SCHEDULING STATUS

S5

1. NAME OF THE MEDICINE

ZOLPIDEM 12,5 mg MR DYNA modified release tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ZOLPIDEM 12,5 mg MR DYNA modified release tablet contains 12,5 mg zolpidem tartrate.

ZOLPIDEM 12,5 mg MR DYNA contains sugar - lactose monohydrate: 120,85 mg.

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Film-coated modified release tablet.

ZOLPIDEM 12,5 mg MR DYNA are blue coloured, round, biconvex, film coated tablets debossed with “E62” on one side and “LU” on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Short term treatment of insomnia.

ZOLPIDEM 12,5 mg MR DYNA is indicated in adults below the age of 65 years, and only when the disorder is severe, disabling or subjecting the individual to extreme distress.

4.2 Posology and method of administration

Posology:

ZOLPIDEM 12,5 mg MR DYNA acts rapidly and therefore should be taken orally immediately before bedtime, or in bed. For faster sleep onset, ZOLPIDEM 12,5 mg MR DYNA should not be administered with or immediately after a meal (see section 5.2).

Tablets should not be halved, crushed or chewed.

ZOLPIDEM 12,5 mg MR DYNA should be taken in a single intake and not be readministered during the same night.

Treatment should be as short as possible. Generally, the duration of treatment varies from four days to two weeks with a maximum, including the tapering process, of four weeks. In certain cases, extension beyond the maximum treatment period may be necessary; if so, it should not take place without re-evaluation of the patient's status. Treatment should be started with the lowest recommended dose. The maximum dose should not be exceeded.

Adults (< 65 years): The recommended daily dose is 12,5 mg. The lowest effective daily dose of ZOLPIDEM 12,5 mg MR DYNA is 12,5 mg, and must not exceed 12,5 mg.

<u>Special populations</u>

Hepatic impairment: ZOLPIDEM 12,5 mg MR DYNA should not be used in patients with severe hepatic impairment (see section 4.3).

Renal impairment: No dosage adjustment is required.

Elderly: As ZOLPIDEM 12,5 mg MR DYNA has not been evaluated in elderly patients (≥ 65 years). ZOLPIDEM 12,5 mg MR DYNA is not recommended in this population.

Paediatric population

As safety and efficacy in paediatric patients below the age of 18 years have not been established ZOLPIDEM 12,5 mg MR DYNA should not be prescribed in this population (see sections 4.3 and 4.4).

Method of administration

Oral administration.

4.3 Contraindications

- hypersensitivity to zolpidem tartrate or to any other ingredient of ZOLPIDEM 12,5 mg MR DYNA (see section 6.1)
- children under the age of 18 years
- sleep apnoea syndrome
- myasthenia gravis

- severe hepatic impairment
- Acute and/ or severe respiratory impairment
- pregnancy and lactation (see section 4.6).

4.4 Special warnings and precautions for use

General information related to effects seen following administration of hypnotics, which should be taken into account by the prescribing medical practitioner are described below:

The cause of insomnia should be identified wherever possible, and the underlying factors treated before a hypnotic is prescribed.

The failure of insomnia to remit after a 7-14 day course of treatment may indicate the presence of a primary psychiatric or physical disorder, and the patient should be carefully re-evaluated at regular intervals.

Amnesia:

ZOLPIDEM 12,5 mg MR DYNA may introduce anterograde amnesia. The condition occurs most often several hours after ingesting the products and therefore to reduce the risk, patients should ensure that they get a full night's sleep (7-8 hours) before being active.

Other psychiatric and paradoxical reactions:

Other psychiatric and paradoxical reactions like restlessness, exacerbated insomnia, agitation, irritability, aggression, delusion, anger, nightmares, hallucinations, abnormal behaviour and other behavioural effects are known to occur when using ZOLPIDEM 12,5 mg MR DYNA.

Should this occur, use of the product should be discontinued. These reactions are most likely to occur in the elderly.

Somnambulism and associated behaviours:

Sleep walking and other associated behaviours such as “sleep driving”, preparing and eating food, making phone calls or having sex, with amnesia for the event have been reported in patients who have taken ZOLPIDEM 12,5 mg MR DYNA and were not fully awake. The use of alcohol and other CNS-depressants with ZOLPIDEM 12,5 mg MR DYNA appears to increase the risk of such behaviours, as does the use of ZOLPIDEM 12,5 mg MR DYNA at doses exceeding the maximum recommended dose. Discontinuation of ZOLPIDEM 12,5 mg MR DYNA should be strongly considered for patients who report such behaviours.

