Professional Information

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

ZITAGLUC 25 (Film coated tablets)

ZITAGLUC 50 (Film coated tablets)

ZITAGLUC 100 (Film coated tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ZITAGLUC 25

Each film coated tablet contains sitagliptin fumarate equivalent to sitagliptin 25 mg.

Sugar free

ZITAGLUC 50

Each film coated tablet contains sitagliptin fumarate equivalent to sitagliptin 50 mg

Sugar free

ZITAGLUC 100

Each film coated tablet contains sitagliptin fumarate equivalent to sitagliptin 100 mg

Sugar free

For full list of excipients, see **section 6.1**

3. PHARMACEUTICAL FORM

Film coated tablets

ZITAGLUC 25

Light pink colour, round film coated tablets debossed with **F1** on one side and plain on the other side.

ZITAGLUC 50

Light beige colour, round film coated tablets debossed with **F2** on one side and plain on the other side

ZITAGLUC 100

Beige colour, round film coated tablets debossed with **F3** on one side and plain on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indication

Monotherapy

ZITAGLUC is indicated as an adjunct to diet and exercise to improve glycaemic control in adult patients with type 2 diabetes mellitus.

Combination Therapy

ZITAGLUC is also indicated in patients with type 2 diabetes mellitus to improve glycaemic control in combination with metformin or a PPARy agonist (e.g. thiazolidinedione) when diet and exercise, plus the single agent do not provide adequate glycaemic control.

The combination of sitagliptin and sulphonylureas has not been adequately studied.

4.2 Posology and method of administration

Posology:

The dose of **ZITAGLUC** in combination with metformin or a PPARy agonist is 100 mg once daily. The dosage of metformin or PPARy agonist should be maintained, and **ZITAGLUC** administered concomitantly.

Special Populations:

Patients with Renal Insufficiency

For patients with mild renal insufficiency (creatinine clearance [CrCl) ≥ 50 ml/min, approximately corresponding to serum creatinine levels of ≤ 150 micromol/litre in men and ≤ 133 micromol/litre in women), no dosage adjustment for **ZITAGLUC** is required.

For patients with moderate renal insufficiency (CrCl ≥ 30 to < 50 ml/min, approximately corresponding to serum creatinine levels of > 150 micromol/litre to ≤ 265 micromol/litre in men and > 133 micromol/1 to not ≤ 221 micromol/litre in women) the dose of **ZITAGLUC** is 50 mg once daily. This dose should be decreased if CrCI decreases to < 30ml/min.

For patients with severe renal insufficiency (CrCl < 30 ml/min, approximately corresponding to serum creatinine levels of > 265 micromol/litre in men and > 221 micromol/litre in women) or with end-stage renal disease requiring haemodialysis, the dose of **ZITAGLUC** is 25 mg once daily.

Sitagliptin may be administered without regard to the timing of haemodialysis.

Patients with Hepatic Insufficiency

No dosage adjustment is necessary for patients with mild to moderate hepatic insufficiency. No data has been reported with Sitagliptin in patients with severe hepatic insufficiency.

Elderly

No dosage adjustment is necessary for elderly patients.

Paediatric Population

There are no reported data available on the use of sitagliptin in patients younger than 18 years of age. Therefore, use of sitagliptin in paediatric patients is not recommended.

Method of administration:

Oral use.

ZITAGLUC can be taken with or without food.

If a dose of **ZITAGLUC** is missed, it should be taken as soon as

the patient remembers. A double dose of **ZITAGLUC** should not be taken on the same day.

4.3 Contraindications

ZITAGLUC is contraindicated in patients who are hypersensitive to any components of this formulation.

A history of serious hypersensitivity reactions, such as anaphylaxis and angioedema to sitagliptin or other gliptins (DPP-4).

No data has been reported with sitagliptin in patients with severe hepatic insufficiency (See section 5.2)

4.4 Special warnings and precautions for use

Pancreatitis

In post-marketing experience there have been reports of acute pancreatitis, including fatal and nonfatal haemorrhagic or necrotising pancreatitis (see section 4.8) in patients taking sitagliptin. Patients should be informed of the characteristic symptom of acute pancreatitis: persistent abdominal pain. Resolution of pancreatitis has been reported after discontinuation of sitagliptin. If pancreatitis is suspected, **ZITAGLUC** and other potentially suspect medicinal products should be discontinued immediately. If acute pancreatitis is confirmed, **ZITAGLUC** should not be restarted. Caution should be exercised in patients with a history of pancreatitis.

