SCHEDULING STATUS: S5

1 NAME OF THE MEDICINE

QUETIAPINE 25 VIATRIS (film-coated tablets)

QUETIAPINE 100 VIATRIS (film-coated tablets)

QUETIAPINE 150 VIATRIS (film-coated tablets)

QUETIAPINE 200 VIATRIS (film-coated tablets)

QUETIAPINE 300 VIATRIS (film-coated tablets)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

QUETIAPINE 25 VIATRIS: Each film-coated tablet contains quetiapine fumarate corresponding to 25 mg quetiapine.

QUETIAPINE 100 VIATRIS: Each film-coated tablet contains quetiapine fumarate corresponding to 100 mg quetiapine.

QUETIAPINE 150 VIATRIS: Each film-coated tablet contains quetiapine fumarate corresponding to 150 mg quetiapine.

QUETIAPINE 200 VIATRIS: Each film-coated tablet contains quetiapine fumarate corresponding to 200 mg quetiapine.

QUETIAPINE 300 VIATRIS: Each film-coated tablet contains quetiapine fumarate corresponding to 300 mg quetiapine.

Contains sugar: lactose monohydrate 4,5 mg (25 mg tablet); 18 mg (100 mg tablet); 27 mg (150 mg tablet); 36 mg (200 mg tablet); 54 mg (300 mg tablet).

3 PHARMACEUTICAL FORM

Film-coated tablet.

QUETIAPINE 25 VIATRIS: Peach coloured, round, biconvex, film-coated tablet engraved ‘Q’ on one side.

QUETIAPINE 100 VIATRIS: Yellow, round, biconvex, film-coated tablet engraved ‘Q’ over ‘100’ on one side.

QUETIAPINE 150 VIATRIS: Pale yellow, round, biconvex, film-coated tablet engraved ‘Q’ over ‘150’ on one side.

QUETIAPINE 200 VIATRIS: White, round, biconvex, film-coated tablet engraved ‘Q’ over ‘200’ on one side.

QUETIAPINE 300 VIATRIS: White, capsule-shaped, biconvex, film-coated tablet engraved ‘Q’ breakline ‘300’ on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

QUETIAPINE VIATRIS is indicated for the treatment of schizophrenia.

QUETIAPINE VIATRIS is also indicated for the treatment of manic episodes associated with a bipolar disorder. Safety and efficacy beyond 12 weeks have not been demonstrated.

4.2 Posology and method of administration

Posology

QUETIAPINE VIATRIS should be administered twice daily, with or without food.

Adults: For the treatment of schizophrenia the total daily dose for the first 4 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 effective dose range of 300-450 mg/day. This may be adjusted, depending on the clinical response and tolerability of the individual patient, within the range 150-750 mg/day.

For the treatment of manic episodes associated with bipolar disorder, the total daily dose for the first 4 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 the clinical response and tolerability of the individual patient, within the range of 200-800 mg/day. The usual effective dose is in the range of 400-800 mg/day.

Special Populations

Elderly:

QUETIAPINE VIATRIS should be used with caution in the elderly, especially during the initial dosing period. Elderly patients should be started on 25 mg/day. The dose should be increased daily, in increments of 25 to 50 mg, to an effective dose, which is likely to be lower than that in younger patients (see section 4.3).

Renal and hepatic impairment:

The oral clearance of QUETIAPINE VIATRIS is reduced by approximately 25 % in patients with renal or hepatic impairment. QUETIAPINE VIATRIS is extensively metabolised by the liver, and therefore should be used with caution in patients with known hepatic impairment.

Patients with renal or hepatic impairment should be started on QUETIAPINE VIATRIS 25 mg/day. The dose should be increased daily in increments of 25 to 50 mg, to an effective dose.

4.3 Contraindications

QUETIAPINE VIATRIS is contraindicated in patients hypersensitive to quetiapine or to any of the excipients listed in section 6.1.

Pregnancy and lactation, as safety has not been demonstrated.

Children and adolescents, under the age of 18 years, as safety and efficacy have not been established.

Advanced liver and renal function impairment, as safety has not been demonstrated.

QUETIAPINE VIATRIS is not indicated for use in elderly patients with dementia exhibiting behavioural disturbance.

