XIPANZ XR
P1528907

XIPANZ XR
P1528907

**PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE**

**SCHEDULING STATUS**

**S5**

## 1. NAME OF THE MEDICINE

**XIPANZ XR 0,5 mg** (tablets)
**XIPANZ XR 1 mg** (tablets)
**XIPANZ XR 2 mg** (tablets)
**XIPANZ XR 3 mg** (tablets)

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

**XIPANZ XR 0,5 mg:**

Each tablet contains 0,5 mg of alprazolam.
Excipients with known effect: Lactose monohydrate 255,680 mg.

**XIPANZ XR 1 mg:**

Each tablet contains 1 mg of alprazolam.
Excipients with known effect: Lactose monohydrate 254,705 mg.

**XIPANZ XR 2 mg:**

Each tablet contains 2 mg of alprazolam.
Excipients with known effect: Lactose monohydrate 253,945 mg.

**XIPANZ XR 3 mg:**

Each tablet contains 3 mg of alprazolam.
Excipients with known effect: Lactose monohydrate 252,485 mg.
For full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

**XIPANZ XR 0,5 mg:**

White to off-white, round, biconvex tablets with bevelled edge, debossed with 'X' on one side and '70' on the other side.

**XIPANZ XR 1 mg:**

Yellow coloured, round, biconvex tablets with bevelled edge, debossed with 'X' on one side and '73' on the other side.

**XIPANZ XR 2 mg:**

Blue coloured, round, biconvex tablets with bevelled edge, debossed with 'X' on one side and '74' on the other side.

**XIPANZ XR 3 mg:**

Green coloured, round, biconvex tablets with bevelled edge, debossed with X on one side and '75' on the other side.

## 4. CLINICAL PARTICULARS

### 4.1. Therapeutic indications

**XIPANZ XR** is indicated for the treatment of:

- Short-term symptomatic relief of anxiety
- Treatment of anxiety disorders

Anxiety disorder is a condition corresponding closely to the latest APA Diagnostic and Statistical Manual [DSM] diagnosis of generalised anxiety disorder.

A. Diagnostic criteria for Generalised Anxiety Disorder:

1. Motor tension: Shakiness, jitteriness, jumpiness, trembling, muscle aches, tension, eyelid twitch, inability to relax, furrowed brow, strained face, restlessness and easily startled.
2. Autonomic hyperactivity:
   Heart pounding or racing, sweating, cold clammy hands, dry mouth, light-headedness, dizziness, paraesthesia, upset stomach, diarrhoea, discomfort in the pit of the stomach, hot or cold spells, lump in the throat, flushing, pallor, high resting pulse and respiration rate.
3. Apprehensive expectation:
   Fear, anxiety, worry, rumination and anticipation of misfortune to self and others.
4. Vigilance and scanning:
   Hyper attentiveness resulting in distractibility, difficulty in concentrating, insomnia, feeling "on edge", impatience and irritability.

B. The anxious mood has been continuous for at least one month.
C. Anxiety not due to another mental disorder, such as Depressive Disorder or Schizophrenia.
D. At least 18 years of age.

- Anxiety Associated with depresssion
- Mixed anxiety-depression
- Depression

Depression can be variously described as neurotic depression, reactive depression, major depressive disorder etc., depending on local psychiatric nosology. Usage has not been established in depression with psychiatric features, in bipolar disorders or in "endogenous" depression (i.e. severely depressed inpatients).

- PANIC DISORDERS

Panic disorder is an illness characterised by recurrent panic attacks. Later in the course of this disturbance, certain issues, e.g. driving a car or being in a crowded place, may become associated with having a panic attack. These panic attacks are not triggered by situations in which the person is the focus of others' attention (as in social phobia).

This includes panic disorders with or without agoraphobia. The essential feature of panic disorder is the unexpected panic attack, a sudden onset of intense apprehension, fear or terror.

Diagnostic criteria for Panic Disorder:

A. At least three panic attacks within a three-week period in circumstances other than during marked exertion or in a life-threatening situation. The attacks are not precipitated by exposure to a circumscribed phobic stimulus.

B. Panic attacks are manifested by discrete periods of apprehension or fear, and at least four of the following symptoms appear during each attack:
Dyspnoea; palpitations; chest pain or discomfort; choking or smothering sensations; dizziness, vertigo or unsteady feelings; feelings of unreality; paraesthesias (tingling in hands or feet); hot and cold flushes; sweating; faintness; trembling or shaking; smothering sensations, dizziness. **XIPANZ XR** is only indicated when the disorder is severe, disabling or when the individual is subject to extreme stress.

**XIPANZ XR** is indicated for use of up to six month's duration for anxiety and depression and for up to eight months in the treatment of panic disorder with or without some phobic avoidance. The effectiveness for long-term use, exceeding six months has not been established.

### 4.2. Posology and method of administration

**Posology**

Patients' should be periodically re-assessed and dosage adjustments made, as appropriate.
The optimum dosage of **XIPANZ XR** should be based upon the severity of the symptoms and individual patient response. The lowest dose which can control symptoms should be used. The usual dosage is stated below; in the few patients who require higher doses, the dosage should be increased cautiously to avoid adverse effects.

The maximum dose should not be exceeded. Treatment should be as short as possible. The patient should be assessed regularly and the need for continued treatment should be re-evaluated, especially when the patient is symptom-free.

When higher dosage is required, the evening dose should be increased before the daytime doses. In general, patients who have not previously received psychotropic medicines will require lower doses than those previously treated with minor tranquilisers, antidepressants or hypnotics, or those with a history of chronic alcoholism. It is recommended that the general principle of using the lowest effective dose be followed in elderly or debilitated patients to preclude the development of ataxia or over sedation.

Paediatric population: The safety and efficacy of **XIPANZ XR** in patients under the age of 18 have not been established (See Section 4.4).

**XIPANZ XR** tablets may be administered once daily, preferably in the morning.

| XIPANZ XR | | |
|---|---|---|
| **XIPANZ XR tablets** | **Usual starting dose*** | **Usual dose range** |
| Anxiety | 1 mg daily, in one or two doses | 0,5 to 4,0 mg daily, in one or two doses |
| Mixed anxiety/depression Anxiety associated with depression | 1 mg daily, in one or two doses | 0,5 to 4,5 mg daily, in one or two doses |
| Panic disorders | 0,5 mg – 1,0 mg given at bedtime or 0,5 mg two times daily | In clinical trials the mean maintenance was between 5 or 6 mg per day, given as a single daily dose or divided between two doses daily, with occasional patients needing up to 10 mg per day. The dose should be adjusted according to patient response, with dose increments of no greater than 1 mg in the daily dose every three to four days. |
| Elderly patients | 0,5 mg – 1,0 mg daily, given in one or two doses | 0,5 to 1 mg daily, may be gradually increased if needed and tolerated. |

* If side effects occur, the dose should be lowered.

