QUETIAPINE

Introduction

Category

Antipsychotic.

Indications

Accepted

Psychotic disorders (treatment)¾Quetiapine is indicated for the treatment of the manifestations of psychotic disorders 1 including schizophrenia 2.

The effectiveness of quetiapine for more than 6 weeks has not been evaluated in controlled trials

Pharmacology/Pharmacokinetics

Physicochemical characteristics:

Chemical group¾Dibenzothiazepine derivative 1.

Molecular weight¾Quetiapine fumarate: 883.11 1

Solubility¾Quetiapine fumarate is moderately soluble in water 1.

Mechanism of action/Effect:

The exact mechanism by which quetiapine exerts its antipsychotic effect is unknown 1.

However, this effect may be mediated through antagonism of dopamine type 2 (D 2) and serotonin type 2 (5-HT 2) receptors 1.

Quetiapine is an antagonist at serotonin 5-HT 1A and 5-HT 2, dopamine D 1 and D 2, histamine H 1, and adrenergic alpha 1 and alpha 2 receptors 1.

Quetiapine has no significant affinity for cholinergic muscarinic or benzodiazepine receptors 1.

Drowsiness and orthostatic hypotension associated with use of quetiapine may be explained by its antagonism of histamine H 1 and adrenergic alpha 1 receptors, respectively 1.

Other actions/effects:

In clinical trials, quetiapine produced a dose-related decrease in total and free thyroxine (T 4) concentrations 1.

This decrease was apparent early in treatment with quetiapine, and no further changes occurred during continued therapy 1.

At the high end of the quetiapine therapeutic dosage range, total and free thyroxine concentrations were decreased by about 20% 1.

About 0.4% (10/2386) of patients in clinical trials experienced increases in thyroid-stimulating hormone (TSH) concentrations and six of these patients required thyroid hormone replacement therapy 1.

Prolactin concentration increases, which were associated with an increased incidence of mammary gland neoplasia, were seen in rat studies with quetiapine 1.

However, prolactin concentration increases were not demonstrated in human clinical trials 1.

Cataracts developed in the eyes of dogs during chronic quetiapine dosing 1.

Also, changes in the lenses of the eyes have been observed in patients during long-term quetiapine therapy, although a causal relationship to quetiapine has not been established 1.

It is thought that quetiapine may have an anti-emetic effect, consistent with its antagonism of dopaminergic receptors. 2

Absorption:

Rapidly and well absorbed 1.

Food increases peak plasma concentration (C max) and area under the plasma concentration-time curve (AUC) by 25% and 15%, respectively 1, 2.

Distribution:

Extensively distributed throughout the body, with an apparent volume of distribution (Vol D) of 10 ± 4 L/kg 1, 2.

Protein binding:

High (83%) to plasma proteins 1 ; does not alter the binding of warfarin or diazepam to human serum albumin in vitro and quetiapine binding is not altered in vitro by warfarin or diazepam 1.

Biotransformation:

Quetiapine is extensively metabolized in the liver 1.

Less than 5% of an orally administered dose is excreted unchanged 1, 2.

The major metabolic pathways are sulfoxidation, which in vitro studies indicate is mediated by the cytochrome P450 3A4 (CYP3A4) isoenzyme, and oxidation 1, 2.

The major metabolites of quetiapine are inactive 1, 2.

Half-life:

Elimination¾

Mean, about 6 to 7 hours 1, 2.

Time to peak concentration:

Peak plasma concentration is reached within 2 hours of dosing 1, 2.

Pharmacokinetic parameters

The pharmacokinetics of quetiapine are linear within the clinical dose range of 50 to 600 mg/day, and are similar in both genders and in smokers and nonsmokers. 2

Elimination:

Renal¾

Approximately 73% of an orally administered dose is excreted renally 1, 2.

Fecal¾

Approximately 20% of an orally administered dose is excreted in the feces 1, 2.

Precautions to Consider

Carcinogenicity/Tumorigenicity

Statistically significant increases in the incidence of thyroid gland follicular cell adenomas were seen in male mice receiving quetiapine at daily dosages that were equivalent to 1.5 and 4.5 times the maximum recommended human dose (MRHD) on a mg per square meter of body surface area (mg/m 2) basis and in male rats receiving three times the MRHD on a mg/m 2 basis, possibly as a result of chronic stimulation of the thyroid gland by thyroid-stimulating hormone (TSH) 1.