Concomitant administration of cytochrome P450 3A4 inhibitors, such as HIV-protease inhibitors, azole antifungal medicines, erythromycin, clarithromycin and nefazodone, is contraindicated (see section 4.5)

4.4 Special warnings and precautions for use

Suicide/suicidal thoughts or clinical worsening:

Depression 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.

Other psychiatric conditions for which QUETIAPINE VIATRIS is prescribed can also be associated with an increased risk of suicide-related events. In addition, these conditions may co-morbid with major depression disorder. The same precaution observed when treating patients with major depressive disorder should therefore be observed when treating with other psychiatric disorders.

Patients with a history of suicide-related events, or those exhibiting a significant degree of suicidal ideation prior to commencement of treatment are known to be at greater risk of suicidal thoughts or suicide attempts and should receive careful monitoring during treatment.

Neutropenia and agranulocytosis:

Severe neutropenia (neutrophil count <0,5 x 10^9/L) without infection has been reported in quetiapine clinical trials. There have been reports of agranulocytosis (severe neutropenia with infection) among all patients treated with quetiapine during clinical trials as well as post-marketing reports (including fatal cases). Most of these cases of severe neutropenia have occurred within the first two months of starting therapy with quetiapine. There was no apparent dose relationship. Possible risk factors for neutropenia include pre-existing low white cell count (WBC) and history of drug induced neutropenia.

There have been cases of agranulocytosis in patients without pre-existing risk factors. Neutropenia should be considered in patients presenting with infection, particularly in the absence of obvious predisposing factor(s), or in patients with unexplained fever, and should be managed as clinically appropriate.

QUETIAPINE VIATRIS should be discontinued in patients with a neutrophil count <1,0 x 10^9/L. These patients should be observed for signs and symptoms of infection and neutrophil counts followed (until they exceed 1,5 x 10^9/L) (see section 4.8).

Hyperglycaemia and diabetes mellitus:

Hyperglycaemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with QUETIAPINE VIATRIS.

Patients with an established diagnosis of diabetes mellitus who are started on QUETIAPINE VIATRIS should be monitored regularly for worsening of glucose control.

Patients with risk factors for diabetes mellitus (e.g. obesity, family history of diabetes) who are starting treatment with QUETIAPINE VIATRIS should be monitored for symptoms of hyperglycaemia including polydipsia, polyuria, polyphagia and weakness. Patients who develop symptoms of hyperglycaemia during treatment with QUETIAPINE VIATRIS should undergo fasting blood glucose testing.
In some cases, hyperglycaemia has resolved when QUETIAPINE VIATRIS was discontinued, however, some patients required continuation of antidiabetic treatment despite discontinuation of the suspect medicine.

Lipids:

Increases in triglycerides and cholesterol and decreases in HDL have been observed with QUETIAPINE VIATRIS (see section 4.8). Lipid changes should be managed as clinically appropriate.

Metabolic factors:

In some patients, a worsening of more than one of the metabolic factors of weight, blood glucose and lipids was observed in clinical studies. Changes in these parameters should be managed as clinically appropriate.

Pancreatitis:

Pancreatitis has been reported in patients treated with QUETIAPINE VIATRIS. 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 (see section 4.4 Lipids), gallstones and alcohol consumption.

Concomitant illness:

QUETIAPINE VIATRIS should be used with caution in patients with known cardiovascular disease, cerebrovascular disease, or other conditions predisposing to hypotension. QUETIAPINE VIATRIS may induce orthostatic hypotension especially during the initial dose-titration period and therefore dose reduction or more gradual titration should be considered if this occurs; this is more common in elderly patients than in younger patients.

In patients who have a history of or are at risk of sleep apnoea and are receiving concomitant central nervous system (CNS) depressants, QUETIAPINE VIATRIS should be used with caution.

Dysphagia:

Dysphagia (see section 4.8) and aspiration have been reported with QUETIAPINE VIATRIS.

QUETIAPINE VIATRIS should be used with caution in patients at risk for aspiration pneumonia.

Constipation and intestinal obstruction:

Constipation represents a risk factor for intestinal obstruction. Constipation and intestinal obstruction have been reported with QUETIAPINE VIATRIS (see section 4.8). This includes fatal reports in patients who are at higher risk of intestinal obstruction, including those that are receiving multiple concomitant medicines 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.

