

Four Seasons team members included a palliative care physician (Dr. Bull), a palliative care nurse practitioner, and administrative support.

Last year, there were 308 admissions to the hospital medical psychiatric unit, of which two-thirds were related to behavioral and psychological symptoms of dementia (BPSD), Dr. Bull explained. "On the palliative care end, we received 242 referrals in 2006 and about two-thirds of those were related to BPSD."

Symptoms of BPSD—seen in 83% of dementia patients and undoubtedly the most common cause of nursing home placement—include aggression, screaming, rest-

lessness, agitation, wandering, sexual disinhibition, hoarding, cursing, and shadowing, she said.

Unfortunately, there are several barriers to quality end-of-life care in the typical psychiatric setting, said Judith A. Adams, the palliative care nurse at Four Seasons.

"Psychiatrists often don't recognize end-of-life symptoms because they're focused on psychological symptoms, and there's a



lack of knowledge of pain medications," Ms. Adams explained, adding that psychiatric patients face many stressors, such as physical restraints and noisy, busy environments.

**Two-thirds of the referrals to palliative care received in 2006 were related to BPSD.**

DR. BULL

Although the psychiatry profession is taking strides to improve end-of-life care, the psychiatry-palliative care partnership approach offers an excellent alternative, she said.

"However, roles have to be clearly de-

finied. In the psychiatry department, the psychiatrist is the attending physician. Our role is strictly one of consultation, and this is a crucial point. We are assessing and treating pain and nonpain symptoms, and we're not going to treat unless the psychiatrist asks us to," Ms. Adams cautioned.

A second pitfall is not having clear communications on the expectations of the palliative care consult.

The partnership has resulted in improved patient quality of care; avoidance of suffering and futile care in future medical admissions related to clear goals; and overall enhancement of the hospital's palliative care service, Ms. Adams said. ■

