PI for QUESARA TABLETS

SCHEDULING STATUS

S5

1. NAME OF THE MEDICINE

QUESARA 25 mg (Film-coated tablet)

QUESARA 100 mg (Film-coated tablet)

QUESARA 200 mg (Film-coated tablet)

QUESARA 300 mg (Film-coated tablet)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

QUESARA 25 mg

Each film-coated tablet contains 25 mg quetiapine (as quetiapine fumarate).

Contains sugar (5,175 mg lactose monohydrate)

QUESARA 100 mg

Each film-coated tablet contains 100 mg quetiapine (as quetiapine fumarate).

Contains sugar (20,70 mg lactose monohydrate)

QUESARA 200 mg

Each film-coated tablet contains 200 mg quetiapine (as quetiapine fumarate).

Contains sugar (41,40 mg lactose monohydrate)

QUESARA 300 mg

Each film-coated tablet contains 300 mg quetiapine (as quetiapine fumarate).

Contains sugar (62,10 mg lactose monohydrate)

Excipients:

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Film-coated tablet.

QUESARA 25 mg

Peach coloured, round, film-coated tablets debossed with 'F 71" on one side and plain on the other side.

QUESARA 100 mg

Yellow coloured, round, film-coated tablets debossed with “F 73” on one side and plain on the other side.

QUESARA 200 mg

White coloured, round, film-coated tablets debossed with “F 75” on one side and plain on the other side.

QUESARA 300 mg

White coloured, capsule shaped, film-coated tablets debossed with “F 76” on one side and plain on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

QUESARA is indicated for the treatment of:

- schizophrenia
- 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:

For the treatment of schizophrenia:

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 range of 300 to 450 mg/day. However, this may be adjusted, depending on the clinical response and tolerability of the individual patient, within the range 150 to 750 mg/day.

For the treatment of manic episodes associated with bipolar disorder:

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 per day by Day 6 should be in increments of no greater than 200 mg per day.

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

Special populations

Elderly

QUESARA should be used with caution in the elderly, especially during the initial dosing period. Elderly patients should be started on **QUESARA 25 mg** per 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 **QUESARA** is reduced by approximately 25 % in patients with renal or hepatic impairment. **QUESARA** 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 **QUESARA 25 mg** per day. The dose should be increased daily in increments of 25 to 50 mg, to an effective dose.

Method of administration:

Oral

QUESARA should be administered twice daily with or without food.

4.3 Contraindications

QUESARA is contraindicated in patients who are hypersensitive to quetiapine or any components of **QUESARA** (see **6.1 List of excipients**).

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.

Concomitant administration of cytochrome P450 3A4 inhibitors, such as HIV-protease inhibitors, azole antifungal medicines, erythromycin, clarithromycin and nefazodone, is contraindicated.

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 **QUESARA** 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 disorder. The same precautions observed when treating patients with major depressive disorder should therefore be observed when treating patients 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 (<0,5 X 10^9/L) without infection has been uncommonly reported in short-term placebo-controlled monotherapy clinical trials with **QUESARA**. There have been reports of agranulocytosis (severe neutropenia with infection) among all patients treated with **QUESARA** during clinical trials (rare) 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 medicine 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. **QUESARA** 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 atypical antipsychotics, including **QUESARA**.

Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics such as **QUESARA**, 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 atypical antipsychotics such as **QUESARA** should be monitored for symptoms of hyperglycaemia including polydipsia, polyuria, polyphagia, and weakness. Patients, who develop symptoms of hyperglycaemia during treatment with atypical antipsychotics such as **QUESARA**, should undergo fasting blood glucose testing. In some cases, hyperglycaemia has resolved when the atypical antipsychotic such as **QUESARA** was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect medicine.

Lipids:

Increases in triglycerides and cholesterol, and decreases in HDL have been observed with **QUESARA** (section see 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. Changes in these parameters should be managed as clinically appropriate.

Pancreatitis:

Pancreatitis has been reported in clinical trials and during the postmarketing experience. Among the post marketing reports, 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:

QUESARA should be used with caution in patients with known cardiovascular disease, cerebrovascular disease, or other conditions predisposing to hypotension. **QUESARA** may induce orthostatic hypotension, especially during the initial dose-titration period; 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, **QUESARA** should be used with caution.

QT prolongation:

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

Dysphagia:

Dysphagia (see section 4.8) and aspiration have been reported with **QUESARA**. **QUESARA** 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 **QUESARA** (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 medications that decrease intestinal motility and/or may not report symptoms of constipation.

Seizures

QUESARA should be used with caution in patients with a history of seizures.

Tardive dyskinesia and Extrapyramidal Symptoms (EPS):

QUESARA has been associated with tardive dyskinesia. If signs and symptoms of tardive dyskinesia appear, discontinuation of **QUESARA** should be considered.