To discontinue treatment in patients taking **XIPANZ XR** tablets, the dosage should be reduced slowly in keeping with good medical practice. It is suggested that the daily dosage of **XIPANZ XR** be decreased by no more than 0,5 mg every three days. Some patients may require an even slower dosage reduction.

**Method of administration**

For oral use. **XIPANZ XR** tablets should be taken intact. They should not be chewed, crushed or broken.

### 4.3. Contraindications

**XIPANZ XR** is contraindicated in patients with known hypersensitivity to benzodiazepines, alprazolam, or to any component of these formulations.

**XIPANZ XR** is not recommended for patients whose primary diagnosis is schizophrenia.
Concomitant administration with antiretroviral protease inhibitors, ketoconazole, as the elimination of **XIPANZ XR** is delayed several fold (see section 4.5).

### 4.4. Special warnings and precautions for use

**XIPANZ XR** usage has not been established in certain types of depression. See section 4.2.

**XIPANZ XR** must be used with caution in patients with impaired renal or hepatic function, pulmonary disease or limited pulmonary reserve.

**XIPANZ XR** produces additive CNS depressant effects when co-administered with alcohol or other medicines producing CNS depression.

Concomitant use of benzodiazepines, **XIPANZ XR**, and opioids may result in profound sedation, respiratory depression (see section 4.5), coma and death.

Habituation and emotional/physical dependence may occur with **XIPANZ XR**. The risk of dependence increases with higher doses and long-term use and is further increased in patients with a history of alcoholism or drug abuse. Caution should be particularly used when prescribing **XIPANZ XR** to patients who are prone to abuse drugs (e.g. alcoholics and drug addicts) because of their predisposition to habituation and dependence.

A transient syndrome which may occur in withdrawal of treatment whereby the symptoms that led to treatment with **XIPANZ XR** recur in an enhanced form. It may be accompanied by other reactions including mood changes, anxiety and restlessness. Since the risk of withdrawal or rebound phenomena is greater after abrupt discontinuation of a treatment, it is recommended that the dosage be decreased gradually.

**XIPANZ XR** is indicated for use of up to six month's duration for anxiety and depression and for up to eight months in the treatment of panic disorder with or without some phobic avoidance. The effectiveness for long-term use, exceeding six months has not been established.

Withdrawal symptoms have occurred following rapid decrease or abrupt discontinuance of **XIPANZ XR**. These can range from mild dysphoria and insomnia to a major syndrome which may include abdominal and muscle cramps, vomiting, sweating, tremor, and convulsions. In addition, withdrawal seizures have occurred upon rapid decrease or abrupt discontinuation of therapy with **XIPANZ XR** and special care must be taken in the treatment of epileptic patients. See section 4.2 for dose reduction during withdrawal period.

**XIPANZ XR** should be avoided in psychotic patients and patients suffering from mental depression unless there is a marked component of anxiety in their illness.
Panic disorders have been associated with primary and secondary major depressive disorders and increased reports of suicide among untreated patients. Therefore, the same precaution must be exercised when using the higher doses of **XIPANZ XR** in treating patients with panic disorders as is exercised with the use of any psychotropic medicines in treating depressed patients or those in whom there is reason to expect concealed suicidal ideation or plans.

Episodes of hypomania and mania have been reported in association with the use of **XIPANZ XR** in patients with depression.

**Paediatric population**
The safety and efficacy of **XIPANZ XR** has not been established in children under the age of 18 years.

**XIPANZ XR** contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take **XIPANZ XR**.

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

**Contraindicated combinations**
**XIPANZ XR** is contraindicated with itraconazole and ketoconazole, and antiretroviral protease inhibitors since these medications significantly impair the oxidative metabolism mediated by cytochrome P450 3A (CYP3A), thus delaying the elimination of **XIPANZ XR** (see section 4.3).

**Combinations not recommended**
The concomitant use of benzodiazepines and opioids increases the risk of respiratory depression because of actions at different receptor sites in the CNS that control respiration. Benzodiazepines interact at GABAA sites and opioids interact primarily at mu receptors. When benzodiazepines and opioids are combined, the potential for benzodiazepines to significantly worsen opioid-related respiratory depression exists. Limit dosage and duration of concomitant use of benzodiazepines and opioids, and monitor patients closely for respiratory depression and sedation (see section 4.3).

**Combinations which require precaution for use**
Pharmacokinetic interactions can occur when **XIPANZ XR** is administered along with medicines that interfere with its metabolism. Compounds which inhibit certain hepatic enzymes (particularly cytochrome P450 3A4) may increase the concentration of **XIPANZ XR** and enhance its activity.

Data from clinical and *in vitro* studies with **XIPANZ XR**, and clinical studies with medicines metabolised similarly to **XIPANZ XR** provide evidence for varying degrees of interaction and possible interaction with **XIPANZ XR** for a number of medicines. Based on the degree of interaction and the type of data available, the following recommendations are made:

- Caution and consideration of dose reduction is recommended when **XIPANZ XR** is co-administered with nefazodone, fluvoxamine, and cimetidine.
- Caution is recommended when **XIPANZ XR** is co-administered with fluoxetine, oral contraceptives, sertraline, diltiazem, or macrolide antibiotics such as erythromycin and troleandomycin.

The steady state plasma concentrations of imipramine and desipramine have been reported to be increased an average of 31 % and 20 %, respectively, by the concomitant administration of alprazolam tablets in doses up to 4 mg/day. The clinical significance of these changes is unknown.

### 4.6. Fertility, pregnancy and lactation

**Pregnancy**

The safety of **XIPANZ XR** during pregnancy and lactation has not been established. The potential for congenital malformations in children of patients who have received **XIPANZ XR** during pregnancy exists.

**XIPANZ XR** should not be administered during labour. Given during labour, it crosses the placenta and may cause the floppy-infant syndrome characterised by central respiratory depression, hypothermia and poor sucking.

**Lactation**

**XIPANZ XR** should not be administered to mothers' breastfeeding their infants, since **XIPANZ XR** is excreted in human breast milk.

**Fertility**

There is no data available on the effect of **XIPANZ XR** on fertility

### 4.7. Effects on ability to drive and use machines

Because of its CNS depressant effects, patients receiving **XIPANZ XR** should be cautioned against engaging in hazardous occupations or activities requiring complete mental alertness such as operating machinery or driving a motor vehicle (see section 4.8).