Psychomotor impairment:

The risk of psychomotor impairment, including impaired driving ability, is increased if:
ZOLPIDEM 12,5 mg MR DYNA is taken within less than 7–8 hours before performing activities that require mental alertness, a dose higher than the recommended dose is taken, or
ZOLPIDEM 12,5 mg MR DYNA is co-administered with other CNS depressants, alcohol, or with other medicines that increase the blood levels of ZOLPIDEM 12,5 mg MR DYNA.

Medicine tolerance:

Some loss of efficacy to the hypnotic effects of ZOLPIDEM 12,5 mg MR DYNA may develop after repeated use for a few weeks.

Dependence:

Use of ZOLPIDEM 12,5 mg MR DYNA may lead to the development of physical and psychological dependence. The risk of dependence increases with dose and duration of treatment; it is also greater in patients with a history of psychiatric disorders and/or alcohol or drug abuse. These patients should be under careful surveillance when receiving hypnotics.
Once physical dependence has developed, abrupt termination of treatment will be accompanied by withdrawal symptoms. These may consist of headaches or muscle pain, extreme anxiety and tension, restlessness, confusion and irritability. In severe cases the following symptoms may occur:
derealisation, depersonalisation, hyperacusis, numbness and tingling of the extremities, hypersensitivity to light, noise and physical contact, hallucinations or epileptic seizures.
Dependence has been reported with ZOLPIDEM 12,5 mg MR DYNA (see section 4.8).

Rebound insomnia:

A transient syndrome, whereby the symptoms that led to treatment with ZOLPIDEM 12,5 mg MR DYNA recur in an enhanced form, may occur on withdrawal of ZOLPIDEM 12,5 mg MR DYNA treatment. It may be accompanied by other reactions including mood changes, anxiety and restlessness. There are indications that, in the case of ZOLPIDEM 12,5 mg MR DYNA with a short duration of action, withdrawal phenomenon can become manifest within the dosage interval, especially when the dosage is high.
The rebound phenomenon, if it occurs with ZOLPIDEM 12,5 mg MR DYNA, was limited to the

first night after the medicine discontinuation in clinical studies (see section 5.2).

It is important that the patients should be aware of the possibility of rebound phenomenon, thereby minimising anxiety over such symptoms should they occur when the medicine is discontinued.

Respiratory impairment:

As hypnotics have the capacity to depress respiratory drive, precautions should be observed if ZOLPIDEM 12,5 mg MR DYNA is prescribed to patients with mild to moderate compromised respiratory function.

Risks from concomitant use with opioids:

Concomitant use of ZOLPIDEM 12,5 mg MR DYNA and other sedative-hypnotic medicines with opioids may result in sedation, respiratory depression, coma and death. Because of these risks, reserve concomitant prescribing of opioids and benzodiazepines for use in patients for whom alternative treatment options are inadequate.

If a decision is made to prescribe ZOLPIDEM 12,5 mg MR DYNA concomitantly with opioids, prescribe the lowest effective dosages and minimum duration of concomitant use, and follow patients closely for signs and symptoms of respiratory depression and sedation (see section 4.5).

Patients with a history of alcohol or drug abuse:

ZOLPIDEM 12,5 mg MR DYNA should be used with extreme caution in these patients (see

section 4.5 and 4.7).

Psychotic illness:

ZOLPIDEM 12,5 mg MR DYNA is not recommended for the primary treatment of psychotic illness.

Suicidality and depression:

ZOLPIDEM 12,5 mg MR DYNA should not be used alone to treat depression or anxiety associated with depression (suicide may be precipitated in such patients). As suicidal tendencies may be present, the least amount of ZOLPIDEM 12,5 mg MR DYNA that is feasible, should be supplied to these patients because of the possibility of intentional overdosage by the patient.

A pre-existing depression may be unmasked during the use of ZOLPIDEM 12,5 mg MR DYNA. Since insomnia may be a symptom of depression, the patient should be re-evaluated if insomnia persists.

