

Size: 240 x 360 mm

Folding size: 30 x 60 mm

Carton size: 36 x 30 x 75 mm

48 x 36 x 85 mm

45 x 36 x 102 mm

↓ Front



QUETIAPINE FUMARATE

Q-WIN™

25 mg/100 mg/200 mg Film Coated Tablet

ANTIPSYCHOTIC

PRODUCT NAME:

Quetiapine

NAME AND STRENGTH:

Quetiapine Tablets 25 mg
Quetiapine Tablets 100 mg
Quetiapine Tablets 200 mg

PHARMACOLOGIC CATEGORY:

ANTIPSYCHOTIC

PRODUCT DESCRIPTION:

Quetiapine Tablets 25 mg - Yellow colored, circular, biconvex film coated tablets
Quetiapine Tablets 100 mg - Yellow colored, circular, biconvex film coated tablets with breakline on one surface
Quetiapine Tablets 200 mg - Yellow colored, circular, biconvex film coated tablets with breakline on one surface

FORMULATION/COMPOSITION:

Each film-coated tablet contains:

Quetiapine (as fumarate) 25 mg/100 mg/200 mg

PHARMACODYNAMICS/PHARMACOKINETICS:

Pharmacodynamics:

Quetiapine is an atypical antipsychotic agent. Quetiapine and the active human plasma metabolite, norquetiapine interact with a broad range of neurotransmitter receptors. Quetiapine and norquetiapine exhibit affinity for brain serotonin (5HT2) and dopamine D1- and D2-receptors. It is this combination of receptor antagonism with a higher selectivity for 5HT2 relative to D2-receptors, which is believed to contribute to the clinical antipsychotic properties and low extrapyramidal side effect (EPS) liability of Quetiapine compared to typical antipsychotics. Quetiapine and norquetiapine have no appreciable affinity at benzodiazepine receptors but high affinity at histaminergic and adrenergic alpha1 receptors and moderate affinity at adrenergic alpha2 receptors. Quetiapine also has low or no affinity for muscarinic receptors, while norquetiapine has moderate to high affinity at several muscarinic receptors, which may explain anti-cholinergic (muscarinic) effects. Inhibition of NET and partial agonist action at 5HT1A sites by norquetiapine may contribute to Quetiapine therapeutic efficacy as an antidepressant.

Pharmacokinetics:

Absorption: Quetiapine is well absorbed and extensively metabolized following oral administration. The bioavailability of quetiapine is not significantly affected by administration with food. Steady-state peak molar concentrations of the active metabolite norquetiapine are 35% of that observed for quetiapine. The pharmacokinetics of quetiapine and norquetiapine are linear across the approved dosing range.

Distribution: Quetiapine is approximately 83% bound to plasma proteins.

Biotransformation: Quetiapine is extensively metabolized by the liver, with parent compound accounting for less than 5% of unchanged drug-related material in the urine or faeces, following the administration of radiolabelled quetiapine. *In vitro* investigations established that CYP3A4 is the primary enzyme responsible for cytochrome P450 mediated metabolism of quetiapine. Norquetiapine is primarily formed and eliminated via CYP3A4. Approximately 73% of the radioactivity is excreted in the urine and 21% in the faeces. Quetiapine and several of its metabolites (including norquetiapine) were found to be weak inhibitors of human cytochrome P450 1A2, 2C9, 2C19, 2D6 and 3A4 activities in vitro. In vitro CYP inhibition is observed only at concentrations approximately 5 to 50 fold higher than those observed at a dose range of 300 to 800 mg/day in humans. Based on these *in vitro* results, it is unlikely that co-administration of quetiapine with other drugs will result in clinically significant drug inhibition of cytochrome P450 mediated metabolism of the other drug. From animal studies it appears that quetiapine can induce cytochrome P450 enzymes. In a specific interaction study in psychotic patients, however, no increase in the cytochrome P450 activity was found after administration of quetiapine.

Elimination: The elimination half-lives of quetiapine and norquetiapine are approximately 7 and 12 hours, respectively. The average molar dose fraction of free quetiapine and the active human plasma metabolite norquetiapine is <5% excreted in the urine.