Hypersensitivity Reactions:

There have been post-marketing reports of serious hypersensitivity reactions in patients treated with sitagliptin. These reactions include anaphylaxis, angioedema and exfoliative skin conditions including Stevens-Johnson syndrome. Onset of these reactions have been reported within the first 3 months after initiation of treatment with sitagliptin, with some reports reported after the first dose. If a hypersensitivity reaction is suspected, discontinue ZITAGLUC immediately, and institute an alternative class of medicines for treatment for diabetes (see section 4.3 and 4.8).

General

Sitagliptin should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.

Hypoglycaemia

In reported clinical trials of sitagliptin as monotherapy and as part of combination therapy with medicinal products not known to cause hypoglycaemia (i.e. metformin and/or a PPARγ agonist), rates of hypoglycaemia reported with sitagliptin were similar to rates in patients taking placebo. Hypoglycaemia has been reported when sitagliptin was used in combination with insulin or a sulphonylurea. Therefore, to reduce the risk of hypoglycaemia, a lower dose of sulphonylurea or insulin may be considered.

Renal insufficiency

A dosage adjustment is recommended in patients with moderate or severe renal insufficiency and in patients with end-stage renal disease requiring haemodialysis (see **Section 4.2**).

When considering the use of sitagliptin in combination with another antidiabetic medicinal product, its conditions for use in patients with renal impairment should be checked.

Bullous pemphigoid

There have been post-marketing reports of bullous pemphigoid in patients taking DPP-4 inhibitors including sitagliptin. If bullous pemphigoid is suspected, sitagliptin should be discontinued.

4.5 Interaction with other medicines and other forms of interaction

Effects of other medicinal products on sitagliptin

Reported clinical data described below suggest that the risk for clinically meaningful interactions by co-administered medicinal products is low.

Reported *in vitro* studies indicated that the primary enzyme responsible for the limited metabolism of sitagliptin is CYP3A4, with contribution from CYP2C8. In patients with normal renal function, metabolism, including via CYP3A4, plays only a small role in the clearance of sitagliptin. Metabolism may play a more significant role in the elimination of sitagliptin in the setting of severe renal impairment or end-stage renal disease (ESRD). For this reason, it is possible that potent CYP3A4 inhibitors (i.e. ketoconazole, itraconazole, ritonavir, clarithromycin) could alter the pharmacokinetics of **ZITAGLUC** in patients with severe renal impairment or ESRD. The effect of potent CYP3A4 inhibitors in the setting of renal impairment has not been reported.

Reported *in vitro* transport studies showed that sitagliptin is a substrate for p-glycoprotein and organic anion transporter-3 (OAT3). OAT3 mediated transport of sitagliptin was inhibited *in vitro* by probenecid,

although the risk of clinically meaningful interactions is considered to be low. Concomitant administration of OAT3 inhibitors has not been reported.

Metformin: Co-administration of multiple twice-daily doses of 1,000 mg metformin with 50 mg sitagliptin has not been reported to significantly alter the pharmacokinetics of sitagliptin in patients with type 2 diabetes.

Ciclosporin: Co-administration of a single 100 mg oral dose of sitagliptin and a single 600 mg oral dose of ciclosporin reported to increase the AUC and C_{max} of sitagliptin by approximately 29% and 68%, respectively. These changes in sitagliptin pharmacokinetics were not considered to be clinically meaningful. The renal clearance of sitagliptin was not meaningfully altered. Therefore, meaningful interactions would not be expected with other p-glycoprotein inhibitors.

Effects of sitagliptin on other medicinal products

Digoxin: Sitagliptin has been reported to have a small effect on plasma digoxin concentrations. Following administration of 0,25 mg digoxin concomitantly with 100 mg of sitagliptin daily for 10 days, the plasma AUC of digoxin was reported to increase on average by 11 %, and the plasma C_{max} on average by 18 %. No dose adjustment of digoxin is recommended. However, patients at risk of digoxin toxicity should be monitored for this when sitagliptin and digoxin are administered concomitantly.

