For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

TRIKA

1. Generic Name

Alprazolam Tablets I.P.

2. Qualitative and quantitative composition

TRIKA 0.25

Each uncoated tablet contains:

Alprazolam I.P……0.25 mg

Excipients……q.s.

Colour: Brilliant Blue FCF

The excipients used are Lactose Monohydrate, Lake of Brilliant Blue, Povidone K-30, Docusate Sodium, Isopropyl Alcohol, Colloidal Silicon Dioxide, Talc, Sodium Starch Glycolate, and Magnesium Stearate.

TRIKA 0.5

Each uncoated tablet contains:

Alprazolam I.P……0.5 mg

Excipients……q.s.

Colour: Erythrosine

The excipients used are Lactose Monohydrate, Povidone K-30, Docusate Sodium, Colour Erythrosine Supra FCF, Isopropyl Alcohol, Colloidal Silicon Dioxide, Talc, Sodium Starch Glycolate and Magnesium Stearate.

TRIKA 1

Each uncoated tablet contains:

Alprazolam I.P……1 mg

Excipients……q.s.

The excipients used are Lactose Monohydrate, Povidone K-30, Docusate Sodium, Isopropyl Alcohol, Colloidal Silicon Dioxide, Talc, Sodium Starch Glycolate and Magnesium Stearate.

3. Dosage form and strength

Dosage form: Uncoated Tablet

Strength: 0.25 mg, 0.5 mg, 1 mg

4. Clinical particulars

4.1 Therapeutic indication

TRIKA is an Anxiolytic agent- Indicated in the treatment of anxiety associated with depression

4.2 Posology and method of administration

Posology

Anxiety

250 micrograms (0.25 mg) to 500 micrograms (0.5 mg) three times daily, increasing if required to a total of 3 mg daily.

The elderly or in the presence of debilitating disease

250 micrograms (0.25 mg) two to three times daily to be gradually increased if needed and tolerated.

If side-effects occur, the dose should be lowered. It is advisable to review treatment regularly and to discontinue use as soon as possible. Should longer term treatment be necessary, then intermittent treatment may be considered to minimize the risk of dependence.

Paediatric population

The safety and efficacy of alprazolam in children and adolescents below the age of 18 years have not been established. No data are available.

Method of administration

For oral use.

Treatment should be as short as possible. It is recommended that the patient be reassessed at the end of no longer than 4 weeks of treatment and the need for continued treatment established, especially in case the patient is symptom free. The overall duration of treatment should not be more than 8-12 weeks, including a tapering off process.

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 with special expertise. As with all benzodiazepines, physicians should be aware that long-term use might lead to dependence in certain patients.

The optimum dosage of TRIKA should be based upon the severity of the symptoms and individual patient response. The lowest dose which can control symptoms should be used. Dosage should be reassessed at intervals of no more than 4 weeks. The usual dosage is stated below; in the few patients who require higher doses, the dosage should be increased cautiously to avoid adverse effects. When higher dosage is required, the evening dose should be increased before the daytime doses. In general, patients who have not previously received psychotropic medications will require lower doses than those so treated, or those with a history of chronic alcoholism.

Treatment should always be tapered off gradually. During discontinuation of

alprazolam treatment, the dosage should be reduced slowly in keeping with good medical practice. It is suggested that the daily dosage of alprazolam be decreased by no more than 0.5 mg every three days. Some patients may require an even slower dosage reduction.

Elderly patients

There is a reduced clearance of the drug and, as with other benzodiazepines, an increased sensitivity to the drug in elderly patients.

4.3 Contraindications

Hypersensitivity to benzodiazepines, alprazolam, or to any of the excipients.

Benzodiazepines are also contraindicated in patients with myasthenia gravis, severe respiratory insufficiency, sleep apnoea syndrome and severe hepatic insufficiency.

4.4 Special warnings and precautions for use

Renal and hepatic impairment

Caution is recommended when treating patients with impaired renal function or mild to moderate hepatic insufficiency.