INDICATIONS:

Quetiapine is indicated for:

- Treatment of Schizophrenia.
- For the treatment of moderate to severe manic episodes in bipolar disorder
- For the treatment of major depressive episodes in bipolar disorder
- For the prevention of recurrence of manic or depressed episodes in patients with bipolar disorder who previously responded to quetiapine treatment.

DOSAGE AND MODEL ROUTE OF ADMINISTRATION:

Different dosing schedules exist for each indication. It must therefore be ensured that patients receive clear information on the appropriate dosage for their condition.

Quetiapine can be administered with or without food.

Adults:

For the treatment of schizophrenia: For the treatment of schizophrenia, Quetiapine should be administered twice a day. The total daily dose for the first four days of therapy is 50 mg (Day 1), 100 mg (Day 2), 200 mg (Day 3) and 300 mg (Day 4). From Day 4 onwards, the dose should be titrated to the usual effective dose of 300 to 450 mg/day. Depending on the clinical response and tolerability of the individual patient, the dose may be adjusted within the range 150 to 750 mg/day.

For the treatment of moderate to severe manic episodes in bipolar disorder: For the treatment of manic episodes associated with bipolar disorder, Quetiapine should be administered twice a day. The total daily dose for the first four days of therapy is 100 mg (Day 1), 200 mg (Day 2), 300 mg (Day 3) and 400 mg (Day 4). Further dosage adjustments up to 800 mg/day by Day 6 should be in increments of no greater than 200 mg/day.

The dose may be adjusted depending on clinical response and tolerability of the individual patient, within the range of 200 to 800 mg/day. The usual effective dose is in the range of 400 to 800 mg/day.

For the treatment of major depressive episodes in bipolar disorder: Quetiapine should be administered once daily at bedtime. The total daily dose for the first four days of therapy is 50 mg (Day 1), 100 mg (Day 2), 200 mg (Day 3) and 300 mg (Day 4). The recommended daily dose is 300 mg. In clinical trials, no additional benefit was seen in the 600 mg group compared to the 300 mg group. Individual patients may benefit from a 600 mg dose. Doses greater than 300 mg should be initiated by physicians experienced in treating bipolar disorder. In individual patients, in the event of tolerance concerns, clinical trials have indicated that dose reduction to a minimum of 200 mg could be considered.

For preventing recurrence in bipolar disorder: For preventing recurrence of manic, mixed or depressive episodes in bipolar disorder, patients who have responded to quetiapine for acute treatment of bipolar disorder should continue therapy at the same dose. The dose may be adjusted depending on clinical response and tolerability of the individual patient, within the range of 300 to 800 mg/day administered twice daily. It is important that the lowest effective dose is used for maintenance therapy.

Elderly: As with other antipsychotics, Quetiapine should be used with caution in the elderly, especially during the initial dosing period. The rate of dose titration may need to be slower, and the daily therapeutic dose lower, than that used in younger patients, depending on the clinical response and tolerability of the individual patient. The mean plasma clearance of quetiapine was reduced by 30 - 50% in elderly subjects when compared to younger patients.

Efficacy and safety has not been evaluated in patients over 65 years with depressive episodes in the framework of bipolar disorder.

Paediatric Population: Quetiapine is not recommended for use in children and adolescents below 18 years of age, due to a lack of data to support use in this age group. The available evidence from placebo-controlled clinical trials is presented in Sections 4.4, 4.8, 5.1 and 5.2.

Renal Impairment: Dosage adjustment is not necessary in patients with renal impairment.

Hepatic Impairment: Quetiapine is extensively metabolized by the liver. Therefore, Quetiapine should be used with caution in patients with known hepatic impairment, especially during the initial dosing period. Patients with known hepatic impairment should be started with 25 mg/day. The dosage should be increased daily with increments of 25 - 50 mg/day until an effective dosage, depending on the clinical response and tolerability of the individual patient.