**SEROQUEL® (quetiapine fumarate) Tablets**

**BRIEF SUMMARY of Prescribing Information (continued)—Before prescribing, please consult complete Prescribing Information.** 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 bid) with lithium had no effect on any of the steady-state pharmacokinetic parameters of lithium. **Antipyrene:** 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 antipyrene or urinary recovery of antipyrene metabolites. These results indicate that quetiapine does not significantly induce hepatic enzymes responsible for cytochrome P450 mediated metabolism of antipyrene. **Carcinogenesis, Mutagenesis, Impairment of Fertility:** **Carcinogenesis:** Carcinogenicity studies were conducted in C57BL mice and Wistar rats. Quetiapine was administered in the diet to mice at doses of 20, 75, 250, and 750 mg/kg and to rats by gavage at doses of 25, 75, and 250 mg/kg for two years. These doses are equivalent to 0.1, 0.5, 1.5, and 4.5 times the maximum human dose (800 mg/day) on a mg/m<sup>2</sup> basis (mice) or 0.3, 0.9, and 3.0 times the maximum human dose on a mg/m<sup>2</sup> basis (rats). There were statistically significant increases in thyroid gland follicular adenomas in male mice at doses of 250 and 750 mg/kg or 1.5 and 4.5 times the maximum human dose on a mg/m<sup>2</sup> basis and in male rats at a dose of 250 mg/kg or 3.0 times the maximum human dose on a mg/m<sup>2</sup> basis. Mammary gland adenocarcinomas were statistically significantly increased in female rats at all doses tested (25, 75, and 250 mg/kg or 0.3, 0.9, and 3.0 times the maximum recommended human dose on a mg/m<sup>2</sup> basis). Thyroid follicular cell adenomas may have resulted from chronic stimulation of the thyroid gland by thyroid stimulating hormone (TSH) resulting from enhanced metabolism and clearance of thyroxine by rodent liver. Changes in TSH, thyroxine, and thyroxine clearance consistent with this mechanism were observed in subchronic toxicity studies in rat and mouse and in a 1-year toxicity study in rat; however, the results of these studies were not definitive. The relevance of the increases in thyroid follicular cell adenomas to human risk, through whatever mechanism, is unknown. Antipsychotic drugs have been shown to chronically elevate prolactin levels in rodents. Serum measurements in a 1-yr toxicity study showed that quetiapine increased median serum prolactin levels a maximum of 32- and 13-fold in male and female rats, respectively. Increases in mammary neoplasms have been found in rodents after chronic administration of other antipsychotic drugs and are considered to be prolactin-mediated. The relevance of this increased incidence of prolactin-mediated mammary gland tumors in rats to human risk is unknown (see **Hyperprolactinemia in PRECAUTIONS, General**). **Mutagenesis:** The mutagenic potential of quetiapine was tested in six *in vitro* bacterial gene mutation assays and in an *in vitro* mammalian gene mutation assay in Chinese Hamster Ovary cells. However, sufficiently high concentrations of quetiapine may not have been used for all tester strains. Quetiapine did not produce a reproducible increase in mutations in one *Salmonella typhimurium* tester strain in the presence of metabolic activation. No evidence of clastogenic potential was obtained in an *in vitro* chromosomal aberration assay in cultured human lymphocytes or in the *in vivo* micronucleus assay in rats. **Impairment of Fertility:** Quetiapine decreased mating and fertility in male Sprague-Dawley rats at oral doses of 50 and 150 mg/kg or 0.6 and 1.8 times the maximum human dose on a mg/m<sup>2</sup> basis. Drug-related effects included increases in interval to mate and in the number of matings required for successful impregnation. These effects continued to be observed at 150 mg/kg even after a two-week period without treatment. The no-effect dose for impaired mating and fertility in male rats was 25 mg/kg, or 0.3 times the maximum human dose on a mg/m<sup>2</sup> basis. Quetiapine adversely affected mating and fertility in female Sprague-Dawley rats at oral doses of 50 mg/kg, or 0.6 times the maximum human dose on a mg/m<sup>2</sup> basis. Drug-related effects included decreases in matings and in matings resulting in pregnancy, and an increase in the interval to mate. An increase in irregular estrus cycles was observed at doses of 10 and 50 mg/kg, or 0.1 and 0.6 times the maximum human dose on a mg/m<sup>2</sup> basis. The no-effect dose in female rats was 1 mg/kg, or 0.01 times the maximum human dose on a mg/m<sup>2</sup> basis. **Pregnancy Category C:** The teratogenic potential of quetiapine was studied in Wistar rats and Dutch Belted rabbits 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/m<sup>2</sup> basis or in rabbits at 25 to 100 mg/kg or 0.6 to 2.4 times the maximum human dose on a mg/m<sup>2</sup> basis. There was, however, evidence of embryofetal 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/m<sup>2</sup> basis) and in rabbits at 50 and 100 mg/kg (1.2 and 2.4 times the maximum human dose on a mg/m<sup>2</sup> 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/m<sup>2</sup> 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/m<sup>2</sup> 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 perinatal 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/m<sup>2</sup> basis. However, in a preliminary pre/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/m<sup>2</sup> 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.