Although the results were not definitive, quetiapine toxicity studies in rats and mice showed changes in thyroxine concentrations, thyroxine clearance, and TSH concentrations that are consistent with the proposed mechanism of increased thyroxine clearance leading to increased TSH concentrations and increased thyroid gland stimulation 1.

Statistically significant increases in the incidence of mammary gland adenocarcinomas were seen in female rats receiving quetiapine at daily dosages that were equivalent to 0.3 to 3 times the MRHD on a mg/m 2 basis 1.

In a 1-year quetiapine toxicity study, median serum prolactin concentrations were increased a maximum of 32-fold in male rats, and 13-fold in female rats 1.

The mammary gland neoplasms seen in rodents after chronic administration of antipsychotic medications are considered to be prolactin-mediated 1.

The relevance of these findings to humans is unknown 1.

Mutagenicity

Quetiapine produced a reproducible increase in mutations in one of six strains in in vitro bacterial gene mutation assays in the presence of metabolic activation 1.

An in vitro chromosomal aberration assay in cultured human lymphocytes and an in vivo micronucleus assay in rats found no evidence of clastogenic potential 1.

Pregnancy/Reproduction

Fertility¾In male Sprague-Dawley rats, the interval to mate and the number of matings required to produce pregnancy increased at quetiapine doses equivalent to 0.6 and 1.8 times the MRHD on a mg/m 2 basis 1.

These effects were still present 2 weeks after discontinuation of quetiapine in the rats that had received 1.8 times the MRHD 1.

No effects on mating or fertility were seen in male rats receiving £ 0.3 times the MRHD on a mg/m 2 basis 1.

In female Sprague-Dawley rats, the interval to mate increased and the number of matings and the number of matings resulting in pregnancy decreased at a quetiapine dose equivalent to 0.6 times the MRHD on a mg/m 2 basis 1.

Irregular estrus cycles increased at doses equivalent to 0.1 and 0.6 times the MRHD on a mg/m 2 basis 1.

No effects on estrus, mating, or fertility were seen in female rats receiving £ 0.01 times the MRHD on a mg/m 2 basis 1.

Pregnancy¾Adequate and well-controlled studies in humans have not been done 1.

Quetiapine showed no teratogenic potential in rats and rabbits dosed at 0.3 to 2.4 and 0.6 to 2.4 times the MRHD on a mg/m 2 basis, respectively, during the period of organogenesis 1.

However, in rats, delays in skeletal ossification were seen in the fetuses at all doses 1.

Also, reduced fetal body weight and reduced maternal weight gain and/or increased maternal deaths were seen at the highest dose used 1.

In rabbits, reduced maternal weight gain and/or increased maternal deaths were seen at all doses, delays in skeletal ossification in the fetuses were seen at doses of 1.2 and 2.4 times the MRHD on a mg/m 2 basis, and reduced fetal body weight and an increased incidence of minor soft tissue anomaly in the fetuses were seen at the highest dose used 1.

In a perinatal/postnatal study in rats receiving 0.01 to 0.24 times the MRHD on a mg/m 2 basis, no drug-related effects were observed 1.

However, in a preliminary perinatal/postnatal study in rats receiving three times the MRHD on a mg/m 2 basis, increases in fetal and pup deaths and decreases in mean litter weight were found 1.

FDA Pregnancy Category C 1.

Labor and delivery¾The effects of quetiapine on labor and delivery are unknown 1.

Breast-feeding

Quetiapine is distributed into the milk of animals 1.

It is not known whether quetiapine is distributed into breast milk, but breast-feeding while taking quetiapine is not recommended 1, 2.

Pediatrics

No information is available on the relationship of age to the effects of quetiapine in pediatric patients. Safety and efficacy have not been established 1 .

Geriatrics

No geriatrics-specific problems that would limit the usefulness of quetiapine in the elderly were seen in studies that included subjects 65 years of age and older 1.

However, the mean plasma clearance of quetiapine in elderly patients was 30 to 50% less than in younger patients 1.

Reduced initial and target dosages, and slower dosage titration may be necessary in elderly patients 1, 2.

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):

Note: Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.

