PROFESSIONAL INFORMATION

SCHEDULING STATUS: S5

1. NAME OF THE MEDICINE

TRAMAZAC SR 100, film-coated tablets

TRAMAZAC SR 150, film-coated tablets

TRAMAZAC SR 200, film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each TRAMAZAC SR 100 tablet contains 100 mg tramadol (as tramadol hydrochloride).

Each TRAMAZAC SR 150 tablet contains 150 mg tramadol (as tramadol hydrochloride).

Each TRAMAZAC SR 200 tablet contains 200 mg tramadol (as tramadol hydrochloride).

Sugar free.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets.

TRAMAZAC SR 100: White to off-white, round shaped, biconvex, film-coated tablets, debossed with “100” on one side and plain on the other side.

TRAMAZAC SR 150: Pale orange, round shaped, biconvex, film-coated tablets, debossed with “150” on one side and plain on the other side.

TRAMAZAC SR 200: Slightly brownish orange, round shaped, biconvex, film-coated tablets, debossed with “200” on one side and plain on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Management of moderate to severe pain.

4.2 Posology and method of administration

Posology

The dosage should be adjusted to the intensity of pain and the sensitivity of the individual patient.

Adults and children over 12 years

The usual initial dose is 100 mg twice daily, preferably in the mornings and evenings.

If pain relief is not adequate, the dose may be increased to 150 mg or 200 mg twice daily.

A total daily dose of 400 mg TRAMAZAC SR should not be exceeded.

Dosage intervals can be adjusted to individual requirements but should be at least 8 hours. The lowest analgesic effective dose should generally be selected.

Special populations

Elderly patients

A downward adjustment of the dose and/or prolongation of the interval between doses are recommended in elderly patients (over 75 years).

Renal insufficiency / dialysis

In patients with renal insufficiency, the elimination of tramadol is delayed. In these patients prolongation of the dosage intervals should be carefully considered according to the patient's requirements. In cases of severe renal insufficiency TRAMAZAC SR is not recommended.

Patients with hepatic impairment

In patients with hepatic insufficiency the elimination of tramadol is delayed. In these patients, prolongation of the dosage intervals should be carefully considered according to the patient's requirements. In cases of severe hepatic insufficiency TRAMAZAC SR is not recommended.

Duration of treatment

Under no circumstances should TRAMAZAC SR be given for longer than absolutely necessary. If the nature and severity of the disease requires long-term pain treatment, careful checks should be carried out initially and at regular intervals to assess efficacy and adverse events, and to what extent further treatment with TRAMAZAC SR is necessary.

Paediatric population

On account of the dosage strength, TRAMAZAC SR is not recommended for children below the age of 12 years.

Method of administration

Oral administration.

Tablets are to be taken whole, not divided or chewed, with sufficient liquid, with or without meals.

4.3 Contraindications

- Hypersensitivity to tramadol hydrochloride, opioids or to any of the excipients in TRAMAZAC SR (see section 6.1).
- Acute intoxication with alcohol, hypnotics, centrally acting analgesics, opioids or psychotropic medicines (due to the risk of respiratory depression).
- Patients taking monoamine oxidase (MAO) inhibitors or within two weeks of their withdrawal (see section 4.5).
- TRAMAZAC SR must not be used for narcotic withdrawal treatment.
- Respiratory depression, or in the presence of cyanosis and excessive bronchial secretions.
- Increased intracranial pressure or central nervous depression due to head injury or cerebral disease.
- Post-operative management in children younger than 18 years of age following tonsillectomy and/or adenoidectomy.
- Epilepsy.

- Pregnancy and lactation (see section 4.6).
- TRAMAZAC SR is not suitable for children under the age of 12 years (see sections 4.2 and 4.4).

4.4 Special warnings and precautions for use

Seizures

Seizures/convulsions have been reported at therapeutic doses and the risk of seizures may be increased in patients exceeding the usual upper daily dose limit. TRAMAZAC SR may increase the seizure risk in patients taking neuroleptics and other medicines that lowers the seizure threshold (see section 4.5). Patients with epilepsy should not take TRAMAZAC SR (see section 4.3).

Shock

TRAMAZAC SR should be used with caution in patients in shock.