In placebo-controlled clinical trials of adult patients with schizophrenia and bipolar mania the incidence of extrapyramidal symptoms was no different from that of placebo across the recommended

therapeutic dose range. This predicts that **QUESARA** has less potential than typical antipsychotic medicines to induce tardive dyskinesia in schizophrenia and bipolar mania patients. In short- term placebo-controlled clinical trials for bipolar depression, the incidence of EPS was higher in **QUESARA** treated patients than in placebo treated patients (see 4.8 Undesirable effects).

Neuroleptic Malignant Syndrome (NMS)

NMS has occurred in association with **QUESARA**. Clinical manifestations include hyperthermia, altered mental status, muscular rigidity, autonomic instability, and increased creatinine phosphokinase. In such an event, **QUESARA** should be discontinued and appropriate medical treatment given.

Cardiomyopathy and Myocarditis:

Cardiomyopathy and myocarditis have been reported in clinical trials and during the postmarketing experience. Treatment with **QUESARA** should be reassessed in patients with suspected cardiomyopathy or myocarditis.

Withdrawal:

Acute withdrawal symptoms such as insomnia, nausea, and vomiting have been described after abrupt cessation of antipsychotic medicines including **QUESARA**. 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 **QUESARA** to patients with a history of alcohol or drug abuse.

Elderly patients with dementia:

QUESARA is not approved for the treatment of patients with dementia-related psychosis. In a meta-analysis of atypical antipsychotic medicines, it has been reported that elderly patients with dementia-related psychosis are at an increased risk of death compared to placebo. In two 10-week placebo-controlled quetiapine studies in the same patient population the incidence of mortality in quetiapine-treated patients was 5,5 % versus 3,2 % in the placebo group. The patients in these trials died from a variety of causes that were consistent with expectations for this population. These data do not

establish a causal relationship between **QUESARA** treatment and death in elderly patients with dementia.

Anticholinergic (muscarinic) effects:

Norquetiapine, an active metabolite of **QUESARA**, has moderate to strong affinity for several muscarinic receptor subtypes. This contributes to adverse drugs reactions (ADRs) reflecting anticholinergic effects when **QUESARA** is used at recommended doses, when used concomitantly with other medications having anticholinergic effects, and in the setting of overdose. **QUESARA** should be used with caution in patients receiving medicines having anticholinergic (muscarinic) effects. **QUESARA** 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. (see sections 4.5 and 4.8).

Paediatric population

QUESARA 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, as contained in **QUESARA**, have shown that in addition to the known safety profile identified in adults (see section 4.8), 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 **QUESARA** on growth and maturation have not been studied beyond 26 weeks. Long-term implications for cognitive and behavioural 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 (see section 4.8).

Hyperprolactinaemia:

QUESARA causes an increase in prolactin levels, and the elevation persists during chronic administration.

Lactose

QUESARA contain lactose. Patients with rare hereditary problems of galactose in tolerance, total galactose intolerance or glucose-galactose malabsorption should not take **QUESARA**. **QUESARA** contains lactose which may have an effect on the glycaemic control of patients with diabetes mellitus.

4.5 Interaction with other medicines and other forms of interaction

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 **QUESARA** with CYP3A4 inhibitors is contraindicated. It is also not recommended to consume grapefruit juice while on quetiapine therapy (see section 4.3).

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

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

Concomitant use of **QUESARA** with a strong hepatic enzyme inducer such as carbamazepine or phenytoin substantially decreases quetiapine plasma concentrations, which could affect the efficacy of **QUESARA** therapy. In patients receiving a hepatic enzyme inducer, initiation of **QUESARA** treatment should only occur if the medical practitioner considers that the benefits of **QUESARA** 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).

Caution should be exercised treating patients receiving other medications having anti-cholinergic (muscarinic) effects (see Section 4.4).

The pharmacokinetics of **QUESARA** 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 altered following co-administration with cimetidine a known P450 enzyme inhibitor.

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

In a 6-week, randomised, study of lithium and quetiapine sustained release formulation versus placebo and quetiapine sustained release formulation 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.

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.

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

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

Food interactions:

It is not recommended to consume grapefruit juice while on **QUESARA** therapy.

4.6 Fertility, pregnancy and lactation

Pregnancy

First trimester

The moderate amount of published data from exposed pregnancies, 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, **QUESARA** is contraindicated in pregnancy.

Third trimester

Neonates exposed to antipsychotics (including **QUESARA**) 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

QUESARA is contraindicated during breastfeeding as safety has not been demonstrated.

Fertility

The effects of **QUESARA** 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.

4.7 Effects on ability to drive and use machines

QUESARA may cause somnolence which may interfere with activities requiring mental alertness. Therefore patients should be advised not to drive or operate machinery, until individual susceptibility is known.