### 4.8. Undesirable effects

**a.** ***Tabulated list of adverse reactions***

| MedDRA System Organ Class | Frequency | Undesirable Effects |
|---|---|---|
| **Metabolism and nutrition disorders** | Frequent | Decreased appetite |
| **Psychiatric disorders** | Frequent | Confusional state, depression, irritability, libido decreased |
| | Less frequent | Aggression, insomnia, loss of libido, mood disorder, Nervousness, abnormal dreams, apathy, anger, bradyphrenia, euphoric mood, logorrhea, mood swings, dysphonia, homicidal ideation, mania, hypomania, impulse control, psychomotor retardation, suicidal ideation, hallucinations, agitation, rage |
| **Nervous system disorders** | Frequent | Sedation, somnolence (see section 4.7), ataxia, balance impaired, coordination abnormal, dizziness, headache, memory impairment, dysarthria, hypersomnia, lethargy |
| | Less frequent | Amnesia, increased activity, tremor Intellectual impairment, slurred speech |
| **Eye disorders** | Frequent | Vision blurred |
| | Less frequent | Increased intraocular pressure |
| **Ear and labyrinth disorders** | Frequent | Vertigo |
| | Less frequent | Tinnitus, ear pain |
| **Cardiac disorders** | Frequent | Palpitation |
| | Less frequent | Sinus tachycardia |
| **Vascular disorders** | Less frequent | Hypotension, hot flushes |
| **Gastrointestinal disorders** | Frequent | Constipation, nausea, dry mouth |
| | Less frequent | Diarrhoea, vomiting |

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**PATIENT INFORMATION LEAFLET**

**SCHEDULING STATUS**

**S5**

**XIPANZ XR 0,5 mg** (tablets)
**XIPANZ XR 1 mg** (tablets)
**XIPANZ XR 2 mg** (tablets)
**XIPANZ XR 3 mg** (tablets)
**Alprazolam**
Contains sugar:
255,680 mg, 254,705 mg, 253,945 mg and 252,485 mg of lactose monohydrate respectively.

**Read all of this leaflet carefully before you start taking XIPANZ XR.**
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- **XIPANZ XR** has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

**What is in this leaflet**:

1. What **XIPANZ XR** is and what it is used for
2. What you need to know before you use **XIPANZ XR**
3. How to use **XIPANZ XR**
4. Possible side effects
5. How to store **XIPANZ XR**
6. Contents of the pack and other information

### 1. What XIPANZ XR is and what it is used for

**XIPANZ XR** falls under the category of anxiolytics (medicines used to relieve anxiety) and contains alprazolam. **XIPANZ XR** belongs to a group of medicines called benzodiazepines.
Benzodiazepines affect chemical activity in the brain to reduce anxiety and worry.
**XIPANZ XR** is only used to treat severe anxiety and severe anxiety associated with depression.
**XIPANZ XR** should only be used for short-term treatment of anxiety.

### 2. What you need to know before you take XIPANZ XR

**Do not take XIPANZ XR:**

- If you are allergic to alprazolam or any of the ingredients of **XIPANZ XR.**
- If you have a condition called schizophrenia (psychotic disorder characterised by distortions of reality and disturbances of thought and language and withdrawal from social contact).
- If you are taking an anti-fungal medicine called ketoconazole or itraconazole or an anti-retroviral medicine class of medicine called protease inhibitors, as these may delay the elimination of **XIPANZ XR.**

**Take special care with XIPANZ XR:**

- If you suffer from depression, unless you suffer from anxiety as well, because **XIPANZ XR** is indicated for use in only certain types of depression.
- If you have problems with your lungs, kidneys or liver.
- If you are younger than 18 years old.
- If you have abused medicines or alcohol in the past or find it difficult to stop taking medicines or drinking.
- If you are taking a class of pain killers called opioids, as taking **XIPANZ XR** with them can result in sedation, breathing problems, coma and death.
- **XIPANZ XR** should not be abruptly stopped as it can cause abdominal and muscle cramps, vomiting, sweating, tremor (trembling) and convulsions (fits).
- If you suffer from depression unless there is some anxiety with the depression.

**Taking other medicines with XIPANZ XR:**

Always tell your healthcare professional if you are taking any other medicine. (This includes all complementary or traditional medicines).

**Other medicines and XIPANZ XR:**

**The following combination is contraindicated:**

- Taking **XIPANZ XR** with ktoconazole, itraconazole, or other azole-type antifungals (medicines used to treat fungal infections).
- Protease inhibitors (for treatment of HIV).

**The following combinations require precautions for use:**

- When using opioids with **XIPANZ XR** (see '**Take special care with XIPANZ XR**).
- Nefazodone, fluvoxamine (medicines used to treat depression) and cimetidine (used to reduce stomach acid)
- When **XIPANZ XR** is co-administered with fluoxetine (an anti-depressant), oral contraceptives, sertraline (an anti-depressant), diltiazem (a medicine used to treat high blood pressure), or macrolide antibiotics such as erythromycin and troleandomycin.
- When **XIPANZ XR** is co-administered with imipramine and desipramine (anti-depressant medicine), because **XIPANZ XR** increases the concentration of these medicines.

**Pregnancy, breastfeeding and fertility**

**XIPANZ XR** may be harmful to the developing baby so you should not take **XIPANZ XR** if you are pregnant or planning to become pregnant or breastfeeding your baby.

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking **XIPANZ XR**.

**Driving and using machines**

**XIPANZ XR** can make you drowsy. Caution is advised when engaging in hazardous occupations or activities requiring complete mental alertness such as operating machinery or driving a motor vehicle.

**Important information about some of the ingredients of XIPANZ XR**
**XIPANZ XR** contains lactose, which is a type of sugar. Before taking **XIPANZ XR**, please consult your doctor for advice if you have intolerance to some sugars.

### 3. How to take XIPANZ XR

Do not share medicines prescribed for you with any other person.

Always take **XIPANZ XR** exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure. Your doctor will tell you how long your treatment with **XIPANZ XR** will last. If you have the impression that the effect of **XIPANZ XR** is too strong or too weak, talk to your doctor or pharmacist.

The tablets should be taken intact; they should not be chewed, crushed on broken.
A. For anxiety or mixed anxiety/depression:
The usual starting dose is 1 mg daily in one or two doses. Your doctor may increase your dose if needed. However, the dose usually is not more than 4 mg a day.
B. For panic disorders:
The usual starting dose is 0,5 mg to 1,0 mg given at bedtime or 0,5 mg taken two times a day. Your doctor may increase your dose if needed. However, the dose usually is not more than 10 mg a day.
C. For elderly patients:
The usual starting dose is 0,5 mg to 1,0 mg taken one or two times a day. Your doctor may increase your dose if needed. However, the dose usually is not more than 1 mg a day.

**Taking XIPANZ XR with food, drink and alcohol**
**XIPANZ XR** should not be taken with alcohol as it will add to the effect of **XIPANZ XR**.

**If you take more XIPANZ XR than you should**

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

These are the possible signs and symptoms of over dosage: slurred speech or confusion, severe drowsiness, staggering or walking unsteadily, difficulty breathing or coma.