Depression/anxiety

In patients presenting with major depression or anxiety associated with depression benzodiazepines and benzodiazepine-like agents should not be prescribed alone to treat depression as they may precipitate or increase the risk of suicide. Therefore, alprazolam should be used with caution and the prescription size should be limited in patients with signs and symptoms of a depressive disorder or suicidal tendencies.

Paediatric population

Safety and efficacy of alprazolam have not been established in children and adolescents below the age of 18 years; therefore, use of alprazolam is not recommended.

Elderly patients

Benzodiazepines and related products should be used with caution in elderly, due to the risk of sedation and / or musculoskeletal weakness that can promote falls, often with serious consequences in this population.

It is recommended that general principle of using the lowest effective dose to be followed in elderly and /or debilitated patients to preclude development of ataxia or over-sedation. A lower dose is also recommended for patients with chronic respiratory insufficiency due to risk of respiratory depression.

Benzodiazepines should be used with extreme caution in patients with a history of alcohol or drug abuse).

Risk from concomitant use of opioids

Concomitant use of TRIKA and opioids may result in sedation, respiratory depression, coma and death. Because of these risks, concomitant prescribing of sedative medicines

such as benzodiazepines or related drugs such as TRIKA with opioids should be reserved for patients for whom alternative treatment options are not possible.

If a decision is made to prescribe TRIKA concomitantly with opioids, the lowest effective dose should be used, and the duration of treatment should be as short as possible.

The patients should be followed closely for signs and symptoms of respiratory depression and sedation. In this respect, it is strongly recommended to inform patients and their environment to be aware of these symptom).

Dependence

Use of benzodiazepines may lead to the development of physical and psychic dependence upon these products. The risk of dependence increases with dose and duration of treatment; it is also greater in patients with a history of alcohol and drug abuse. Pharmacodependency may occur at therapeutic doses and/or in patients with no individualised risk factor. There is an increased risk of Pharmacodependency with the combined use of several benzodiazepines regardless of the anxiolytic or hypnotic indication. Cases of abuse have also been reported.

Withdrawal symptoms: Once physical dependence has developed; abrupt termination of treatment will be accompanied by withdrawal symptoms. These may consist of headaches, muscle pain, extreme anxiety, tension, restlessness, confusion, irritability and insomnia. 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.

During discontinuation of alprazolam treatment, the dosage should be reduced slowly in keeping with good medical practice. It is suggested that the daily dosage of alprazolam be decreased by no more than 0.5 mg every three days. Some patients may require even slower dosage reduction.

Rebound insomnia and anxiety: a transient syndrome whereby the symptoms that led to treatment with a benzodiazepine recur in an enhanced form may occur on withdrawal of treatment. It may be accompanied by other reactions including mood changes, anxiety or sleep disturbances and restlessness. Since the risk of withdrawal phenomena/rebound phenomena is greater after abrupt discontinuation of treatment, it is recommended that the dosage be decreased gradually by no more than 0.5 mg every three days. Some patients may require an even slower dose reduction).

Duration of treatment

The duration of treatment should be as depending on the indication, but should not exceed eight to twelve weeks including tapering off process. Extension beyond these periods should not take place without re-evaluation of the situation.

It may be useful to inform the patient when treatment is started that it will be of limited duration and to explain precisely how the dosage will be progressively decreased. Moreover, it is important that the patient should be aware of the possibility of rebound phenomena, thereby minimising anxiety over such symptoms should they occur while the medicinal product is being discontinued. There are indications, that in the case of

benzodiazepines with a short duration of action, withdrawal phenomena can become manifest within the dosage interval, especially when the dosage is high. When benzodiazepines with a long duration of action are being used it is important to warn against changing to a benzodiazepine with a short duration of action, as withdrawal symptoms may develop.

Amnesia

Benzodiazepines may induce anterograde amnesia. The condition occurs most often several hours after ingesting the product and therefore to reduce the risk patients should ensure that they will be able to have uninterrupted sleep of 7-8 hours.

Psychiatric and paradoxical reactions

Reactions like restlessness, agitation, irritability, aggressiveness, delusion, rages, nightmares, hallucinations, psychoses, inappropriate behaviour and other adverse behavioural effects are known to occur when using benzodiazepines. Should this occur, use of the medicinal product should be discontinued. They are more likely to occur in children and the elderly.

