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QUETAPINE

100 mg Film-Coated Tablet
ANTIPSYCHOTICS

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FORMULATION:
Each film coated tablet contains:
Quetiapine Fumarate equivalent to
Quetiapine……. 100 mg

PRODUCT DESCRIPTION:
A yellow colour, round shape, film coated tablet, plain on both sides.

PHARMACODYNAMICS:
Quetiapine fumarate is a dibenzothiazepine atypical antipsychotic. It is reported to have affinity for serotonin (5-HT2), histamine (H1), and adrenergic (α1 and α2) receptors as well as dopamine D1 and D2 receptors.

PHARMACOKINETIC:
Quetiapine is well absorbed after oral doses and widely distributed throughout the body. Peak plasma concentrations are reached in about 1.5 hours. It is about 83% bound to plasma proteins. Quetiapine is extensively metabolised in the liver by sulfoxidation mediated mainly by the cytochrome P450 isoenzyme CYP3A4 and by oxidation. It is excreted mainly as inactive metabolites with about 73% of a dose appearing in the urine and about 20% in the faeces. The elimination half-life has been reported to be about 6 to 7 hours. It is distributed into breast milk

INDICATIONS:
Quetiapine is used in the treatment of schizophrenia and of bipolar disorder.

DOSAGE AND ADMINISTRATION:
Schizophrenia: The usual initial daily dose in schizophrenia is the equivalent of 50 mg of the base on day one. The dose is increased on days two and three in increments of 50 to 150 mg, as tolerated, to a target of 300 to 400 mg daily by day four. The daily dose on the first day is given in 2 divided doses, but may be given in 3 divided doses thereafter. The daily dosage may be further adjusted as necessary in steps of 50 to 100 mg at intervals of not less than 2 days to a maximum daily of dose 750 mg.
In the treatment of acute manic episodes associated with bipolar disorder, the initial dose is 50 mg twice daily on day one, 100 mg twice daily on day two, 150 mg twice daily on day three, and 200 mg twice daily on day four. The dose may then be adjusted according to response to a usual range of 400 to 800 mg daily, although in some patients, 200 mg daily may be adequate. Increments in dosage should be no greater than 200 mg daily.
Quetiapine used in the depressive phase of bipolar disorder. The initial dose is 50 mg once daily at bedtime increased to 100 mg on day two, 200 mg on day three, and 300 mg on day four. The dose may be further increased to 400 mg on day five and 600 mg on day eight, if necessary. For the maintenance treatment of bipolar disorder as an adjunct to lithium or valproate; patients should be continued on the dose that controlled their initial symptoms.
Quetiapine should be given in reduced doses for elderly patients; a recommended starting dose is 25 mg daily, which may be increased every day in increments of 25 to 50 mg according to response; the effective dose range is likely to be lower than in younger adults. Reduced doses are also recommended in patients with hepatic or renal impairment.
Administration in hepatic or renal impairment: Quetiapine should be given in reduced doses to patients with hepatic impairment; a recommended initial oral dose is 25 mg daily, increased in steps of 25 to 50 mg daily according to response.

CONTRAINDICATIONS:
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.

WARNINGS AND PRECAUTIONS:
Asymptomatic changes in the lens of the eye have occurred in patients during long-term treatment with Quetiapine; Quetiapine should be used with caution in patients with hepatic or renal impairment, with cardiovascular disease or other conditions predisposing to hypotension, with cerebrovascular disease, or with a history of seizures or conditions that lower the seizure threshold.
When Quetiapine is used for the depressive phase in bipolar disorder, patients should be closely monitored during early therapy until significant improvement in depression is observed because suicide is an inherent risk in depressed patients.
Quetiapine may affect the performance of skilled tasks including driving. Gradual withdrawal of quetiapine is recommended because of the risk of withdrawal symptoms, including nausea, vomiting, insomnia, and rebound psychosis, with abrupt cessation.

DRUG INTERACTIONS:
The central effects of other CNS depressants, including alcohol, may be enhanced by Quetiapine. Quetiapine should be used with caution in patients also receiving antihypertensives or drugs that
prolong the QT interval.
Quetiapine may antagonise the actions of dopaminergics such as levodopa. CYP3A4 is the main isoenzyme responsible for cytochrome P450-mediated metabolism of Quetiapine and caution is advised when quetiapine is used with potent inhibitors of CYP3A4 such as erythromycin, fluconazole, itraconazole and ketoconazole; lower doses of quetiapine should be used when given with such drugs.
Conversely, enzyme inducers such as carbamazepine and phenytoin may decrease the plasma concentrations of quetiapine, and higher doses of quetiapine may be necessary. Thioridazine has also been reported to increase the clearance of quetiapine.
Antibacterials: Antibacterials such as *erythromycin* inhibited Quetiapine's metabolism by the cytochrome P450 isoenzyme CYP3A4. Modification of dosage was recommended in this patient group taking these two drugs together.