Severe injuries:

Due to its pharmacological properties, ZOLPIDEM 12,5 mg MR DYNA can cause drowsiness and a decreased level of consciousness, which may lead to falls and consequently to severe injuries.

Patients with Long QT syndrome:

An *in vitro* cardiac electrophysiological study showed that under experimental conditions using very high concentration and pluripotent stem cells ZOLPIDEM 12,5 mg MR DYNA may reduce the hERG (human Ether-à-go-go-Related Gene) related potassium currents. The potential consequence in patients with congenital long QT syndrome is unknown. As a precaution, the benefit/risk ratio of ZOLPIDEM 12,5 mg MR DYNA treatment in patients with known congenital long QT syndrome should be carefully considered.

Special populations:

Hepatic impairment:

ZOLPIDEM 12,5 mg MR DYNA should be used with caution in patients with mild to moderate hepatic impairment. ZOLPIDEM 12,5 mg MR DYNA should not be used in patients with severe hepatic impairment as it may contribute to encephalopathy (see section 4.3 and 5.2).

Paediatric population

As safety and efficacy in subjects below the age of 18 have not been established ZOLPIDEM 12,5 mg MR DYNA should not be used in this population (see section 4.3).

Information on excipients of ZOLPIDEM 12,5 mg MR DYNA:

ZOLPIDEM 12,5 mg MR DYNA contains lactose monohydrate. Patients with the rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take ZOLPIDEM 12,5 mg MR DYNA.

4.5 Interaction with other medicines and other forms of interaction

Combination not recommended:

Concomitant use with alcohol:

The sedative effect may be enhanced when the product is used in combination with alcohol. This affects the ability to drive or use machines.

Combinations to be taken into account:

CNS depressants:

Enhancement of the central depressive effect may occur in cases of concomitant use with antipsychotics (neuroleptics), hypnotics, anxiolytics/sedatives, antidepressant medicines, narcotic analgesics, antiepileptic medicines, anaesthetics and sedative antihistamines.
Concomitant use of ZOLPIDEM 12,5 mg MR DYNA with these medicines may increase drowsiness and psychomotor impairment, including impaired driving ability.
Concomitant use with hypnotics may enhance the euphoric effect of narcotic analgesics, which may lead to an increase in psychological dependence.

Opioids:

The concomitant use of benzodiazepines and other sedative-hypnotic medicines, including ZOLPIDEM 12,5 mg MR DYNA, and opioids increases the risk of sedation, respiratory depression, coma, and death because of additive CNS depressant effect. The dosage and duration of concomitant use should be limited (see section 4.4).

Cytochrome P450 inhibitors:

Compounds, which inhibit cytochrome P450, may enhance the activity of ZOLPIDEM 12,5 mg MR DYNA. Coadministration of ZOLPIDEM 12,5 mg MR DYNA with ketoconazole (200 mg twice daily), a potent CYP3A4 inhibitor, produced a 64 % increase in ZOLPIDEM 12,5 mg MR DYNA plasma levels. A routine dosage adjustment of ZOLPIDEM 12,5 mg MR DYNA is not necessary, but patients should be advised that the sedative effects might be enhanced.

However, co-administration of ZOLPIDEM 12,5 mg MR DYNA with itraconazole or fluconazole did not produce any significant changes in ZOLPIDEM 12,5 mg MR DYNA pharmacokinetics and pharmacodynamics.

Fluvoxamine is a strong inhibitor of CYP1A2 and a moderate to weak inhibitor of CYP2C9 and CYP3A4. Coadministration of fluvoxamine may increase blood levels of ZOLPIDEM 12,5 mg MR DYNA; concurrent use is not recommended.

Ciprofloxacin has been shown to be a moderate inhibitor of CYP1A2 and CYP3A4. Co-administration of ciprofloxacin may increase blood levels of ZOLPIDEM 12,5 mg MR DYNA concurrent use is not recommended.

Rifampicin (CYP3A4 inducer):

The pharmacodynamic effect of ZOLPIDEM 12,5 mg MR DYNA is decreased due to an increase in liver metabolism.

St. John's Wort (CYP3A4 inducer):

Use of St. John's Wort, a CYP3A4 inducer, in combination with ZOLPIDEM 12,5 mg MR DYNA may decrease blood levels of zolpidem and is not recommended.