Seizures:

Caution is recommended when treating patients with a history of seizures.

Tardive dyskinesia and Extrapyramidal Symptoms (EPS):

There is a potential for QUETIAPINE VIATRIS to cause tardive dyskinesia. If signs and symptoms of tardive dyskinesia appear, discontinuation of QUETIAPINE VIATRIS should be considered.

Neuroleptic malignant syndrome:

Neuroleptic malignant syndrome has been associated with QUETIAPINE VIATRIS treatment. Clinical manifestations include hyperthermia, altered mental status, muscular rigidity, autonomic instability, and increased creatine phosphokinase. In such an event, QUETIAPINE VIATRIS should be discontinued and appropriate medical treatment given.

QT prolongation:

Caution should be exercised when QUETIAPINE VIATRIS is prescribed in patients with cardiovascular disease or family history of QT prolongation. Also, caution should be exercised when QUETIAPINE VIATRIS is prescribed either with medicines known to increase QT interval or with concomitant neuroleptics, especially for patients with increased risk of QT prolongation, i.e. the elderly, patients with congenital long QT syndrome, congestive heart failure, heart hypertrophy, hypokalaemia, or hypomagnesaemia (see section 4.5).

Cardiomyopathy and myocarditis:

Cardiomyopathy and myocarditis have been reported. Treatment with QUETIAPINE VIATRIS should be reassessed in patients with suspected cardiomyopathy or myocarditis.

Severe Cutaneous Adverse Reactions:

Severe cutaneous adverse reactions (SCARs), including Stevens-Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN), Acute Generalised Exanthematous Pustulosis (AGEP), Erythema multiforme (EM) and Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) are potentially life-threatening adverse drug reactions that have been reported during QUETIAPINE VIATRIS exposure. SCARs commonly present with one or more of the following symptoms: extensive cutaneous rash which may be pruritic or associated with pustules, exfoliative dermatitis, fever, lymphadenopathy and possible eosinophilia or neutrophilia. Discontinue QUETIAPINE VIATRIS if severe cutaneous adverse reactions occur.

Withdrawal:

Acute withdrawal symptoms such as insomnia, nausea, and vomiting have been described after abrupt cessation of antipsychotic medicines including QUETIAPINE VIATRIS.
Recurrence of psychotic symptoms may also occur and the emergence of involuntary movement disorders (such as akathisia, dystonia and dyskinesias) have been reported.
Gradual withdrawal over a period of at least one to two weeks is advisable (see section 4.8).

Misuse and abuse:

Cases of misuse and abuse have been reported. Caution may be needed when prescribing QUETIAPINE VIATRIS to patients with a history of alcohol or drug abuse.

Elderly patients with dementia:

QUETIAPINE VIATRIS is not approved for the treatment of patients with dementia-related psychosis. Before prescribing QUETIAPINE VIATRIS, clinicians are advised to carefully assess the risks and benefits of the use of QUETIAPINE VIATRIS in elderly patients with dementia as there has been an increase in the cerebrovascular events (see section 4.3).

In these cases, the risk prediction for stroke in the individual patient (e.g. hypertension, diabetes, current smoking, atrial fibrillation and age > 80 years) must be taken into account.

Where the use of QUETIAPINE VIATRIS in the elderly is considered essential, the lowest effective dose should be used. These patients should be carefully monitored to avoid or reduce hypotension, gait disturbances, oversedation and complications associated with hyperglycaemia.

Anticholinergic (muscarinic) effects:

Norquetiapine, an active metabolite of quetiapine, has moderate to strong affinity for several muscarinic receptor subtypes. This contributes to adverse drug reactions (ADRs) reflecting anticholinergic effects when QUETIAPINE VIATRIS is used at recommended doses, when used concomitantly with other medicines having anticholinergic effects, and in the setting of overdose. QUETIAPINE VIATRIS should be used with caution in patients receiving medicines having anticholinergic (muscarinic) effects.

QUETIAPINE VIATRIS should be used with caution in patients with a current diagnosis or prior history of urinary retention, clinically significant prostatic hypertrophy, intestinal obstruction or related conditions, increased intraocular pressure or narrow angle glaucoma.

