# Professional Information for TUERIZIN 10 & 25

**SCHEDULING STATUS** S4

## 1. NAME OF THE MEDICINE

**TUERIZIN 10** mg film-coated tablets

**TUERIZIN 25** mg film-coated tablets

**TUERIZIN IS CONTRAINDICATED FOR USE IN TYPE 1 DIABETES.**

**TUERIZIN IS NOT INDICATED FOR USE IN WEIGHT CONTROL PROGRAMMES AND NOT INDICATED FOR THE TREATMENT OF ANY OTHER CONDITIONS EXCEPT TYPE 2 DIABETES.**

**There have been reports of metabolic acidosis, including ketoacidosis which were serious life threatening or fatal in patients taking TUERIZIN.**

**Patients who present with signs and symptoms including nausea, vomiting, abdominal pain, malaise and shortness of breath, should be assessed for metabolic acidosis, even if blood glucose levels are below 11 mmol/L. TUERIZIN should be discontinued and the patient should be promptly evaluated and managed accordingly.**

**Predisposing factors for metabolic acidosis include insulin dose reduction, reduced caloric intake, reduced fluid intake or increased insulin requirements due to infections, illness, surgery or alcohol abuse. Caution is advised in treating these patients with TUERIZIN.**

**Predisposing factors for ketoacidosis include low beta-cell function reserve resulting from**

**pancreatic disorders, e.g. history of pancreatitis or pancreatic surgery. TUERIZIN is contraindicated in these patients.**

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

TUERIZIN 10: Each film-coated tablet contains 10 mg empagliflozin.

TUERIZIN 25: Each film-coated tablet contains 25 mg empagliflozin.

*Excipients with known effect*

TUERIZIN 10: Each film-coated tablet contains 22,4 mg lactose anhydrous.

TUERIZIN 25: Each film-coated tablet contains 56,0 mg lactose anhydrous.

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Film-coated tablets.

TUERIZIN 10: White to off-white, round, film-coated tablets debossed with “1453” on one side and plain on the other side.

TUERIZIN 25: White to off-white, oval, film-coated tablets debossed with “1454” on one side and plain on the other side.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

TUERIZIN film-coated tablets are indicated as an adjunct to diet and exercise to improve glycaemic control in adults with type 2 diabetes mellitus.

*Add-on combination therapy:*

In combination with glucose-lowering medicines, including metformin, a thiazolidinedione, a

sulphonylurea, a dipeptidyl peptidase 4 (DPP4) inhibitor, or insulin, when these together with diet and exercise do not provide adequate glycaemic control.

*Prevention of cardiovascular events:*

TUERIZIN is indicated in patients with type 2 diabetes mellitus and high cardiovascular risk* to reduce the risk of:

- cardiovascular death due to myocardial infarction
- cardiovascular death or hospitalisation for heart failure.

*e.g. previous myocardial infarction, multi vessel coronary artery disease, previous coronary revitalisation, single vessel coronary disease, at least 50 % narrowing of coronary artery lumen.

## 4.2 Posology and method of administration

***Posology***

Assess hydration status and renal function before initiating treatment with TUERIZIN. Do not initiate treatment if the estimated glomerular filtration rate (eGFR) < 30 mL/min/1,73 $m^2$ (or creatinine clearance < 30 mL/min) and/or in patients who are volume depleted or acidotic (see sections 4.3 and 4.4).

The recommended starting dose of TUERIZIN is 10 mg once daily.
In patients tolerating TUERIZIN 10 once daily and requiring additional glycaemic control, the dose may be increased to 25 mg once daily.

***Special populations***

*Patients with renal insufficiency:*

No dose adjustment is required for patients with eGFR ≥ 30 mL/min/1,73 $m^2$).
TUERIZIN is not recommended for use in patients with severe renal impairment (defined as eGFR < 30 mL/min/1,73 $m^2$ by modification of diet in renal disease or creatinine clearance < 30 mL/min by Cockroft-Gault) (see sections 4.3 and 4.4).

*Patients with hepatic insufficiency:*

Dose adjustment may be necessary fo patients with severe hepatic impairment.

*Elderly patients:*

No dosage adjustment is recommended based on age if the creatinine clearance is ≥ 30 mL/min. Therapeutic experience in patients aged 85 years and older is limited. Initiation of TUERIZIN therapy in this population is not recommended (see section 4.4).