**ADVERSE REACTIONS:** The information below is derived from a clinical trial database for SEROQUEL consisting of over 3700 patients. Of these approximately 3700 subjects, approximately 3400 (2300 in schizophrenia, 405 in acute bipolar mania, and 698 in bipolar depression) were patients who participated in multiple dose effectiveness trials, and their experience corresponded to approximately 992.6 patient-years. (Refer to full Prescribing Information for details of adverse event data collection.) **Adverse Findings Observed in Short-Term, Controlled Trials: Adverse Events Associated with Discontinuation of Treatment in Short-Term, Placebo-Controlled Trials: Bipolar Disorder: Depression:** Overall, discontinuations due to adverse events were 12.3% for SEROQUEL 300 mg vs 19.0% for SEROQUEL 600 mg and 5.2% for placebo. **Mania:** Overall, discontinuations due to adverse events were 5.7% for SEROQUEL vs. 5.1% for placebo in monotherapy and 3.6% for SEROQUEL vs. 5.9% for placebo in adjunct therapy. **Schizophrenia:** Overall, there was little difference in the incidence of discontinuation due to adverse events (4% for SEROQUEL vs. 3% for placebo) in a pool of controlled trials. However, discontinuations due to somnolence (0.8% for SEROQUEL vs. 0% for placebo) and hypotension (0.4% for SEROQUEL vs. 0% for placebo) were considered to be drug related (see **PRECAUTIONS, Adverse Events Occurring at an Incidence of 1% or More Among SEROQUEL Treated Patients in Short-Term, Placebo-Controlled Trials:** The following treatment-emergent adverse events occurred during acute therapy of schizophrenia (up to 6 weeks) and bipolar mania (up to 12 weeks) in 1% or more of patients treated with SEROQUEL (doses ranging from 75 to 800 mg/day) where the incidence in patients treated with SEROQUEL was greater than the incidence in placebo-treated patients. **Body as a Whole:** Headache 21% vs. 14%; Pain 7% vs. 5%; Asthenia 5% vs. 3%; Abdominal Pain 4% vs. 1%; Back Pain 3% vs. 1%; Fever 2% vs. 1%; **Cardiovascular:** Tachycardia 6% vs. 4%; Postural Hypotension 4% vs. 1%; **Digestive:** Dry Mouth 9% vs. 3%; Constipation 8% vs. 3%; Vomiting 6% vs. 5%; Dyspepsia 5% vs. 1%; Gastroenteritis 2% vs. 0%; Gamma Glutamyl Transpeptidase Increased 1% vs. 0%; **Metabolic and Nutritional:** Weight Gain 5% vs. 1%; SGPT Increased 5% vs. 1%; SGOT Increased 3% vs. 1%; **Nervous:** Agitation 20% vs. 17%; Somnolence 18% vs. 8%; Dizziness 11% vs. 5%; Anxiety 4% vs. 3%; **Respiratory:** Pharyngitis 4% vs. 3%; Rhinitis 3% vs. 1%; **Skin and Appendages:** Rash 4% vs. 2%; **Special Senses:** Amblyopia 2% vs. 1%. (Events for which the SEROQUEL incidence was equal to or less than placebo are not listed, but included the following: accidental injury, akathisia, chest pain, cough increased, depression, diarrhea, extrapyramidal syndrome, hostility, hypertension, hypertonnia, hypotension, increased appetite, infection, insomnia, leukopenia, malaise, nausea, nervousness, paresthesia, peripheral edema, sweating, tremor, and weight loss.) In these studies, the most commonly observed adverse events associated with the use of SEROQUEL (incidence of 5% or greater) and observed at a rate on SEROQUEL at least twice that of placebo were somnolence (18%), dizziness (11%), dry mouth (9%), constipation (8%), SGPT increased (5%), weight gain (5%), and dyspepsia (5%). The following treatment-emergent adverse events occurred during therapy (up to 3-weeks) of acute mania in 5% or more of patients treated with SEROQUEL (doses ranging from 100 to 800 mg/day) used as adjunct therapy to lithium and divalproex where the incidence in patients treated with