**If you forget to take XIPANZ XR**
If you forgot to take a dose, take it as soon as you remember unless it is nearly time for your next dose. Do not take a double dose to make up for forgotten individual doses.

**If you stop taking XIPANZ XR**
Withdrawal symptoms on discontinuing **XIPANZ XR** can range from mild dysphoria (a state of unease or dissatisfaction) and insomnia (difficulty sleeping) to abdominal and muscle cramps, vomiting, sweating, tremor, and convulsions. In addition, withdrawal seizures have occurred upon rapid decrease or abrupt discontinuation of therapy with **XIPANZ XR** (see '**Take special care with XIPANZ XR**')

### 4. Possible side effects

**XIPANZ XR** can have side effects.

Not all side effects reported for **XIPANZ XR** are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking **XIPANZ XR**, please consult your healthcare provider for advice.

If any of the following happens, stop taking **XIPANZ XR** and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Swelling of the hands, feet, ankles, face, lips and mouth or throat, which may cause difficulty in swallowing or breathing,
- rash or itching,
- fainting.

These are all very serious side effects. If you have them, you may have had a serious reaction to **XIPANZ XR**. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:
- Chest pain,
- fast or irregular heartbeat.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:
*Frequent side effects:*
- Decreased appetite,
- inability to sleep (insomnia), sleepiness (somnolence), feeling confused, depression, irritability, decreased libido,
- symptoms of ataxia which can be impaired balance and coordination, slurring,
- dizziness, headache, impaired memory, feeling a general lack of energy or enthusiasm,
- spinning sensation (vertigo),
- blurred vision,
- nausea, dry mouth, constipation, sweating,
- involuntary urination, frequent urination,
- irregular menstruation,
- fatigue (feeling tired), malaise (feeling sick or unwell), weakness.

*Less frequent side effects:*
- Aggression, difficulty sleeping, nervousness, abnormal dreams, apathy, anger, feeling like it's taking longer to process information,
- a sudden feeling of intense excitement and happiness, mood swings, hallucination, feeling suicidal, an extreme increase in activity and talking (hypomania),
- becoming forgetful, experiencing tremor,
- ear pain, ringing in the ears,
- feeling dizzy and uneasy on your feet (symptoms of hypotension),
- diarrhoea and vomiting,
- abnormal liver function (yellowing of skin and eyes, abdominal pain, selling of legs and ankles),
- if your body breaks out in a rash,
- muscle twitching or muscle weakness,
- unable to pass urine, sexual dysfunction,
- fever, feeling thirsty, feeling hot and cold,
- feeling sluggish, chest tightness, loss of control of your legs,
- increase or decrease in weight.

If you notice any side effects not mentioned in this leaflet, inform your doctor or pharmacist.

**Reporting of side effects**

If you get side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via the **"6.04 Adverse Drug Reaction Reporting Form"**, found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of this medicine.

### 5. How to store XIPANZ XR

Store at or below 25 °C.
Keep HDPE containers tightly closed.

**KEEP OUT OF REACH OF CHILDREN.**

Return all unused medicine to your pharmacist.
Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

### 6. Contents of the pack and other information

**What XIPANZ XR contains**

The active substance is alprazolam 0, 5 mg, 1 mg, 2 mg and 3 mg.
The other ingredients are:
- Colloidal silicon dioxide,
- hypromellose (Methocel K 4M-CR Premium),
- hypromellose (Methocel K 100LV-CR Premium),
- lactose monohydrate,
- magnesium stearate.

In addition, 1 mg tablet contains D&C Yellow No. 10 aluminium lake (C.I. No. 47005), 2 mg tablet contains FD&C Blue No. 2 lake (C.I. No: 73015) and 3 mg contains both D&C Yellow No. 10 aluminium lake (C.I. No. 47005) & FD&C Blue No. 2 lake (C.I. No: 73015).

**What XIPANZ XR looks like and contents of the pack**

**XIPANZ XR 0,5 mg:**

White to off-white, round, biconvex tablets with bevelled edge, debossed with 'X' on one side and '70' on the other side.

**XIPANZ XR 1 mg:**

Yellow coloured, round, biconvex tablets with bevelled edge, debossed with 'X' on one side and '73' on the other side.

**XIPANZ XR 2 mg:**

Blue coloured, round, biconvex tablets with bevelled edge, debossed with 'X' on one side and '74' on the other side.

**XIPANZ XR 3 mg:**

Green coloured, round, biconvex tablets with bevelled edge, debossed with X on one side and '75' on the other side.

**XIPANZ XR 0,5 mg, 1 mg & 2 mg:**

**1) HDPE Pack:**

Tablets are packed in white opaque round 75 mL Heavy weight HDPE container with 38 mm neck finish closed with 38 mm – 400 CR white opaque polypropylene child resistant closure with wad having induction sealing liner. The HDPE container also contains 2 gm silica gel sachet and 9 gm per yard cotton.

<u>**Pack size:**</u> 60's – One HDPE container contains 60 tablets.

**XIPANZ XR 3 mg:**

**1) HDPE Pack:**

Tablets are packed in white opaque round 40 mL Heavy weight HDPE container with 33 mm neck finish closed with 33 mm – 400 CR white opaque polypropylene child resistant closure with wad having TEKNIPLEX HS 123 induction sealing liner. The HDPE container also contains 1 gm silica gel sachet and 9 gm per yard cotton.

<u>**Pack size:**</u> 30's – One HDPE container contains 30 tablets.

**NAME, BUSINESS ADDRESS AND TELEPHONE NUMBER OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION**

Aurogen South Africa (Pty) Ltd
Woodhill Office Park, Building 1, First floor
53 Phillip Engelbrecht Avenue
Meyersdal, Ext. 12
1448, Johannesburg
South Africa

**Registration number**
**XIPANZ XR 0,5 mg:** 50/2.6/0094
**XIPANZ XR 1 mg:** 50/2.6/0095
**XIPANZ XR 2 mg:** 50/2.6/0096
**XIPANZ XR 3 mg:** 50/2.6/0097

**This leaflet was last revised in:**
14 September 2021

| MedDRA System Organ Class | Frequency | Undesirable Effects |
|---|---|---|
| **Hepatobiliary disorders** | Less frequent | Abnormal liver function |
| **Skin and subcutaneous tissue disorders** | Frequent | Sweating |
| | Less frequent | Dermatitis |
| **Musculoskeletal and connective tissue disorders** | Less frequent | Muscle twitching, muscle weakness |
| **Renal and urinary disorders** | Frequent | Enuresis, urinary frequency |
| | Less frequent | Urinary retention |
| **Reproductive system and breast disorders** | Frequent | Menstrual irregularities |
| | Less frequent | Sexual dysfunction |
| **General disorders and administration site conditions** | Frequent | Fatigue, Malaise, Weakness, chest pains, hyperventilation |
| | Less frequent | Fall, pyrexia, thirst, feeling hot and cold, oedema, feeling jittery, sluggishness, asthenia, feeling drunk, chest tightness, increased energy, feeling of relaxation, hangover, loss of control of legs, rigors |
| **Investigations** | Less frequent | Jaundice, weight decreased, weight increased |