*Combination therapy:*

When TUERIZIN is used in combination with a sulphonylurea or with insulin, a lower dose of the sulphonylurea or insulin should be considered to reduce the risk of hypoglycaemia (see section 4.8).

*Missed dose:*

If a dose is missed, it should be taken as soon as the patient remembers. A double dose should not be taken on the same day.

*Paediatric population:*

Safety and effectiveness of TUERIZIN in children under 18 years of age have not been established.

***Method of administration***

TUERIZIN can be taken with or without food.

## 4.3 Contraindications

- Hypersensitivity to empagliflozin or any of the excipients listed in section 6.1.
- Treatment of type I diabetes mellitus.
- Treatment of ketoacidosis.

- Severe renal impairment (creatinine clearance < 30 mL/min), end-stage renal disease or dialysis.
- Pregnancy and lactation.

## 4.4 Special warnings and precautions for use

*Lower limb amputations*

An increase in cases of lower limb amputation (primarily of the toe) has been observed in long-term clinical studies with another SGLT2 inhibitor. It is unknown whether this constitutes a class effect. Like for all diabetic patients it is important to counsel patients on routine preventative foot-care.

*Urine laboratory assessments*

Due to its mechanism of action, patients taking TUERIZIN will test positive for glucose in their urine.

TUERIZIN should not be used in patients with type 1 diabetes.

***Ketoacidosis with atypical presentation***

Cases of ketoacidosis, which may be serious, life threatening or fatal, have been reported in patients treated with empagliflozin, as in TUERIZIN. Such cases require hospitalisation. The presentation of ketoacidosis is frequently atypical with either euglycaemia or with blood glucose values mildly or moderately increased below 11 mmol/L (196 mg/dL).

The risk of ketoacidosis must be considered in the event of non-specific symptoms such as nausea, vomiting, anorexia, abdominal pain, excessive thirst, difficulty breathing, confusion, unusual fatigue or sleepiness.

Patients should be assessed for ketoacidosis immediately if these symptoms occur, regardless of blood glucose level. Treatment with TUERIZIN should be discontinued immediately in such cases

and treatment instituted. Treatment, amongst others, may require fluids, carbohydrate and insulin.

The risk of developing ketoacidosis while taking TUERIZIN, is increased in patients with a reduced fluid and food intake, patients on a very low carbohydrate diet, severely dehydrated patients, insulin dose reduction in patients also requiring insulin, patients with a history of ketoacidosis or who are known to have a low beta-cell function reserve, or any pancreatic disease/disorder with or without an insulin deficiency, or patients with alcohol abuse or misusing alcohol.

A progressive increase in blood and urine ketones and a progressive increase in metabolic acidosis may be indicative of the development of ketoacidosis irrespective of blood glucose levels.

Blood and urine ketones as well as blood pH should be regularly monitored.

In clinical situations known to predispose to ketoacidosis (e.g. prolonged fasting due to an acute illness or surgery), the treatment with TUERIZIN should be temporarily discontinued.

The underlying mechanism for SGLT2 inhibition-associated ketoacidosis has not been established.

Atypical metabolic acidosis (no ketone bodies) may present in a very similar manner to ketoacidosis.

***Haemoconcentration***

An increase in the haematocrit of patients on treatment with TUERIZIN can be expected.

***Hypoglycaemia with concomitant use with insulin and insulin secretagogues***

The risk of hypoglycaemia is increased when TUERIZIN is used in combination with insulin secretagogues (e.g. sulphonylurea) or insulin (see section 4.8). Therefore, a lower dose of the insulin secretagogue or insulin may be required to reduce the risk of hypoglycaemia when used in combination with TUERIZIN (see section 4.4).

***Use in patients with renal impairment***

The efficacy of TUERIZIN is dependent on renal function. Therefore, assessment of renal function is recommended prior to TUERIZIN initiation and periodically during treatment, i.e. at least 6-monthly.

Consider renal function when used in conjunction with metformin.

***Hepatic injury***

Cases of hepatic injury have been reported.