Antipsychotics: Asymptomatic QT prolongation associated with Quetiapine in a patient receiving *Risperidone*.

ADVERSE DRUG REACTIONS:
Quetiapine has been associated with a low incidence of extrapyramidal symptoms but tardive dyskinesia may occur after long-term treatment.
Rises in prolactin concentrations may be less than with chlorpromazine.
The most frequent adverse effects with Quetiapine are somnolence and dizziness. Mild asthenia, anxiety, fever, rhinitis, peripheral edema, constipation, dyspepsia, dry mouth and raised liver enzyme values are also relatively common. Orthostatic hypotension associated with dizziness, tachycardia, and syncope has been reported, particularly during initial dose-titration. Prolongation of QT interval is rarely significant with Quetiapine. Hyperglycaemia and exacerbation of pre-existing diabetes have been reported rarely. Clinical monitoring for hyperglycaemia has been recommended, especially in patients with, or at risk of developing, diabetes. Weight

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gain, particularly during early treatment, has also been noted. Neuroleptic malignant syndrome is rare with Quetiapine. Leucopenia, neutropenia and eosinophilia have also been reported. Other adverse effects have included rises in plasma-triglyceride and cholesterol concentrations, and reduced plasma- thyroid hormone concentrations. There have been rare reports of seizures, hypersensitivity reactions including angiedema, and priapism.
Breastfeeding: Mother receiving Quetiapine 200 mg daily by mouth has been reported to excretion of the drug through breast milk, the patients receiving Quetiapine should not breastfeed.
Dementia: In the treatment of behavioural problems in elderly patients with dementia showed an increased risk of mortality with certain drugs of this class, including Quetiapine; most of the deaths appeared due to cardiovascular events or infection.
Effects on the blood: There have been reports of leucopenia, neutropenia and pancytopenia associated with Quetiapine therapy; when the drug was stopped. Thrombotic thrombocytopenic purpura has also been reported in a patient who received Quetiapine.
Effects on body-weight: The increased risk of weight gain with some atypical antipsychotics.
Effects on carbohydrate metabolism: The increased risk of glucose intolerance and diabetes mellitus with some atypical antipsychotics, including Quetiapine has been reported.
Effects on lipid metabolism: The increased risk of hyperlipidaemia with some atypical antipsychotics is reported.
Effects on the pancreas: Severe haemorrhagic pancreatitis and necrotising pancreatitis may occur.
Effects on the respiratory system: Hyperventilation and respiratory alkalosis have been reported with Quetiapine use. Acute respiratory failure may develop in patients with a history of chronic obstructive pulmonary disease with even a single 50-mg dose of Quetiapine.
Quetiapine has been associated with mania. In old man with schizophrenia developed manic symptoms after starting treatment with Quetiapine; the symptoms resolved when Quetiapine was withdrawn.

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, hypertonia, hypotonia, tremor, somnolence, respiratory distress, or feeding disorder. Consequently, newborns should be monitored carefully.

Breastfeeding
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 breastfeeding 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.

Effects on ability to drive and use machines
Given its primary central nervous system effects, quetiapine may interfere with activities requiring mental alertness. Therefore, patients should be advised not to drive or operate machinery, until individual susceptibility to this is known.

OVERDOSE AND TREATMENT:
Hypotension, tachycardia, and somnolence were the main clinical events seen in a patient who had taken an overdose of 3 g of Quetiapine. Tachycardia of an unexpectedly long duration was also noted. Management was symptomatic, including maintenance of fluids. Asymptomatic prolongation of the QT interval was seen who had taken a 2-g overdose of Quetiapine. The considerable QT interval prolongation may occur when patients overdose on Quetiapine while taking therapeutic doses of Risperidone. Quetiapine overdosage was primarily associated with CNS and respiratory depression and sinus tachycardia.

CAUTION:
Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph. Seek medical attention immediately at the first sign of any adverse drug reaction.

STORAGE CONDITION:
Store at temperatures not exceeding 30°C.

Keep out of reach of children.

AVAILABILITY:
Alu/Alu Blister Pack x10's (Box of 30's)

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