**Post Marketing data**

| MedDRA System Organ Class | Frequency | Undesirable Effects |
|---|---|---|
| **Endocrine disorders** | Frequency unknown | Hyperprolactinaemia |
| **Psychiatric disorders** | Frequency unknown | Hypomania, mania (see section 4.4), hallucination, anger, aggression, hostility, agitation, libido disorder, abnormal thinking, psychomotor hyperactivity |
| **Nervous system disorders** | Frequency unknown | Dystonia, autonomic nervous system imbalance |
| **Gastrointestinal disorders** | Frequency unknown | Gastrointestinal disorder |
| **Hepatobiliary disorders** | Frequency unknown | Hepatitis, abnormal hepatic function, jaundice |
| **Skin and subcutaneous tissue disorders** | Frequency unknown | Dermatitis, angioedema |
| **Renal and urinary disorders** | Frequency unknown | Incontinence, urinary retention |
| **Reproductive system and breast disorders** | Frequency unknown | Sexual dysfunction, irregular menstruation |
| **General disorders and administration site conditions** | Frequency unknown | Peripheral oedema, photophobia |
| **Investigations** | Frequency unknown | Increased intraocular pressure |

**b. Description of selected adverse reactions**

**Physical and Psychological Dependence**

While it is difficult to distinguish withdrawal and recurrence for certain patients, the time course and the nature of the symptoms may be helpful. A withdrawal syndrome typically includes the occurrence of new symptoms, tends to appear toward the end of taper or shortly after discontinuation, and will decrease with time. In recurring panic disorder, symptoms similar to those observed before treatment may recur either early or late, and they will persist.

While the severity and incidence of withdrawal phenomena appear to be related to dose and duration of treatment, withdrawal symptoms, including seizures, have been reported after only brief therapy with alprazolam at doses within the recommended range for the treatment of anxiety (e.g., 0.75 to 4 mg/day). Signs and symptoms of withdrawal are often more prominent after rapid decrease of dosage or abrupt discontinuance. The risk of withdrawal seizures may be increased at doses above 4 mg/day.

Patients, especially individuals with a history of seizures or epilepsy, should not be abruptly discontinued from any CNS depressant agent, including alprazolam. It is recommended that all patients on alprazolam who require a dosage reduction be gradually tapered under close supervision (see section 4.2 and 4.4).

**c. 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 providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Medicine Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

**4.9. Overdose**

Symptoms of overdose with **XIPANZ XR** are extensions of its pharmacological action and include drowsiness, slurred speech, motor in-coordination, coma and respiratory depression. Serious sequela are rare unless other medicines and/or ethanol are concomitantly ingested. Treatment of overdosage is primarily supportive of respiratory and cardiovascular function. The value of dialysis has not been determined. Flumazenil, a specific benzodiazepine receptor antagonist, may be used as an adjunct to the management of respiratory and cardiovascular function associated with overdose.

**5. PHARMACOLOGICAL PROPERTIES**

**5.1. Pharmacodynamic properties**

Pharmacological classification: A 26 - Tranquillisers

Pharmacotherapeutic group: Other antipsychotics, ATC code: N05BA12

**Mechanism of action**

Alprazolam is an anxiolytic agent of the benzodiazepine group. Benzodiazepines, including alprazolam, are thought to bind to central nervous system benzodiazepine receptors, thereby increasing the affinity of the receptor for gamma-aminobutyric acid (GABA). GABA, an inhibitory neurotransmitter, modulates the activity of other neurotransmitter systems, including the noradrenergic system.

**5.2. Pharmacokinetic properties**

**Absorption**

The mean absolute bioavailability of alprazolam from alprazolam extended-release tablets is approximately 90 %, and the relative bioavailability compared to alprazolam tablets is 100 %. The bioavailability and pharmacokinetics of alprazolam following administration of alprazolam extended-release tablets are similar to that for alprazolam tablets, with the exception of a slower rate of absorption. The slower absorption rate results in a relatively constant concentration that is maintained between 5 and 11 hours after the dosing. The pharmacokinetics of alprazolam and two of its major active metabolites (4-hydroxyalprazolam and α-hydroxyalprazolam) are linear, and concentrations are proportional up to the recommended maximum daily dose of 10 mg given once daily. Multiple dose studies indicate that the metabolism and elimination of alprazolam are similar for the immediate-release and the extended-release products.

Food has a significant influence on the bioavailability of alprazolam extended-release tablets. A high-fat meal given up to 2 hours before dosing with alprazolam extended-release tablets increased the mean $C_{max}$ by about 25 %. The effect of this meal on $T_{max}$ depended on the timing of the meal, with a reduction in $T_{max}$ by about $^{1}/_{3}$ for subjects eating immediately before dosing and an increase in $T_{max}$ by about $^{1}/_{3}$ for subjects eating 1 hour or more after dosing. The extent of exposure (AUC) and elimination half-life ($t_{1/2}$) were not affected by eating.

There were significant differences in absorption rate for the alprazolam extended-release tablet, depending on the time of day administered, with the $C_{max}$ increased by 30 % and the $T_{max}$ decreased by an hour following dosing at night, compared to morning dosing.

**Distribution**

The apparent volume of distribution of alprazolam is similar for alprazolam extended-release and alprazolam tablets. *In vitro*, alprazolam is bound (80 %) to human serum protein. Serum albumin accounts for the majority of the binding.

**Metabolism**

Alprazolam is extensively metabolized in humans, primarily by cytochrome P450 3A4 (CYP3A4), to two major metabolites in the plasma: 4-hydroxyalprazolam and α-hydroxyalprazolam. A benzophenone derived from alprazolam is also found in humans. Their half-lives appear to be similar to that of alprazolam. The pharmacokinetic parameters at steady-state for the two hydroxylated metabolites of alprazolam (4-hydroxyalprazolam and α-hydroxyalprazolam) were similar for alprazolam and alprazolam extended-release tablets, indicating that the metabolism of alprazolam is not affected by absorption rate. The plasma concentrations of 4-hydroxyalprazolam and α-hydroxyalprazolam relative to unchanged alprazolam concentration after both alprazolam extended-release and alprazolam tablets were always less than 10 % and 4 %, respectively. The reported relative potencies in benzodiazepine receptor binding experiments and in animal models of induced seizure inhibition are 0,2 and 0,66, respectively, for 4-hydroxyalprazolam and α-hydroxyalprazolam. Such low concentrations and the lesser potencies of 4-hydroxyalprazolam and α-hydroxyalprazolam suggest that they are unlikely to contribute much to the pharmacological effects of alprazolam. The benzophenone metabolite is essentially inactive.

