During clinical trials, seizures occurred in 0.8% (18/2387) of patients treated with SEROQUEL. Asymptomatic, transient and reversible elevations in serum creatinine phosphokinase (CPK) were noted in patients treated with SEROQUEL. In a pool of 3- to 6-week placebo-controlled trials, a mean 25% decrease in CPK was observed in 10% of patients treated with SEROQUEL compared to 3% of patients treated with placebo; however, this difference was not statistically significant. This decrease in CPK was not associated with any concomitant clinical symptoms of muscular toxicity, such as muscle weakness, myalgia, or rash. The mechanism of action of SEROQUEL, as with other antipsychotics, is unknown. However, SEROQUEL has been shown to be metabolized through a combination of dopamine type 2 (D2) and serotonin type 2 (5HT2) antagonism. SEROQUEL is extensively metabolized in vivo by cytochromes P450 1A2, 2C9, 2C19, 2D6 and 3A4. The contribution of each of these enzymes to the overall metabolism of SEROQUEL is unknown. In patients with normal renal and hepatic function, the half-life of SEROQUEL is approximately 6-7 hours. In patients with renal impairment, the half-life of SEROQUEL is increased by approximately 50%. In patients with hepatic impairment, the elimination of SEROQUEL is decreased. The safety and efficacy of SEROQUEL have been demonstrated in clinical studies of patients with acute exacerbations of schizophrenia and in maintenance studies of patients with stable schizophrenia. The safety and efficacy of SEROQUEL in patients with other mental disorders have not been studied. The safety and efficacy of SEROQUEL in children and adolescents have not been established. The safety and efficacy of SEROQUEL in elderly patients have not been studied. The safety and efficacy of SEROQUEL in patients with renal impairment have not been studied. 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Infrequent: conjunctivitis, abnormal vision, dry eyes, tinnitus, taste dysmenorrhea*, vaginitis*, urinary incontinence, serotonin syndrome, depression, delusions, pharyngitis, dry skin, dysuria and urinary tract infection.

Explanations for interactions on the basis of gender, age, and race did not reveal any clinically meaningful differences in the frequency of adverse events or reactions. However, there were some differences in the relative frequency of adverse events in the two placebo-controlled trials in patients who were African American (220 in the short-term trial, 240 in the maintenance trial) and non-African American (234 in the short-term trial, 241 in the maintenance trial).

Adverse Events in Short-Term, Placebo-controlled Trials

Dose-related Adverse Events: Spontaneously reported adverse event data from a study conducted in patients 65 years of age and older, who received SEROQUEL during the initial dosing period for up to 3-6 weeks, are summarized in Table 1. The frequency of adverse events increased with higher doses of SEROQUEL and with longer duration of treatment. As shown in Table 1, the relative frequency of the 600 mg/day dose in comparison with the 100 mg/day dose was increased in patients 65 years of age and older.

Five fixed doses of SEROQUEL (25, 50, 100, 200, 400 mg/day) were compared to placebo in a 6-week, double-blind, placebo-controlled, rivastigmine-assisted, fixed-ratio bioequivalence trial. Mean steady-state rivastigmine concentrations were consistent with those observed in previous bioequivalence trials. The bioavailability of rivastigmine was similar for doses of 25 mg, 50 mg, and 100 mg. Mean maximum rivastigmine concentrations were approximately proportional to dose over the range of 25 mg to 100 mg/day.

SEROQUEL was excreted in milk of treated animals during lactation. It is not known whether SEROQUEL is excreted in human milk. Maternal milk should be avoided in nursing women during treatment with SEROQUEL. The effect of SEROQUEL on labor and delivery in humans is unknown.

There are no adequate and well-controlled studies in pregnant women and the pharmacokinetics of SEROQUEL in pregnant women has not been established. Labor and Delivery: There are no adequate and well-controlled studies in pregnant women and the pharmacokinetics of SEROQUEL in pregnant women has not been established. Labor and Delivery: There are no adequate and well-controlled studies in pregnant women and the pharmacokinetics of SEROQUEL in pregnant women has not been established.

DOSAGE AND ADMINISTRATION

Usual Dose: SEROQUEL should be administered with an initial dose of 25 mg bid with increments in increments of 3.75 mg/day in 6-week stages until the target dose is reached. Further dosage adjustments, if indicated, should generally occur at intervals of not less than 4 weeks.

Adverse Events

In placebo-controlled trials, approximately 2400 patients with schizophrenia were treated with SEROQUEL. There are no adequate and well-controlled studies in pregnant women and the pharmacokinetics of SEROQUEL in pregnant women has not been established. Labor and Delivery: There are no adequate and well-controlled studies in pregnant women and the pharmacokinetics of SEROQUEL in pregnant women has not been established.

DOSAGE AND ADMINISTRATION

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SEROQUEL tablets are available in the following dosage and strength combinations: 25 mg (NDC 0310-0268) white, capsule-shaped, biconvex, film coated tablets, identified with ‘SEROQUEL’ and ‘25’ on one side and ‘S’ on the other side, are supplied in bottles of 100 tablets and hospital unit dose packages of 100 tablets.

200 mg tablets (NDC 0310-0267) white, capsule-shape, biconvex, film coated tablets, identified with ‘SEROQUEL’ and ‘300’ on one side and plain on the other side, are supplied in bottles of 60 tablets and hospital unit dose packages of 100 tablets. The tablets may be reconstituted to a 25 mg/ml solution by adding 0.9% sodium chloride injection to the vials to provide a 25 mg/ml solution for intravenous use.

300 mg tablets (NDC 0310-0278) white, capsule-shaped, biconvex, film coated tablets, identified with ‘SEROQUEL’ and ‘300’ on one side and plain on the other side, are supplied in bottles of 100 tablets and hospital unit dose packages of 100 tablets. The tablets may be reconstituted to a 25 mg/ml solution by adding 0.9% sodium chloride injection to the vials to provide a 25 mg/ml solution for intravenous use.

25 mg tablets (NDC 0310-0277) white, round, biconvex, film coated tablets, identified with ‘SEROQUEL’ and ‘25’ on one side and on the other side, are supplied in bottles of 100 tablets and hospital unit dose packages of 100 tablets.

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