***Use in patients at risk for volume depletion***

Based on the mode of action of SGLT2 inhibitors, osmotic diuresis accompanying therapeutic glycosuria may lead to intravascular volume contraction with a decrease in blood pressure. Therefore, caution should be exercised in patients for whom an empagliflozin-induced drop in blood pressure could pose a risk, such as patients with known cardiovascular disease, patients on anti-hypertensive therapy and/or diuretics, and with a history of hypotension, or the elderly especially patients aged 75 years and older. In conditions that may lead to fluid loss (e.g. gastrointestinal illness), careful monitoring of volume status (e.g. physical examination, blood pressure measurements, laboratory tests including haematocrit) and electrolytes is recommended for patients receiving TUERIZIN. Temporary interruption of treatment with TUERIZIN should be considered until the fluid loss is corrected.

***Urinary tract infections and genital infections***

The overall frequency of urinary tract infection, and/or genital infection, reported as an adverse event was higher than placebo in patients treated with TUERIZIN especially mycotic infections in females. Genital infections occurred more frequently in females than in males.

Patients with a history of chronic or recurrent urinary tract infection (UTI) were more likely to experience UTI. Post-marketing cases of complicated urinary tract infections including pyelonephritis and urosepsis have been reported in patients treated with TUERIZIN (see section

4.8). Temporary interruption of TUERIZIN should be considered in patients with complicated urinary tract infections.

*Necrotising fasciitis of the perineum (Fournier's gangrene)*

Post-marketing cases of necrotising fasciitis of the perineum (also known as Fournier's gangrene), a rare, but serious and life-threatening necrotising infection, have been reported in female and male patients with diabetes mellitus treated with SGLT2 inhibitors, including empagliflozin. Serious outcomes have included hospitalisation, multiple surgeries and death. Patients treated with TUERIZIN who present with pain or tenderness, erythema, swelling in the genital or perineal area, fever, malaise should be evaluated for necrotising fasciitis. If suspected, TUERIZIN should be discontinued and prompt treatment should be instituted (including broad-spectrum antibiotics and surgical debridement if necessary).

***Elderly patients***

Patients aged 75 years and older are at increased risk of volume depletion, therefore, TUERIZIN should be prescribed with caution in these patients (see section 4.8). Therapeutic experience in patients aged 85 years and older is limited. Initiation of TUERIZIN therapy in this population is not recommended.

***Paediatrics and children***

TUERIZIN is not recommended for use in children below 18 years due to lack of data on safety and efficacy.

*Lactose*

TUERIZIN tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency, or glucose-galactose malabsorption should not take TUERIZIN.

## 4.5 Interaction with other medicines and other forms of interaction

***Pharmacodynamic interactions***

*Diuretics*

Empagliflozin may add to the diuretic effect of thiazide and loop diuretics and may increase the risk of dehydration and hypotension (see section 4.4).

*Insulin and insulin secretagogues*

Insulin and insulin secretagogues, such as sulphonylureas, may increase the risk of hypoglycaemia. Therefore, a lower dose of insulin or an insulin secretagogue may be required to reduce the risk of hypoglycaemia when used in combination with empagliflozin (see sections 4.2 and 4.8).

***Pharmacokinetic interactions***

*Effects of other medicines on empagliflozin*

*In vitro* data suggest that the primary route of metabolism of empagliflozin in humans is glucuronidation by uridine 5'-diphosphoglucuronosyltransferases UGT1A3, UGT1A8, UGT1A9, and UGT2B7. Empagliflozin is a substrate of the human uptake transporters OAT3, OATP1B1, and OATP1B3, but not OAT1 and OCT2. Empagliflozin is a substrate of P-glycoprotein (P-gp) and breast cancer resistance protein (BCRP).

Co-administration of empagliflozin with probenecid, an inhibitor of UGT enzymes and OAT3, resulted in a 26 % increase in peak empagliflozin plasma concentrations ($C_{max}$) and a 53 % increase in area under the concentration-time curve (AUC). These changes were not considered to be clinically meaningful.

The effect of UGT induction (e.g. induction by rifampicin or phenytoin) on empagliflozin has not been studied. Co-treatment with known inducers of UGT enzymes is not recommended due to a potential risk of decreased efficacy. If an inducer of these UGT enzymes must be co-administered, monitoring of glycaemic control to assess response to TUERIZIN is appropriate.

An interaction study with gemfibrozil, an *in vitro* inhibitor of OAT3 and OATP1B1/1B3 transporters, showed that empagliflozin $C_{max}$ increased by 15 % and AUC increased by 59 % following co-administration. These changes were not considered to be clinically meaningful.

