

Economic Woes May Not Slow SCHIP Expansion

BY ALICIA AULT
Associate Editor, Practice Trends

Even though the Bush administration has made it nearly impossible to expand the State Children’s Health Insurance Program, and the economic downturn has put a squeeze on Medicaid budgets, many states are keeping children covered and some are even expanding eligibility, according to two new studies by Families USA.

Officials at the advocacy organization, based in Washington, D.C., said that at the end of 2007, 17 states were considering expanding coverage for children under SCHIP and Medicaid. But those plans were largely put on hold or scaled back because of President Bush’s vetoes of the original SCHIP reauthorization package. A law authorizing the program at 2007 levels expires in March 2009.

Another setback for states came last August, when the Bush administration is-

sued a directive that limited the SCHIP eligibility, going forward, of families with incomes at or below 250% of the federal poverty level.

That directive has remained essentially unchanged, although the Centers for Medicare and Medicaid Services announced in May that it would look at expansion programs on a case-by-case basis.

Expansion plans by New York and Ohio were rejected by CMS, but New York used state funds to expand coverage to children

living in families with incomes up to 400% of the poverty level. Ohio is using state money to cover children who can’t get private health coverage, but the expansion is not through Medicaid or SCHIP, according to the Families USA report, “Detour on the Road to Kids Coverage: Administration Creates Roadblocks, So States Seek Alternative Routes.”

Ohio also raised eligibility to the federal ceiling (250% of the poverty level).

Indiana, Louisiana, Oklahoma, and Wis-

SEROQUEL® (quetiapine fumarate) Tablets

the introduction to the ADVERSE REACTIONS section reported by patients treated with SEROQUEL at multiple doses ≥ 75 mg/day during any phase of a trial within the premarketing database of approximately 2200 patients treated for schizophrenia. All reported reactions are included except those already listed in the tables or elsewhere in labeling, those reactions for which a drug cause was remote, and those reaction terms which were so general as to be uninformative. It is important to emphasize that, although the reactions reported occurred during treatment with SEROQUEL, they were not necessarily caused by it. Reactions are further categorized by body system and listed in order of decreasing frequency according to the following definitions: frequent adverse reactions are those occurring in at least 1/100 patients (only those not already listed in the tabulated results from placebo-controlled trials appear in this listing); infrequent adverse reactions are those occurring in 1/100 to 1/1000 patients; rare reactions are those occurring in fewer than 1/1000 patients. **Nervous System:** *Frequent:* hypertonia, dysarthria; *Infrequent:* abnormal dreams, dyskinesia, thinking abnormal, tardive dyskinesia, vertigo, involuntary movements, confusion, amnesia, psychosis, hallucinations, hyperkinesia, libido increased*, urinary retention, incoordination, paranoid reaction, abnormal gait, myoclonus, delusions, manic reaction, apathy, ataxia, depersonalization, stupor, bruxism, catatonic reaction, hemiplegia; *Rare:* aphasia, buccoglossal syndrome, choreoathetosis, delirium, emotional lability, euphoria, libido decreased*, neuralgia, stuttering, subdural hematoma. **Body as a Whole:** *Frequent:* flu syndrome; *Infrequent:* neck pain, pelvic pain*, suicide attempt, malaise, photosensitivity reaction, chills, face edema, moniliasis; *Rare:* abdomen enlarged. **Digestive System:** *Frequent:* anorexia; *Infrequent:* increased salivation, increased appetite, gamma glutamyl transpeptidase increased, gingivitis, dysphagia, flatulence, gastroenteritis, gastritis, hemorrhoids, stomatitis, thirst, tooth caries, fecal incontinence, gastroesophageal reflux, gum hemorrhage, mouth ulceration, rectal hemorrhage, tongue edema; *Rare:* glossitis, hematemesis, intestinal obstruction, melena, pancreatitis. **Cardiovascular System:** *Frequent:* palpitation; *Infrequent:* vasodilatation, QT interval prolonged, migraine, bradycardia, cerebral ischemia, irregular pulse, T wave abnormality, bundle branch block, cerebrovascular accident, deep thrombophlebitis, T wave inversion; *Rare:* angina pectoris, atrial fibrillation, AV block first degree, congestive heart failure, ST elevated, thrombophlebitis, T wave flattening, ST abnormality, increased QRS duration. **Respiratory System:** *Frequent:* pharyngitis, rhinitis, cough increased, dyspnea; *Infrequent:* pneumonia, epistaxis, asthma; *Rare:* hiccup, hyperventilation. **Metabolic and Nutritional System:** *Frequent:* peripheral edema; *Infrequent:* weight loss, alkaline phosphatase increased, hyperlipemia, alcohol intolerance, dehydration, hyperglycemia, creatinine increased, hypoglycemia; *Rare:* glycosuria, gout, hand edema, hypokalemia, water intoxication. **Skin and Appendages System:** *Frequent:* sweating; *Infrequent:* pruritus, acne, eczema, contact dermatitis, maculopapular rash, seborrhea, skin ulcer; *Rare:* exfoliative dermatitis, psoriasis, skin discoloration. **Urogenital System:** *Infrequent:* dysmenorrhea*, vaginitis*, urinary incontinence, metrorrhagia*, impotence*, dysuria, vaginal moniliasis*, abnormal ejaculation*, cystitis, urinary frequency, amenorrhea*, female lactation*, leukorrhea*, vaginal hemorrhage*, vulvovaginitis* orchitis*; *Rare:* gynecomastia*, nocturia, polyuria, acute kidney failure. **Special Senses:** *Infrequent:* conjunctivitis, abnormal vision, dry eyes, tinnitus, taste perversion, blepharitis, eye pain; *Rare:* abnormality of accommodation, deafness, glaucoma. **Musculoskeletal System:** *Infrequent:* pathological fracture, myasthenia, twitching, arthralgia, arthritis, leg cramps, bone pain. **Hemic and Lymphatic System:** *Frequent:* leukopenia; *Infrequent:* leukocytosis, anemia, ecchymosis, eosinophilia, hypochromic anemia; lymphadenopathy, cyanosis; *Rare:* hemolysis, thrombocytopenia. **Endocrine System:** *Infrequent:* hypothyroidism, diabetes mellitus; *Rare:* hyperthyroidism.