Antiretrovirals:

HIV-protease inhibitors such as *ritonavir* may increase plasma concentrations of zolpidem with a risk of extreme sedation and respiratory depression; use together is possible provided the patient is carefully monitored for excessive sedative effects.

Other:

No significant pharmacokinetic interactions were observed, when ZOLPIDEM 12,5 mg MR DYNA was administered with warfarin, digoxin, ranitidine or cimetidine.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

If ZOLPIDEM 12,5 mg MR DYNA is prescribed to a woman of childbearing potential, she should be warned to contact her medical practitioner about stopping ZOLPIDEM 12,5 mg MR DYNA if she intends to become, or suspects that she is pregnant.

Pregnancy

Safety in pregnancy have not been established. The use of ZOLPIDEM 12,5 mg MR DYNA

during pregnancy should be avoided.

If for compelling medical reasons ZOLPIDEM 12,5 mg MR DYNA is administered during the late phase of pregnancy or during labour, effects on the neonate, such as hypothermia, hypotonia and moderate respiratory depression, can be expected due to the pharmacological action of zolpidem.

Infants born to mothers who took hypnotics including ZOLPIDEM 12,5 mg MR DYNA, chronically during the latter stages of pregnancy may have developed physical dependence and may be at risk of developing withdrawal symptoms in the postnatal period.

Breastfeeding

As zolpidem is excreted in breast milk, the use of ZOLPIDEM 12,5 mg MR DYNA in breastfeeding mothers is not recommended.

Fertility

There is no data on fertility with ZOLPIDEM 12,5 mg MR DYNA.

4.7 Effects on ability to drive and use machines:

Vehicle drivers and machine operators should be warned that, there might be a possible risk of adverse reactions including drowsiness, prolonged reaction time, dizziness, feeling drugged, sleepiness, blurred/double vision, reduced alertness and impaired driving the morning after the therapy. In order to minimise this risk a full night of sleep (7-8 hours) is recommended. The risk is increased by concomitant intake of alcohol and other CNS depressants. Patients should be

warned not to use alcohol or other psychoactive substances when taking ZOLPIDEM 12,5 mg MR DYNA (see section 4.4, 4.5 and 4.8).

4.8 Undesirable effects

Summary of the safety profile

The reaction most commonly associated with discontinuation in a 3-week study was somnolence, whilst in a 6-month study, anxiety, restlessness or agitation, (depression, major depression or depressed mood) were the most common adverse effects that resulted after discontinuation of treatment.

Short-term studies indicate the most common adverse effects to be headache, next-day somnolence and dizziness. A six month study revealed the most common adverse effects to be the same as those indicated in short-term use, with the addition of higher incidence of anxiety.

There is evidence of a dose-relationship for adverse effects associated with ZOLPIDEM 12,5 mg MR DYNA use, particularly for certain CNS events. The occurrence is most frequently in elderly patients.

Tabulated list of adverse effects

System Organ Class	Frequency	Side effects

Infections and Infestations	Frequent Less frequent	Influenza Gastroenteritis, labyrinthitis, lower respiratory tract infection, otitis externa, upper respiratory tract infection
Blood and lymphatic system disorders	Less frequent	Anaemia, hyperhaemoglobinaemia, leukopenia, lymphadenopathy, macrocytic anaemia, thrombosis
Immune system disorders	Less frequent Frequency unknown	Infection, abscess, herpes simplex zoster, otitis externa, otitis media, allergic reaction, allergy aggravated, anaphylactic shock Angioedema
Metabolism and nutrition disorders	Less frequent	Appetite disorder, hyperglycaemia, thirst, gout, hypercholesterolaemia, hyperlipidaemia, increased alkaline phosphatase, increased BUN, periorbital oedema, appetite increased, weight decreased

Psychiatric disorders	Frequent	Anxiety, psychomotor retardation, disorientation
	Less frequent	Depression, hallucination, apathy, binge eating, confusional state, depersonalisation, depressed mood, disinhibition, euphoric mood, hallucination visual, hypnagogic hallucination, mood swings, nightmares, stress symptoms
	Frequency unknown	Sleep walking, restlessness, aggression, delusion, anger, abnormal behaviour (see section 4.4), dependence (withdrawal symptoms, or rebound effects may occur after treatment discontinuation)