4.8 Undesirable effects

The most frequent reported adverse reactions with **QUESARA** 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.

Table 1 ADRs associated with QUESARA therapy

System Organ Class	Frequency	Undesirable effects
Blood and lymphatic system disorders	Frequent	Decreased haemoglobin, Leucopoenia, decreased neutrophil count, increased eosinophils
	Less frequent	Neutropenia, thrombocytopenia, anaemia, platelet count decreased, agranulocytosis
Immune system disorders	Less frequent	Hypersensitivity, including allergic skin reactions), agranulocytosis, anaphylactic reaction
Endocrine disorders	Frequent	Hyperprolactinaemia, decreases in total T_4, decreases in free total T_3, increases in TSH
	Less frequent	Decreases in free T_3 Hypothyroidism, inappropriate antidiuretic hormone secretion
Metabolism and nutrition disorders	Frequent	Elevations in serum triglyceride levels, elevations in total cholesterol (predominantly LDL cholesterol), decreases in HDL cholesterol, weight gain Increased appetite, blood glucose increased to hyperglycaemic levels
	Less frequent	Hyponatraemia, diabetes mellitus, exacerbation of pre-existing diabetes, metabolic syndrome
Psychiatric disorders	Frequent	Abnormal dreams and nightmares, suicidal ideation and suicidal behaviour
	Less frequent	Somnambulism and related reactions such as sleep talking and sleep related eating disorder.
Nervous system disorders	Frequent	Dizziness, somnolence, headache, Extrapyramidal symptoms, dysarthria.

	Less frequent	Seizure, restless legs syndrome, tardive dyskinesia, syncope
Eye disorders	Frequent	Blurred vision
Cardiac disorders	Frequent	Tachycardia, palpitations
	Less frequent	QT prolongation, bradycardia
Vascular disorders	Frequent	Orthostatic hypotension
	Less frequent	Venous thromboembolism
	Frequency unknown	stroke
Respiratory, thoracic and mediastinal disorders	Frequent	Rhinitis, dyspnoea
Gastrointestinal disorders	Frequent	Dry mouth, constipation, dyspepsia, vomiting,
	Less frequent	Dysphagia, pancreatitis, intestinal obstruction/ileus
Hepatobiliary disorders	Frequent	Elevations in serum alanine aminotransferase (ALT), elevations in gamma-GT levels
	Less frequent	Jaundice, Hepatitis
Skin and subcutaneous tissue disorders	Less frequent	Angioedema, Stevens-Johnson syndrome
	Frequency unknown	Toxic epidermal necrolysis, erythema multiforme, drug rash with eosinophilia and systemic symptoms (DRESS)
Musculoskeletal and connective tissue disorders	Less frequent	Rhabdomyolysis
Renal and urinary disorders	Less frequent	Urinary retention

Pregnancy, puerperium and perinatal conditions	Frequency unknown	Drug withdrawal syndrome neonatal
Reproductive system and breast disorders	Less frequent	Sexual dysfunction, Priapism, galactorrhoea, breast swelling and menstrual disorder
General disorders and administration site conditions	Frequent	Withdrawal (discontinuation) symptoms, mild asthenia, peripheral oedema, irritability, pyrexia
	Less frequent	Neuroleptic malignant syndrome, hypothermia
Investigations	Less frequent	Elevations in blood creatinine phosphokinase

Somnolence may occur, usually during the first two weeks of treatment and generally resolves with the continued administration of **QUESARA**

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

In clinical trials, experience with **QUESARA** in overdosage is limited. In postmarketing experience, there have been very rare reports of overdose of **QUESARA** alone resulting in death or coma.

In general, reported signs and symptoms of overdosage were those resulting from an exaggeration of the active medicines known pharmacological effects, i.e., drowsiness and sedation, tachycardia and hypotension.

There is no specific antidote to **QUESARA**. Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmaceutical groups: Central nervous system depressants: Miscellaneous structure.

ATC code: N05AH04

Quetiapine is an atypical antipsychotic medicine which interacts with a broad range of neurotransmitter receptors. Quetiapine exhibit higher affinity for brain serotonin ($5HT_2$) receptors than it does for dopamine D_1 and D_2 receptors in the brain. Quetiapine also has high affinity at histaminergic and adrenergic α_1 receptors, with a lower affinity at adrenergic α_2 receptors, but no appreciable affinity at cholinergic muscarinic or benzodiazepine receptors.

Quetiapine does not produce sustained elevations in prolactin in man.

Quetiapine, when given twice a day, maintains $5HT_2$ and D_2 receptor occupancy for up to 12 hours after dosing.

5.2 Pharmacokinetic properties

Quetiapine is well absorbed and extensively metabolised 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.

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

In vitro investigations established that CYP3A4 is the primary enzyme responsible for cytochrome P450 mediated metabolism of quetiapine.