Method of administration:

Orally administer

CONTRAINDICATIONS & PRECAUTION(S), WARNING(S):

Hypersensitivity to the active substance or to any of the excipients of this product. Concomitant administration of cytochrome P450 3A4 inhibitors, such as HIV-protease inhibitors, azole-antifungal agents, erythromycin, clarithromycin and nefazodone, is contraindicated.

PRECAUTIONS & WARNINGS:

As Quetiapine has several indications, the safety profile should be considered with respect to the individual patient's diagnosis and the dose being administered.

Paediatric population: Quetiapine is not recommended for use in children and adolescents below 18 years of age, due to a lack of data to support use in this age group. Clinical trials with quetiapine have shown that in addition to the known safety profile identified in adults, certain adverse events occurred at a higher frequency in children and adolescents compared to adults (increased appetite, elevations in serum prolactin, vomiting, rhinitis and syncope), or may have different implications for children and adolescents (extrapyramidal symptoms and irritability) and one was identified that has not been previously seen in adult studies (increases in blood pressure). Changes in thyroid function tests have also been observed in children and adolescents. Furthermore, the long-term safety implications of treatment with quetiapine on growth and maturation have not been studied beyond 26 weeks. Long-term implications for cognitive and behavioral development are not known. In placebo-controlled clinical trials with children and adolescent patients, quetiapine was associated with an increased incidence of extrapyramidal symptoms (EPS) compared to placebo in patients treated for schizophrenia, bipolar mania and bipolar depression.

Suicide/suicidal thoughts or clinical worsening: Depression in bipolar disorder is associated with an increased risk of suicidal thoughts, self-harm and suicide (suicide-related events). This risk persists until significant remission occurs. As improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored until such improvement occurs. It is general clinical experience that the risk of suicide may increase in the early stages of recovery.

In addition, physicians should consider the potential risk of suicide-related events after abrupt cessation of quetiapine treatment, due to the known risk factors for the disease being treated. Other psychiatric conditions for which quetiapine is prescribed can also be associated with an increased risk of suicide related events. In addition, these conditions may be co-morbid with major depressive episodes. The same precautions observed when treating patients with major depressive episodes should therefore be observed when treating patients with other psychiatric disorders.

Metabolic Risk: Given the observed risk for worsening of their metabolic profile, including changes in weight, blood glucose (see hyperglycaemia) and lipids, which was seen in clinical studies, patients' metabolic parameters should be assessed at the time of treatment initiation and changes in these parameters should be regularly controlled for during the course of treatment. Worsening in these parameters should be managed as clinically appropriate.

Extrapyramidal symptoms: In placebo controlled clinical trials of adult patients quetiapine was associated with an increased incidence of extrapyramidal symptoms (EPS) compared to placebo in patients treated for major depressive episodes in bipolar disorder. The use of quetiapine has been associated with the development of akathisia, characterised by a subjectively unpleasant or distressing restlessness and need to move often accompanied by an inability to sit or stand still. This is most likely to occur within the first few weeks of treatment. In patients who develop these symptoms, increasing the dose may be detrimental.

Tardive Dyskinesia: If signs and symptoms of tardive dyskinesia appear, dose reduction or discontinuation of quetiapine should be considered. The symptoms of tardive dyskinesia can worsen or even arise after discontinuation of treatment.

Somnolence and dizziness: Quetiapine treatment has been associated with somnolence and related symptoms, such as sedation. In clinical trials for treatment of patients with bipolar depression, onset was usually within the first 3 days of treatment and was predominantly of mild to moderate intensity. Patients experiencing somnolence of severe intensity may require more frequent contact for a minimum of 2 weeks from onset of somnolence, or until symptoms improve and treatment discontinuation may need to be considered.

QT Prolongation: In clinical trials and use in accordance with the SPC, quetiapine was not associated with a persistent increase in absolute QT intervals. In post-marketing, QT prolongation was reported with quetiapine at the therapeutic doses and in overdose. As with other antipsychotics, caution should be exercised when quetiapine is prescribed in patients with cardiovascular disease or family history of QT prolongation. Also, caution should be exercised when quetiapine is prescribed either with medicines known to increase QT interval or with concomitant neuroleptics, especially in the elderly, in patients with congenital long QT syndrome, congestive heart failure, heart hypertrophy, hypokalemia or hypomagnesaemia.