>> Alcohol or

>> Central nervous system (CNS) depression-producing medications, other (see Appendix II)

(quetiapine has been shown to potentiate the cognitive and motor effects of alcohol 1, 2)

Antihypertensive agents

(hypotensive effects of these medications may be enhanced 1)

Cimetidine

(oral clearance of quetiapine was decreased by 20% when coadministered with cimetidine 400 mg three times a day 1)

>> Cytochrome P450 3A (CYP3A) isoenzyme inhibitors, such as:

Clarithromycin

Diltiazem

Erythromycin

Fluconazole

Itraconazole

Ketoconazole

Nefazodone

Verapamil

(although there is no experience with the combination of quetiapine and a potent CYP3A enzyme inhibitor, caution is advised since quetiapine's major route of metabolism involves CYP3A4 1, 2)

Dopamine agonists or

Levodopa

(effects of these medications may be antagonized by quetiapine 1)

>> Enzyme inducers, hepatic, cytochrome P450 (see Appendix II)

(mean oral clearance of quetiapine was increased fivefold in patients receiving phenytoin 1, 2 ; higher doses of quetiapine may be required during concomitant therapy with an enzyme-inducing medication 1 ; a decrease in quetiapine dosage may be required when enzyme-inducer therapy is discontinued 1, 2)

Lorazepam

(mean oral clearance of lorazepam was decreased by 20% when coadministered with quetiapine 250 mg three times a day 1)

Thioridazine

(oral clearance of quetiapine was increased by 65% when coadministered with thioridazine 200 mg two times a day 1, 2)

Laboratory value alterations

The following have been selected on the basis of their potential clinical significance (possible effect in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):

With physiology/laboratory test values

Alanine aminotransferase (ALT [SGPT]) and

Aspartate transaminase (AST [SGOT])

(elevated values have been reported, usually during the first 2 months of quetiapine use 1, 2 ; approximately 6% of patients in a sample of clinical trials experienced elevations of greater than

three times the upper limit of normal 1 ; all patients were asymptomatic, and most elevations (80%) returned to baseline with continued use of quetiapine 1, 2)

Blood counts

(Transient leukopenia, neutropenia, and eosinophilia have been reported during quetiapine therapy 2)

Cholesterol, total and

Triglycerides

(increases from baseline of 11% and 17%, respectively, which were weakly related to body weight increases, were reported in patients in short-term, placebo-controlled trials 1, 2)

Gamma glutamyl transpepsidase (GGT)

(elevated values have been reported; patients were asymptomatic, and values returned to baseline during continued quetiapine therapy)

Thyroid function tests

(a dose-related decrease in total and free thyroxine [T 4] concentrations, which averaged 20%, but was ³50% in some cases, at the higher end of the therapeutic dose range, was seen in clinical trials 1, 2 ; this decrease was apparent early in treatment with quetiapine, and no further changes occurred with continued therapy 1 ; about 0.4% [10/2386] of patients in clinical trials experienced increases in thyroid-stimulating hormone [TSH] concentrations and six of these patients required thyroid hormone replacement therapy 1)

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)¾ not necessarily inclusive (>> = major clinical significance).

Except under special circumstances, this medication should not be used when the following medical problem exists

>> Hypersensitivity to quetiapine 1, 2

Risk-benefit should be considered when the following medical problems exist

Alzheimer's dementia

(dysphagia associated with use of antipsychotic medications may increase risk of aspiration pneumonia 1)

(possible increased risk of seizures because of lowered seizure threshold with Alzheimer's dementia 1)

>> Breast cancer, or history of

(although elevated prolactin concentrations have not been demonstrated in clinical trials of quetiapine, elevations have occurred with use of other antipsychotic medications and in animal studies of quetiapine 1 ; studies have found approximately one third of human breast cancers to be prolactin-dependent in vitro1, 2)

>> Cardiovascular disease, including:

Conduction abnormalities or

Heart failure or

Myocardial infarction or ischemia, or history of or

>> Cerebrovascular disease or

>> Conditions that would predispose to hypotension, including:

Dehydration or

Hypovolemia

(orthostatic hypotension may be exacerbated or may exacerbate pre-existing cardiovascular or cerebrovascular conditions 1, 2 ; if hypotension occurs during dosage titration, it is recommended that dosage be returned to the previous level 1)

(dehydration may predispose patient to increased core body temperature, and antipsychotic medications may disrupt the body's ability to lower core body temperature, thus increasing the risk of heatstroke 1)

Drug abuse or dependence, history of

(patients should be observed closely for signs of misuse or abuse of quetiapine, as with any new CNS medication 1)

>> Hepatic function impairment or

Renal function impairment, severe

(higher blood concentrations of quetiapine may occur; dosage adjustments may be necessary, especially in the initial dosing period 1, 2)

Hypothyroidism

(decreases in total and free thyroxine (T 4) occurred during clinical trials of quetiapine) 2