Central nervous system (CNS) depressants

Concomitant use of TRAMAZAC SR and sedating medicines such as benzodiazepines or related substances, may result in sedation, respiratory depression, coma and death. The use of TRAMAZAC SR concurrently with other central nervous system medicines is likely to intensify and prolong CNS effects (see section 4.5). Because of these risks, concomitant prescribing with these sedating medicines should be reserved for patients for whom alternative treatment options are not possible. If a decision is made to prescribe TRAMAZAC SR concomitantly with sedating medicines, the lowest effective dose of TRAMAZAC SR should be used, and the duration of the concomitant treatment should be as short as possible. The patients should be monitored closely for signs and symptoms of respiratory depression and sedation. In this respect, it is strongly recommended to inform patients and their caregivers to be aware of these symptoms (see section 4.5).

TRAMAZAC SR should be used with caution in patients with a reduced level of consciousness of

uncertain origin.

Sleep-related breathing disorders

Opioids, such as TRAMAZAC SR, may cause sleep-related breathing disorders, including central sleep apnoea (CSA) and sleep-related hypoxaemia. Opioid use increases the risk of CSA in a dose-dependent fashion. In patients who present with CSA, consider decreasing the total opioid dosage.

Serotonin syndrome

TRAMAZAC SR alone or in combination with other serotonergic medicines may cause serotonin syndrome, a potentially life-threatening condition (see sections 4.5, 4.8 and 4.9).

In the case of concomitant treatment with other serotonergic medicines, careful observation of the patient is advised, particularly during treatment initiation and dose escalations.

Symptoms of serotonin syndrome may include mental status changes, autonomic instability, neuromuscular abnormalities and/or gastrointestinal symptoms.

If serotonin syndrome is suspected, a dose reduction or discontinuation of therapy should be considered depending on the severity of the symptoms. Withdrawal of the serotonergic medicines usually brings about a rapid improvement.

Risk of tolerance, dependence and withdrawal symptoms

Tolerance, psychic and physical dependence may develop, especially after long-term use. At therapeutic doses, TRAMAZAC SR has the potential to cause withdrawal symptoms. Symptoms of medicine withdrawal syndrome, similar to those occurring during opiate withdrawal, may occur as follows: agitation, anxiety, nervousness, insomnia, hyperkinesia, tremor and gastrointestinal symptoms. Other symptoms that have been seen with TRAMAZAC SR discontinuation include:

panic attacks; severe anxiety, hallucinations, paraesthesia, tinnitus and unusual CNS symptoms (i.e. confusion, delusions, depersonalisation, derealisation and paranoia).

Cases of dependence and abuse have been reported. The risks are increased in individuals with current or past history or family history of substance misuse disorder (including alcohol misuse) or with a mental health disorder (e.g. major depression or anxiety). Because of this potential, the clinical need for continued analgesic treatment should be reviewed regularly. When a patient no longer requires therapy with TRAMAZAC SR, it may be advisable to taper the dose gradually to prevent symptoms of withdrawal.

TRAMAZAC SR should not be used in opioid-dependent patients. TRAMAZAC SR can reinstate physical dependence in patients that have been previously dependent or chronically using other opioids. In patients with a tendency to abuse drugs, a history of drug dependence or who are chronically using opioids, treatment with TRAMAZAC SR is not recommended.

A comprehensive patient history should be taken to document concomitant medicines, including over-the-counter medicines and medicines obtained online, as well as past and present medical and psychiatric conditions.

Patients may find that treatment is less effective with chronic use and express a need to increase the dose to obtain the same level of pain control as initially experienced. Patients may also supplement their treatment with additional pain relievers. These could be signs that the patient is developing tolerance. The risks of developing tolerance should be explained to the patient.

Overuse or misuse may result in overdose and/or death. It is important that patients only use medicines that are prescribed for them at the dose they have been prescribed and do not give this medicine to anyone else. Patients should be closely monitored for signs of misuse, abuse or addiction.

TRAMAZAC SR is not a suitable substitute in opioid-dependent patients. TRAMAZAC SR does not suppress morphine withdrawal symptoms although it is an opioid agonist.

TRAMAZAC SR should not be used in patients who are suicidal.

Opioid-sensitive patients

TRAMAZAC SR should be used with care in patients with increased reactivity to opioids.

