Applicant: **Zimbili Pharma CC**
Product name: Zimbiquet 25
Zimbiquet 100
Zimbiquet 200
Zimbiquet 300
Dosage form and strength: Film coated tablets, Quetiapine fumarate equivalent to quetiapine 25,100,200,300 mg free base

PROFESSIONAL INFORMATION FOR HUMAN MEDICINES

SCHEDULING STATUS

S5

1 NAME OF THE MEDICINE

ZIMBIQUET 25

ZIMBIQUET 100

ZIMBIQUET 200

ZIMBIQUET 300

Strength

Quetiapine fumarate equivalent to quetiapine 25 mg free base.

Quetiapine fumarate equivalent to quetiapine 100 mg free base**.**

Quetiapine fumarate equivalent to quetiapine 200 mg free base.

Quetiapine fumarate equivalent to quetiapine 300 mg free base.

Pharmaceutical form

Film coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

ZIMBIQUET 25

Each film coated tablet contains:

Quetiapine fumarate equivalent to quetiapine 25 mg free base.

Contains sugar: Lactose monohydrate 7,881 mg

ZIMBIQUET 100

Each film coated tablet contains:

Quetiapine fumarate equivalent to quetiapine 100 mg free base**.**

Contains sugar: Lactose monohydrate 31,524 mg

ZIMBIQUET 200

Each film coated tablet contains:

Quetiapine fumarate equivalent to quetiapine 200 mg free base.

Contains sugar: Lactose monohydrate 63,050 mg

ZIMBIQUET 300

Each film coated tablet contains:

Quetiapine fumarate equivalent to quetiapine 300 mg free base.

Contains sugar: Lactose monohydrate 94,575 mg

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

ZIMBIQUET 25

Peach coloured, film coated, round tablets.

ZIMBIQUET 100

Yellow, film coated, round tablets.

ZIMBIQUET 200

White coloured, film coated, round tablets.

ZIMBIQUET 300

White coloured, film coated, capsule-shaped tablets.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

ZIMBIQUET tablets are indicated for the treatment of schizophrenia.

Zimbiquet is also indicated for the treatment of manic episodes associated with a bipolar disorder.

Safety and efficacy beyond 12 weeks has not been demonstrated.

4.2 Posology and method of administration

Posology

Adults:

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 to 450 mg/day. Depending on the clinical response and tolerability of the individual patient, the dose may be adjusted in some patients within the range 150 to 750 mg/day.

***Elderly*:**

ZIMBIQUET should be used with caution in the elderly, especially during the initial dosing periods. Elderly patients should be started on **ZIMBIQUET** 25mg/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.

***Renal and hepatic impairment*:**

The oral clearance of quetiapine is reduced by approximately 25 % in patients with renal or hepatic impairment. Quetiapine is extensively metabolized 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 **ZIMBIQUET,** tablets 25 mg/day. The dose should be increased daily in increments of 25 to 50 mg, to an effective dose.

Method of Administration

ZIMBIQUET should be administered twice daily, with or without food.

4.3 Contraindications

ZIMBIQUET is contraindicated in:

- Patients who are hypersensitive to any component of this product.
- Pregnancy and lactation, as safety has not been demonstrated.
- Safety and efficacy in children and adolescents have not been demonstrated.
- Advanced liver and renal function impairment, as safety has not been demonstrated.
- Elderly patients with dementia exhibiting behavioural disturbances.

4.4 Special warnings and precautions for use

Hyperglycaemia and Diabetes mellitus

Hyperglycaemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, may occur in patients treated with **ZIMBIQUET.**

Patients with an established diagnosis of diabetes mellitus who are started on **ZIMBIQUET** 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 **ZIMBIQUET** should be monitored for symptoms of hyperglycaemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycaemia during treatment with **ZIMBIQUET** should undergo fasting blood glucose testing. Hyperglycaemia may be resolved when **ZIMBIQUET** is discontinued; however, some patients may require continuation of the anti-diabetic treatment despite discontinuation of the suspected medicine.

Elderly patients with dementia

Before prescribing, clinicians are advised to carefully assess the risks and benefits of the use of atypical antipsychotics in elderly patients with dementia.

