Professional information for STILNOX MR 12,5

SCHEDULING STATUS

S5

1. NAME OF THE MEDICINE

STILNOX MR 12,5 mg, modified release tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 12,5 mg zolpidem tartrate.

Excipients with known effects:

Contains sugar (138,913 mg lactose monohydrate per tablet).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Modified release tablets.

Blue, round, biconvex tablet engraved ZMR on one face.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Short-term treatment of insomnia.

STILNOX MR 12,5 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

STILNOX MR 12,5 acts rapidly and therefore should be taken immediately before bedtime, or in bed.

For a faster sleep onset, STILNOX MR 12,5 should not be administered with or immediately after a meal (see section 5.2, Pharmacokinetic properties).

STILNOX MR 12,5 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 off 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 STILNOX MR 12,5 should be used and must not exceed 12,5 mg.

Special populations

Hepatic impairment:

STILNOX MR 12,5 should not be used in patients with severe hepatic impairment (see section 4.3 and section 4.4).

Renal impairment:

No dosage adjustment is required.

Children:

Safety and effectiveness of STILNOX MR 12,5 in paediatric patients under the age of 18 years have not been established. Therefore, STILNOX MR 12,5 should not be prescribed in this population (see section 4.3).

***Elderly**:*

As STILNOX MR 12,5 has not been evaluated in elderly patients (≥ 65 years), STILNOX MR 12,5 is not recommended in this population.

Method of administration:

Oral administration.

Tablets should not be halved, crushed or chewed.

4.3 Contraindications

- A hypersensitivity to the active substance zolpidem tartrate or any of the excipients listed in 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 considered 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.

Respiratory impairment:

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

Risks from concomitant use with opioids:

Concomitant use of opioids with benzodiazepines or other sedative-hypnotic medicines, including STILNOX MR 12,5, 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 STILNOX MR 12,5 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.

Paediatric patients:

STILNOX MR 12,5 is contraindicated in patients under the age of 18 years because the safety and effectiveness of STILNOX MR 12,5 have not been established (see section 4.3).

In an 8-week study in paediatric patients (aged 6 – 17 years) with insomnia associated with attention-deficit/hyperactivity disorder (ADHD), psychiatric and nervous system disorders comprised the most frequent treatment emergent adverse events observed with zolpidem versus placebo and included dizziness (23,5 % vs. 1,5 %), headache (12,5 % vs. 9,2 %), and hallucinations (7,4 % vs. 0 %).

Elderly patients:

See section 4.2 for dose recommendations.

Amnesia:

STILNOX MR 12,5 may induce anterograde amnesia. The condition occurs most often several hours after ingesting STILNOX MR 12,5 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 STILNOX MR 12,5. Should this occur, use of STILNOX MR 12,5 should be discontinued. These reactions are more 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 STILNOX MR 12,5 and were not fully awake.
Isolated cases of self-harming behaviour have also been reported.
The use of alcohol and other CNS-depressants, or medicines which act on the central nervous system, with STILNOX MR 12,5 appears to increase the risk of such behaviours, as does the use of STILNOX MR 12,5 at doses exceeding the maximum recommended dose.
Discontinuation of STILNOX MR 12,5 should be strongly considered for patients who report such behaviours, due to the risk to the patient and others.

Psychomotor impairment:

The risk of psychomotor impairment, including impaired driving ability, is increased if:
STILNOX MR 12,5 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 STILNOX MR 12,5 is co-administered with other CNS depressants, alcohol, or with other medicines that increase the blood levels of STILNOX MR 12,5.

Tolerance:

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

Dependence:

Use of STILNOX MR 12,5 may lead to the development of abuse and/or physical and psychological dependence. The risk of dependence increases with dose and duration of treatment, or in predisposed patients. Cases of dependence have been reported more frequently in patients treated with STILNOX MR 12,5 for longer than 4 weeks. The risk of abuse and dependence is also greater in patients with a history of psychiatric disorders and/or alcohol or medicine abuse. STILNOX MR 12,5 should be used with extreme caution in patients with current or a history of alcohol or medicine abuse.

Patients with a history of alcohol or drug abuse – see Patients with a history of alcohol and drug abuse.

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 STILNOX MR 12,5 (see section 4.8).

Withdrawal symptoms occur after abrupt termination and are limited, in the mildest cases, to tremors, restlessness, sleep disturbances, anxiety, headaches and impaired concentration. However, other symptoms such as sweating, muscle and abdominal cramps, perception

disturbances, and rarely, delusions and epileptic seizures may occur. Depending on the duration of action of zolpidem, as in STILNOX MR 12,5, withdrawal symptoms develop a few hours to one week or more after discontinuation of treatment.