Opioid-induced hyperalgesia

Opioid-induced hyperalgesia (OIH) is a paradoxical response to an opioid, such as TRAMAZAC SR, in which there is an increase in pain perception despite stable or increased opioid exposure. It differs from tolerance, in which higher opioid doses are required to achieve the same analgesic effect or treat recurring pain. OIH may manifest as increased levels of pain, more generalised pain (i.e. less focal), or pain from ordinary (i.e. non-painful) stimuli (allodynia) with no evidence of disease progression. When OIH is suspected, the dose of TRAMAZAC SR should be reduced or tapered off, if possible.

CYP2D6 metabolism

Tramadol, as in TRAMAZAC SR, is metabolised by the liver enzyme CYP2D6. If a patient has a deficiency or is completely lacking this enzyme, an adequate analgesic effect may not be obtained. However, if the patient is an ultra-rapid metaboliser of the CYP2D6 enzyme, there is a risk of developing side effects of opioid toxicity even within the recommended dosage range.

General symptoms of opioid toxicity include confusion, somnolence, shallow breathing, small pupils, nausea, vomiting, constipation and lack of appetite. In severe cases this may include symptoms of circulatory and respiratory depression, which may be life-threatening and very rarely fatal.

Renal or hepatic impairment

TRAMAZAC SR should be used with caution in patients with renal or hepatic impairment and avoided if severe (see section 4.2).

Respiratory disorders

TRAMAZAC SR should be used with caution in patients with disorders of the respiratory function, including asthma.

Adrenal insufficiency

Opioid analgesics, such as TRAMAZAC SR, may occasionally cause reversible adrenal insufficiency requiring monitoring and glucocorticoid replacement therapy. Symptoms of acute or chronic adrenal insufficiency may include severe abdominal pain, nausea and vomiting, low blood pressure, extreme fatigue, decreased appetite and weight loss.

Hyponatraemia

Hyponatraemia may occur with the use of TRAMAZAC SR, usually in patients with predisposing risk factors, such as elderly patients and/or patients using concomitant medicines that may cause hyponatraemia. This hyponatraemia appears to be the result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH) and resolves with discontinuation of TRAMAZAC SR and appropriate treatment (e.g. fluid restriction). During TRAMAZAC SR treatment, monitoring for signs and symptoms of hyponatraemia is recommended for patients with predisposing risk factors.

Minor pain

TRAMAZAC SR should not be used for the treatment of minor pain.

Other conditions

TRAMAZAC SR should be used with caution in patients with hypothyroidism, prostatic hyperplasia,

hypotension, inflammatory or obstructive bowel disorders or myasthenia gravis.

Paediatric population

Children under 12 years

TRAMAZAC SR is not suitable for children under the age of 12 years (see sections 4.2 and 4.3).

Post-operative use in children

TRAMAZAC SR should not be given post-operatively to children (under 18 years of age) after tonsillectomy and/or adenoidectomy for obstructive sleep apnoea or for post-operative pain relief as it may lead to rare, but life-threatening adverse events (see section 4.3).

Children with compromised respiratory function

TRAMAZAC SR is not recommended for use in children in whom respiratory function may be compromised, including neuromuscular disorders, severe cardiac or respiratory conditions, upper respiratory or lung infections, multiple trauma or extensive surgical procedures. These factors may worsen symptoms of opioid toxicity.

4.5 Interaction with other medicines and other forms of interaction

Monoamine oxidase inhibitors (MAOIs)

Because of its inhibitory effect on serotonin uptake, TRAMAZAC SR should not be used concomitantly with MAOIs or within 14 days after discontinuing such treatment (see section 4.3). Life-threatening interactions with MAO-inhibitors affecting the central nervous system, respiratory and cardiovascular function may occur during treatment with TRAMAZAC SR.

Central nervous system (CNS) depressants

Concomitant administration of TRAMAZAC SR with other CNS depressants, including alcohol and anaesthetics, may potentiate the CNS depressant effects (see section 4.4). The duration of anaesthesia may be prolonged when TRAMAZAC SR is combined with barbiturates.