Seizures, or history of

(seizures occurred rarely in premarketing studies of quetiapine; it is recommended that quetiapine be used with caution in patients with a history of seizures or a decreased seizure threshold 1, 2)

Patient monitoring

The following may be especially important in patient monitoring (other tests may be warranted in some patients, depending on condition; >> = major clinical significance):

Abnormal hepatic function

(transaminase values should be measured prior to quetiapine use in patients with known or suspected hepatic function impairment; periodic re-assessment should occur in these patients, as well as in patients who develop signs or symptoms suggestive of new onset liver disorders 2)

Careful supervision of patients with suicidal tendencies

(recommended in high-risk patients, since the possibility of suicide attempt is inherent in schizophrenia 1 ; prescribing the smallest quantity of medication necessary for good patient management is recommended to prevent overdosing 1, 2)

>> Ophthalmologic exams

(examination of the lens of the eye by methods adequate to detect cataract formation, such as slit lamp examination, is recommended at baseline and every 6 months during treatment with quetiapine 1 ; lens changes have been observed in patients during long-term quetiapine therapy and cataracts developed in dogs during chronic quetiapine dosing 1, 2)

Side/Adverse Effects

Note: Disturbances of body temperature regulation have been associated with use of other antipsychotic agents 1.

Caution is advised in administering quetiapine to patients who will be experiencing conditions that may contribute to an elevation in core body temperature, such as strenuous exercise, exposure to extreme heat, dehydration, or concomitant treatment with anticholinergic medications 1.

The neuroleptic malignant syndrome (NMS) has been associated with the use of antipsychotic agents 1.

Two possible cases were reported during clinical trials with quetiapine 1.

NMS is a potentially fatal symptom complex that may include: hyperpyrexia; muscle rigidity; altered mental status; and autonomic instability seen as irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia 1.

Elevated creatine kinase, myoglobinuria (rhabdomyolysis), and acute renal failure also may occur 1.

Differential diagnosis should exclude serious medical illnesses, such as pneumonia or systemic infection, presenting in conjunction with extrapyramidal effects, as well as central anticholinergic toxicity, heatstroke, drug fever, and primary CNS pathology 1.

Tardive dyskinesia, a syndrome of potentially irreversible, involuntary, dyskinetic movements, has been reported in patients taking other antipsychotic medications 1.

Tardive dyskinesia occurs more frequently in elderly patients, especially women, than in younger patients 1.

The risk of developing the syndrome and of experiencing irreversible effects appears to increase with treatment duration and total cumulative dose, although it may develop at any time during antipsychotic therapy 1.

There is no known treatment for tardive dyskinesia, although partial or complete remission may occur when the antipsychotic medication is withdrawn 1.

Alternatively, the antipsychotic medication may suppress the signs of the syndrome, masking the underlying process 1.

For these reasons, quetiapine should be used only in those patients with chronic illness that is responsive to antipsychotic medication, and for whom potentially less harmful treatments are unavailable or inappropriate 1.

Also, the smallest effective dose of quetiapine should be used and the need for continuing treatment should be assessed periodically 1.

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)¾not necessarily inclusive:

Those indicating need for medical attention

Incidence less frequent

Dysarthria 1trouble in speaking); dyspnea 1 trouble in breathing); extrapyramidal symptoms, parkinsonian 1trouble in speaking or swallowing); loss of balance control); mask-like face); shuffling walk); slowed movements); stiffness of arms or legs); trembling and shaking of hands and fingers); flu-like symptoms 1fever); chills); muscle aches); leukopenia 1 fever, chills, or sore throat); orthostatic hypotension (dizziness, lightheadedness, or fainting, especially when getting up from a lying or sitting position); peripheral edema 1swelling of feet or lower legs); skin rash 1

Incidence rare

Changes in lenses of eyes 1, 2¾usually asymptomatic; galactorrhea (unusual secretion of milk)¾ in females; hypothyroidism 1 loss of appetite); weight gain); dry, puffy skin); tiredness); hypotension 1 low blood pressure); menstrual changes 1; neuroleptic malignant syndrome (NMS) 1, 2 difficult or unusually fast breathing); fast heartbeat or irregular pulse); high fever); high or low [irregular] blood pressure); increased sweating); loss of bladder control); severe muscle stiffness); seizures); unusually pale skin); unusual tiredness or weakness); seizures 1; tachycardia 2 (fast, pounding, or irregular heartbeat; fainting)

Note: Changes in the lenses of the eyes have been observed in patients during long-term quetiapine therapy and cataracts have developed in dogs during chronic quetiapine dosing 1.