**Elimination**

Alprazolam and its metabolites are excreted primarily in the urine. The mean plasma elimination half-life of alprazolam following administration of alprazolam extended-release tablet ranges from 11 to 15 hours in healthy adults.

**Special Populations**

While pharmacokinetic studies have not been performed in special populations with alprazolam extended-release tablets, the factors (such as age, gender, hepatic or renal impairment) that would affect the pharmacokinetics of alprazolam after the administration of alprazolam tablets would not be expected to be different with the administration of alprazolam extended-release tablets. Alprazolam clearance has been reported to be delayed in patients with impaired hepatic and renal function, alcoholism, in elderly or obese patients; and by the co-administration of certain medicines.

**6. PHARMACEUTICAL PARTICULARS**

**6.1. List of excipients**

Colloidal silicon dioxide, hypromellose (Methocel K 4M-CR Premium), hypromellose (Methocel K 100LV-CR Premium), lactose monohydrate and magnesium stearate.

In addition, 1 mg tablet contains D&C Yellow No. 10 aluminium lake (C.I. No. 47005), 2 mg tablet contains FD&C Blue No. 2 lake (C.I. No: 73015) and 3 mg contains both D&C Yellow No. 10 aluminium lake (C.I. No. 47005) & FD&C Blue No. 2 lake (C.I. No: 73015).

**6.2. Incompatibilities**

Not applicable

**6.3. Shelf life**

2 years

**6.4. Special precautions for storage**

Store at or below 25 °C.

Keep HDPE containers tightly closed.

**KEEP OUT OF REACH OF CHILDREN.**

**6.5. Nature and contents of container**

**XIPANZ XR 0,5 mg, 1 mg & 2 mg:**

**1) HDPE Pack:**

Tablets are packed in white opaque round 75 mL Heavy weight HDPE container with 38 mm neck finish closed with 38 mm – 400 CR white opaque polypropylene child resistant closure with wad having induction sealing liner. The HDPE container also contains 2 gm silica gel sachet and 9 gm per yard cotton.

**Pack size:** 60's – One HDPE container contains 60 tablets.

**XIPANZ XR 3 mg:**

**1) HDPE Pack:**

Tablets are packed in white opaque round 40 mL heavy weight HDPE container with 33 mm neck finish closed with 33 mm – 400 CR white opaque polypropylene child resistant closure with wad having TEKNIPLEX HS 123 induction sealing liner. The HDPE container also contains 1 gm silica gel sachet and 9 gm per yard cotton.

**Pack size:** 30's – One HDPE container contains 30 tablets.

**6.6. Special precautions for disposal of a used medicine or waste materials derived from such medicine and other handling of the product**

No special requirements for the disposal and handling of **XIPANZ XR**.

**7. NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION**

Aurogen South Africa (Pty) Ltd
Woodhill Office Park, Building 1, First floor
53 Phillip Engelbrecht Avenue
Meyersdal, Ext. 12, 1448
Johannesburg
South Africa

**8. REGISTRATION NUMBER**

**XIPANZ XR 0,5 mg:** 50/2.6/0094
**XIPANZ XR 1 mg:** 50/2.6/0095
**XIPANZ XR 2 mg:** 50/2.6/0096
**XIPANZ XR 3 mg:** 50/2.6/0097

**9. DATE OF FIRST AUTHORISATION**

14 September 2021

P1528907

**PASIËNTINLIGTINGSBLAD**

**SKEDULERINGSTATUS**

**S5**

**XIPANZ XR 0,5 mg** (tablette)
**XIPANZ XR 1 mg** (tablette)
**XIPANZ XR 2 mg** (tablette)
**XIPANZ XR 3 mg** (tablette)

**Alprasolaam**

Bevat suiker:

255,680 mg, 254,705 mg, 253,945 mg en 252,485 mg laktosemonohidraat onderskeidelik.

**Lees die hele pamflet sorgvuldig deur voordat u begin om XIPANZ XR te gebruik.**

- Hou hierdie pamflet. U moet dit dalk weer lees.
- Indien u verdere vrae het, vra asseblief u dokter of u apteker.
- **XIPANZ XR** is vir u persoonlik voorgeskryf en u moet nie u medisyne met ander mense deel nie. Dit kan skadelik vir hulle wees, selfs al het hulle dieselfde simptome as u.

**Wat is in hierdie pamflet**:

1. Wat **XIPANZ XR** is en waarvoor dit gebruik word
2. Wat u moet weet voor u **XIPANZ XR** gebruik
3. Hoe om **XIPANZ XR** te gebruik
4. Moontlike newe-effekte
5. Hoe om **XIPANZ XR** te berg
6. Inhoud van die verpakking en ander inligting

**1. Wat XIPANZ XR is en waarvoor dit gebruik word**

**XIPANZ XR** val onder die kategorie van angsiolitika (medisyne wat gebruik word om angs te verlig) en bevat alprasolaam. **XIPANZ XR** behoort aan 'n groep medisyne wat bensodiasepiene genoem word.

Bensodiasepiene beïnvloed chemiese aktiwiteit in die brein om angs en bekommernis te verminder.

**XIPANZ XR** word slegs gebruik om ernstige angs en ernstige angs geassosieer met depressie te behandel.

**XIPANZ XR** moet slegs vir korttermynbehandeling van angs gebruik word.

**2. Wat u moet weet voor u XIPANZ XR gebruik**

**Moenie XIPANZ XR neem nie:**

- Indien u allergies is vir alprasolaam of enige van die bestanddele van **XIPANZ XR**.
- Indien u 'n toestand het wat skisofrenie genoem word (psigotiese versteuring wat gekenmerk word deur verdraaiings van werklikheid en versteurings van denke en taal en onttrekking van sosiale kontak).
- Indien u 'n antifungale medisyne neem, genaamd ketokonasool of itrakonasool, of 'n klas antiretrovirale medisyne genaamd protease inhibeerders, aangesien dit die uitskeiding van **XIPANZ XR** kan vertraag.

**Neem spesiale sorg met XIPANZ XR:**

- Indien u aan depressie ly, tensy u ook aan angs ly, aangesien **XIPANZ XR** slegs vir sekere tipes depressie gebruik word.
- Indien u probleme met u longe, niere of lewer het.
- Indien u jonger as 18 jaar oud is.
- Indien u in die verlede medisyne of alkohol misbruik het of indien u dit moeilik vind om op te hou om medisyne of alkohol te drink.
- Indien u 'n klas pynstillers, genaamd opioïede, neem, aangesien die gelyktydige inname van **XIPANZ XR** met hulle, sedasie, asemhalingsprobleme, koma en dood kan veroorsaak.
- **XIPANZ XR** moet nie skielik gestop word nie, aangesien dit buik- en spierkrampe, braking, sweet, bewing en konvulsies (stuipe) kan veroorsaak.
- Indien u aan depressie ly, tensy daar 'n mate van angs met die depressie is.