Special Precautions

Cardiovascular disease

ZIMBIQUET may induce orthostatic hypotension especially during the initial dose titration period; this is more common in elderly patients than in younger patients. **ZIMBIQUET may be** associated with a persistent increase in QTc intervals. However, caution should be exercised when quetiapine is prescribed with medicines known, to prolong the QTc interval, especially in the elderly.

ZIMBIQUET should be used with caution in patients with known cardiovascular disease, cerebrovascular disease; or other conditions predisposing to hypotension.

Seizures

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

Tardive Dyskinesia

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

Neuroleptic Malignant Syndrome (NMS)

Neuroleptic Malignant Syndrome may be associated with **ZIMBIQUET** treatment. Clinical manifestations include hyperthermia, altered mental status, muscular rigidity, autonomic instability, and increased creatinine phosphokinase. In such an event, **ZIMBIQUET** should be discontinued and appropriate medical treatment given.

Gradual withdrawal

Gradual withdrawal of **ZIMBIQUET** is recommended because of the risk of withdrawal symptoms, including nausea, vomiting, insomnia, and rebound psychoses with abrupt cessation.

Contains lactose monohydrate. Patients with the rare hereditary conditions of galactose intolerance e.g. galactosaemia, Lapp lactase deficiency, glucose-galactose malabsorption should not take **ZIMBIQUET**.

Metabolic risk

There may be a risk for worsening of the patient’s metabolic profile, such as changes in weight, blood glucose (see hyperglycaemia) and lipids. 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 appropriately (see also section 4.8).

Extrapyramidal symptoms

Quetiapine usage may be associated with an increased incidence of extrapyramidal symptoms (EPS), in patients treated for major depressive episodes in bipolar disorder (see sections 4.8 and 5.1). The use of quetiapine may be 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 may be most likely to occur within the first few weeks of treatment. In patients who develop these symptoms, increasing the dose may be detrimental.

Somnolence and dizziness

Quetiapine treatment may be associated with somnolence and related symptoms, such as sedation (see section 4.8). During treatment of patients with bipolar depression, an onset may usually be within the first 3 days of treatment and may be 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.

Sleep apnoea syndrome

Sleep apnoea syndrome may be reported in patients using quetiapine. In patients receiving concomitant central nervous system depressants and who have a history of or are at risk of sleep apnoea, such as those who are overweight/obese or are male, quetiapine should be used with caution.

Severe neutropenia and agranulocytosis

Severe neutropenia (neutrophil count $<0.5 \times 10^9$/L) may be reported. Most cases of severe neutropenia may occur within a couple of months of starting therapy with quetiapine. There may be no apparent dose relationship. Possible risk factors for neutropenia include pre-existing low white blood cell count (WBC) and history of medicine induced neutropenia. However, some cases may occur in patients without pre-existing risk factors.

Quetiapine should be discontinued in patients with a neutrophil count <1.0 x 109/L. Patients should be observed for signs and symptoms of infection and neutrophil counts followed (until they exceed 1.5 x 109/L) (see section 5.1). Neutropenia should be considered in patients presenting with infection or fever, particularly in the absence of obvious predisposing factor(s), and should be managed as clinically appropriate. Patients should be advised to immediately report the appearance of signs/symptoms consistent with agranulocytosis or infection (e.g., fever, weakness, lethargy, or sore throat) at any time during quetiapine therapy. Such patients should have a WBC count and an absolute neutrophil count (ANC) performed promptly, especially in the absence of predisposing factors.

Anti-cholinergic (muscarinic) effects

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

Interactions

See also section 4.5.

Concomitant use of quetiapine with a strong hepatic enzyme inducer such as carbamazepine or phenytoin substantially decreases quetiapine plasma concentrations, which could affect the efficacy of quetiapine therapy. 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).

Weight

Weight gain has been reported in patients who have been treated with quetiapine, and should be monitored and managed as clinically appropriate as in accordance with utilised antipsychotic guidelines (see sections 4.8 and 5.1).

Lipids

Increases in triglycerides, LDL and total cholesterol and decreases in HDL cholesterol may be observed with quetiapine (see section 4.8). Lipid changes should be managed as clinically appropriate.

QT Prolongation

Caution should be exercised when ZIMBIQUET is prescribed with medicines known to prolong the QTc interval, especially in the elderly.