Tolerance

Some loss of efficacy to the hypnotic effects of benzodiazepines may develop after repeated use for a few weeks.

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

Benzodiazepines are not recommended for the primary treatment of psychotic illness.

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Drugs interactions

Opioids

The concomitant use of sedative medicines such as benzodiazepines or related drugs such as TRIKA with opioids increases the risk of sedation, respiratory depression, coma and death because of additive central nervous system (CNS) depressant effect. The dosage and duration of concomitant use should be limited. Concomitant intake with alcohol is not recommended. Alprazolam should be used with caution when combined with CNS depressants.

Enhancement of the central depressive effect may occur in cases of concomitant use with antipsychotics (neuroleptics), hypnotics, anxiolytics/sedatives, antidepressant agents, narcotic analgesics, anti-epileptic drugs, anaesthetics and sedative antihistamines. In the case of narcotic analgesics enhancement of the euphoria may also occur leading to an increase in psychic dependence.

Pharmacokinetic interactions can occur when alprazolam is administered along with drugs that interfere with its metabolism.

CYP3A Inhibitors

Compounds that inhibit certain hepatic enzymes (particularly cytochrome P450 3A4)

may increase the concentration of alprazolam and enhance its activity. Data from clinical studies with alprazolam, in-vitro studies with alprazolam and clinical studies with drugs metabolised similarly to alprazolam provide evidence for varying degrees of interaction and possible interaction with alprazolam for a number of drugs. Based on the degree of interaction and the type of data available, the following recommendations are made:

• The co-administration of alprazolam with ketoconazole, itraconazole, or other azole-type antifungals is not recommended.

• The co-administration of nefazodone or fluvoxamine increases the AUC of alprazolam by approximately 2-fold. Caution and consideration of dose reduction is recommended when alprazolam is co-administered with nefazodone, fluvoxamine and cimetidine.

• Caution is recommended when alprazolam is co-administered with fluoxetine, propoxyphene, oral contraceptives, sertraline, diltiazem, or macrolide antibiotics such as erythromycin, clarithromycin and troleandomycin.

CYP3A4 Inducers

Since alprazolam is metabolized by CYP3A4, inducers of this enzyme may enhance the metabolism of alprazolam. Interactions involving HIV protease inhibitors (e.g. ritonavir) and alprazolam are complex and time dependent. Short term, low doses of ritonavir resulted in a large impairment of alprazolam clearance, prolonged its elimination half-life and enhanced clinical effects. However, upon extended exposure to ritonavir, CYP3A induction offset this inhibition. This interaction will require a dose-adjustment or discontinuation of alprazolam.

Digoxin

Increased digoxin concentrations have been reported when alprazolam was given, especially in elderly (>65 years of age). Patients who receive alprazolam and digoxin should therefore be monitored for signs and symptoms related to digoxin toxicity.

4.6 Use in special populations

Pregnancy

The data concerning teratogenicity and effects on postnatal development and behaviour following benzodiazepine treatment are inconsistent. A large amount of data based on cohort studies indicate that first trimester exposure to benzodiazepine is not associated with an increase in the risk of major malformation. However, some early case-control epidemiological studies have found a twofold increased risk of oral clefts.

Benzodiazepine treatment at high dose, during the second and/or the third trimester of pregnancy, has revealed a decrease of fetal active movements and a variability of fetal cardiac rhythm.

When treatment has to be administered for medical reasons during the last part of pregnancy, even at low doses, floppy infant syndrome such as axial hypotonia, sucking

troubles leading to a poor weight gain may be observed. These signs are reversible but they may last from 1 up to 3 weeks, according to the half-life of the product. At high

doses, respiratory depression or apnoea and hypothermia in new-born may appear. Moreover, neonatal withdrawal symptoms with hyper excitability, agitation and tremor may be observed a few days after birth, even if no floppy infant syndrome is observed. The apparition of withdrawal symptoms after birth depends on the half-life of the substance.