**Die neem van ander medisyne saam met XIPANZ XR:**

Vertel altyd u gesondheidsorgkundige indien u enige ander medisyne neem. (Dit sluit alle komplementêre of tradisionele medisyne in).

**Ander medisyne en XIPANZ XR:**

**Die volgende kombinasie is teenaangedui:**

- Die gebruik van **XIPANZ XR** met ketokonasool, itrakonasool, of ander azool-tipe antifungale medisyne (medisyne wat gebruik word om swaminfeksies te behandel).
- Protease inhibeerders (vir die behandeling van MIV).

**Die volgende kombinasies benodig voorsorgmaatreëls met gebruik:**

- Wanneer opioïede met **XIPANZ XR** gebruik word (sien **'Neem spesiale sorg met XIPANZ XR'**).
- Nefazodoon, fluvoksamien (medisyne gebruik om depressie te behandel) en simetidien (gebruik om maagsuur te verminder)
- Wanneer **XIPANZ XR** saam met fluoksetien ('n antidepressant), orale voorbehoedmiddels, sertralien ('n antidepressant), diltiazem ('n medisyne wat gebruik word om hoë bloeddruk te behandel), of makroliedantibiotika soos eritromisien en troleandomisien gebruik word.
- Wanneer **XIPANZ XR** saam met imipramien en desipramien (antidepressante medisyne) gebruik word, omdat **XIPANZ XR** die konsentrasie van hierdie medisyne verhoog.

**Swangerskap, borsvoeding en fertiliteit**

**XIPANZ XR** kan skadelik wees vir die baba wat ontwikkel, daarom moet u nie **XIPANZ XR** neem indien u swanger is of beplan om swanger te raak of u baba borsvoed nie.

Indien u swanger is of u baba borsvoed, raadpleeg asseblief u dokter, apteker of ander gesondheidsorgkundige vir advies voordat u **XIPANZ XR** neem.

**Bestuur en gebruik van masjinerie**

**XIPANZ XR** kan u lomerig maak. Wees versigtig wanneer u aan gevaarlike beroepe of atiwiteite deelneem wat volledige geestelike waaksaamheid vereis, soos om masjinerie te gebruik of om 'n motor te bestuur.

**Belangrike inligting oor sommige van die bestanddele van XIPANZ XR**

**XIPANZ XR** bevat laktose, 'n tipe suiker. Indien u 'n intoleransie vir sommige suikers het, raadpleeg u dokter vir advies voordat u **XIPANZ XR** neem.

**3. Hoe om XIPANZ XR te gebruik**

Moenie medisyne wat vir u voorgeskryf is met enige ander persoon deel nie.

Neem **XIPANZ XR** altyd presies soos u dokter u voorgeskryf het. Raadpleeg u dokter of apteker indien u onseker is. U dokter sal u vertel hoe lank u behandeling met **XIPANZ XR** sal duur. Indien u die indruk het dat die effek van **XIPANZ XR** te sterk of te swak is, raadpleeg u dokter of apteker.

Die tablette moet heel geneem word; dit moet nie gekou, verbrysel of gebreek word nie.

A. Vir angs of gemengde angs/depressie:

Die gewone aanvangsdosis is 1 mg daagliks in een of twee dosisse. U dokter kan u dosis verhoog indien nodig. Die dosis is egter nie gewoonlik meer as 4 mg per dag nie.

B. Vir paniekversteurings:

Die gewone aanvangsdosis is 0,5 mg tot 1,0 mg voor bedtyd of 0,5 mg twee keer per dag. U dokter kan u dosis verhoog indien nodig. Die dosis is egter nie gewoonlik meer as 10 mg per dag nie.

C. Vir bejaarde pasiënte:

Die gewone aanvangsdosis is 0,5 mg tot 1,0 mg een of twee keer per dag. U dokter kan u dosis verhoog indien nodig. Die dosis is egter nie gewoonlik meer as 1 mg per dag nie.

**Die neem van XIPANZ XR met voedsel, drank en alkohol**

**XIPANZ XR** moet nie met alkohol geneem word nie, aangesien dit die effek van **XIPANZ XR** sal verhoog.

**Indien u meer XIPANZ XR neem as wat u moet**

In die geval van oordosering, raadpleeg u dokter of apteker. Indien geeneen beskikbaar is nie, kontak die naaste hospital of gifbeheersentrum.

Hierdie is die moontlike tekens en simptome van oordosering: onduidelike spraak of verwarring, erge lomerigheid, steier of onstabiel loop, moeilike asemhaling of koma.

**Indien u vergeet om XIPANZ XR te neem**

Indien u vergeet om 'n dosis te neem, neem dit so gou as wat u onthou, tensy dit amper tyd is vir u volgende dosis. Moenie 'n dubbeldosis neem om op te maak vir vergete individuele dosisse nie.

**Indien u ophou om XIPANZ XR te neem**

Ontrekkingsimptome by die staking van **XIPANZ XR** kan wissel van ligte disforie ('n toestand van ongemak of ontevredenheid) en slapeloosheid (slaapprobleme) tot buik- en spierkrampe, braking, sweet, bewing, en konvulsies. Daarbenewens het ontrekkingsaanvalle plaasgevind na 'n vinnige afname of skielike staking van behandeling met **XIPANZ XR** (sien **'Neem spesiale sorg met XIPANZ XR'**).

**4. Moontlike newe-effekte**

**XIPANZ XR kan newe-effekte hê.**

Nie alle newe-effekte aangemeld vir **XIPANZ XR** is in hierdie pamflet ingesluit nie. Indien u algemene gesondheid agteruitgaan of indien u enige ongewensde effekte ervaar terwyl u **XIPANZ XR** neem, raadpleeg asseblief u gesondheidsorgverskaffer vir advies.

Indien enige van die volgende gebeur, hou op om **XIPANZ XR** te neem en vertel u dokter onmiddellik of gaan na die ongevalle-afdeling van u naaste hospitaal:

- Swelling van die hande, voete, gesig, lippe en mond of keel, wat moeilike sluk of asemhaling kan veroorsaak,
- uitslag of jeuk,
- floute.

Hierdie is almal baie ernstige newe-effekte. Indien u dit ervaar, het u 'n ernstige reaksie vir **XIPANZ XR**. U benodig moontlik dringende mediese behandeling of hospitalisasie.