Regular ophthalmologic examinations are recommended during quetiapine therapy 1.

Those indicating need for medical attention only if they continue or are bothersome

Incidence more frequent

Constipation 1; dizziness 1; drowsiness 1; dry mouth 1; dyspepsia 1 (indigestion); increased weight 1

Note: Dyspepsia and increased weight are dose-related 1.

In pooled data from 3- to 6-week trials, 23% of patients receiving quetiapine and 6% of patients receiving placebo gained ³ 7% of their baseline body weight 1.

Incidence less frequent

Abdominal pain 1; abnormal vision 1; anorexia 1 (decrease in appetite); asthenia 1 (decreased strength and energy); headache 1; hypertonia 1 (increased muscle tone); increased sweating 1; palpitation 1 (feeling of fast or irregular heartbeat); pharyngitis 1 (sore throat); rhinitis 1 (stuffy or runny nose)

Note: Abdominal pain is dose-related 1.

Overdose

For specific information on the agents used in the management of quetiapine overdose, see:

· Antidyskinetics (Systemic) monograph;

· Charcoal, Activated (Oral-Local) monograph;

· Laxatives (Local) monograph; and/or

· Sympathomimetic Agents-Cardiovascular Use (Parenteral-Systemic) monograph.

For more information on the management of overdose or unintentional ingestion, contact a Poison Control Center (see Poison Control Center Listing).

Clinical effects of overdose

Note: Effects of overdose may be similar to side effects experienced at therapeutic doses, but may be more severe or several effects may occur together 1.

The following effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)¾not necessarily inclusive:

Acute

Drowsiness 1; heart block 1 slow or irregular heartbeat); hypotension 1 low blood pressure); hypokalemia 1 weakness); tachycardia 1 fast heartbeat)

Note: First degree heart block and hypokalemia were seen in one patient after an estimated overdose of 9600 mg of quetiapine 1.

Doses in excess of 10 grams have been taken; patients recovered without sequelae, and no fatalities were reported. 2

Treatment of overdose

Treatment is symptomatic and supportive 1, 2.

To decrease absorption¾Gastric lavage, following intubation in unconscious patients, and administration of charcoal with a laxative should be considered 1.

Induction of emesis is not recommended due to risk of aspiration if patient is obtunded or experiencing seizures or dystonic reactions of the head and neck 1.

Specific treatment¾Administering antiarrhythmic therapy, if needed 1.

However, disopyramide, procainamide, and quinidine have the potential to add to the possible QT-interval-prolonging effects of quetiapine overdosage 1.

Also, bretylium may add to the hypotensive effect of quetiapine, due to additive alpha-adrenergic receptor blockade 1.

Hypotension may be treated with intravenous fluids and/or sympathomimetic agents 1.

However, epinephrine and dopamine may exacerbate hypotension through beta-adrenergic stimulation in the presence of quetiapine-induced alpha-adrenergic receptor blockade 1.

Anticholinergic (antidyskinetic) medication should be administered in the presence of severe extrapyramidal symptoms 1.

Monitoring¾Continuous electrocardiographic (ECG) monitoring is recommended to detect possible arrhythmias 1.

Supportive care¾Establish and maintain airway and ensure adequate oxygenation and ventilation 1.

Patients in whom intentional overdose is confirmed or suspected should be referred for psychiatric consultation.

Patient Consultation

In providing consultation, consider emphasizing the following selected information (>> = major clinical significance):

Before using this medication

>> Conditions affecting use, especially:

Breast-feeding¾Distributed into milk of animals; use in nursing mothers not recommended

Other medications, especially alcohol, CYP3A isoenzyme inhibitors, other CNS depression-producing medications, or hepatic enzyme inducers

Other medical problems, especially breast cancer or history of breast cancer, cardiovascular disease, cerebrovascular disease, conditions that would predispose to hypotension, hepatic function impairment, hypersensitivity to quetiapine, or severe renal function impairment

Proper use of this medication

Compliance with therapy; not taking more or less medicine than prescribed

Taking with or without food, on a full or empty stomach, as directed by physician

>> Proper dosing

Missed dose: Taking as soon as remembered; skipping if almost time for next dose; not doubling doses.