Cardiomyopathy and Myocarditis: Cardiomyopathy and myocarditis have been reported in clinical trials and during the post-marketing experience; however, a causal relationship to quetiapine has not been established. Treatment with quetiapine should be reassessed in patients with suspected cardiomyopathy or myocarditis.

Withdrawal: Acute withdrawal symptoms such as insomnia, nausea, headache, diarrhoea, vomiting, dizziness and irritability have been described after abrupt cessation of quetiapine. Gradual withdrawal over a period of at least one to two weeks is advisable.

Constipation and intestinal obstruction: Constipation represents a risk factor for intestinal obstruction. Constipation and intestinal obstruction have been reported with quetiapine. This includes fatal reports in patients who are at higher risk of intestinal obstruction, including those that are receiving multiple concomitant medications that decrease intestinal motility and/or may not report symptoms of constipation. Patients with intestinal obstruction/ileus should be managed with close monitoring and urgent care.

Venous Thromboembolism (VTE): Cases of venous thromboembolism (VTE) have been reported with antipsychotic drugs. Since patients treated with antipsychotics often present with acquired risk factors for VTE, all possible risk factors for VTE should be identified before and during treatment with quetiapine and preventive measures undertaken.

Pancreatitis: Pancreatitis has been reported in clinical trials and during post marketing experience. Among post marketing reports, while not all cases were confounded by risk factors, many patients had factors which are known to be associated with pancreatitis such as increased triglycerides, gallstones, and alcohol consumption.

Additional Information: Quetiapine data in combination with divalproex or lithium in acute moderate to severe manic episodes is limited; however, combination therapy was well tolerated. The data showed an additive effect at week 3.

Lactose: Quetiapine tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency, or glucose-galactose malabsorption should not take this medicine.

PREGNANCY AND LACTATION:

Pregnancy:

First trimester: The moderate amount of published data from exposed pregnancies (i.e. between 300-1000 pregnancy outcomes), including individual reports and some observational studies do not suggest an increased risk of malformations due to treatment. However, based on all available data, a definite conclusion cannot be drawn. Animal studies have shown reproductive toxicity. Therefore, quetiapine should only be used during pregnancy if the benefits justify the potential risks.

Third trimester: Neonates exposed to antipsychotics (including quetiapine) during the third trimester of pregnancy are at risk of adverse reactions including extrapyramidal and/or withdrawal symptoms that may vary in severity and duration following delivery. There have been reports of agitation, hypertension, hypotonia, tremor, somnolence, respiratory distress, or feeding disorder. Consequently, newborns should be monitored carefully.

Lactation: Based on very limited data from published reports on quetiapine excretion into human breast milk, excretion of quetiapine at therapeutic doses appears to be inconsistent. Due to lack of robust data, a decision must be made whether to discontinue breast-feeding or to discontinue Quetiapine therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

Fertility: The effects of quetiapine on human fertility have not been assessed. Effects related to elevated prolactin levels were seen in rats, although these are not directly relevant to humans.

INTERACTIONS:

f) Clinically significant drug interactions

Given the primary central nervous system effects of quetiapine, quetiapine should be used with caution in combination with other centrally acting medicinal products and alcohol.

Caution should be exercised treating patients receiving other medications having anti-cholinergic (muscarinic) effects.