Misuse and abuse

Caution may be needed when prescribing quetiapine to patients with a history of alcohol or drug abuse.

Dysphagia

Dysphagia (see section 4.8) may occur with the use of quetiapine. Quetiapine 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 may occur with the use of quetiapine (see section 4.8), especially 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) may occur with antipsychotic medicines. 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.

4.5 Interaction with other medicines and other forms of interaction

Centrally acting drugs and alcohol

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

Lithium

The pharmacokinetics of lithium were not altered when co-administered with **ZIMBIQUET.**

Antipyrine

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

Enzyme inducers

Carbamazepine: 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, and hence in each patient, consideration for a higher dose of **ZIMBIQUET**, depending on clinical response, should be considered. It should be noted that the recommended maximum daily dose of **ZIMBIQUET**, is 750 mg/day and continued treatment at higher doses should only be considered as a result of careful consideration of the benefit risk assessment of an individual patient.

Phenytoin: Co-administration of **ZIMBIQUET,** with phenytoin, a microsomal enzyme inducer, causes increases in clearance of quetiapine. Increased doses of **ZIMBIQUET,** may be required to maintain control of psychotic symptoms in patients co-administered **ZIMBIQUET,** and phenytoin and other hepatic enzyme inducers (e.g., barbiturates, rifampicin etc.). The dose of **ZIMBIQUET**, may need to be reduced if phenytoin or **carbamazepine** or other hepatic enzyme inducers are withdrawn and replaced with a non-inducer (e.g., sodium valproate).

Antipsychotics

The pharmacokinetics of quetiapine were not significantly altered following co-administration with the antipsychotics, risperidone or haloperidol. However, co-administration of **ZIMBIQUET**, and thioridazine caused increases in clearance of quetiapine.

Antidepressants

The pharmacokinetics of quetiapine were not significantly altered following co-administration with the antidepressants, imipramine (a known CYP2D6 inhibitor) or fluoxetine (a known CYP3A4 and CYP2D6 inhibitor).

CYP3A4 enzyme inhibitors

CYP3A4 is the primary enzyme responsible for cytochrome P450 mediated metabolism of quetiapine. The pharmacokinetics of quetiapine was not altered following co-administration with cimetidine or fluoxetine, both of which known P450 enzyme inhibitors.

In a multiple-dose trial in healthy volunteers to assess the pharmacokinetics of quetiapine given before and during treatment with ketoconazole, co-administration of ketoconazole resulted in an increase in mean C_{max} and AUC of quetiapine by 235 % and 522 %, respectively, with a corresponding decrease in mean oral clearance of 84 %. The mean half-life of quetiapine increased from 2,6 to 6,8 hours, the mean t_{max}, was unchanged.

Due to the potential for an interaction of similar magnitude in a clinical setting; the dosage of **ZIMBIQUET**, should be reduced during concomitant use of quetiapine and potent CYP3A4 inhibitors (such as azole antifungals and macrolide antibiotics).

4.6 Fertility, pregnancy and lactation

The safety of **ZIMBIQUET**, in pregnancy and lactation has not been established. (See section 4.3). Pregnant women should notify their healthcare provider if they become pregnant or intend to become pregnant during treatment with **ZIMBIQUET**. **ZIMBIQUET** may cause extrapyramidal and/or withdrawal symptoms (agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress, and feeding disorder) in a neonate.

Breast-feeding

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

ZIMBIQUET may impair fertility due to an increase in serum prolactin levels. The effects on fertility are reversible.

4.7 Effects on ability to drive and use machines

Because **ZIMBIQUET** may cause somnolence, patients should be cautioned about operating hazardous machines, including motor vehicles, until individual susceptibility is known.

4.8 Undesirable effects

Side-effects

The side-effects are listed below by body system, organ class and frequency (wherever applicable). The most frequent and significant adverse events reported for **ZIMBIQUET**, were somnolence, dizziness, constipation, postural hypotension, dry mouth and liver enzyme abnormalities.
ZIMBIQUET may be associated with asthenia, rhinitis and dyspepsia.
ZIMBIQUET may also be associated with weight gain, predominantly during the early weeks of

treatment.

ZIMBIQUET may induce orthostatic hypotension, associated with dizziness, tachycardia and, in some patients, syncope; these events occur especially during the initial dose- titration period (see section 4.4).