Vertel u dokter onmiddellik of gaan na die ongevalle-afdeling van u naaste hospitaal indien u enige van die volgende opmerk:

- Borspyn,
- vinnige of onreëlmatige hartklop.

Hierdie is almal ernstige newe-effekte. U benodig moontlik dringende behandeling.

Vertel u dokter indien u enige van die volgende opmerk:

*Gereelde newe-effekte:*

- Verminderde eetlus,
- onvermoë om te slaap (slapeloosheid), slaperigheid, verwardheid, depressie, geïrriteerdheid, verminderde libido,
- simptome van ataksie wat 'n verswakte balans en koördinasie, onduidelike spraak kan wees,
- duiseligheid, hoofpyn, verswakte geheue, 'n algemene gebrek aan energie of entoesiasme,
- spin-sensasie (vertigo),
- dowwe visie,
- naarheid, droë mond, hardlywigheid, sweet,
- onwillekeurige urinering, gereelde urinering,
- onreëlmatige menstruasie,
- uitputting (moeg voel), malaise (siek voel of onwel), swakheid.

*Minder gereelde newe-effekte:*

- Aggressie, slaapprobleme, senuweeagtigheid, abnormale drome, apatie, woede, voel of dit langer neem om inligting te verwerk,
- 'n skielike gevoel van intense opgewondenheid en geluk, gemoedswisselings, halusinasie, selfmoordgevoelens, 'n uiterste toename in aktiwiteit en praat (hipomanie),
- vergeetagtig word, bewing ervaar,
- oorpyn, lui in die ore,
- duiselig voel en ongemaklik op u voete (simptome van hipotensie),
- diarree en braking,
- abnormale lewerfunksie (vergeling van vel en oë, buikpyn, swelling van bene en enkels),
- indien 'n uitslag op u liggaam uitbreek,
- spiertrekkings of spierswakheid,
- kan nie urineer nie, seksuele disfunksie,
- koors, dors voel, warm en koud voel,
- traag voel, benoudheid op die bors, verlies van beheer oor u bene,
- toename of afname in gewig.

Indien u enige newe-effekte opmerk wat nie in hierdie pamflet genoem word nie, lig asseblief u dokter of apteker in.

**Aanmelding van newe-effekte**

Indien u newe-effekte ervaar, praat met u dokter, apteker of verpleegster. Dit sluit enige moontlike newe-effekte in wat nie in hierdie pamflet gelys is nie. U kan ook newe-effekte aanmeld aan SAHPRA via die **"6.04 Adverse Drug Reaction Reporting Form"**, wat aanlyn gevind kan word onder SAHPRA se publikasies: https://www.sahpra.org.za/Publications/Index/8. Deur newe-effekte aan te meld, kan u meer inligting verskaf oor die veiligheid van hierdie medisyne.

**5. Hoe om XIPANZ XR te berg**

Berg teen of benede 25 °C.

Hou die HDPE houers dig toe.

**HOU BUITE BEREIK VAN KINDERS.**

Neem alle ongebruikte medisyne terug na u apteker.
Moenie ongebruikte medisyne in dreine of rioolstelsels (bv. toilette) weggooi nie.

**6. Inhoud van die verpakking en ander inligting**

**Wat XIPANZ XR bevat:**

Die aktiewe bestanddeel is alprasolaam 0,5 mg, 1 mg, 2 mg en 3 mg.

Die ander bestanddele is:

- Kolloïdale silikondioksied,
- hipromellose (Methocel K 4M-CR Premium),
- hipromellose (Methocel K 100LV-CR Premium),
- laktosemonohidraat,
- magnesiumstearaat.

Daarbenewens, 1 mg tablet bevat D&C Geel No. 10 aluminiumlak (C.I. No. 47005), 2 mg tablet bevat FD&C Blou No. 2 lak (C.I. No. 73015), 3 mg tablet bevat beide D&C Geel No. 10 aluminiumlak (C.I. No. 47005) & FD&C Blou No. 2 lak (C.I. No. 73015).

**Hoe XIPANZ XR lyk en inhoud van die verpakking**

**XIPANZ XR 0,5 mg:**

Wit tot naaswit, ronde, bikonvekse tablette met 'n skuinsrand, gebosseleer met 'X' aan die een kant en '70' aan die anderkant.

**XIPANZ XR 1 mg:**

Geel gekleurde, ronde, bikonvekse tablette met 'n skuinsrand, gebosseleer met 'X' aan die een kant en '73' aan die ander kant.

**XIPANZ XR 2 mg:**

Blou gekleurde, ronde, bikonvekse tablette met 'n skuinsrand, gebosseleer met 'X' aan die een kant en '74' aan die ander kant.

**XIPANZ XR 3 mg:**

Groen gekleurde, ronde, bikonvekse tablette met 'n skuinsrand, gebosseleer met 'X' aan die een kant en '75' aan die ander kant.

**XIPANZ XR 0,5 mg, 1 mg & 2 mg:**

**1) HDPE-Verpakking**

Die tablette word verpak in 'n wit, ondeursigtige ronde 75 mL Swaar gewig HDPE-houer met 'n nekafwerking van 38 mm gesluit met 38 mm - 400 CR wit, ondeursigtige polipropileen kindweerstandige sluiting met watte en induksie seëlvoering. Die HDPE-houer bevat ook 'n sakkie van 2 gm silikajel en 9 gm per meter katoen.

**Verpakkingsgrootte:** 60's - Een HDPE-houer bevat 60 tablette.

**XIPANZ XR 3 mg:**

**1) HDPE-Verpakking**

Die tablette word verpak in 'n wit, ondeursigtige ronde 40 mL swaar gewig HDPE-houer met 'n nekafwerking van 33 mm gesluit met 33 mm - 400 CR wit, ondeursigtige polipropileen kindweerstandige sluiting met watte en TEKNIPLEX HS 123 induksie seëlvoering. Die HDPE-houer bevat ook 'n sakkie van 1 gm silikajel en 9 gm per meter katoen.

**Verpakkingsgrootte:** 30's - Een HDPE-houer bevat 30 tablette.

**NAAM, BESIGHEIDSADRES EN TELEFOONNOMMER VAN DIE HOUER VAN DIE REGISTRASIESERTIFIKAAT**

Aurogen South Africa (Edms.) Bpk
Woodhill Office Park, Gebou 1, Eerste vloer
Philip Engelbrechtlaan 53
Meyersdal, Uitbr. 12
1448, Johannesburg
Suid-Afrika

**Registrasienommer**

**XIPANZ XR 0,5 mg**: 50/2.6/0094
**XIPANZ XR 1 mg**: 50/2.6/0095
**XIPANZ XR 2 mg**: 50/2.6/0096
**XIPANZ XR 3 mg**: 50/2.6/0097

**Hierdie blad is laas hersien op:**
14 September 2021