Cytochrome P450 (CYP) 3A4 is the enzyme that is primarily responsible for the cytochrome P450 mediated metabolism of quetiapine. In an interaction study in healthy volunteers, concomitant administration of quetiapine (dosage of 25 mg) with ketoconazole, a CYP3A4 inhibitor, caused a 5- to 8-fold increase in the AUC of quetiapine. On the basis of this, concomitant use of quetiapine with CYP3A4 inhibitors is contraindicated. It is also not recommended to consume grapefruit juice while on quetiapine therapy. In a multiple dose trial in patients to assess the pharmacokinetics of quetiapine given before and during treatment with carbamazepine (a known hepatic enzyme inducer), co-administration of carbamazepine significantly increased the clearance of quetiapine. This increase in clearance reduced systemic quetiapine exposure (as measured by AUC) to an average of 13% of the exposure during administration of quetiapine alone; although a greater effect was seen in some patients. As a consequence of this interaction, lower plasma concentrations can occur, which could affect the efficacy of quetiapine therapy. Co-administration of quetiapine and phenytoin (another microsomal enzyme inducer) caused a greatly increased clearance of quetiapine by approx. 450%. In patients receiving a hepatic enzyme inducer, initiation of quetiapine treatment should only occur if the physician considers that the benefits of quetiapine outweigh the risks of removing the hepatic enzyme inducer. It is important that any change in the inducer is gradual, and if required, replaced with a non-inducer (e.g. sodium valproate).

The pharmacokinetics of quetiapine were not significantly altered by co-administration of the antidepressants imipramine (a known CYP 2D6 inhibitor) or fluoxetine (a known CYP 3A4 and CYP 2D6 inhibitor).

The pharmacokinetics of quetiapine were not significantly altered by co-administration of the antipsychotics risperidone or haloperidol. Concomitant use of quetiapine and thioridazine caused an increased clearance of quetiapine with approx. 70%.

The pharmacokinetics of quetiapine were not altered following co-administration with cimetidine.

In a 6-week, randomised, study of lithium and quetiapine prolonged release versus placebo and quetiapine prolonged release in adult patients with acute mania, a higher incidence of extrapyramidal related events (in particular tremor), somnolence, and weight gain were observed in the lithium add-on group compared to the placebo add-on group (see section 5.1).

The pharmacokinetics of sodium valproate and quetiapine were not altered to a clinically relevant extent when co-administered. A retrospective study of children and adolescents who received valproate, quetiapine, or both, found a higher incidence of leucopenia and neutropenia in the combination group versus the monotherapy groups.

Formal interaction studies with commonly used cardiovascular medicinal products have not been performed.

Caution should be exercised when quetiapine is used concomitantly with medicinal products known to cause electrolyte imbalance or to increase QT interval.

There have been reports of false positive results in enzyme immunoassays for methadone and tricyclic antidepressants in patients who have taken quetiapine. Confirmation of questionable immunoassay screening results by an appropriate chromatographic technique is recommended.

ADVERSE EFFECTS:

The most commonly reported Adverse Drug Reactions (ADRs) with quetiapine ($\geq 10\%$) are somnolence, dizziness, headache, dry mouth, withdrawal (discontinuation) symptoms, elevations in serum triglyceride levels, elevations in total cholesterol (predominantly LDL cholesterol), decreases in HDL cholesterol, weight gain, decreased haemoglobin and extrapyramidal symptoms.

The incidences of ADRs associated with quetiapine therapy, are tabulated below (Table 1) according to the format recommended by the Council for International Organizations of Medical Sciences (CIOMS III Working Group; 1995).

Table 1 ADRs associated with quetiapine therapy

The frequencies of adverse events are ranked according to the following: Very common ($\geq 1/10$), common ($\geq 1/100, < 1/10$), uncommon ($\geq 1/1000, < 1/100$), rare ($\geq 1/10000, < 1/1000$), very rare ($< 1/10000$) and not known (cannot be estimated from the available data).