SEROQUEL was greater than the incidence in placebo-treated patients. (SEROQUEL vs. placebo) **Body as a Whole:** Headache 17% vs. 13%; Asthenia 10% vs. 4%; Abdominal Pain 7% vs. 3%; Back Pain 5% vs. 3%; **Cardiovascular:** Postural Hypotension 7% vs. 2%; **Digestive:** Dry Mouth 19% vs. 3%; Constipation 10% vs. 5%; **Metabolic and Nutritional:** Weight Gain 6% vs. 3%; **Nervous:** Somnolence 34% vs. 9%; Dizziness 9% vs. 6%; Tremor 8% vs. 7%; Agitation 6% vs. 4%; **Respiratory:** Pharyngitis 6% vs. 3%. (Events for which the SEROQUEL incidence was equal to or less than placebo are not listed, but included the following: akathisia, diarrhea, insomnia, and nausea.) In these studies, the most commonly observed adverse events associated with the use of SEROQUEL (incidence of 5% or greater) and observed at a rate on SEROQUEL at least twice that of placebo were somnolence (34%), dry mouth (19%), asthenia (10%), constipation (10%), abdominal pain (7%), postural hypotension (7%), pharyngitis (6%), and weight gain (6%). The following treatment-emergent adverse events occurred during therapy (up to 8-weeks) of bipolar depression in 5% or more of patients treated with SEROQUEL (doses of 300 and 600 mg/day) where the incidence in patients treated with SEROQUEL was greater than the incidence in placebo-treated patients. (SEROQUEL vs. placebo) **Gastrointestinal Disorders:** Dry Mouth 44% vs. 13%; Constipation 10% vs. 4%; Dyspepsia 7% vs. 4%; **General Disorders and Administrative Site Conditions:** Fatigue 10% vs. 8%; **Metabolism and Nutrition Disorders:** Increased Appetite 5% vs. 2%; **Nervous System Disorders:** Sedation 30% vs. 8%; Somnolence 28% vs. 7%; Dizziness 18% vs. 7%; Lethargy 5% vs. 3%; **Respiratory, Thoracic, and Mediastinal Disorders:** Nasal Congestion 5% vs. 3%. (Events for which the SEROQUEL incidence was equal to or less than placebo are not listed, but included the following: nausea, upper respiratory tract infection, and headache.) In these studies, the most commonly observed adverse events associated with the use of SEROQUEL (incidence of 5% or greater) and observed at a rate on SEROQUEL at least twice that of placebo were dry mouth (44%), sedation (30%), somnolence (28%), dizziness (18%), constipation (10%), lethargy (5%), and nasal congestion (5%). Explorations for interactions on the basis of gender, age, and race did not reveal any clinically meaningful differences in the adverse event occurrence on the basis of these demographic factors. **Dose Dependency of Adverse Events in Short-Term, Placebo-Controlled Trials: Dose-related Adverse Events:** Spontaneously elicited adverse event data from a study of schizophrenia comparing five fixed doses of SEROQUEL (75 mg, 150 mg, 300 mg, 600 mg, and 750 mg/day) to placebo were explored for dose-relatedness of adverse events. Logistic regression analyses revealed a positive dose response (p<0.05) for the following adverse events: dyspepsia, abdominal pain, and weight gain. **Extrapyramidal Symptoms:** Data from one 6-week clinical trial of schizophrenia comparing five fixed doses of SEROQUEL (75, 150, 300, 600, 750 mg/day) provided evidence for the lack of treatment-emergent extrapyramidal symptoms (EPS) and dose-relatedness for EPS associated with SEROQUEL treatment. Three methods were used to measure EPS: (1) Simpson-Angus total score (mean change from baseline) which evaluates parkinsonism and akathisia, (2) incidence of spontaneous complaints of EPS (akathisia, akinesia, cogwheel rigidity, extrapyramidal syndrome, hypertonnia, hypokinesia, neck rigidity, and tremor), and (3) use of anticholinergic medications to treat emergent