Quetiapine and several of its metabolites are weak inhibitors of human cytochrome P450, 1A2, 2C9, 2C19, 2D6 and 3A4 activities, 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.

Quetiapine is extensively metabolised with the 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 % is excreted in the urine and 21 % in the faeces.

The elimination half-life of quetiapine is approximately 7 hours.

Special populations

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

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

The mean plasma clearance of quetiapine is 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 individual clearance values are within the range for normal subjects.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Contains microcrystalline cellulose, dibasic calcium phosphate, sodium starch glycolate, lactose monohydrate, povidone, colloidal silicon dioxide, magnesium stearate. The tablets are coated with coating made up of hypromellose, titanium dioxide (Colour Index No. 77891), polyethylene glycol 400,

In addition **QUESARA 25 mg** contains iron oxide yellow (Colour Index No.:77492), iron oxide red (Colour Index No.:77491) and **QUESARA 100 mg** contains, iron oxide yellow (Colour Index No.:77492).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

48 months from the manufacturing date.

6.4 Special precautions for storage

Store at or below 25 °C. Protect from light.

Keep the blisters in the carton until required for use.

Keep the HDPE container tightly closed.

Store in the original package in order to protect from light and moisture.

KEEP OUT OF REACH OF CHILDREN

6.5 Nature and contents of container

QUESARA 25 mg:

1) Blister Pack:

Tablets are packed in white opaque PVC/PVdC 250/60 PVC film coated with 60 gsm PVdC as the forming material and plain 25 micron, aluminum foil, 6-8 gsm HSL, as the lidding material. Each blister contains 10 tablets.

Pack size: 100's – Each carton contains 10 blisters of 10 tablets each.

2) HDPE Container Pack:

Tablets are packed in white round 60 ml HDPE bottle with 33 neck finish closed with 33 mm child resistant closure with pulp and heat seal. Each container contains 100 tablets.

Pack size: 100's - One HDPE container contains 100 tablets.

QUESARA 100 mg:

1) Blister Pack:

Tablets are packed in white opaque PVC/PVdC 250/60 PVC film coated with 60 gsm PVdC as the forming material and plain 25 micron, aluminum foil, 6-8 gsm HSL, as the lidding material. Each blister contains 10 tablets.

Pack size: 100's – Each carton contains 10 blisters of 10 tablets each.

90's – Each carton contains 9 blisters of 10 tablets each.

2) HDPE Container Pack:

Tablets are packed in white round 60 ml HDPE bottle with 33 neck finish closed with 33 mm child resistant closure with pulp and heat seal. Each container contains 100 tablets.

Pack size: 100's - One HDPE container contains 100 tablets.

QUESARA 200 mg:

1) Blister Pack:

Tablets are packed in white opaque PVC/PVdC 250/60 PVC film coated with 60 gsm PVdC as the forming material and plain 25 micron, aluminum foil, 6-8 gsm HSL, as the lidding material. Each blister contains 10 tablets.

Pack size: **100's** – Each carton contains 10 blisters of 10 tablets each.

60's – Each carton contains 6 blisters of 10 tablets each.

2) HDPE Container Pack:

Tablets are packed in white round 100 ml HDPE bottle with 38-400 neck finish closed with 38 mm child resistant closure with pulp and heat seal. Each container contains 100 tablets.

Pack size: **100's -** One HDPE container contains 100 tablets.

QUESARA 300 mg:

1) Blister Pack:

Tablets are packed in white opaque PVC/PVdC 250/60 PVC film coated with 60 gsm PVdC as the forming material and plain 25 micron, aluminum foil, 6-8 gsm HSL, as the lidding material. Each blister contains 10 tablets

Pack size: **90's** – Each carton contains 9 blisters of 10 tablets each.

60's – Each carton contains 6 blisters of 10 tablets each.

2) HDPE Container Pack:

Tablets are packed in white round 75 ml HDPE bottle with 38-400 neck finish closed with 38 mm child resistant closure with pulp and heat seal. Each container contains 60 tablets.

Pack size: **60's -** One HDPE container contains 60 tablets.

Not all packs and pack sizes are necessarily marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

Any unused product or waste material should be disposed of in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Macleods Pharmaceuticals SA (Pty) Ltd

Office block 1, Bassonia Estate Office Park (East),

1 Cussonia Drive, Bassonia Rock, Ext. 12,

Alberton, South Africa.

8. REGISTRATION NUMBER(S)

QUESARA 25 mg: 47/2.6.5/0144

QUESARA 100 mg: 47/2.6.5/0145

QUESARA 200 mg: 47/2.6.5/0146

QUESARA 300 mg: 47/2.6.5/0147

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

09 February 2021

10. DATE OF REVISION OF THE TEXT

24 March 2023

PM0051-01

Vanita Rajool

Digitally signed by Vanita Rajool
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