SOC	Very Common	Common	Uncommon	Rare	Very Rare	Not known
Blood and lymphatic system disorders	Decreased haemoglobin ²²	Leucopenia ^{1,23} , decreased neutrophil count, eosinophils increased ²⁷	Neutropenia ¹ , Thrombocytopenia, Anaemia, platelet count decreased ¹	Agranulocytosis ²⁶		
Immune system disorders			Hypersensitivity (including allergic skin reactions)		Anaphylactic reaction ⁵	
Endocrine disorders		Hyperprolactinaemia ¹⁵ , decreases in total T ₄ ²⁴ , decreases in free T ₄ ²⁴ , decreases in total T ₃ ²⁴ , increases in TSH ²⁴	Decreases in free T ₃ ²⁴ , Hypothyroidism ²¹		Inappropriate antiidiuretic hormone secretion	
Metabolism and nutritional disorders	Elevations in serum triglyceride levels ^{23,21} Elevations in total cholesterol (predominantly LDL cholesterol) ^{23,11} Decreases in HDL cholesterol ^{17,30} , Weight gain ^{8,30}	Increased appetite, blood glucose increased to hyperglycaemic levels ^{6,30}	Hyponatremia ¹⁹ , Diabetes Mellitus ^{1,5} Exacerbation of pre-existing diabetes	Metabolic syndrome ²⁹		
Psychiatric disorders		Abnormal dreams and nightmares, Suicidal ideation and suicidal behaviour ²⁰		Somnambulism and related reactions such as sleep talking and sleep related eating disorder		
Nervous system disorders	Dizziness ^{4,16} , somnolence ^{2,16} , headache, Extrapyramidal symptoms ^{1,21}	Dysarthria	Seizure ¹ , Restless legs syndrome, Tardive dyskinesia ^{1,5} , Syncope ^{4,16}			
Cardiac disorders		Tachycardia ⁴ , Palpitations ²³	QT prolongation ^{1,12,18} Bradycardia ³²			
Eye disorders		Vision blurred				
Vascular disorders		Orthostatic hypotension ^{1,4}		Venous thromboembolism ¹		
Respiratory, thoracic and mediastinal disorder		Dyspnoea ²³	Rhinitis			
Gastrointestinal disorders	Dry mouth	Constipation, dyspepsia, vomiting ²⁵	Dysphagia ⁷	Pancreatitis ¹ , Intestinal obstruction/Ileus		
Hepatobiliary disorders		Elevations in serum alanine aminotransferase (ALT) ³ . Elevations in gamma-GT levels ³	Elevations in serum aspartate aminotransferase (AST) ³	Jaundice ⁵ , Hepatitis		
Skin and subcutaneous tissue disorders					Angioedema ⁵ , Stevens-Johnson syndrome ⁵	Toxic Epidermal Necrolysis, Erythema Multiforme
Musculoskeletal and connective tissue disorders					Rhabdomyoly-sis	
Renal and urinary disorders			Urinary retention			
Pregnancy, puerperium and perinatal conditions						Drug withdrawal syndrome neonatal ³
Reproductive system and breast disorders			Sexual dysfunction	Priapism, Galactorrhea, breast swelling, menstrual disorder		
General disorders and administration site conditions	Withdrawal (discontinuation) symptoms ^{1,9}	Mild asthenia, peripheral oedema, irritability, pyrexia		Neuroleptic malignant syndrome ¹ , hypothermia		
Investigations				Elevations in blood creatine phosphokinase ¹		

(1) See section 4.4

(2) Somnolence may occur, usually during the first two weeks of treatment and generally resolves with the continued administration of quetiapine.

(3) Asymptomatic elevations (shift from normal to > 3 x ULN at any time) in serum transaminase (ALT, AST) or gamma-GT levels have been observed in some patients administered quetiapine. These elevations were usually reversible on continued quetiapine treatment.

(4) As with other antipsychotics with alpha1 adrenergic blocking activity, quetiapine may commonly induce orthostatic hypotension, associated with dizziness, tachycardia and, in some patients, syncope, especially during the initial dose-titration period. (See section 4.4).

(5) Calculation of frequency for these ADRs have been taken from post-marketing data only.

(6) Fasting blood glucose ≥ 126 mg/dL (≥ 7.0 mmol/L) or a non fasting blood glucose ≥ 200 mg/dL (≥ 11.1 mmol/L) on at least one occasion.

(7) An increase in the rate of dysphagia with quetiapine vs. placebo was only observed in the clinical trials in bipolar depression.

(8) Based on $> 7\%$ increase in body weight from baseline. Occurs predominantly during the early weeks of treatment in adults.

(9) The following withdrawal symptoms have been observed most frequently in acute placebo-controlled, monotherapy clinical trials, which evaluated discontinuation symptoms: insomnia, nausea, headache, diarrhoea, vomiting, dizziness, and irritability. The incidence of these reactions had decreased significantly after 1 week post-discontinuation.