Nervous system disorders	Frequent	Headache, somnolence, dizziness, memory disorders (memory impairment, amnesia, anterograde amnesia), disturbance in attention, drugged feeling, euphoria, insomnia, lethargy, light-headedness, dry mouth
	Less frequent	Balance disorder, hypoaesthesia, paraesthesia, ataxia, burning sensation, dizziness postural, dysgeusia, involuntary muscle contractions, tremor, agitation, decreased cognition, detached, difficulty concentrating, dysarthria, emotional lability, illusion, leg cramps, migraine, nervousness, sleeping (after daytime dosing)

		speech disorder, stupor, abnormal gait, abnormal thinking, aggressive reaction, apathy, decreased libido, delusion, dementia, depersonalisation, neuralgia, neuritis, neuropathy, neurosis, panic attacks, paresis, personality disorder, somnambulism, suicide attempts, tetany, yawning, increased sweating, pallor, syncope, altered saliva, flushing, impotence, increased saliva, tenesmus
Eye disorders	Frequent Less frequent	Visual disturbance, diplopia Eye redness, vision blurred, altered visual depth perception, asthenopia, eye irritation, eye pain, scleritis, conjunctivitis, corneal ulceration, abnormal lacrimation, photopsia, abnormal accommodation, glaucoma
Ear and labyrinth disorders	Less frequent	Vertigo, tinnitus

Cardiac disorders	Less frequent	Palpitations, tachycardia, angina pectoris, dysrhythmia, circulatory failure, extrasystoles, myocardial infarction, pulmonary embolism, pulmonary oedema, ventricular tachycardia
Vascular disorders	Less frequent	Postural hypotension, hypotension, cerebrovascular disorder, hypertension, arteritis, hypertension aggravated, phlebitis, varicose veins
Respiratory, thoracic and mediastinal disorders	Frequent Less frequent	Sinusitis Cough, dry throat, throat irritation, bronchitis, dyspnoea, bronchospasm, respiratory depression, epistaxis, hypoxia, laryngitis, pneumonia
Gastrointestinal disorders	Frequent Less frequent	Nausea, constipation, diarrhoea, dyspepsia, hiccup Vomiting, abdominal discomfort, flatulence, frequent bowel movements, gastro-oesophageal reflux disease, enteritis, eructation, gastritis, haemorrhoids, intestinal obstruction, rectal haemorrhage, tooth caries

Blood and lymphatic disorder	Less frequent	Anaemia, hyperhaemoglobinaemia, leukopenia, lymphadenopathy, macrocytic anaemia, purpura, porphyria
Hepato-biliary disorders	Frequency unknown	Hepatocellular, cholestatic or mixed liver injury
Skin and subcutaneous tissue disorders	Less frequent	Rash, urticaria, contact dermatitis, skin wrinkling, pruritus, acne, bullous eruption, furunculosis
Musculoskeletal, connective tissue and bone disorders	Frequent Less frequent Frequency unknown	Myalgia, muscle cramp, neck pain, back pain Arthralgia, arthritis, arthrosis, sciatica, tendonitis Muscle weakness
Renal and urinary disorders	Frequent Less frequent	Urinary tract infection Dysuria, cystitis, urinary incontinence, acute renal failure, micturition frequency, nocturia, polyuria, pyelonephritis, renal pain, urinary retention

Reproductive system and breast disorders	Less frequent	Dysmenorrhoea, menorrhagia, vulvovaginal dryness, menstrual disorder, vaginitis, breast fibroadenosis, breast neoplasm, breast pain
General disorders and administrative site conditions	Frequent Less frequent	Fatigue Asthenia, chest discomfort, feeling drunk, influenza-like illness, lethargy, pain, oedema, falling, pyrexia, malaise, trauma, face oedema, hot flashes, restless legs, rigors, tolerance increased, medicine tolerance
Investigations	Less frequent	Increased body temperature, heart rate increased, increased ESR

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. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via online service for adverse drug reaction reporting by following the link:

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

An email can be sent directly to the company,

pharmacovigilance@pharmadynamics.co.za to ensure safety of the product.

4.9 Overdose

Signs and symptoms:

In cases of overdose involving ZOLPIDEM 12,5 mg MR DYNA alone or with other CNS-depressant agents (including alcohol), impairment of consciousness up to coma, and more severe symptomatology, including fatal outcomes have been reported.