>> Proper storage

Precautions while using this medication

Possible drowsiness, especially during first 3 to 5 days of therapy; caution when driving, operating machinery, or doing other jobs that require alertness

Possible orthostatic hypotension; rising slowly from a sitting or lying position

Possible impairment of ability to regulate core body temperature; avoiding overheating and dehydration

Avoiding use of alcoholic beverages; not taking other CNS depressants unless prescribed by physician

Side/adverse effects

Signs of potential side effects, especially dysarthria, dyspnea, parkinsonian extrapyramidal symptoms, flu-like symptoms, galactorrhea, leukopenia, orthostatic hypotension, peripheral edema, skin rash, changes in lenses of eyes, hypothyroidism, hypotension, menstrual changes, neuroleptic malignant syndrome (NMS), seizures, and tachycardia,

General Dosing Information

Since the possibility of suicide is inherent in schizophrenia, patients should not have access to large quantities of quetiapine 1.

To reduce the risk of overdose, the patient should be supplied with the smallest quantity of medication necessary for satisfactory patient management 1.

Diet/Nutrition

Quetiapine may be administered with or without food, on a full or empty stomach. Food marginally increases quetiapine absorption 1.

For treatment of adverse effects

Neuroleptic malignant syndrome (NMS)¾Recommended treatment consists of the following 1 :

· Discontinuing quetiapine and other medications not essential to current therapy.

· Providing intensive symptomatic treatment and medical monitoring.

· Treating any concomitant serious medical problems for which specific treatments are available.

· After recovery, giving careful consideration to the reintroduction of antipsychotic drug therapy in patients with severe psychosis requiring treatment, because of possible recurrence of NMS; closely monitoring patients in whom antipsychotic drug therapy is reintroduced after recovery from NMS.

Tardive dyskinesia¾There is no known effective treatment 1.

If signs and symptoms of tardive dyskinesia appear, discontinuation of quetiapine treatment should be considered if clinically feasible 1, 2.

To minimize the occurrence of tardive dyskinesia, chronic antipsychotic treatment should be in the smallest effective dose for the shortest duration necessary to produce a satisfactory clinical response 1, 2.

Oral Dosage Form

Note: The available dosage form contains quetiapine fumarate, but dosage and strength are expressed in terms of the base 1.

QUETIAPINE TABLETS

Usual adult dose

Antipsychotic¾

Oral, initially 25 mg (base) two times a day, with increases of 25 to 50 mg (base) two or three times a day to a target dosage range of 300 to 400 mg (base) a day, in divided doses given two or three times a day, by the fourth to seventh day 1, 2.

Further dosage adjustments may be made in increments or decrements of 25 to 50 mg (base) two times a day at intervals of two days 1.

Some patients may require as little as 150 mg a day. 2

Note: A slower rate of dosage titration and a lower target dosage should be considered in geriatric patients and in patients with hepatic impairment, predisposition to hypotension, or other debilitation 1.

A dose-response study did not find dosages above 300 mg (base) a day to be more efficacious than a dosage of 300 mg (base) a day [1].

When reinstituting quetiapine therapy in a patient who has discontinued quetiapine for more than one week, the initial titration schedule should be followed [1].

If discontinuation has been for less than one week, quetiapine may be reinstituted at the previous maintenance dosage [1].

Usual adult prescribing limits

800 mg (base) a day [1, 2].

Usual pediatric dose

Antipsychotic¾

Safety and efficacy have not been established [1, 2].

Strength(s) usually available

U.S.¾25 mg (base) (Rx)[Seroquel] [1]

100 mg (base) (Rx)[Seroquel] [1]

200 mg (base) (Rx)[Seroquel] [1]

Canada¾25 mg (base) (Rx)[Seroquel (film-coated) (red ferric oxide)] [2]

100 mg (base) (Rx)[Seroquel (film-coated)] [2]

200 mg (base) (Rx)[Seroquel (film-coated)] [2]

Packaging and storage:

Store at temperatures between 15 and 30 °C (59 to 86 °F) 1, 2 , unless otherwise specified by manufacturer.

Auxiliary labeling:

· Avoid alcoholic beverages.

· May cause dizziness or drowsiness.

References

1 Seroquel package insert (Zeneca¾US), Rev 7/97, Rec 10/97.

2 Product Information: SeroquelÒ, quetiapine fumarate, Zeneca. In: Welbanks L (ed): Compendium of Pharmaceuticals and Specialties, 35th ed. Canadian Pharmaceutical Association, Ottawa, Ontario, Canada, 2000. p.1451-1453.