Alprazolam should not be used during pregnancy unless the clinical condition of the woman requires treatment with alprazolam. If alprazolam is used during pregnancy, or of the patient becomes pregnant while taking alprazolam, the patient should be apprised of the potential hazard to the fetus.

If alprazolam treatment is necessary during last part of pregnancy, high doses should be avoided and withdrawal symptoms and/or floppy infant syndrome should be monitored in new-born.

Breast-feeding

Alprazolam is excreted in breast milk at low level. However, alprazolam is not recommended during breast-feeding.

4.7 Effects on ability to drive and use machines

Sedation, amnesia, impaired concentration and impaired muscle function may adversely affect the ability to drive and use machines. If insufficient sleep occurs, the likelihood of impaired alertness may be increased.

These effects are potentiated by alcohol.

Patients should be cautioned about operating motor vehicles or engaging in other dangerous activities while taking TRIKA.

This medicine can impair cognitive function and can affect a patient's ability to drive safely.

4.8 Undesirable effects

Adverse events, if they occur, are generally observed at the beginning of therapy and usually disappear upon continued medication or decreased dosage.

The following undesirable effects have been observed and reported during treatment with alprazolam with the following frequencies: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).

MedDRA System Organ Class	**Frequency**	**Undesirable Effects**
Endocrine disorders	**Not known**	Hyperprolactinaemia*
Metabolism and nutrition	**Common**	Decreased appetite

disorders		
Psychiatric disorders	**Very common**	Depression
	Common	Confusional state, disorientation, libido decreased, anxiety, insomnia, nervousness, libido increased*
	Uncommon	Mania* , hallucination*, anger*, agitation*
	Not known	Hypomania*, aggression*, hostility*, thinking abnormal*, psychomotor hyperactivity*
Nervous system disorders	**Very common**	Sedation, somnolence, ataxia, memory impairment, dysarthria, dizziness, headache
	Common	Balance disorder, coordination abnormal, disturbance in attention, hypersomnia, lethargy, tremor
	Uncommon	Amnesia
	Not Known	Autonomic nervous system imbalance*, dystonia*
Eye disorders	**Common**	Vision blurred
Gastrointestinal disorders	**Very common**	Constipation, dry mouth
	Common	Nausea
	Not known	Gastrointestinal disorder*
Hepatobiliary disorders	**Not known**	Hepatitis*, hepatic function abnormal*, jaundice*
Skin and subcutaneous tissue disorders	**Common**	Dermatitis*
	Not Known	Angioedema*, photosensitivity reaction*
Musculoskeletal and connective tissue disorders	**Uncommon**	Muscular weakness

Renal and urinary disorders	**Uncommon**	Incontinence*
	Not known	Urinary retention*
Reproductive system and breast disorders	**Common**	Sexual dysfunction*
	Uncommon	Menstruation irregular*
General disorders and administration site conditions	**Very common**	Fatigue, irritability
	Not Known	Oedema peripheral*
Investigations	**Common**	Weight increased, weight decreased
	Not known	Intraocular pressure increased*

* ADR identified post-marketing

Withdrawal symptoms have occurred following rapid decrease or abrupt discontinuance of benzodiazepines including alprazolam. 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 alprazolam.

Amnesia

Anterograde amnesia may occur at therapeutic dosages, the risk increasing at higher dosages. Amnesic effects may be associated with inappropriate behaviour.

Depression

Pre-existing depression may be unmasked during benzodiazepine use.

Psychiatric and paradoxical reactions

Reactions like restlessness, agitation, irritability, aggressiveness, delusion, rages, nightmares, hallucinations, psychoses, inappropriate behaviour and other adverse behavioural effects are known to occur when using benzodiazepines or benzodiazepine-like agents. They may be quite severe with this product. They are more likely to occur in children and the elderly.

In many of the spontaneous case reports of adverse behavioural effects, patients were receiving other CNS drugs concomitantly and/or were described as having underlying psychiatric conditions. Patients who have borderline personality disorder, a prior history of violent or aggressive behaviour, or alcohol or substance abuse may be at risk of such events. Instances of irritability, hostility and intrusive thoughts have been reported during discontinuance of alprazolam in patients with post-traumatic stress disorder.