Inhibition of OATP1B1/1B3 transporters by co-administration with rifampicin resulted in a 75 % increase in $C_{max}$ and a 35 % increase in AUC of empagliflozin. These changes were not considered to be clinically meaningful.

Empagliflozin exposure was similar with and without co-administration with verapamil, a P-gp inhibitor, indicating that inhibition of P-gp does not have any clinically relevant effect on empagliflozin.

Interaction studies suggest that the pharmacokinetics of empagliflozin were not influenced by co-administration with metformin, glimepiride, pioglitazone, sitagliptin, linagliptin, warfarin, verapamil, ramipril, simvastatin, torasemide, digoxin, diuretics, oral contraceptives and hydrochlorothiazide in patients with type 2 diabetes mellitus.

*Effects of empagliflozin on other medicines*

Based on *in vitro* studies, empagliflozin does not inhibit, inactivate, or induce CYP450 isoforms. Empagliflozin does not inhibit UGT1A1, UGT1A3, UGT1A8, UGT1A9 or UGT2B7. Medicine-medicine interactions involving the major CYP450 and UGT isoforms with empagliflozin and concomitantly administered substrates of these enzymes are therefore considered unlikely.

Empagliflozin does not inhibit P-gp at therapeutic doses. Based on *in vitro* studies, empagliflozin is considered unlikely to cause interactions with active substances that are P-gp substrates. Co-administration of digoxin, a P-gp substrate, with empagliflozin resulted in a 6 % increase in AUC and 14 % increase in $C_{max}$ of digoxin. These changes were not considered to be clinically meaningful.

Empagliflozin does not inhibit human uptake transporters such as OAT3, OATP1B1, and OATP1B3 *in vitro* at clinically relevant plasma concentrations and, as such, medicine-medicine interactions with substrates of these uptake transporters are considered unlikely.

## 4.6 Fertility, pregnancy and lactation

### Pregnancy

TUERIZIN is contraindicated in pregnancy (see section 4.3). Animal studies showed that empagliflozin, as contained in TUERIZIN, crosses the placenta.

### Breastfeeding

TUERIZIN is contraindicated in lactation (see section 4.3). Mothers should not breastfeed their infants while taking TUERIZIN. Animal studies have shown excretion empagliflozin as contained in TUERIZIN, in milk of animals. A risk to human newborns/infants cannot be excluded.

## 4.7 Effects on ability to drive and use machines

Hypoglycaemia may impair driving and machinery use capabilities. Patients should be aware of symptoms that may herald the onset of hypoglycaemia and act appropriately.

## 4.8 Undesirable effects

Table 1: Tabulated list of adverse reactions (MedDRA) from reported placebo-controlled studies and from post-marketing experience

| System Organ Class | Frequent | Less frequent | Not known |
|---|---|---|---|
| ***Infections and infestations*** | vaginal moniliasis, vulvovaginitis, balanitis and other genital infection (including pyelonephritis and | | necrotising fasciitis of the perineum (Fournier's gangrene) |

| | | | |
|---|---|---|---|
| | urosepsis), urinary tract infection | | |
| ***Metabolism and nutrition disorders*** | hypoglycaemia (when used with sulphonylurea or insulin), weight loss, increased serum lipids | diabetic ketoacidosis | |
| ***Skin and subcutaneous tissue disorders*** | pruritus (generalised), rash | urticaria | angioedema |
| ***Vascular disorders*** | | volume depletion (hypotension and dehydration) | |
| ***Gastro- intestinal disorders*** | thirst | | |
| ***Renal and urinary disorders*** | increased urination, glycosuria | dysuria, ketonuria | |
| ***Investigations*** | increased serum lipids | increased blood creatinine, decreased glomerular filtration rate, increased haematocrit. | |

**Description of selected adverse reactions**

*Volume depletion*

The overall frequency of volume depletion (including the predefined terms blood pressure (ambulatory) decreased, blood pressure systolic decreased, dehydration, hypotension, hypovolaemia, orthostatic hypotension, and syncope) was similar to placebo. The effect of empagliflozin, as in TUERIZIN, on urinary glucose excretion is associated with osmotic diuresis,

which could affect hydration status of patients aged 75 years and older or those otherwise at risk. In patients ≥ 75 years of age the frequency of volume depletion events was similar for empagliflozin 10 mg compared to placebo, but it increased with empagliflozin 25 mg.