The concomitant use of opioids, such as TRAMAZAC SR, with sedating medicines (e.g. benzodiazepines or related substances) increases the risk of sedation, respiratory depression, coma and death because of the additive CNS depressant effect. The dose of TRAMAZAC SR and the duration of concomitant use should be limited (see section 4.4).

Serotonergic medicines

Concomitant therapeutic use of TRAMAZAC SR and serotonergic medicines, such as lithium, selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), MAO inhibitors (see section 4.3), tricyclic antidepressants and mirtazapine may cause serotonin syndrome, a potentially life-threatening condition (see sections 4.4, 4.8 and 4.9).

Seizure threshold-lowering medicines

TRAMAZAC SR can induce convulsions and increase the potential for selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants, antipsychotics and other seizure threshold-lowering medicines (such as neuroleptics, bupropion, mirtazapine, tetrahydrocannabinol) to cause convulsions (see section 4.4).

Anticoagulants

Caution should be exercised during concomitant treatment with TRAMAZAC SR and anticoagulants (e.g. warfarin) as it may cause increased international normalised ratio (INR) with major bleeding and ecchymoses.

The action of warfarin on blood clotting may be affected and small areas of bleeding under the skin may appear when used in combination with TRAMAZAC SR.

CYP2D6 and CYP3A4 inhibitors

CYP2D6 inhibitors (such as amitriptyline, fluoxetine, paroxetine) and CYP3A4 inhibitors (such as ketoconazole and erythromycin) may inhibit the metabolism of tramadol (*N*-demethylation) and the

metabolism of the active *O*-demethylated metabolite.

CYP3A4 inducers

CYP3A4 inducers (such as rifampicin and St John's wort) may induce the metabolism of tramadol (*N*-demethylation) and the metabolism of the active *O*-demethylated metabolite, reducing the therapeutic effect.

Carbamazepine

Administration of TRAMAZAC SR with carbamazepine (enzyme inducer) may reduce the serum concentrations, lower the analgesic effect and shorten the duration of action of TRAMAZAC SR.

Ondansetron

The antiemetic 5-HT3 antagonist ondansetron may increase the requirement of TRAMAZAC SR in patients with post-operative pain. TRAMAZAC SR may decrease the antiemetic efficacy of ondansetron.

Cimetidine

Simultaneous administration with cimetidine (enzyme inhibitor) is associated with clinically insignificant changes in serum concentrations of tramadol.

4.6 Fertility, pregnancy and lactation

TRAMAZAC SR is contraindicated during pregnancy and lactation (see section 4.3).

Pregnancy

Safety during pregnancy and lactation has not been established.

Therefore, TRAMAZAC SR tablets should not be used in pregnant women. TRAMAZAC SR crosses the placenta. Animal studies with TRAMAZAC SR revealed effects on organ development, ossification and neonatal mortality.

The repeated administration of TRAMAZAC SR tablets during pregnancy may lead to habituation in the unborn child. The child may experience withdrawal symptoms after birth (see section 4.3).

Breastfeeding

TRAMAZAC SR passes into breastmilk. Mothers on TRAMAZAC SR tablets should not breastfeed their infants.

Fertility

Post-marketing surveillance does not suggest an effect of tramadol, as in TRAMAZAC SR on fertility. Animal studies did not show an effect of tramadol on fertility.

4.7 Effects on ability to drive and use machines

TRAMAZAC SR may cause side effects, such as somnolence and dizziness (see section 4.8) and therefore affect the ability to drive a vehicle or use machinery. This applies particularly in conjunction with other psychotropic medicines, including alcohol (see section 4.5). Caution is advised before driving a vehicle or operating machinery until the effects of TRAMAZAC SR are known.

4.8 Undesirable effects

Summary of the safety profile

The most frequent side effects during treatment with TRAMAZAC SR are nausea and dizziness, both occurring in more than 10 % of patients.