Management of overdose:

General symptomatic and supportive measures should be used. Activated charcoal should be given to reduce absorption. Sedating medicines should be withheld even if excitation occurs. Use of flumazenil may be considered where serious symptoms are observed. However, flumazenil administration may contribute to the appearance of neurological symptoms (convulsions).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Hypnotics and Sedatives

ATC code: N05CF02

Pharmacological classification: A 2.2. Sedatives, hypnotics

Zolpidem is a benzodiazepine receptor agonist. Benzodiazepine receptor agonists

(BZRAs) exert their pharmacological effects by binding to a site associated with GABA-A receptors. Zolpidem shows selectively for a subtype of GABA-A receptors containing alpha-1 subunits. Scientific evidence suggests that this receptor subtype mediates drug-induced sedative /hypnotic effects.

5.2 Pharmacokinetic properties

Absorption:

After oral intake, the absolute bioavailability is around 70 % and the peak plasma concentration is reached between 1,5 and 2,5 hours. The inter-individual variability (CV) is around 40 – 60 % for AUC and 30 – 40 % for C_{max}.

The elimination $t_{1/2}$ is 2,8 hours in healthy volunteers.

When zolpidem is administered after food C_{max} and AUC are decreased by 30 and 23 % respectively and the time to maximal plasma concentration is delayed by 2 hours.

Distribution:

The *in vivo* plasma protein binding is around 92 %. The distribution volume in adults is 0,54 L/kg following intravenous administration.

Biotransformation:

Zolpidem is mainly metabolised by the hepatic cytochrome P450 CYP 3A4 (around 60 % of the net CYP -mediated hepatic clearance). Other P450 isoenzymes such as CYP2C9, CYP1A2, CYP2D6 and CYP2C19 also contribute to the oxidation of the drug. All of

zolpidem's metabolites are pharmacologically inactive. Zolpidem itself is not a significant inhibitor or inducer of human CYP isoforms.

Elimination:

Zolpidem is excreted in the form of inactive metabolites in the urine (around 60 %) and faeces (around 40 %). Clearance is around 212 mL/min. Reduced clearance of 100 mL/min has been noticed in the elderly.

Zolpidem plasma concentrations were measured approximately 9 hours post-dose on day 1 and day 15 in adult patients who were treated for 3 weeks with zolpidem 12,5 mg. Zolpidem concentrations did not change upon repeated dosing, indicating no evidence of accumulation with zolpidem.

Pharmacokinetics in special patient groups

Hepatic impairment:

In patients with liver impairment, the clearance of zolpidem is decreased, and the elimination half-life is modified (around 10 hours) (see section 4.2 and 4.4). In liver cirrhosis a 5-fold increase of AUC and a 3-fold increase of half-life have been observed.

Renal impairment:

In patients with renal impairment, whether dialysed or not, there is a moderate increase (around 30 %) of the volume of distribution compared to healthy subjects. Other pharmacokinetic parameters such as clearance, AUC and elimination half-life are not

affected. Therefore, no dose adjustment is necessary in patients with renal impairment.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cores:

Colloidal silicon dioxide

FD and C blue aluminium lake

Hypromellose

Lactose monohydrate

Magnesium stearate

Microcrystalline cellulose

Potassium bitartrate

Sodium starch glycolate

Film Coating:

12,5 mg: Opadry blue:

FD and C blue / indigo carmine aluminium lake

Hypromellose

Polyethylene glycol 400

Titanium dioxide

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 30 °C in original container. Keep the blisters in the carton until required for use.

Keep the HDPE bottle tightly closed.

6.5 Nature and contents of container

Round opaque white HDPE bottle with child resistant closure along with one silica gel sachet 1 g. Pack sizes of 30 or 100 film coated tablets.

PVC/aclar blister consisting of clear PVC/aclar film forming base material and hard tampered aluminium foil, one side bright, and other side dull and lacquered. Pack size of 3 x 10 film coated tablets.

6.6 Special precautions for disposal and other handling of the product

No special requirements.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION:

Pharma Dynamics (Pty) Ltd

1st Floor Grapevine House, Steenberg Office Park

Silverwood Close

Westlake, Cape Town

7945, South Africa

8. REGISTRATION NUMBER

ZOLPIDEM 12,5 mg MR DYNA 12,5 mg: 54/2.2/0180.178

9. DATE OF FIRST AUTHORISATION

05 September 2023