Post Marketing Experience The following adverse reactions were identified during post approval of SEROQUEL. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Adverse reactions reported since market introduction which were temporally related to SEROQUEL therapy include: anaphylactic reaction and restless legs. Other adverse reactions reported since market introduction, which were temporally related to SEROQUEL therapy, but not necessarily causally related, include the following: agranulocytosis, cardiomyopathy, hyponatremia, myocarditis, rhabdomyolysis, syndrome of inappropriate antidiuretic hormone secretion (SIADH), and Stevens- Johnson syndrome (SJS).

*adjusted for gender

SEROQUEL® (quetiapine fumarate) Tablets

335% increase in maximum plasma concentration of quetiapine. Caution (reduced dosage) is indicated when SEROQUEL is administered with ketoconazole and other inhibitors of cytochrome P450 3A (e.g., itraconazole, fluconazole, erythromycin, and protease inhibitors). *Fluoxetine, Imipramine, Haloperidol, and Risperidone:* Coadministration of fluoxetine (60 mg once daily); imipramine (75 mg bid), haloperidol (7.5 mg bid), or risperidone (3 mg bid) with quetiapine (300 mg bid) did not alter the steady-state pharmacokinetics of quetiapine.

Effect of Quetiapine on Other Drugs *Lorazepam:* The mean oral clearance of lorazepam (2 mg, single dose) was reduced by 20% in the presence of quetiapine administered as 250 mg tid dosing. *Divalproex:* The mean maximum concentration and extent of absorption of total and free valproic acid at steady state were decreased by 10 to 12% when divalproex (500 mg bid) was administered with quetiapine (150 mg bid). The mean oral clearance of total valproic acid (administered as divalproex 500 mg bid) was increased by 11% in the presence of quetiapine (150 mg bid). The changes were not significant. *Lithium:* Concomitant administration of quetiapine (250 mg tid) with lithium had no effect on any of the steady-state pharmacokinetic parameters of lithium. *Antipyrine:* Administration of multiple daily doses up to 750 mg/day (on a tid schedule) of quetiapine to subjects with selected psychotic disorders had no clinically relevant effect on the clearance of antipyrine or urinary recovery of antipyrine metabolites. These results indicate that quetiapine does not significantly induce hepatic enzymes responsible for cytochrome P450 mediated metabolism of antipyrine.