*Blood creatinine increased/Glomerular filtration rate decreased*

The overall frequency of patients with increased blood creatinine and decreased glomerular filtration rate were similar between empagliflozin, as in TUERIZIN, and placebo.
In placebo controlled, double-blind studies up to 76 weeks, initial transient increases in creatinine and initial decreases in estimated glomerular filtration rates have been observed. These changes were generally reversible during continuous treatment or after medicine discontinuation.

***Reporting of suspected adverse reactions***

Reporting suspected adverse reactions after authorisation of TUERIZIN is important. It allows continued monitoring of the benefit/risk balance of TUERIZIN. Health care providers are asked to report any suspected adverse reactions 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

The risk and severity of undesirable effects may be increased (see section 4.8). In the event of an overdose, symptomatic and supportive treatment should be initiated as appropriate to the patient's clinical status. The removal of TUERIZIN by haemodialysis has not been studied. Hypoglycaemia should be monitored for, especially when other antidiabetic medication has been co-administered.

## 5. PHARMACOLOGICAL PROPERTIES

**Category and class:** A 21.2 Oral hypoglycaemics

**Pharmacotherapeutic group:** Drugs used in diabetes, Other blood glucose lowering drugs, excluding insulins

**ATC code:** A10BK03

**5.1 Pharmacodynamic properties**

Empagliflozin is a reversible inhibitor of SGLT2 (sodium glucose cotransporter 2) with an IC50 of 1,3 nM. It has a 5 000-fold selectivity over human SGLT1 (IC50 of 6 278 nM), responsible for glucose absorption in the gut. Furthermore, high selectivity could be shown toward other glucose transporters (GLUTs) responsible for glucose homeostasis in the different tissues.

SGLT2 is highly expressed in the kidney, whereas expression in other tissues is absent or very low. It is responsible as the predominant transporter for reabsorption of glucose from the glomerular filtrate back into the circulation. In patients with type 2 diabetes mellitus (T2DM) and hyperglycaemia a higher amount of glucose is filtered and reabsorbed.

Empagliflozin improves glycaemic control in patients with T2DM by reducing renal glucose reabsorption. The amount of glucose removed by the kidney through this glucuretic mechanism is dependent upon the blood glucose concentration and GFR (glomerular filtration rate). Through inhibition of SGLT2 in patients with T2DM and hyperglycaemia, excess glucose is excreted in the urine.

The mechanism of action of empagliflozin is independent of beta-cell function and insulin pathway and this contributes to a low risk of hypoglycaemia.
Urinary glucose excretion triggers calorie loss, associated with body fat loss and body weight reduction.

The glycosuria observed with empagliflozin is accompanied by mild diuresis which may contribute to sustained and moderate reduction of blood pressure.

## 5.2 Pharmacokinetic properties

### *Absorption*

The pharmacokinetics of empagliflozin have been extensively characterised in healthy volunteers and patients with type 2 diabetes. After oral administration, empagliflozin was rapidly absorbed with peak plasma concentrations occurring at a median $t_{max}$ of 1,5 hours post-dose. Thereafter, plasma concentrations declined in a biphasic manner with a rapid distribution phase and a relatively slow terminal phase. For single doses of 10 mg and 25 mg, the terminal phase half-life is 13,1 ± 4,0 h and 10,2 ± 2,1 h respectively. The steady state mean plasma AUC and $C_{max}$ were 4 740 nmol.h/L and 687 nmol/L with empagliflozin 25 mg once daily. Systemic exposure of empagliflozin increased in a dose-proportional manner. The single-dose and steady-state pharmacokinetic parameters of empagliflozin were similar suggesting linear pharmacokinetics with respect to time. There were no clinically relevant differences in empagliflozin pharmacokinetics between healthy volunteers and patients with type 2 diabetes.

Administration of empagliflozin 25 mg after intake of a high-fat and high-calorie meal resulted in slightly lower exposure; AUC decreased by approximately 16 % and $C_{max}$ by approximately 37 % compared to fasted condition. The observed effect of food on empagliflozin pharmacokinetics was not considered clinically relevant and empagliflozin may be administered with or without food.

### *Distribution*

The apparent steady-state volume of distribution was estimated to be 73,8 L based on the population pharmacokinetic analysis. Following administration of an oral [$^{14}$C] empagliflozin solution to healthy volunteers, the red blood cell partitioning was approximately 36,8 % and plasma protein binding was 86,2 %.