List of adverse reactions

Immune system disorders

Frequent:	allergic reactions (e.g. dyspnoea, bronchospasm, wheezing) and anaphylaxis
Less frequent:	angioedema

Metabolism and nutrition disorders

Frequent: anorexia

Less frequent: changes in appetite

Frequency unknown: hypoglycaemia

Psychiatric disorders

Frequent: depression

Less frequent: medicine dependence, withdrawal reactions (see section 4.4), mood changes (euphoria, dysphoria), confusion, hallucinations, sleep disorders, delirium, agitation, anxiety, nervousness, restlessness, nightmares, changes in activity (usually suppression, occasionally increase), decreased cognitive and sensory perception (such as decision behaviour, perception disorders)

Nervous system disorders

Frequent: sedation, somnolence, dizziness, vertigo, muzziness, headache

Less frequent: speech disorders, hypaesthesia, paraesthesia, amnesia, epileptiform convulsions, involuntary muscle contractions, abnormal coordination, syncope, abnormal gait, abnormal sensations, trembling, tremors. Convulsions occur mainly after administration of high doses of TRAMAZAC SR or after concomitant treatment with medicines which can lower the seizure threshold (see sections 4.4 and 4.5).

Frequency unknown: serotonin syndrome

Eye disorders

Less frequent: miosis, mydriasis, blurred vision

Cardiac disorders

Less frequent: bradycardia, tachycardia, palpitations, dysrhythmia, chest pain, myocardial infarction

Vascular disorders

Less frequent: flushing, orthostatic hypotension, cardiovascular collapse, fainting, hypertension

Respiratory, thoracic and mediastinal disorders

Less frequent: bronchospasm, nasal congestion, rhinorrhoea, respiratory depression, dyspnoea

Frequency unknown: slow breathing, worsening of asthma, bronchitis, hiccups

Gastrointestinal disorders

Frequent: nausea, vomiting, dry mouth, dyspepsia, constipation, diarrhoea, abdominal pain

Less frequent: retching, appendicitis, bloating, cholecystitis, cholelithiasis, pancreatitis.

Hepatobiliary disorders

Less frequent: increase in liver enzymes (ALT and AST)

Skin and subcutaneous tissue disorders

Frequent: hyperhidrosis, dermal reactions (e.g. pruritis, skin rash)

Less frequent: toxic epidermal necrolysis, Stevens-Johnson syndrome, urticaria, vesicles, cellulitis, dermatitis

Musculoskeletal and connective tissue disorders

Less frequent: muscle weakness, arthralgia, myalgia, joint stiffness or swelling, back pain

Renal and urinary disorders

Less frequent: micturition disorders (urinary retention, urinary frequency, haematuria, dysuria)

General disorders and administration site conditions

Frequent: asthenia, influenza-like illness, fatigue

Less frequent: hypothermia (rigors).

Description of selected adverse reactions

Hyponatraemia:

Hyponatraemia and/or SIADH may occur with TRAMAZAC SR, usually in patients with predisposing risk factors, such as the elderly or those using concomitant medicines that may cause hyponatraemia (see section 4.4).

Post-marketing experience

The following side effects have been reported for opioid-containing medicines, such as contained in TRAMAZAC SR:

Gastrointestinal disorders: increased risk of abdominal pain, including pancreatitis.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of TRAMAZAC SR is important. It allows continued monitoring of the benefit/risk balance of TRAMAZAC SR. Health care providers are asked to report any suspected adverse reactions to the South African Health Products Regulatory Authority (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

Symptoms

Following an overdose with TRAMAZAC SR, symptoms similar to those of other centrally acting analgesics (opioids) are to be expected. These include in particular constriction of the pupil of the eye, vomiting, slow heartbeat, hypotension, cardiovascular collapse, weakness, consciousness disorders, coma, convulsions, cold clammy skin, dizziness, rhabdomyolysis progressing to renal failure, respiratory depression and respiratory arrest.

Serotonin syndrome has also been reported (see section 4.4).

Treatment

The general emergency measures apply. Keep the respiratory tract open, maintain respiration and circulation depending on the symptoms. Suitable measures should be taken to avoid aspiration dangers.
Treatment of restlessness is symptomatic and supportive.

Respiratory depression can be antagonised with a pure opiate antagonist (naloxone).
Administration of naloxone should be done with caution because it may precipitate seizures.

Convulsions should be treated with intravenous diazepam.

Gastrointestinal decontamination with activated charcoal is only recommended within 2 hours after TRAMAZAC SR intake. Gastrointestinal decontamination at a later time point may be useful in case of intoxication with exceptionally large quantities.