Dependence

Use (even at therapeutic doses) may lead to the development of physical dependence: discontinuation of the therapy may result in withdrawal or rebound phenomena. Psychic dependence may occur. Abuse of benzodiazepines has been reported

Reporting of side effects

If you get any 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 directly via any point of contact of Torrent Pharma available at:

http://www.torrentpharma.com/index.php/site/info/adverse_event_reporting.

By reporting side effects, you can help provide more information on the safety of this medicine.

4.9 Overdose

As with other benzodiazepines, overdose should not present a threat to life unless combined with other CNS depressants (including alcohol). In the management of overdose with any medicinal product, it should be borne in mind that multiple agents have been taken.

Following overdose with oral benzodiazepines, vomiting may be induced (within 1 hour) if the patient is conscious or gastric lavage undertaken with the airway protected if the patient is unconscious. If there is no advantage in emptying the stomach, activated charcoal should be given to reduce absorption.

Special attention should be paid to respiratory and cardiovascular functions in intensive care.

Overdose of benzodiazepines is usually manifested by degrees of central nervous system depression ranging from drowsiness to coma. In mild cases, symptoms include drowsiness, mental confusion and lethargy, in more serious cases, symptoms may include ataxia, hypotonia, hypotension, respiratory depression, rarely coma and very rarely death.

Flumazenil may be useful as an antidote.

5. Pharmacological properties

5.1 Mechanism of Action

The exact mechanism of action of alprazolam is unknown. Benzodiazepines bind to gamma aminobutyric acid (GABA) receptors in the brain and enhance GABA mediated synaptic inhibition; such actions may be responsible for the efficacy of alprazolam in anxiety disorder and panic disorder.

5.2 Pharmacodynamicproperties

Pharmacotherapeutic group: Benzodiazepine derivatives, ATC code: N05BA12

Alprazolam, like other benzodiazepines, has a high affinity for the benzodiazepine binding site in the brain. It facilitates the inhibitory neurotransmitter action of gamma-aminobutyric acid, which mediates both pre- and post-synaptic inhibition in the central nervous system (CNS).

5.3 Pharmacokinetic properties

Alprazolam is readily absorbed. Following oral administration peak concentration in the plasma occurs after 1 - 2 hours.

The mean half-life is 12 - 15 hours. Repeated dosage may lead to accumulation and this should be borne in mind in elderly patients and those with impaired renal or hepatic function. Alprazolam and its metabolites are excreted primarily in the urine. *In vitro* alprazolam is bound (80%) to human serum protein.

6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

Mutagenesis and Carcinogenesis

Non-clinical data reveal no special hazard for humans based on conventional studies of genotoxicity and carcinogenic potential.

Ocular Effects

When rats were treated orally with alprazolam for 2 years, a tendency for a dose related increase in the number of cataracts (females) and corneal vascularization (males) was observed. These lesions did not appear until after 11 months of treatment.

Fertility

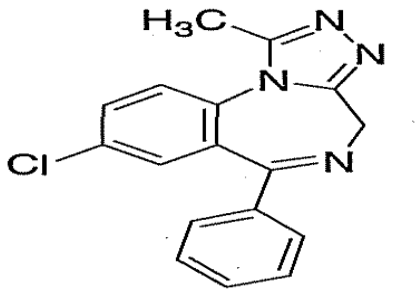
In reproductive toxicity studies administration of alprazolam in rats and rabbits is associated at very high doses with developmental delay and an increased incidence of fetal death and skeletal malformations. In fertility studies, treatment of male rats at high doses prior to mating resulted in a decrease in the percentage of dams conceiving.

Effect of anesthetic and sedative drugs

Nonclinical research has shown that administration of anesthetic and sedation drugs that block N-Methyl-D-aspartate (NMDA) receptors and/or potentiate gamma-aminobutyric acid (GABA) activity can increase neuronal cell death in the brain and result in long term deficits in cognition and behavior of juvenile animals when administered during the period of peak brain development. Based on comparisons across nonclinical species, the window of vulnerability of the brain to these effects is believed to correlate with human exposures in the third trimester of pregnancy through the first year of life, but may extend to approximately 3 years of age. While there is limited information of this effect with alprazolam, since the mechanism of action includes potentiation of GABA activity, a similar effect may occur. The relevance of these nonclinical findings to human use is unknown.