To minimise the risk of dependence, STILNOX MR 12,5 should only be prescribed after carefully reviewing the indication and should be taken for the shortest time possible (generally not longer than 4 weeks). The need to continue treatment should be reviewed periodically. Prolonged treatment is only indicated in some patients.

To avoid withdrawal symptoms, a tapering-off period, during which doses are reduced gradually, is advised. If withdrawal symptoms develop, very close medical supervision and patient management are essential.

Rebound insomnia:

A transient syndrome, whereby the symptoms that led to treatment with STILNOX MR 12,5 recur in an enhanced form, may occur on withdrawal of STILNOX MR 12,5 treatment.

It may be accompanied by other reactions including mood changes, anxiety and restlessness.

There are indications that, in the case of STILNOX MR 12,5 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 STILNOX MR 12,5, was limited to the first night after the medicine discontinuation in clinical studies (see Pharmacodynamic properties).

It is important that the patient should be aware of the possibility of rebound phenomenon, thereby minimising anxiety over such symptoms should they occur when STILNOX MR 12,5 is discontinued.

Patients with a history of alcohol or drug abuse:

STILNOX MR 12,5 should not be used in patients with a history of alcohol or medicine abuse.

Hepatic impairment:

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

Psychotic illness:

STILNOX MR 12,5 is not recommended for the primary treatment of psychotic illness.

Suicidality and depression:

Several epidemiological studies show an increased incidence of suicide and suicide attempt in patients with or without depression, treated with benzodiazepines and other hypnotics, including STILNOX MR 12,5. A causal relationship has not been established. STILNOX MR 12,5 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 STILNOX MR 12,5 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 STILNOX MR 12,5. Since insomnia may be a symptom of depression, the patient should be re-evaluated if insomnia persists.

Drowsiness:

Due to its pharmacological properties, STILNOX MR 12,5 can cause drowsiness and a decreased level of consciousness, which may lead to falls and consequently to severe injuries. It may be accompanied by other reactions including mood changes, anxiety and restlessness.

Patients with long QT syndrome:

An *in vitro* cardiac electrophysiological study showed that under experimental conditions using very high concentration and pluripotent stem cells STILNOX MR 12,5 may reduce the hERG (human ether-a-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

STILNOX MR 12,5 treatment in patients with known congenital long QT syndrome should be carefully considered.

Lactose intolerance:

Since STILNOX MR 12,5 tablets contain lactose monohydrate, patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption, should not take STILNOX MR 12,5.

4.5 Interaction with other medicines and other forms of interaction

Alcohol:

Concomitant use with alcohol is not recommended. The sedative effect may be enhanced when STILNOX MR 12,5 is used in combination with alcohol. This affects the ability to drive or use machines.

CNS depressants:

Enhancement of the central depressive effect may occur in cases of concomitant use with antipsychotics (neuroleptics), hypnotics, anxiolytics/sedatives, antidepressant agents, opioids (analgesics and antitussives), narcotic analgesics, antiepileptic medicines, anaesthetics and sedative antihistamines.

Concomitant use of STILNOX MR 12,5 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.

Combination of STILNOX MR 12,5 with fluoxetine or sertraline, SSRI (selective serotonin reuptake inhibitors) antidepressants, it should be noted that:

- with fluoxetine, no clinically significant interaction, either for pharmacokinetics or pharmacodynamics, has been observed
- with sertraline, the maximum concentration of zolpidem is significantly elevated and the

T_{max} is decreased. Although it has not been demonstrated clinically, these changes could theoretically accelerate the hypnotic effect of zolpidem.

Opioids:

The concomitant use of benzodiazepines and other sedative-hypnotic medicines, including STILNOX MR 12,5, 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).

CYP450 inhibitors and inducers:

Compounds which inhibit cytochrome P450 may enhance the activity of STILNOX MR 12,5. STILNOX MR 12,5 is metabolised via several hepatic cytochrome P450 enzymes, the main enzyme being CYP3A4 with the contribution of CYP1A2.
Co-administration of STILNOX MR 12,5 with ketoconazole (200 mg twice daily), a potent CYP3A4 inhibitor, produced a 64 % increase in STILNOX MR 12,5 plasma levels. A routine dosage adjustment of STILNOX MR 12,5 is not necessary, but patients should be advised that the sedative effects might be enhanced.

However, co-administration of STILNOX MR 12,5 with itraconazole or fluconazole did not produce any significant changes in STILNOX MR 12,5 pharmacokinetics and pharmacodynamics. It is not necessary to change the dose of STILNOX MR 12,5 with itraconazole use.