Blood and the lymphatic system disorders:

Frequent: Decreased Haemoglobin, transient, asymptomatic leucopaenia and/or neutropaenia, eosinophilia.

Less Frequent: Thrombocytopenia, Anaemia, platelet count decreased, Agranulocytosis

Immune system disorder:

Less frequent: Hypersensitivity (angioedema, anaphylaxis, urticaria, rash).

Endocrine disorders:

Frequent: Hyperprolactinaemia, decreases in total T4, decreases in free T4, decreases in total T3, increases in TSH.

Less Frequent: Decreases in free T3, Hypothyroidism, Inappropriate antidiuretic hormone secretion

Metabolic and nutrition disorders:

Frequent: Elevations in serum triglyceride levels, Elevations in total cholesterol (predominantly LDL cholesterol), Decreases in HDL cholesterol, Weight gain, Increased appetite, Hyperglycaemia

Less frequent: Hyponatraemia, diabetes mellitus (or exacerbation of pre- existing diabetes), Metabolic syndrome, psychiatric disorders.

Nervous system disorders:

Frequent: Somnolence, dizziness, headache, syncope, Extrapyramidal symptoms, dysarthria

Less frequent: Seizures (see section 4.4), tardive dyskinesia may occur after long term treatment. Extrapyramidal symptoms (akathisia, akinesia, cogwheel rigidity, extrapyramidal syndrome,

hypertonia, hypokinesia, neck rigidity and tremor) occur and are not dose related, restless legs syndrome.

Frequency unknown: Anxiety.

Eye disorders:

Less frequent: Dry eyes, Vision Blurred

Frequency unknown: Asymptomatic changes in the lens of the eye with long term treatment.

Ear and labyrinth disorders:

Frequency unknown: Ear pain.

Cardiac disorders:

Frequent: Tachycardia, palpitations.

Less frequent: Prolongation of the QTc interval (see section 4.4). Bradycardia

Vascular disorders:

Frequent: Postural hypotension.

Frequency unknown: Hypertension, Venous thromboembolism.

Respiratory, thoracic and mediastinal disorders:

Frequent: Dyspnoea, Rhinitis.

Gastro-intestinal disorders:

Frequent: Constipation, dry mouth, dyspepsia, Vomiting.

Less frequent: Abdominal pain, dysphagia, Pancreatitis, intestinal obstruction.

Frequency unknown: Diarrhoea. Hepato-biliary disorders

Skin and subcutaneous tissue disorders:

Frequency unknown: Rash, Angioedema, Steven Johnsons syndrome, toxic epidermal necrolysis, erythema multiforme, drug reaction with eosinophilia and systemic symptoms (DRESS)

Musculoskeletal, connective tissue and bone disorders:

Frequency unknown: Myalgia, back pain, chest pain, Rhabdomyolysis

Reproductive system and breast disorders:

Less frequent: Sexual dsysfunction, Priapism, galactorrhoea, breast swelling, menstrual disorder. Pregnancy, puerperium and perinatal conditions. Drug withdrawal syndrome neonatal.

Renal and urinary disorders:

Frequency unknown: Urinary tract infection.

General disorders and administration site conditions:

Frequent: Mild Asthenia, pyrexia, irritability, peripheral oedema

Less frequent: Fever, peripheral oedema, weight gain. Cases of hypothermia, neuroleptic malignant syndrome has been reported in patients treated with quetiapine (see section 4.4).

Investigations:

Frequent: ALT increased; AST increased.

Less frequent: GGT increased, elevations in non-fasting serum triglyceride levels, elevations in blood creatine phosphokinase.

ZIMBIQUET treatment was associated with dose related decreases in thyroid hormone levels, particularly total T_4 and free T_4. The reduction in total and free T_4 was maximal within the first 2 to 4 weeks of quetiapine 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 **ZIMBIQUET** treatment was associated with a reversal of the effects on total and free T_4

irrespective of the duration of treatment.