(10) Triglycerides ≥ 200 mg/dL (≥ 2.258 mmol/L) (patients ≥ 18 years of age) or ≥ 150 mg/dL (≥ 1.694 mmol/L) (patients < 18 years of age) on at least one occasion.

(11) Cholesterol ≥ 240 mg/dL (≥ 6.2064 mmol/L) (patients ≥ 18 years of age) or ≥ 200 mg/dL (≥ 5.172 mmol/L) (patients < 18 years of age) on at least one occasion. An increase in LDL cholesterol of ≥ 30 mg/dL (≥ 0.769 mmol/L) has been very commonly observed. Mean change among patients who had this increase was 41.7 mg/dL (≥ 1.07 mmol/L).

(12) See text below.

(13) Platelets $\leq 100 \times 10^9$ /L on at least one occasion.

(14) Based on clinical trial adverse event reports of blood creatine phosphokinase increase not associated with neuroleptic malignant syndrome.

(15) Prolactin levels (patients > 18 years of age): > 20 µg/L (> 869.56 pmol/L) males; > 30 µg/L (> 1304.34 pmol/L) females at any time.

(16) May lead to falls.

(17) HDL cholesterol: < 40 mg/dL (1.025 mmol/L) males; < 50 mg/dL (1.282 mmol/L) females at any time.

(18) Incidence of patients who have a QTc shift from < 450 msec to ≥ 450 msec with a ≥ 30 msec increase. In placebocontrolled trials with quetiapine the mean change and the incidence of patients who have a shift to a clinically significant level is similar between quetiapine and placebo.

(19) Shift from < 132 mmol/L to ≤ 132 mmol/L on at least one occasion.

(20) Cases of suicidal ideation and suicidal behaviours have been reported during quetiapine therapy or early after treatment discontinuation (see Sections 4.4 and 5.1).

(21) See Section 5.1

(22) Decreased haemoglobin to ≤ 13 g/dL (8.07 mmol/L) males, ≤ 12 g/dL (7.45 mmol/L) females on at least one occasion occurred in 11% of quetiapine patients in all trials including open label extensions. For these patients, the mean maximum decrease in hemoglobin at any time was -1.50 g/dL.

(23) These reports often occurred in the setting of tachycardia, dizziness, orthostatic hypotension, and/or underlying cardiac/respiratory disease.

(24) Based on shifts from normal baseline to potentially clinically important value at any time post-base-line in all trials. Shifts in total T₄, free T₄, total T₃ and free T₃ are defined as $< 0.8 \times LLN$ (pmol/L) and shift in TSH is > 5 mIU/L at any time.

(25) Based upon the increased rate of vomiting in elderly patients (≥ 65 years of age).

(26) Shift in neutrophils from $> 1.5 \times 10^9$ /L at baseline to $< 0.5 \times 10^9$ /L at any time during treatment.

(27) Based on shifts from normal baseline to potentially clinically important value at anytime post-base-line in all trials. Shifts in eosinophils are defined as $> 1 \times 10^9$ cells/L at any time.

(28) Based on shifts from normal baseline to potentially clinically important value at anytime post-base-line in all trials. Shifts in WBCs are defined as $\leq 3 \times 10^9$ cells/L at any time.

(29) Based on adverse event reports of metabolic syndrome from all clinical trials with quetiapine.

(30) In some patients, a worsening of more than one of the metabolic factors of weight, blood glucose and lipids was observed in clinical studies (See Section 4.4).

(31) See section 4.6

(32) May occur at or near initiation of treatment and be associated with hypotension and/or syncope. Frequency based on adverse reports of bradycardia and related events in all clinical trials with Quetiapine. Cases of QT prolongation, ventricular arrhythmia, sudden unexplained death, cardiac arrest and torsades de pointes have been reported very rarely with the use of neuroleptics and are considered class effect.

OVERDOSAGE AND TREATMENT:

Symptoms: In general, reported signs and symptoms were those resulting from an exaggeration of the active substance's known pharmacological effects, i.e., drowsiness and sedation, tachycardia, hypotension and anti-cholinergic effects.