Fluvoxamine is a strong inhibitor of CYP1A2 and a moderate to weak inhibitor of CYP2C9 and CYP3A4. Co-administration of fluvoxamine may increase blood levels of STILNOX MR 12,5; 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 STILNOX MR 12,5; concurrent use is not recommended.

The pharmacodynamic effect of STILNOX MR 12,5 is decreased when it is administered with a CYP3A4 inducer such as rifampicin due to an increase in liver metabolism.
The pharmacodynamic effect of STILNOX MR 12,5 is decreased when it is administered with a CYP3A4 inducer such as St John's Wort. Co-administration of St. John's Wort may decrease blood levels of STILNOX MR 12,5; concurrent use is not recommended.

Other:

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

4.6 Fertility, pregnancy and lactation

Safety in pregnancy and lactation has not been established (see section 4.3).

Pregnancy:

The use of STILNOX MR 12.5 during pregnancy should be avoided.
Zolpidem, as in STILNOX MR 12,5 crosses the placenta.
Cases of reduced fetal movement and fetal heart rate variability have been described after administration of benzodiazepines during the second and/or third trimester of pregnancy.
The data collected from cohort studies has not demonstrated evidence of the occurrence of malformations following exposure to benzodiazepines (like zolpidem) during the first trimester of pregnancy. However, in certain epidemiological case-control studies, an increased incidence of cleft lip and palate was observed with benzodiazepines.
Administration of STILNOX MR 12,5 during the late phase of pregnancy or during labour, has been associated with effects on the neonate, such as hypothermia, hypotonia, feeding difficulties

and moderate respiratory depression, can be expected due to the pharmacological action of STILNOX MR 12,5. Cases of severe neonatal respiratory depression have been reported.
Infants born to mothers who took hypnotics, including STILNOX MR 12,5, 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.
If STILNOX MR 12,5 is prescribed to a woman of childbearing potential, she should be warned to contact her medical practitioner about stopping STILNOX MR 12,5 if she intends to become, or suspects that she is pregnant.

Lactation:

Small quantities of zolpidem is excreted in breast milk, the use of STILNOX MR 12,5 in breastfeeding mothers is not recommended (see section 4.3).

4.7 Effects on ability to drive and use machines

Vehicle drivers and machine operators should be warned that there may be a possible risk of adverse reactions including drowsiness, prolonged reaction time, dizziness, sleepiness, blurred/double vision, reduced alertness and impaired driving the morning after therapy.
In order to minimise this risk, a full night of sleep (7 - 8 hours) is recommended.
Furthermore, the co-administration of STILNOX MR 12,5 with alcohol and other CNS depressants increases the risk of such effects. Patients should be warned not to use alcohol or other psychoactive substances when taking STILNOX MR 12,5 (see section 4.4 and section 4.5).
The risk related to anterograde amnesia should also be taken into consideration.

4.8 Undesirable effects

Adverse reactions have been ranked under headings of system-organ class and frequency using the following: very common (≥ 10 %); common (≥ 1 and < 10 %); uncommon (≥ 0,1 % and < 1 %); rare (≥ 0,01 % and < 0,1 %); very rare (< 0,01 %).

Not known: Cannot be estimated based on available data.

There is evidence of a dose-relationship for adverse effects associated with STILNOX MR 12,5 use, particularly for certain CNS events. They occur most frequently in elderly patients.

Infections and Infestations

Common: influenza

Uncommon: gastroenteritis, labyrinthitis, lower respiratory tract infection, otitis externa, upper respiratory tract infection

Immune system disorders

Not known: angioneurotic oedema

Metabolism and nutrition disorders

Uncommon: appetite disorder

Psychiatric disorders

Common: anxiety, psychomotor retardation, disorientation

Uncommon: restlessness, aggression, depression, hallucination, including visual and hypnagogic hallucination, apathy, binge eating, confusional state, depersonalisation, depressed mood, disinhibition, euphoric mood, mood swings, nightmares, stress symptoms, somnambulism (see section 4.4, Somnambulism and associated behaviours)

Rare: libido disorder

Very rare: delusion, dependence (withdrawal symptoms, or rebound effects may occur after treatment discontinuation)

Not known: anger, abnormal behaviour

Most of these psychiatric undesirable effects are related to paradoxical reactions.