EPS. In six additional placebo-controlled clinical trials (3 in acute mania and 3 in schizophrenia) using variable doses of SEROQUEL, there were no differences between the SEROQUEL and placebo treatment groups in the incidence of EPS, as assessed by Simpson-Angus total scores, spontaneous complaints of EPS and the use of concomitant anticholinergic medications to treat EPS. In two placebo-controlled clinical trials for the treatment of bipolar depression using 300 mg and 600 mg of SEROQUEL, the incidence of adverse events potentially related to EPS was 12% in both dose groups and 6% in the placebo group. In these studies, the incidence of the individual adverse events (eg, akathisia, extrapyramidal disorder, tremor, dyskinesia, dystonia, restlessness, muscle contractions involuntary, psychomotor hyperactivity and muscle rigidity) were generally low and did not exceed 4% in any treatment group. The 3 treatment groups were similar in mean change in SAS total score and BARS Global Assessment score at the end of treatment. The use of concomitant anticholinergic medications was infrequent and similar across the three treatment groups. **Vital Signs and Laboratory Studies: Vital Sign Changes:** SEROQUEL is associated with orthostatic hypotension (see **PRECAUTIONS, Weight Gain:** In schizophrenia trials the proportions of patients meeting a weight gain criterion of ≥7% of body weight were compared in a pool of four 3- to 6-week placebo-controlled clinical trials, revealing a statistically significantly greater incidence of weight gain for SEROQUEL (23%) compared to placebo (6%). In mania monotherapy trials the proportions of patients meeting the same weight gain criterion were 21% compared to 7% for placebo and in mania adjunct therapy trials the proportion of patients meeting the same weight gain criterion were 13% compared to 4% for placebo. In bipolar depression trials, the proportions of patients meeting the same weight gain criterion were 8% compared to 2% for placebo. **Laboratory Changes:** An assessment of the premarketing experience for SEROQUEL suggested that it is associated with asymptomatic increases in SGPT and increases in both total cholesterol and triglycerides (see **PRECAUTIONS**). In post-marketing clinical trials, elevations in total cholesterol (predominantly LDL cholesterol) have been observed. An assessment of hematological parameters in short-term, placebo-controlled trials revealed no clinically important differences between SEROQUEL and placebo. **ECG Changes:** Between group comparisons for pooled placebo-controlled trials revealed no statistically significant SEROQUEL/placebo differences in the proportions of patients experiencing potentially important changes in ECG parameters, including QT, QTc, and PR intervals. However, the proportions of patients meeting the criteria for tachycardia were compared in four 3- to 6-week placebo-controlled clinical trials for the treatment of schizophrenia revealing a 1% (4/399) incidence for SEROQUEL compared to 0.6% (1/156) incidence for placebo. In acute (monotherapy) bipolar mania trials the proportions of patients meeting the criteria for tachycardia was 0.5% (1/192) for SEROQUEL compared to 0% (0/178) incidence for placebo. In acute bipolar mania (adjunct) trials the proportions of patients meeting the same criteria was 0.6% (1/166) for SEROQUEL compared to 0% (0/171) incidence for placebo. In bipolar depression trials, no patients had heart rate increases to >120 beats per minute. SEROQUEL use was associated with a mean increase in heart rate, assessed by ECG, of 7 beats per minute compared to a mean increase of 1 beat per minute among placebo patients. This slight tendency to tachycardia may be related to SEROQUEL's potential for inducing orthostatic changes (see **PRECAUTIONS**). **Other Adverse Events Observed During the Pre-Marketing Evaluation of SEROQUEL:** Following is a list of COSTART terms that reflect treatment-emergent adverse events as defined in 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 events are included except those already listed in Table 1 or elsewhere in labeling, those events for which a drug cause was remote, and those event terms which were so general as to be uninformative. It is important to emphasize that, although the events reported occurred during treatment with SEROQUEL, 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 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 events are those occurring in 1/100 to 1/1000 patients; rare events are those occurring in fewer than 1/1000 patients. **Nervous System: Frequent:** hypertonnia, 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:** vasodilation, QT interval prolonged, migraine, bradycardia, cerebral ischemia, irregular pulse, I wave abnormal, 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: Frequent:** 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, echthymosis, eosinophilia, hypochromic anemia, lymphadenopathy, cyanosis; **Rare:** hemolytic thrombocytopenia. **Endocrine System: Infrequent:** hypothyroidism, diabetes mellitus; **Rare:** hyperthyroidism. (\*adjusted for gender) **Post Marketing Experience:** Adverse events reported since market introduction which were temporally related to SEROQUEL therapy include: leukopenia/ neutropenia. If a patient develops a low white cell count and history of drug induced leukopenia/neutropenia. Other adverse events reported since market introduction, which were temporally related to SEROQUEL therapy, but not necessarily causally related, include the following: agranulocytosis, anaphylaxis, cardiomyopathy, hyponatremia, myocarditis, rhabdomyolysis, syndrome of inappropriate antidiuretic hormone secretion (SIADH), and Stevens-Johnson Syndrome (SJS).