Lactose:

QUETIAPINE VIATRIS contains lactose. Patients with hereditary galactose intolerance e.g. galactosaemia, the Lapp lactase deficiency or glucose-galactose malabsorption should not take QUETIAPINE VIATRIS.

4.5 Interaction with other medicines and other forms of interaction

QUETIAPINE VIATRIS must be used with caution in combination with alcohol and other centrally acting medicines.

Caution should be exercised when QUETIAPINE VIATRIS is used concomitantly with antihypertensives, or medicines known to cause electrolyte imbalance or to increase QT interval (see section 4.4).

Caution should be exercised treating patients receiving other medicines having anticholinergic (muscarinic) effects (see section 4.4).

Lithium pharmacokinetics were not altered when used with QUETIAPINE VIATRIS.

The pharmacokinetics of sodium valproate and QUETIAPINE VIATRIS are not altered to a clinically relevant extent when co-administered.

QUETIAPINE VIATRIS may antagonise the actions of dopaminergics, such as levodopa.

The pharmacokinetics of QUETIAPINE VIATRIS were not significantly altered after co-administration with antipsychotics such as risperidone or haloperidol.
However, co-administration of QUETIAPINE VIATRIS and thioridazine caused an increase in clearance of QUETIAPINE VIATRIS.

QUETIAPINE VIATRIS did not induce the hepatic enzyme systems involved in the metabolism of antipyrine.

The co-administration of carbamazepine (a known hepatic enzyme inducer) and QUETIAPINE VIATRIS significantly increased the clearance of quetiapine. This increase in clearance significantly reduced systemic QUETIAPINE VIATRIS exposure. Because of this interaction, lower plasma concentrations can

occur, hence in each patient consideration for a higher dose of QUETIAPINE VIATRIS, depending on clinical response, should be considered.

It should be noted that the recommended maximum daily dose of QUETIAPINE VIATRIS is 750 mg/day, for the treatment of schizophrenia and 800 mg/day for the treatment of manic episodes associated with bipolar disorder.
Continued treatment at higher doses should only be considered as a result of careful consideration of the benefit-risk assessment for an individual patient.

The co-administration of QUETIAPINE VIATRIS with another microsomal enzyme inducer, phenytoin, caused increases in clearance of QUETIAPINE VIATRIS. Increased doses of QUETIAPINE VIATRIS may be required to maintain control of psychotic symptoms in patients co-administered with QUETIAPINE VIATRIS and phenytoin and other hepatic enzyme inducers (e.g. barbiturates, rifampicin etc). The QUETIAPINE VIATRIS dose may have to be reduced when phenytoin or carbamazepine or other hepatic enzyme inducers are withdrawn and replaced with a non-inducer (e.g. sodium valproate).

The pharmacokinetics of QUETIAPINE VIATRIS 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.

CYP3A4 is the primary enzyme responsible for cytochrome P450 mediated metabolism of QUETIAPINE VIATRIS. The pharmacokinetics of QUETIAPINE VIATRIS were not altered after co-administration with cimetidine, a known P450 enzyme inhibitor.

The co-administration of ketoconazole and QUETIAPINE VIATRIS may result in a significant (5-fold) increase in the AUC of QUETIAPINE VIATRIS. On the basis of this, concomitant use of QUETIAPINE VIATRIS and CYP3A4 inhibitors, such as HIV protease inhibitors, azole antifungals, erythromycin, clarithromycin and nefazodone, is contraindicated (see section 4.3).

Concomitant administration of clarithromycin and atypical antipsychotics that are predominantly metabolised through the CYP3A4 pathway, for example quetiapine, cariprazine, and aripiprazole may result in an increase in plasma levels of these antipsychotics as a result of inhibition which may present a potential for serious adverse reactions.

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

4.6 Fertility, pregnancy and lactation

Pregnancy

QUETIAPINE VIATRIS is contraindicated during pregnancy and lactation as safety and efficacy have not been established (see section 4.3).

Following some pregnancies in which quetiapine was used, neonatal withdrawal symptoms have been reported.

Breastfeeding

There have been published reports of quetiapine excretion into human breast milk, however the degree of excretion was not consistent.

4.7 Effects on ability to drive and use machines

QUETIAPINE VIATRIS may cause somnolence which may interfere with activities requiring mental alertness. Patients should be advised not to operate hazardous machines, or drive vehicles, until individual susceptibility is known.