Nervous system disorders

Very common: headache, somnolence

Common: dizziness, cognitive disorders such as memory disorders (memory impairment, amnesia, anterograde amnesia), disturbance in attention

Uncommon: balance disorder, hypoaesthesia, paraesthesia, ataxia, burning sensation, postural dizziness, dysgeusia, involuntary muscle contractions, tremor

Rare: depressed level of consciousness, speech disorder

Eye disorders

Common: visual disturbance

Uncommon: eye redness, blurred vision, altered visual depth perception, asthenopia

Ear and labyrinth disorders

Uncommon: vertigo, tinnitus

Cardiac disorders

Uncommon: palpitations

Respiratory, thoracic and mediastinal disorders

Uncommon: cough, dry throat, throat irritation

Very rare: respiratory depression

Gastrointestinal disorders

Common: nausea, constipation

Uncommon: vomiting, abdominal discomfort, flatulence, frequent bowel movements, gastro-oesophageal reflux disease

Hepato-biliary disorders:

Rare: bilirubinaemia, severe hepatitis with jaundice, raised liver enzymes, hepatocellular, cholestatic or mixed liver injury

Skin and subcutaneous tissue disorders

Uncommon: rash, urticaria, contact dermatitis, skin wrinkling

Musculoskeletal and connective tissue disorders

Common: myalgia, muscle cramp, neck pain, back pain

Uncommon: arthralgia, muscular weakness

Renal and urinary disorders

Uncommon: dysuria

Reproductive system and breast disorders

Uncommon: dysmenorrhoea, menorrhagia, vulvovaginal dryness

General disorders and administration site conditions

Common: fatigue

Uncommon: asthenia, chest discomfort, feeling drunk, influenza-like illness, lethargy, pain, pyrexia

Rare: gait disturbances, fall (predominantly in elderly patients and when STILNOX MR 12,5 was not taken in accordance with prescribing recommendation)

Not known: drug tolerance

Investigations

Uncommon: increased blood pressure, increased body temperature, increased heart rate

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of STILNOX MR 12,5 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 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
Side effects can be reported directly to Sanofi's Pharmacovigilance Unit at za.drugsafety@sanofi.com (email) or 011 256 3700 (tel).

4.9 Overdose

Signs and symptoms:

In cases of overdose involving STILNOX MR 12,5 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:

General symptomatic and supportive measures should be used. If there is no advantage in emptying the stomach, 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. It may be
useful for diagnosis and/or treatment of an intentional or accidental STILNOX MR 12,5 overdose. However, flumazenil administration may contribute to the appearance of neurological symptoms (convulsions).
STILNOX MR 12,5 is not dialysable.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 2.2. Sedatives, hypnotics.

Pharmacotherapeutic groups: Nervous system, Psycholeptics, Hypnotics and sedatives, Benzodiazepine related drugs

ATC code: N05CF02

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 selectivity 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

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 t½ 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 vitro* plasma protein binding is around 92 %. The distribution volume in adults is 0,54 l/kg following intravenous administration.

Metabolism:

Zolpidem is mainly metabolised by the hepatic cytochrome P450 CYP3A4 (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 and excretion:

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

Special populations:

Hepatic impairment:

In patients with liver impairment, the clearance of zolpidem is decreased and the elimination half-life is extended (around 10 hours) (see section 4.4 and section 4.2. 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.

5.3 Preclinical safety data

Preclinical safety data have not identified any particular risks for humans based on a battery of standard pharmacology tests on safety, repeat dose toxicity, genotoxicity, reproductive toxicity, and carcinogenicity. Zolpidem is considered to have no effects on reproduction parameters and has shown no teratogenic, genotoxic or carcinogenic potential.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Colloidal anhydrous silica (200)

Hypromellose (6 mPa.s, 4000 mPa.s)

Iron oxide yellow (E172)

Lactose monohydrate

Magnesium stearate

Microcrystalline cellulose (Avicel PH101)

Potassium hydrogen tartrate

Sodium starch glycolate (type A)

Film coating:

Opadry II 32F20797X containing:

Hypromellose (15 mPa.s)

Indigotine (E132) aluminium lake

Lactose monohydrate

Macrogol 3350

Titanium dioxide (E171)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

Store at or below 30 °C.

6.4 Special precautions for storage

Protect from light and moisture.

Tablets must be kept in blisters in the carton at all times until required for use.

6.5 Nature and contents of container

Clear, colourless, transparent, rigid PVC/Aluminium foil blister containing 7, 14 , 28 or 100 tablets in a carton.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

sanofi-aventis south africa (pty) ltd

Hertford Office Park, Building I, 5th Floor

90 Bekker Road, Vorna Valley

Midrand 2196

South Africa

011 256 3700

8. REGISTRATION NUMBER

A40/2.2/0441

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of registration: 10 October 2008

10. DATE OF REVISION OF THE TEXT

15 June 2023