Tramadol, as in TRAMAZAC SR, is minimally eliminated from the serum by haemodialysis or haemofiltration. Treatment of acute intoxication with TRAMAZAC SR with haemodialysis or haemofiltration alone is therefore not suitable for detoxification.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 2.9 Other analgesics.

Pharmacotherapeutic group: Other opioids.

ATC code: N02AX02.

Mechanism of action

Tramadol hydrochloride is a centrally acting synthetic opioid analgesic binding to specific opioid receptors. It is a non-selective, pure agonist at mu (μ), delta (δ) and kappa (κ) opioid receptors with a higher affinity for the μ receptor. Other mechanisms, which may contribute to its analgesic effect, are inhibition of neuronal re-uptake of norepinephrine (noradrenaline) and enhancement of serotonin release.

Tramadol hydrochloride does not promote histamine release.

5.2 Pharmacokinetic properties

Absorption

Tramadol hydrochloride is readily absorbed following oral administration. Oral bioavailability is approximately 68 % after a single dose and increases to 90 % at steady state. Onset of action is dose dependent but generally occurs within one hour of dosing, peaking within 2 to 3 hours. Duration of analgesia is about 6 hours. The rate or extent of absorption is not significantly affected by co-administration with food.

Distribution

The relationship between serum concentrations and the analgesic effect is dose dependent but varies considerably. Patients devoid of CYP2D6 may need higher doses of tramadol to achieve adequate analgesia.

Biotransformation

The inhibition of one or both types of isoenzymes CYP3A4 and CYP2D6 involved in the biotransformation of tramadol may affect the plasma concentration of tramadol or its active metabolite. Tramadol crosses the blood-brain and placental barriers. Small amounts are excreted in breast milk unchanged or as the metabolite mono-*O*-desmethyltramadol (M1).

Elimination

Tramadol is mainly metabolised in the liver (90 %). Tramadol has a linear pharmacokinetic profile within the therapeutic dosage range. Tramadol is metabolised by *N*- and *O*-demethylation via the cytochrome P450 isoenzymes CYP3A4, CYP2D6, glucuronidation or sulphation in the liver. The metabolite *O*-desmethyltramadol is pharmacologically active.

Tramadol hydrochloride and its metabolites are almost completely excreted in the urine. The elimination half-life is 5 to 7 hours, but is prolonged in impaired hepatic and renal function.

Biliary excretion of these components is quantitatively insignificant and is therefore subject to hepatic metabolism and renal elimination. In patients with liver cirrhosis, elimination half-lives of 13,3 ± 4,9 h (tramadol) and 18,5 ± 9,4 h (*O*-desmethyltramadol), have been determined. In patients with renal insufficiency (creatinine clearance < 5 mL/min) the values were 11,0 ± 3,2 h (tramadol) and 16,9 ± 3,0 h (M1) respectively.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core

Magnesium stearate

Microcrystalline cellulose

Polyethylene oxide

Povidone K-30.

Tablet coating

TRAMAZAC SR 100: Opadry White 03F58750 (containing hypromellose, titanium dioxide, polyethylene glycol and talc).

TRAMAZAC SR 150: Opadry Orange 03F53885 (containing hypromellose, titanium dioxide, polyethylene glycol, talc, iron oxide yellow and iron oxide red).

TRAMAZAC SR 200: Opadry Pink 03F84640 (containing hypromellose, titanium dioxide, polyethylene glycol, talc, iron oxide red, iron oxide yellow and quinoline yellow).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

Store at or below 25 °C.

6.4 Special precautions for storage

Protect from light and moisture.

Keep the blister strips in the outer carton until required for use.

6.5 Nature and contents of container

White opaque PVC/PVDC/aluminium blister strips containing 10 tablets per blister strip. 10, 30, 60 or 100 tablets will be packed into a cardboard box.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Zydus Healthcare SA (Pty) Ltd

Southdowns Office Park

Building B, Ground Floor

22 Karee Street

Centurion 0157

8. REGISTRATION NUMBERS

TRAMAZAC SR 100: 44/2.9/0496

TRAMAZAC SR 150: 44/2.9/0497

TRAMAZAC SR 200: 44/2.9/0498

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

19 April 2013

10. DATE OF REVISION OF THE TEXT

07 June 2024