Reported *in vitro* data suggest that sitagliptin does not inhibit nor induce CYP450 isoenzymes. In reported clinical studies, sitagliptin did not meaningfully alter the pharmacokinetics of metformin, glyburide, simvastatin, rosiglitazone, warfarin, or oral contraceptives, providing in vivo evidence of a low propensity for causing interactions with substrates of CYP3A4, CYP2C8, CYP2C9, and organic cationic transporter (OCT). Sitagliptin may be a mild inhibitor of p-glycoprotein *in vivo*.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no reported studies in pregnant women; therefore, sitagliptin is not recommended for use in pregnancy. Studies in animals have reported reproductive toxicity at high doses.

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Breastfeeding

Sitagliptin has been reported to be secreted in the milk of lactating rats. It is not known whether sitagliptin is secreted in human milk. Therefore, sitagliptin should not be used by a woman who is breast-feeding

Fertility

Animal data do not report an effect of treatment with sitagliptin on male and female fertility. Reported human data are lacking.

4.7 Effects on ability to drive and use machines

No data has been reported of the effects of sitagliptin on the ability to drive and use machines. However, when driving or using machines, it should be taken into account that dizziness and somnolence have been reported. In addition, patients should be alerted to the risk of hypoglycaemia when **ZITAGLUC** is used in combination with a sulphonylurea or with insulin.

4.8 Undesirable effects

Serious adverse reactions including pancreatitis and hypersensitivity reactions have been reported. Hypoglycaemia has been reported in combination with sulphonylurea (4,7 % - 13,8 %) and insulin (9,6 %) (see **Section 4.4**).

Adverse reactions considered as medicine related reported in patients treated with sitagliptin occurring

in excess (> 0,2 % and difference more than one patient) of that in patients treated with placebo are listed below (below Table) by system organ class and frequency

Table: The frequency of adverse reactions identified from placebo-controlled clinical studies and post-marketing experience			
Adverse Reaction	**Frequency of adverse reaction by treatment regimen**		
	Sitagliptin with Metformin	**Sitagliptin with a PPARγ Agent (pioglitazone)**	**Post-marketing experience**
Blood and lymphatic system disorders			
Thrombocytopenia		Less frequent	
Immune system disorders			
Hypersensitivity reactions including anaphylactic responses†			Frequency not known
Metabolism and nutrition disorders			
Hypoglycaemia		Frequent	
Nervous system disorders			
Somnolence	Less frequent		
Headache	Frequent		
Dizziness	Less frequent		
Respiratory, thoracic and mediastinal disorders			

Interstitial lung disease			Frequency not known
Nasopharyngitis			Frequency not known
Upper respiratory tract infection			Frequency not known
Gastrointestinal disorders			
Diarrhoea	Less frequent		
Nausea	Frequent		
Flatulence		Frequent	
Upper abdominal pain	Less frequent		
Constipation	Less frequent		
Vomiting			Frequency not known
Acute pancreatitis			Frequency not known
Fatal and non-fatal haemorrhagic and necrotizing pancreatitis			Frequency not known
Skin and subcutaneous tissue disorders			
Pruritus	Less frequent		
Angioedema†			Frequency not known
Rash†			Frequency not known
Urticaria†			Frequency not known

Cutaneous vasculitis†			Frequency not known
Exfoliative skin conditions including Stevens-Johnson syndrome†			Frequency not known
Bullous pemphigoid			Frequency not known
Anaphylaxis			Frequency not known
Musculoskeletal and connective tissue disorders			
Arthralgia			Frequency not known
Myalgia			Frequency not known
Back pain			Frequency not known
Arthropathy			Frequency not known
Renal and urinary disorders			
Impaired renal function (worsening renal function)			Frequency not known
Acute renal failure (sometimes requiring dialysis)			Frequency not known
General disorders			
Peripheral oedema		Frequent	
Investigations			

Decreased blood glucose levels	Less frequent		
†Special warnings and precautions for use			

In addition, adverse reactions considered as medicine-related reported in patients treated with sitagliptin in excess (> 0,2 % and difference more than 1 patient) of that in patients receiving placebo are headache, hypoglycaemia, constipation and dizziness.