**DRUG ABUSE AND DEPENDENCE: Controlled Substance Class:** SEROQUEL is not a controlled substance. **Physical and Psychological dependence:** 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 events or recovered fully from the reported events. 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 drug's known pharmacological effects, i.e., 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 **PRECAUTIONS: Orthostatic Hypotension**). 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 Overdose:** In case of acute overdose, 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 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 overdose 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.

**DOSAGE AND ADMINISTRATION: Dosing in Special Populations:** Consideration should be given to a slower rate of dose titration and a lower target dose in the elderly and in patients who are debilitated or who have a predisposition to hypotensive reactions. When indicated, dose escalation should be performed with caution in these patients. Patients with hepatic impairment should be started on 25 mg/day. The dose should be increased daily in increments of 25-50 mg/day to an effective dose, depending on the clinical response and tolerability of the patient. The elimination of quetiapine was enhanced in the presence of phenytoin. Higher maintenance doses of quetiapine may be required when it is coadministered with phenytoin and other enzyme inducers such as carbamazepine and phenobarbital (See **Drug Interactions under PRECAUTIONS, Maintenance Treatment:** While there is no body of evidence available to answer the question of how long the patient treated with SEROQUEL should be maintained, it is generally recommended that responding patients be continued beyond the acute response, but at the lowest dose needed to maintain remission. Patients should be periodically reassessed to determine the need for maintenance treatment. **Reinitiation of Treatment in Patients Previously Discontinued:** Although there are no data to specifically address reinitiation of treatment, it is recommended that when restarting patients who have had an interval of less than one week off SEROQUEL, titration of SEROQUEL is not required and the maintenance dose may be reinitiated. When restarting therapy of patients who have been off SEROQUEL for more than one week, the initial titration schedule should be followed. **Switching from Antipsychotics:** There are no systematically collected data to specifically address switching patients with schizophrenia from antipsychotics to SEROQUEL, or concerning concomitant administration with antipsychotics. While immediate discontinuation of the previous antipsychotic treatment may be acceptable for some patients with schizophrenia, more gradual discontinuation may be most appropriate for others. In all cases, the period of overlapping antipsychotic administration should be minimized. When switching patients with schizophrenia from depot antipsychotics, if medically appropriate, initiate SEROQUEL therapy in place of the next scheduled injection. The need for continuing existing EPS medication should be reevaluated periodically. SEROQUEL is a trademark of the AstraZeneca group of companies. ©AstraZeneca 2006, 2007 30417-00 Rev 01/07 AstraZeneca Pharmaceuticals LP, Wilmington, DE 19850 Made in USA 248500

# Dementia Care: Go Beyond Patient

BALTIMORE — Supportive care for patients with dementia and their caregivers is an important component of overall dementia care, Dr. Constantine G. Lyketsos said at a meeting on Alzheimer's disease and related disorders sponsored by Johns Hopkins University.

Supportive care for the patient should provide comfort and emotional support, safety, structure, activity and stimulation, planning/assistance with decision making, management of medical comorbidities, and good nursing care for advanced stages, said Dr. Lyketsos, chair of psychiatry at Johns Hopkins Bayview Medical Center in Baltimore.

In terms of safety, "many patients with dementia, in fact most of them, should stop driving," said Dr. Lyketsos. "Most of them can't live alone entirely. That doesn't mean that there needs to be someone in the house 24 hours a day, but there needs to be some support."

Providing structure means ensuring a safe, predictable place to live with support for activities of daily living. "Because of diminishing cognition, making sure that structure is available is critical. ... The more dementia advances, the more important it is to have daily structure in place that's predictable," he said.

Participation in activities can make a big difference. "One of the things we found in the Maryland Assisted Living Study was that the more participation there was in activities, the longer patients were able to stay in their assisted living facility," Dr. Lyketsos said.

Support for caregivers includes emotional support and comfort, education, instruction in the skills of caregiving, problem-solving and crisis-intervention help, respite, and attention to personal needs and wants.

"The piece that we don't have a good way to deliver yet is respite. Caregivers need breaks. They can get easily overwhelmed," he said. Caregivers tend to overlook their own health, so they need to pay attention to their personal needs and wants as well. They also need to maintain touch with social contacts, which is an important part of the support network.

—Kerri Wachter