### *Biotransformation*

No major metabolites of empagliflozin were detected in human plasma and the most abundant metabolites were three glucuronide conjugates (2-, 3-, and 6-*O*-glucuronide). Systemic exposure

of each metabolite was less than 10 % of total medicine-related material. *In vitro* studies suggested that the primary route of metabolism of empagliflozin in humans is glucuronidation by the uridine 5'-diphospho-glucuronosyltransferases UGT2B7, UGT1A3, UGT1A8, and UGT1A9.

***Elimination***

Based on the population pharmacokinetic analysis, the apparent terminal elimination half-life of empagliflozin was estimated to be 12,4 hours and apparent oral clearance was 10,6 L/hour. The inter-subject and residual variabilities for empagliflozin oral clearance were 39,1 % and 35,8 %, respectively. With once-daily dosing, steady-state plasma concentrations of empagliflozin were reached by the fifth dose. Consistent with the half-life, up to 22 % accumulation, with respect to plasma AUC, was observed at steady state. Following administration of an oral [$^{14}$C] empagliflozin solution to healthy volunteers, approximately 95,6 % of the medicine-related radioactivity was eliminated in faeces (41,2 %) or urine (54,4 %). The majority of medicine-related radioactivity recovered in faeces was unchanged parent medicine and approximately half of medicine-related radioactivity excreted in urine was unchanged parent medicine.

***Specific populations***

*Renal impairment*

In patients with mild (eGFR: 60 – < 90 mL/min/1,73 m$^2$), moderate (eGFR: 30 – < 60 mL/min/1,73 m$^2$), severe (eGFR: < 30 mL/min/1,73 m$^2$) renal impairment and patients with kidney failure/ESRD (end stage renal disease) patients, AUC of empagliflozin increased by approximately 18 %, 20 %, 66 % and 48 %, respectively, compared to subjects with normal renal function.

*Hepatic impairment*

In subjects with mild, moderate, and severe hepatic impairment according to the Child-Pugh classification, AUC of empagliflozin increased approximately by 23 %, 47 % and 75 % and $C_{max}$ by approximately 4 %, 23 % and 48 %, respectively, compared to subjects with normal hepatic

function. Based on pharmacokinetics, dosage adjustment may be necessary in patients with severe hepatic impairment.

*Body mass index (BMI)*

No dosage adjustment is necessary based on BMI. Body mass index had no clinically relevant effect on the pharmacokinetics of empagliflozin based on the population pharmacokinetic analysis.

*Gender*

No dosage adjustment is necessary based on gender.

*Elderly patients*

Age did not have a clinically meaningful impact on the pharmacokinetics of empagliflozin based on the population pharmacokinetic analysis.

*Paediatric population*

Studies characterising the pharmacokinetics of empagliflozin in paediatric patients have not been performed.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

***Tablet core:***

Copovidone

Lactose anhydrous

Microcrystalline cellulose

Crospovidone

Colloidal silicon dioxide

Magnesium stearate.

***Film coating:***

*Opadry White containing:*

Hypromellose (E464)

Titanium dioxide (E171)

Macrogol (E1521)

Talc (E553b).

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

24 months.

### 6.4 Special precautions for storage

- Store at or below 25 °C. Protect from moisture.
- Keep blister strip in outer carton until required for use.
- Keep bottle tightly closed.

### 6.5 Nature and contents of container

- Silver aluminium/aluminium blister strip packed in an outer carton. Pack size: 10 tablets.
- White, heavy weight, 60 mL, high-density polyethylene (HDPE) bottle with blue 1 g silica gel sachet and with 33 mm child-resistant closure.

  Pack sizes: 30 and 90 tablets.

Not all pack sizes may be marketed.

### 6.6 Special precautions for disposal and other handling

Any unused medicine should be disposed of in accordance with local requirements.

## 7. HOLDER OF CERTIFICATE OF REGISTRATION

Zydus Healthcare SA (Pty) Ltd

Southdowns Office Park

Building B, Ground Floor

22 Karee Street

Centurion, Pretoria

0157

## 8. REGISTRATION NUMBER(S)

**TUERIZIN 10:** 55/21.2/0628

**TUERIZIN 25:** 55/21.2/0629

## 9. DATE OF FIRST AUTHORISATION

01 August 2023.

## 10. DATE OF REVISION OF THE TEXT

Not applicable.