USE IN SPECIFIC POPULATIONS

Pregnancy The teratogenic potential of quetiapine was studied in Wistar rats and Dutch Belted rabbits dosed during the period of organogenesis. No evidence of a teratogenic effect was detected in rats at doses of 25 to 200 mg/kg or 0.3 to 2.4 times the maximum human dose on a mg/m² basis or in rabbits at 25 to 100 mg/kg or 0.6 to 2.4 times the maximum human dose on a mg/m² basis. There was, however, evidence of embryo/fetal toxicity. Delays in skeletal ossification were detected in rat fetuses at doses of 50 and 200 mg/kg (0.6 and 2.4 times the maximum human dose on a mg/m² basis) and in rabbits at 50 and 100 mg/kg (1.2 and 2.4 times the maximum human dose on a mg/m² basis). Fetal body weight was reduced in rat fetuses at 200 mg/kg and rabbit fetuses at 100 mg/kg (2.4 times the maximum human dose on a mg/m² basis for both species). There was an increased incidence of a minor soft tissue anomaly (carpal/tarsal flexure) in rabbit fetuses at a dose of 100 mg/kg (2.4 times the maximum human dose on a mg/m² basis). Evidence of maternal toxicity (i.e., decreases in body weight gain and/or death) was observed at the high dose in the rat study and at all doses in the rabbit study. In a peri/postnatal reproductive study in rats, no drug-related effects were observed at doses of 1, 10, and 20 mg/kg or 0.01, 0.12, and 0.24 times the maximum human dose on a mg/m² basis. However, in a preliminary peri/postnatal study, there were increases in fetal and pup death, and decreases in mean litter weight at 150 mg/kg, or 3.0 times the maximum human dose on a mg/m² basis. There are no adequate and well-controlled studies in pregnant women and quetiapine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Labor and Delivery The effect of SEROQUEL on labor and delivery in humans is unknown.

Nursing Mothers SEROQUEL was excreted in milk of treated animals during lactation. It is not known if SEROQUEL is excreted in human milk. It is recommended that women receiving SEROQUEL should not breast feed.

Pediatric Use The safety and effectiveness of SEROQUEL in pediatric patients have not been established. Anyone considering the use of SEROQUEL in a child or adolescent must balance the potential risks with the clinical need.

Geriatric Use Of the approximately 3700 patients in clinical studies with SEROQUEL, 7% (232) were 65 years of age or over. In general, there was no indication of any different tolerability of SEROQUEL in the elderly compared to younger adults. Nevertheless, the presence of factors that might decrease pharmacokinetic clearance, increase the pharmacodynamic response to SEROQUEL, or cause poorer tolerance or orthostasis, should lead to consideration of a lower starting dose, slower titration, and careful monitoring during the initial dosing period in the elderly. The mean plasma clearance of SEROQUEL was reduced by 30% to 50% in elderly patients when compared to younger patients (see **Dosage and Administration**).

DRUG ABUSE AND DEPENDENCE

Controlled Substance SEROQUEL is not a controlled substance.

Abuse SEROQUEL has not been systematically studied, in animals or humans, for its potential for abuse, tolerance or physical dependence. While the clinical trials did not reveal any tendency for any drug-seeking behavior, these observations were not systematic and it is not possible to predict on the basis of this limited experience the extent to which a CNS-active drug will be misused, diverted, and/or abused once marketed. Consequently, patients should be evaluated carefully for a history of drug abuse, and such patients should be observed closely for signs of misuse or abuse of SEROQUEL, e.g., development of tolerance, increases in dose, drug-seeking behavior.

OVERDOSAGE

Human Experience In clinical trials, survival has been reported in acute overdoses of up to 30 grams of quetiapine. Most patients who overdosed experienced no adverse reactions or recovered fully from the reported reactions. Death has been reported in a clinical trial following an overdose of 13.6 grams of quetiapine alone. In general, reported signs and symptoms were those resulting from an exaggeration of the drugs known pharmacological effects, ie, drowsiness and sedation, tachycardia and hypotension. Patients with pre-existing severe cardiovascular disease may be at an increased risk of the effects of overdose (see **Warnings and Precautions**). One case, involving an estimated overdose of 9600 mg, was associated with hypokalemia and first degree heart block. In post-marketing experience, there have been very rare reports of overdose of SEROQUEL alone resulting in death, coma, or QTc prolongation.

Management of Overdosage In case of acute overdosage, establish and maintain an airway and ensure adequate oxygenation and ventilation. Gastric lavage (after intubation, if patient is unconscious) and administration of activated charcoal together with a laxative should be considered. The

consin had planned to raise eligibility for their programs to 300% of the poverty level, but have now scaled that back to 250%, according to the Detour report. Finally, North Carolina, Washington state, and West Virginia also had expansion plans, but have not yet submitted them to CMS, according to the report. It is not clear yet how those states will proceed.

