outcomes.*

Table II: MIC Breakpoints for Gatifloxacin

NCCLS* Organism Group	Equivalent MIC† Breakpoints (mcg/mL)		
	Susceptible	Intermediate	Resistant
Enterobacteriaceae, non-Enterobacteriacea, Staphylococcus species, Enterococcus species	<2	4	>8
S. pneumoniae, other *Streptococcus species*	<1	2	>4
Haemophilus species	<0.5		
N. gonorrhoeae	<0.125	0.25	>0.5

*NCCLS = National Committee on Clinical Laboratory Standards.
†MIC = minimum inhibitory concentration.

Table III: Normal Dosing of Gatifloxacin

Infection	Daily Dose	Duration
Acute bacterial exacerbation of chronic bronchitis	400 mg	7-10 days
Acute sinusitis	400 mg	10 days
Community-acquired pneumonia	400 mg	7-14 days
Uncomplicated urinary tract infections (UTIs)	200 or 400 mg	Single dose or 3 days
Complicated UTIs	400 mg	7-10 days
Acute pyleonephritis	400 mg	7-10 days
Uncomplicated urethral gonorrhea (men), cervical and anal (women)	400 mg	Single dose

Table IV: Renal Dose Adjustment of Gatifloxacin

Renal	Initial Dose	Subsequent Doses
CrCl > 40 mL/min	no dose adjustment necessary	no dose adjustment necessary
CrCl < 40 mL/min	400 mg	200 mg once daily
Hemodialysis	400 mg	200 mg once daily
Continuous peritoneal dialysis	400 mg	200 mg once daily

Source: The tables in this supplement were provided by Claire Merinar, PharmD, of the Medical University of South Carolina in Charleston. See references in *Drug Criteria & Outcomes.*