4.8 Undesirable effects

The most commonly reported adverse drug reactions (ADRs) with QUETIAPINE VIATRIS (≥10 %) are somnolence, dizziness, 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 following adverse drug reactions have been reported:

Blood and lymphatic system disorders:

Frequent: Leucopenia.

Less frequent: Eosinophilia, neutropenia, thrombocytopenia, agranulocytosis.

Immune system disorders:

Less frequent: Hypersensitivity (angioedema, anaphylaxis, urticaria/rash), Stevens-Johnson syndrome.

Metabolism and nutritional disorders:

Frequent: Increased appetite.

Less frequent: Hyperglycaemia, diabetes mellitus (or exacerbation of pre-existing diabetes).

Psychiatric disorders:

Frequent: Abnormal dreams, nightmares.

Less frequent: Somnambulism and other related events.

Nervous system disorders:

Frequent: Dizziness, somnolence, headache, anxiety, extrapyramidal symptoms, dysarthria.

Less frequent: Seizures, syncope, restless legs syndrome, tardive dyskinesia, confusional state.

Eye disorders:

Frequent: Blurred vision.

Reported but frequency unknown: Dry eyes, asymptomatic changes in the lens of the eye with long-term treatment.

Ear and labyrinth disorders:

Reported but frequency unknown: Ear pain.

Cardiac disorders:

Frequent: Tachycardia, palpitations.

Less frequent: QTc prolongation (see section 4.4), bradycardia.

Vascular disorders:

Frequent: Orthostatic hypotension, hypertension (associated with dizziness, tachycardia and syncope in some patients).

Less frequent: Venous thromboembolism.

Respiratory, thoracic and mediastinal disorders:

Frequent: Dyspnoea.

Less frequent: Rhinitis.

Gastrointestinal disorders:

Frequent: Dry mouth, constipation, dyspepsia, vomiting, abdominal pain, diarrhoea.

Less frequent: Dysphagia, intestinal obstruction/ileus.

Hepato-biliary disorders:

Less frequent: Jaundice, hepatitis.

Skin and subcutaneous tissue disorders:

Reported but frequency unknown: Drug reaction with eosinophilia and systemic symptoms (DRESS), Acute Generalised Exanthematous Pustulosis (AGEP), Erythema multiforme (EM), cutaneous vasculitis.

Musculoskeletal, connective tissue and bone disorders:

Less frequent: Myalgia, back pain, rhabdomyolysis.

Renal and urinary disorders:

Less frequent: Urinary retention.

Reported but frequency unknown: Urinary tract infection.

Reproductive system and breast disorders:

Less frequent: Priapism, galactorrhoea.

General disorders and administration site conditions:

Frequent: Asthenia, peripheral oedema, withdrawal (discontinuation) symptoms see section 4.4), irritability, pyrexia.

Less frequent: Neuroleptic malignant syndrome, hypothermia.

Reported but frequency unknown: Neonatal withdrawal, chest pain.

Investigations:

Frequent: Elevations in serum triglyceride levels, elevations in total cholesterol, decreases in HDL cholesterol, weight gain, decreased haemoglobin, elevations in serum alanine aminotransferase (ALT), elevations in gamma-GT levels, neutrophils count decreased, eosinophils increased, blood glucose increased to hyperglycaemic level, elevations in serum prolactin, decreases in total T_4, decreases in free T_4, decreases in total T_3, increases in TSH.

Less frequent: Elevations in serum aspartate aminotransferase (AST), platelet count decreased, decreases in free T_3, elevations in blood creatinine phosphokinase.

QUETIAPINE VIATRIS was associated with dose-related decreases in thyroid hormone levels, particularly total T4 and free T4. The reduction in total T4 and free T4 was maximally within the first 2 to 4 weeks of QUETIAPINE VIATRIS treatment with no further reduction during long-term treatment. There was no evidence of clinically significant changes in TSH concentration over time. In nearly all cases, cessation of QUETIAPINE VIATRIS treatment has been associated with a reversal of the effects on total and free T4, irrespective of the duration of treatment. Smaller decreases in total T3 and reverse T3 were seen only at

higher doses. Levels of TBG were unchanged and in general, reciprocal increases in TSH were not observed, with any indication that QUETIAPINE VIATRIS causes clinically relevant hypothyroidism.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