Despite the CMS directive and the bleak economic outlook, some states—including Colorado, Florida, Iowa, and Kansas—are planning to expand coverage next year. The expansions in Iowa and Kansas, however, depend on a reauthorization of the SCHIP program, according to the Detour report.

There also may be a ballot measure in Montana this fall aimed at increasing eligibility from 175% to 250% of poverty level.

California is currently wrangling over the state's budget, which included an increase in cost sharing for SCHIP (which is called "Healthy Families" in California) as well as reduced Medicaid coverage for parents. Rhode Island is also looking at paring back its SCHIP coverage in fiscal 2009 and increasing cost sharing for families.

"States are committed to covering kids, but they are clearly hampered by the roadblocks the administration has put up," said Families USA senior policy analyst Jenny Sullivan in a briefing with reporters.

SEROQUEL® (quetiapine fumarate) Tablets

possibility of obtundation, seizure or dystonic reaction of the head and neck following overdose may create a risk of aspiration with induced emesis. Cardiovascular monitoring should commence immediately and should include continuous electrocardiographic monitoring to detect possible arrhythmias. If antiarrhythmic therapy is administered, disopyramide, procainamide and quinidine carry a theoretical hazard of additive QT-prolonging effects when administered in patients with acute overdosage of SEROQUEL. Similarly it is reasonable to expect that the alpha-adrenergic-blocking properties of bretylium might be additive to those of quetiapine, resulting in problematic hypotension. There is no specific antidote to SEROQUEL. Therefore appropriate supportive measures should be instituted. The possibility of multiple drug involvement should be considered. Hypotension and circulatory collapse should be treated with appropriate measures such as intravenous fluids and/or sympathomimetic agents (epinephrine and dopamine should not be used, since beta stimulation may worsen hypotension in the setting of quetiapine-induced alpha blockade). In cases of severe extrapyramidal symptoms, anticholinergic medication should be administered. Close medical supervision and monitoring should continue until the patient recovers.

PATIENT COUNSELING INFORMATION

Prescribers or other health professionals should inform patients, their families, and their caregivers about the benefits and risks associated with treatment with SEROQUEL 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 SEROQUEL. 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 SEROQUEL.

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 antidepressant 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.

Increased Mortality in Elderly Patients with Dementia-Related Psychosis Patients and caregivers should be advised that elderly patients with dementia-related psychoses treated with atypical antipsychotic drugs are at increased risk of death compared with placebo. Quetiapine is not approved for elderly patients with dementia-related psychosis.

Neuroleptic Malignant Syndrome (NMS) Patients should be advised to report to their physician any signs or symptoms that may be related to NMS. These may include muscle stiffness and high fever.

Hyperglycemia and Diabetes Mellitus Patients should be aware of the symptoms of hyperglycemia (high blood sugar) and diabetes mellitus. Patients who are diagnosed with diabetes, those with risk factors for diabetes, or those that develop these symptoms during treatment should be monitored.

Orthostatic Hypotension Patients should be advised of the risk of orthostatic hypotension (symptoms include feeling dizzy or lightheaded upon standing) especially during the period of initial dose titration, and also at times of re-initiating treatment or increases in dose.

Leukopenia/Neutropenia Patients with a pre-existing low WBC or a history of drug induced leukopenia/neutropenia should be advised that they should have their CBC monitored while taking SEROQUEL (see **Warnings and Precautions**).

Interference with Cognitive and Motor Performance Patients should be advised of the risk of somnolence or sedation, especially during the period of initial dose titration. Patients should be cautioned about performing any activity requiring mental alertness, such as operating a motor vehicle (including automobiles) or operating machinery, until they are reasonably certain quetiapine therapy does not affect them adversely. Patients should limit consumption of alcohol during treatment with quetiapine.

Pregnancy and Nursing Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during therapy. Patients should be advised not to breast feed if they are taking quetiapine.

Concomitant Medication As with other medications, patients should be advised to notify their physicians if they are taking, or plan to take, any prescription or over-the-counter drugs.

Heat Exposure and Dehydration Patients should be advised regarding appropriate care in avoiding overheating and dehydration.

SEROQUEL is a trademark of the AstraZeneca group of companies © AstraZeneca 2008
AstraZeneca Pharmaceuticals LP
Wilmington, DE 19850
Made in USA
35018-00 05/08 265755

AstraZeneca

Most states are also feeling the pinch as tax revenues recede while Medicaid costs—increasingly a larger proportion of most state budgets—continue to rise, according to the second Families USA report, "Precarious Position: States Must Balance Declining Revenues With a Growing Need for Medicaid." The report found that 16 states and Puerto Rico are looking at budget deficits in fiscal year 2008, and 29 states and the District of Columbia are looking at shortfalls in fiscal 2009.