In addition to the medicine-related adverse experiences described above, adverse experiences reported regardless of causal relationship to medication and occurring in at least 5 % and more frequently in patients treated with sitagliptin included upper respiratory tract infection and nasopharyngitis.

Additional adverse experiences reported regardless of causal relationship to medication that occurred more frequently in patients treated with sitagliptin (not reaching the 5 % level, but occurring with an incidence of greater than 0,5 % higher with sitagliptin than that in the control group) included osteoarthritis and pain in extremity.

Some adverse reactions were reported more frequently in studies of combination use of sitagliptin with other anti-diabetic medicinal products than in studies of sitagliptin monotherapy. These included influenza (frequent with insulin [with or without metformin]), and dry mouth (less frequent with insulin [with or without metformin]).

Paediatric population

In reported clinical trials with sitagliptin in paediatric patients with type 2 diabetes mellitus aged 10 to 17 years, the profile of adverse reactions was comparable to that reported in adults.

Trial Evaluating Cardiovascular Outcomes with Sitagliptin (TECOS) Cardiovascular Safety Study

In the reported trial which evaluated the cardiovascular outcomes with sitagliptin included patients treated with sitagliptin, 100 mg daily (or 50 mg daily if the baseline eGFR was ≥ 30 and < 50 mL/min/1,73 m^2), and patients treated with placebo in the intention-to-treat population. Both treatments were added to usual care targeting regional standards for HbA1c and CV risk factors. The overall reported incidence of serious adverse events in patients receiving sitagliptin was similar to that in patients receiving placebo.

In the intention-to-treat population, it was reported that among patients who were using insulin and/or a sulfonylurea at baseline, the incidence of severe hypoglycaemia was 2,7 % in sitagliptin-treated patients and 2,5 % in placebo-treated patients; among patients who were not using insulin and/or a sulfonylurea at baseline, the incidence of severe hypoglycaemia was 1,0 % in sitagliptin-treated patients and 0,7 % in placebo-treated patients. The incidence of adjudication-confirmed reported that pancreatitis events was 0,3 % in sitagliptin-treated patients and 0,2 % in placebo-treated patients.

Laboratory test findings

A small mean increase in uric acid (approximately 12 micromol/litre difference from placebo; mean baseline 297 to 327 micromol/litre) was reported in patients treated with sitagliptin 100 or 200 mg daily. No increase in the incidence of gout was reported. A small mean decrease in total alkaline phosphatase (up to approximately 5 IU/l difference from placebo; mean baseline approximately 56 to 62 IU/l) was also reported, partly related to a small decrease in bone alkaline phosphatase. A small increase in white blood cell count (WBC) (approximately 200 cells/microlitre difference in WBC versus placebo; mean baseline WBC approximately 6 600 cells/microlitre) was reported due to *an* increase in neutrophils. This observation was reported in most but not all studies. These changes in laboratory parameters are not considered to be clinically relevant.

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 Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Single doses of up to 800 mg sitagliptin has been reported to be generally well tolerated in healthy subjects. Minimal increases in QTc, not considered to be clinically relevant, were reported in at a dose of 800 mg sitagliptin. There is no experience with doses above 800 mg in humans.

In the event of an overdose, it is reasonable to employ the usual supportive measures e.g. remove unabsorbed material from the gastrointestinal tract, employ clinical monitoring (including obtaining an electrocardiogram), and institute supportive therapy if required.

Sitagliptin is modestly dialysable. In reported clinical studies, approximately 13,5 % of the dose was removed over a 3 to 4 hour haemodialysis session. Prolonged haemodialysis may be considered if clinically appropriate. It is not known if sitagliptin is dialysable by peritoneal dialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Medicines used in diabetes, Dipeptidyl peptidase 4 (DPP-4) inhibitors,

ATC code: A10BH01

A21.2 Oral hypoglycaemics

Mechanism of action:

Sitagliptin is an orally-active, potent and selective inhibitor of the dipeptidyl peptidase 4 (DPP-4) enzyme for *the* treatment of type 2 diabetes. The DPP-4 inhibitors are a class of agents that act as incretin enhancers. By inhibiting the DPP-4 enzyme, sitagliptin increases the levels of two known active incretin hormones, glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP). Lncretin hormones physiologically regulate blood glucose levels by increasing insulin response from pancreatic beta cells and suppressing glucagon secretion from pancreatic alpha cells when blood

glucose levels are normal or elevated. These effects are not reported when blood glucose levels are low.