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 asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Symptoms

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. Therefore, appropriate symptomatic and supportive measures should be instituted. In cases of severe intoxication, the possibility of multiple medicine 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. Close medical supervision and monitoring should continue until the patient recovers.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 2.6.5 Central nervous system depressants: Miscellaneous structures

Pharmacodynamic properties

Quetiapine is an atypical antipsychotic agent, which interacts with broad range of neurotransmitter receptors. Quetiapine exhibits a higher affinity for serotonin (5-HT_2) receptors in the brain than it does for dopamine D_1 and D_2 receptors in the brain. Quetiapine also has the high affinity at histaminergic and adrenergic α-1 receptors, with a lower affinity at α-2 receptors, but no appreciable affinity at cholinergic, muscarinic or benzodiazepine receptors. In animal models, quetiapine is active in tests for antipsychotic activity, such as conditioned avoidance. Quetiapine does not produce sustained elevations in prolactin in man. Quetiapine when given twice a day, maintains 5-HT_2 and D_2 receptor occupancy for up to 12 hours after dosing.

5.2 Pharmacokinetic properties

Quetiapine is absorbed and extensively metabolized following oral administration. The principal human plasma metabolites do not have significant pharmacological activity. The bioavailability of quetiapine is not significantly affected by administration with food. The elimination half-life of quetiapine is approximately 7 hours. Quetiapine is approximately 65 %-83 % bound to plasma proteins. Quetiapine is extensively metabolized with parent compound accounting for less than 5 % of unchanged drug-related material in the urine or faeces, following the administration of radio labelled quetiapine. Approximately 73 % of the radioactivity is excreted in the urine and 21 % in the faeces. *In vitro* investigations 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 lA2, 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.

Special populations

***Elderly*:** The mean clearance of quetiapine in the elderly is approximately 30 % to 50 % lower than that seen in adults aged 18 to 65 years.

***Renally and hepatically impaired*:** The mean plasma clearance of quetiapine was reduced by approximately 25 % in subjects with severe renal impairment (creatinine clearance less than 30

ml/min/l,73 m^2) and in subjects with hepatic impairment (stable alcoholic cirrhosis), but the individual clearance values are within the range for normal subjects.

***Gender*:** The pharmacokinetics of quetiapine are variable, but do not differ significantly between men and women.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Excipients: calcium hydrogen phosphate, lactose monohydrate, magnesium stearate, microcrystalline cellulose, povidone, sodium starch glycollate and a coating agent.

ZIMBIQUET 25

The coating agent contains hypromellose, titanium dioxide (CI No. 77891), macrogol, iron oxide yellow (CI No. 77492) and iron oxide red (CI No. 77491).

ZIMBIQUET 100, 200 and 300

The coating agent contains hypromellose, titanium dioxide (CI No. 77891), macrogol and talc.

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25 °C and protect from moisture. Do not remove the blisters from the carton until required for use.

6.5 Nature and contents of container

ZIMBIQUET 25:

Cartons contain 100 tablets of 10 or 20 tablets per blister

ZIMBIQUET 100:

Cartons contain 90 tablets of 10 tablets per blister.

ZIMBIQUET 200:

Cartons contain 60 tablets of 10 tablets per blister.

ZIMBIQUET 300:

Cartons contain 60 tablets of 10 tablets per blister.

6.6 Special precautions for disposal and other handling

Tablets are packed in PVC/PE/PVdC blister and PVC/Aclar blister packs. The PVC/PE/PVdC blister pack comprises of clear, transparent PVC film, laminated with polyethylene (PE) and coated with PVdC on the inner side having a backing of hard tempered, heat sealable aluminium foil coated with heat seal lacquer on inner side. The PVC/ACLAR blister pack comprises of PVC clear film, biaxially oriented well thermoformable laminated uniformly with Aclar on the inner a side with backing of aluminium foil coated with heat seal lacquer on the inner side.

7 HOLDER OF CERTIFICATE OF REGISTRATION

Zimbili Pharma CC

24 Parrot Avenue, Extension 1

Lenasia, 1827

Gauteng

South Africa

8 REGISTRATION NUMBER(S)

ZIMBIQUET 25: 43/2.6.5/0318

ZIMBIQUET 100: 43/2.6.5/0319

ZIMBIQUET 200: 43/2.6.5/0321

ZIMBIQUET 300: 43/2.6.5/0684

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of registration: 07 December 2012

Date of the most recently revised professional information for medicines for human use: 20 June 2018

10 DATE OF REVISION OF THE TEXT

September 2020