Overdose could lead to QT-prolongation, seizures, status epilepticus, rhabdomyolysis, respiratory depression, urinary retention, confusion, delirium and/or agitation, coma and death. Patients with pre-existing severe cardiovascular disease may be at an increased risk of the effects of overdose.

Management of overdose: There is no specific antidote to quetiapine. In cases of severe signs, the possibility of multiple drug involvement should be considered, and intensive care procedures are recommended, including establishing and maintaining a patent airway, ensuring adequate oxygenation and ventilation, and monitoring and support of the cardiovascular system.

Based on public literature, patients with delirium and agitation and a clear anti-cholinergic syndrome may be treated with Physostigmine, 1-2 mg (under continuous ECG monitoring). This is not recommended as standard treatment, because of potential negative effect of Physostigmine on cardiac conductance. Physostigmine may be used if there are no ECG aberrations. Do not use Physostigmine in case of dysrhythmias, any degree of heart block or QRS-widening.

Whilst the prevention of absorption in overdose has not been investigated, gastric lavage can be indicated in severe poisonings and if possible to perform within one hour of ingestion. The administration of activated charcoal should be considered.

In cases of quetiapine overdose, refractory hypotension should be treated with appropriate measures such as intravenous fluids and/or sympathomimetic agents. Epinephrine and dopamine should be avoided, since beta stimulation may worsen hypotension in the setting of quetiapine-induced alpha blockade. Close medical supervision and monitoring should be continued until the patient recovers.

STORAGE CONDITION:

Store at temperatures not exceeding 30°C.

DOSAGE FORMS AND PACKAGING AVAILABLE:

Quetiapine (Q Win) Tablets 25 mg/100 mg/200 mg are packed in Alu/PVC Blister pack of 10's (Box of 50's)

INSTRUCTIONS AND SPECIAL PRECAUTIONS FOR HANDLING AND DISPOSAL (IF APPLICABLE):

Not Applicable

NAME AND ADDRESS OF MARKETING AUTHORIZATION HOLDER:

Marketing Authorization Holder

Brown & Bur PHILIPPINES INC.
U-501, 5/F, SEDCCO 1 Bldg, 120 Rada cor., Legaspi Sts., Legaspi Village, Makati City, Philippines

NAME AND ADDRESS OF MANUFACTURER:

MICRO LABS LIMITED

92, Sipcot Industrial Complex,
Hosur - 635 126, Tamil Nadu, India

CAUTION STATEMENT:

FOODS, DRUGS, DEVICES, AND COSMETICS ACT PROHIBITS DISPENSING WITHOUT PRESCRIPTION.

ADR REPORTING STATEMENT:

"FOR SUSPECTED ADVERSE DRUG REACTION, REPORT TO THE FDA: www.fda.gov.ph

Seek medical attention immediately at the first sign of Adverse Drug Reaction.

REGISTRATION NUMBER:

Quetiapine Tablets 25 mg : DRP-7200

Quetiapine Tablets 100 mg : DRP-7868

Quetiapine Tablets 200 mg : DRP-7203

DATE OF FIRST AUTHORIZATION:

Quetiapine Tablets 25 mg - 6th July 2015

Quetiapine Tablets 100 mg - 6th July 2015

Quetiapine Tablets 200 mg - 6th July 2015

DATE OF REVISION OF PACKAGE INSERT:

Feb. 2017

EXG-ML01-1587/A

MICRO LABS LIMITED, BANGALORE, INDIA				
1	Product Name	Q-WIN		
2	Strength	25 mg, 100 mg & 200 mg		
3	Component	Leaflet		
4	Category	Export - Philippines		
5	Dimension	240 x 360 mm		
6	Artwork Code	EXG-ML01I-1587/A		
7	Pharma Code	N/A		
8	Reason for Change	Text corrections as per Customer		
Prepared by (DTP)		Checked by (PD)	Approved by	
Sign	Kantharaju L.		Head CQA	Head Production/ Packing (Site)
Date	24-05-2021		Head QC (Site)	Head QA (Site)