In general, reported signs and symptoms of overdosage were those resulting from an exaggeration of the pharmacological effects, namely drowsiness, sedation, tachycardia, hypotension and anticholinergic effects. There is no specific antidote to QUETIAPINE VIATRIS. Treatment is symptomatic and supportive.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 2.6.5 Central nervous system depressants: Tranquillisers - miscellaneous structures

Quetiapine is an atypical antipsychotic agent which interacts with a broad range of neurotransmitter receptors. Quetiapine exhibits affinity for brain serotonin ($5HT_2$) and dopamine D_1 and D_2 receptors. Quetiapine also has high affinity at histaminergic and adrenergic alpha-1 receptors, with a lower affinity at adrenergic alpha-2 receptors, but no appreciable affinity at cholinergic, muscarinic or benzodiazepine receptors. Quetiapine, when administered twice daily, maintains $5HT_2$ and D_2 receptor occupancy for up to 12 hours after dosing.

5.2 Pharmacokinetic properties

After oral administration, quetiapine is absorbed and extensively metabolised. The principal human plasma metabolites do not have significant pharmacological activity. Food does not significantly affect the bioavailability of quetiapine. Elimination half-life is approximately 7 hours.

Quetiapine is approximately 65 % - 83 % bound to plasma proteins.

Quetiapine pharmacokinetics are variable but do not differ significantly between men and women.

Quetiapine mean clearance in the elderly is approximately 30 % to 50 % lower than that seen in adults aged 18 to 65 years.

Quetiapine mean plasma clearance was reduced by approximately 25 % in subjects with severe renal impairment (creatinine clearance less than 30 ml/min/1,73 m^2) and in subjects with hepatic impairment (stable alcoholic cirrhosis) but the individual clearance values are within the range for normal subjects.

Metabolism of quetiapine is extensive with parent compound accounting for less than 5 % of unchanged medicine-related material in the urine or faeces after the administration of radio-labelled quetiapine.

Approximately 73 % of the radioactivity is excreted in the urine and 21 % in the faeces.

Investigations, *in vitro,* established that CYP3A4 is the primary enzyme responsible for cytochrome P450 mediated metabolism of quetiapine.

Quetiapine and several of its metabolites were found to be weak inhibitors of human cytochrome P450 1A2, 2C9, 2C19, 2D6, and 3A4 activities, but only at concentrations at least 10 to 50-fold higher than those observed in the usual effective dose range of 300 to 450 mg/day in humans.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Lactose monohydrate

Microcrystalline cellulose

Povidone

Magnesium stearate

Sodium starch glycolate

Calcium hydrogen phosphate dihydrate

Tablet coating:

Titanium dioxide

Hydroxypropyl methylcellulose

Macrogol

Polysorbate 80 ((150 mg, 200 mg, 300 mg tablets)

Iron oxide, yellow (100 mg, 150 mg tablets)

Iron oxide, red (25 mg tablets)

Iron oxide, black (150 mg tablets)

Talc (100 mg tablets)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at or below 25 ^{o}C. Keep containers dry and tightly closed.

6.5 Nature and contents of container

Packs of 1, 3, 6, 7, 10, 14, 20, 28, 30, 50, 56, 60, 84, 90, 98, 100, 250, 500, 1000 * tablets in PVC/PVDC aluminium foil blister strips in an outer carton and/or white HDPE bottles with white polyethylene caps.

*Not all pack sizes will be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7 HOLDER OF THE CERTIFICATE OF REGISTRATION

Viatris South Africa (Pty) Ltd

4 Brewery Street

Isando

Kempton Park

Gauteng, 1601

Tel. no.: +27 11 451 1300

8 REGISTRATION NUMBER(S)

QUETIAPINE 25 VIATRIS: 41/2.6.5/0951

QUETIAPINE 100 VIATRIS: 41/2.6.5/0952

QUETIAPINE 150 VIATRIS: 41/2.6.5/0953

QUETIAPINE 200 VIATRIS: 41/2.6.5/0954

QUETIAPINE 300 VIATRIS: 41/2.6.5/0955

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

25 November 2011

10 DATE OF REVISION OF TEXT

27 February 2026