Increasing unemployment means more Americans will turn to Medicaid for health coverage for them and their children, said the organization. The Medicaid report cited a study by the Kaiser Family Foundation showing that a 1% rise in unemployment increases Medicaid and SCHIP enrollment by 1 million, leaving states with an additional \$1.4 billion obligation.

In California, Gov. Arnold Schwarzenegger (R) has proposed \$1 billion in Medic-

aid and SCHIP cuts. That means the state would lose an additional \$1 billion in federal matching funds—a danger that all states face as they look to balance their budgets through Medicaid cuts, according to the Medicaid report. Mississippi is also considering Medicaid cuts in a special legislative session. Maine instituted some cost-sharing measures; New Jersey is considering shifting more of the burden onto Medicaid recipients. In Rhode Island's 2008 budget, eligibility was reduced for parents and cost sharing was increased; premium payments based on income are required, and the state is looking at further cuts in 2009, according to the report.

Families USA is pushing for federal relief, such as a temporary increase in the matching rate given to states for Medicaid. Congress passed such a fix in 2003, but it is unclear whether a proposed fix could make it out of Congress this year, said a Families USA staffer in the briefing. ■

International Graduates Fill Gaps in Physician Supply

BY JOYCE FRIEDEN

Senior Editor

ARLINGTON, VA. — International medical graduates have become an integral part of providing medical care in federally designated physician shortage areas, according to results from a recent study.

"Compared to U.S.-trained physicians, IMGs provide more primary care and more [overall] medical care to populations living in primary care shortage areas" as well as to minorities, immigrants, patients in poor areas, and Medicaid recipients, said Esther Hing of the National Center for Health Statistics, in Hyattsville, Md.

Ms. Hing and her colleague Susan Lin, Dr.P.H., studied 2005-2006 data from the National Ambulatory Medical Care Survey. The survey was nationally representative, and the data used by the researchers included information from 2,390 physicians in office-based practices. Ms. Hing presented the survey results at the 2008 Physician Workforce Research Conference.

The survey showed that IMGs make up 25% of office-based physicians. They also tend to be a little older than U.S.-trained doctors, with an average age of 52 years, compared with 50 years for physicians trained in the United States. The racial and ethnic differences were more pronounced: 71% of U.S. medical graduates were non-Hispanic white, compared with 26% of IMGs. Asian/Pacific Islanders made up 32% of IMGs, compared with 5% of U.S. medical graduates. Hispanic and Latino physicians accounted for 7% of IMGs, compared with 2% of U.S. graduates.

More of the IMGs than U.S. medical graduates were working as primary care physicians—57% vs. 46%—a statistically significant difference, Ms. Hing noted.

IMGs also practiced more often in counties that included primary care shortage areas than did U.S.-trained physicians—87% vs. 79%. IMGs also were more likely to accept new patients and to accept Medicaid—nearly one-third of IMGs surveyed derived 20% or more of their incomes

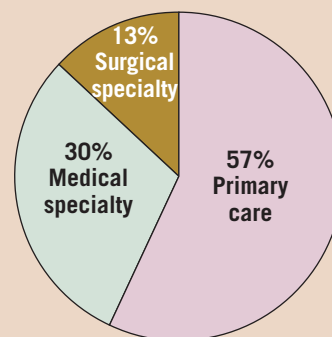
from Medicaid, compared with less than one-fourth of U.S.-trained physicians.

"This study illustrates how the U.S. health care system continues to rely on IMGs to address shortages in primary care," Ms. Hing said at the conference, which was sponsored by the Association of American Medical Colleges and Harvard Medical School.

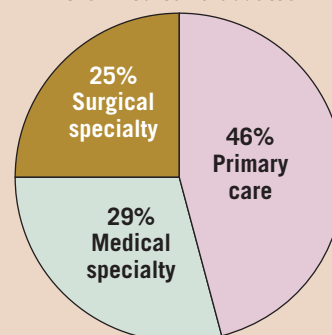
"The U.S. health care system faces challenges if the future supply and use of IMGs is constrained by recent changes in visa policy that reduce the number of incoming" medical graduates, she said. ■

Most International Medical Graduates Work as Primary Care Physicians

International Medical Graduates



U.S. Medical Graduates



Note: Based on 2005-2006 data from the National Ambulatory Medical Care Survey for 2,390 physicians in office-based practices.

Source: Ms. Hing