Sitagliptin differs in chemical structure and pharmacological action from GLP-1 analogues, insulin, sulphonylureas or meglitinides, biguanides, peroxisome proliferator-activated receptor gamma (PPARy) agonists, alpha-glucosidase inhibitors and amylin analogues.

5.2. Pharmacokinetic properties

The pharmacokinetics of sitagliptin have been reported to be extensively characterised in healthy subjects and patients with type 2 diabetes. After oral administration of a 100 mg dose to healthy subjects, sitagliptin was reported to be absorbed with peak plasma concentrations (median T_{max}) occurring 1 to 4 hours post-dose. Plasma Area Under the Curve (AUC) of sitagliptin reported to be increased in a dose-proportional manner. Following a single oral 100 mg dose to healthy volunteers, mean plasma AUC of sitagliptin was reported to be 8,52 micromolar hours, C_{max} was 950 nanomol and apparent terminal half-life ($t_{1/2}$) was 12,4 hours. Plasma AUC of sitagliptin was reported to be increased approximately 14 % following 100 mg doses at steady-state compared to the first dose. The intra-subject and inter-subject coefficients of variation for sitagliptin AUC were reported to be small (5,8 % and 15,1 %). The pharmacokinetics of sitagliptin were reported to be generally similar in healthy subjects and in patients with type 2 diabetes.

Absorption

The absolute bioavailability of sitagliptin is reported to be approximately 87 %. Co-administration of a high fat meal with sitagliptin has no effect on the pharmacokinetics (**see section 4.2**).

Distribution

The mean volume of distribution at steady state following a single 100 mg intravenous dose of sitagliptin to healthy subjects is reported to be approximately 198 litres. The fraction of sitagliptin reversibly bound to plasma proteins is low (38 %).

Biotransformation

Sitagliptin is reported to be primarily eliminated unchanged in urine, and metabolism is a minor pathway. Approximately 79 % of sitagliptin is excreted unchanged in the urine. Following a radioactively-labelled ^{14}C sitagliptin oral dose, approximately 16 % of the radioactivity was reported to be excreted as metabolites of sitagliptin. Six metabolites were detected at trace levels and are not expected to contribute to the plasma DPP-4 inhibitory activity of sitagliptin. Reported *in vitro* studies indicated that the primary enzyme responsible for the limited metabolism of sitagliptin was CYP3A4, with contribution from CYP2C8.

Elimination

Following administration of an oral radioactively-labelled ^{14}C sitagliptin dose to healthy subjects, approximately 100 % of the administered radioactivity was reported to be eliminated in faeces (13 %) or urine (87 %) within one week of dosing. The apparent terminal $t_{1/2}$ following a 100 mg oral dose of sitagliptin was reported to be approximately 12,4 hours and renal clearance was approximately 350 ml/min.

Elimination of sitagliptin occurs primarily via renal excretion and involves active tubular secretion. Sitagliptin is a substrate for human organic anion transporter-3 (hOAT-3), which may be involved in the renal elimination of sitagliptin. The clinical relevance of hOAT-3 in sitagliptin transport has not been established. Sitagliptin is also a substrate of p-glycoprotein, which may also be involved in mediating the renal elimination of sitagliptin. However, cyclosporin, a p-glycoprotein inhibitor did not reduce the renal clearance of sitagliptin.

Pharmacokinetics in Special Patient Groups

Renal insufficiency

In a reported single-dose, open-label study which was conducted to evaluate the pharmacokinetics of sitagliptin (50 mg dose) in patients with varying degrees of chronic renal insufficiency compared to

normal healthy control subjects. The study included patients with renal insufficiency, classified on the basis of creatinine clearance as mild (50 to < 80 ml/min), moderate (30 to < 50 ml/min), and severe (< 30 ml/min), as well as patients with end-stage renal disease on haemodialysis. Creatinine clearance was measured by 24 hour urinary creatinine clearance measurements or estimated from serum creatinine based on the Cockcrott-Gault formula:

CrCI = [140 - age (years)] x weight 1kg) (x 1 2)/ [serum creatinine (micromol/1)]

For female patients: 0,85 x value calculated for males

Compared to normal healthy control subjects, an approximate 1,6-fold increase in plasma AUG of sitagliptin was reported in patients with mild renal insufficiency. An approximately 2,3-fold increase in the plasma AUG of sitagliptin was reported in patients with moderate renal insufficiency, an approximately 3,8-fold increase was reported in patients with severe renal insufficiency and an approximately 4,5-fold increase was reported in patients with end-stage renal disease on haemodialysis, as compared to normal healthy control subjects. Sitagliptin was not meaningfully removed by haemodialysis (13,5 % over a 3- to 4-hour haemodialysis session starting 4 hours post-dose). To achieve plasma concentrations of sitagliptin similar to those in patients with normal renal function, lower dosages are recommended in patients with moderate and severe renal insufficiency, as well as in end-stage renal disease patients requiring haemodialysis (see **Section 4.2**).

Hepatic insufficiency

In patients with moderate hepatic insufficiency (Child-Pugh score 7 to 9), mean AUC and C_{max} of sitagliptin was reported to increase approximately 21 % and 13 %, respectively, compared to healthy matched controls following administration of a single 100-mg dose of sitagliptin. These differences are not considered to be clinically meaningful. There is no clinical experience in patients with severe hepatic insufficiency (Child-Pugh score > 9) (see **Section 4.3**)

Elderly

Age has not been reported to have a clinically meaningful impact on the pharmacokinetics of sitagliptin. Elderly subjects (65 to 80 years) had approximately 19 % higher plasma concentrations of sitagliptin compared to younger subjects.

Paediatric

No studies with sitagliptin have been reported in paediatric patients.

Gender:

Gender has not been reported to have a clinically meaningful impact on the pharmacokinetics of sitagliptin.

Body Mass Index (BMI)

Body mass index has not been reported to have a clinically meaningful impact on the pharmacokinetics of sitagliptin

Type 2 diabetes

The pharmacokinetics of sitagliptin in patients with type 2 diabetes are generally reported to be similar to those in healthy subjects

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Calcium hydrogen phosphate, crospovidone (type-a), glycerol dibehenate, hydrogenated castor oil, magnesium stearate

Film coating

Opadry Pink 02F540038 (25 mg)

HPMC 2910/Hypromellose, iron oxide yellow, iron oxide red, macrogol/peg (mw 6000), talc, titanium dioxide

Opadry Beige 02F570009 (50 mg)

HPMC 2910/Hypromellose, iron oxide yellow, iron oxide red, macrogol/peg (mw 6000), talc, titanium dioxide

Opadry Beige 02F570006 (100 mg)

HPMC 2910/Hypromellose, iron oxide yellow, iron oxide red, isopropyl alcohol, macrogol/peg (mw 6000), methylene chloride, talc, titanium dioxide

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Store at or below 25 ºC. Protect from moisture.

Do not remove the blisters from the carton until required for use.

6.5 Nature and contents of container

HDPE Bottle Pack:

The product can be supplied in pack sizes of 90’s comprising of an HDPE bottle with silica gel desiccants and child resistant closure with induction seal liner.

Blister packs:

The product can be supplied in blister packs of 3 x 10's comprising of a desiccant embedded cold form laminate with the oriented polyamide, aluminium foil, polyethylene, desiccant and HDPE coating with a backing of lidding laminate comprising of aluminum foil and heat seal extrusion coating.

6.6 Special precautions for disposal and other handling

Return all unused or expired medicines to your pharmacist for safe disposal. Do not dispose of unused medicines in drains or sewerage systems (e.g. toilets).

7 HOLDER OF CERTIFICATE OF REGISTRATION

Ranbaxy Pharmaceuticals (Pty) Ltd

14 Lautre Road

Stormill, Ext. 1

Roodepoort, 1724

South Africa

8 REGISTRATION NUMBER(S)

ZITAGLUC 25: 57/21.2/0009

ZITAGLUC 50: 57/21.2/0010

ZITAGLUC 100: 57/21.2/0011

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

21 January 2025

10 DATE OF REVISION OF THE TEXT

21 January 2025