7. Description

Alprazolarn is 8-chloro-1-methyl-6-phenyl-4H-1, 2, 4-triazolo[4,3-a] [1,4]benzodiazepine. Having molecular formula $C_{17}H_{13}ClN_4$ and molecular weight 308.8. The chemical structure is:



Alprazolam is a white to off-white, crystalline powder.

TRIKA 0.25

Alprazolam Tablets are Round, flat, bevel edged, light blue uncoated tablets one side plain and 'Trika' debossed on one half and picture of butterfly on the other half of other side. The excipients used are Lactose Monohydrate, Lake of Brilliant Blue, Povidone K-30, Docusate Sodium, Isopropyl Alcohol, Colloidal Silicon Dioxide, Talc, Sodium Starch Glycolate, and Magnesium Stearate.

TRIKA 0.5

Alprazolam Tablets are Round, flat, bevel edged, light Pink uncoated tablets one side plain and 'Trika' debossed on one half and picture of butterfly on the other half of other side. The excipients used are Lactose Monohydrate, Povidone K-30, Docusate Sodium, Colour Erythrosine Supra FCF, Isopropyl Alcohol, Colloidal Silicon Dioxide, Talc, Sodium Starch Glycolate and Magnesium Stearate.

TRIKA 1

Alprazolam Tablets are Round, flat, bevel edged, White uncoated tablets one side plain and 'Trika' debossed on one half and picture of butterfly on the other half of other side. The excipients used are Lactose Monohydrate, Povidone K-30, Docusate Sodium, Isopropyl Alcohol, Colloidal Silicon Dioxide, Talc, Sodium Starch Glycolate and Magnesium Stearate.

8. Pharmaceutical particulars

8.1 Incompatibilities

Not applicable.

8.2 Shelf-life

Do not use later than the date of expiry

8.3 Packaging information

TRIKA 0.25 and TRIKA 0.5 is available in 15 COMPOSITE PACKS OF 4X15 TABLETS EACH
TRIKA 1 is available in 5 COMPOSITE PACKS OF 6X10 TABLETS EACH

8.4 Storage and handing instructions

STORE IN A COOL, DRY & DARK

PLACE. Keep all medicines out of reach of

children.

9. Patient Counselling Information

TRIKA

0.25 mg, 0.5mg and 1 mg Tablets alprazolam

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

· Keep this leaflet. You may need to read it again.

· If you have any further questions, ask your doctor or pharmacist.

· This medicine has been prescribed for you only. Do not pass it on to others; it may harm them, even if their signs of illness are the same as yours.

· If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

What is in this leaflet

9.1 What TRIKA is and what it is used for

TRIKA is a tranquilliser containing the active ingredient alprazolam. Alprazolam belongs to one of a group of medicines called benzodiazepines. Benzodiazepines affect chemical activity in the brain to promote sleep and to reduce anxiety and worry.

TRIKA tablets are only used to treat severe anxiety and severe anxiety associated with depression. TRIKA is not recommended for the treatment of depression. TRIKA tablets should only be used for short-term treatment of anxiety. The overall duration of treatment should not be more than 12 weeks including a period where the dose is gradually reduced (this is called dose 'tapering').

You must talk to a doctor if you do not feel better or if you feel worse.

9.2. What you need to know before you take

TRIKA Do not use TRIKA:

- If you are allergic to alprazolam or other similar benzodiazepine medicines, or to any of the other inactive ingredients of this medicine.

- If you suffer from a disease called 'myasthenia gravis' where you suffer from very weak and tired muscles.

- If you have severe chest problems or breathing difficulties (e.g. chronic bronchitis or emphysema).

- If you have 'sleep apnoea' - this is a condition where your breathing becomes irregular, even stopping for short periods, while you are asleep.

- If you have severe liver problems.

- If you are pregnant, think you might be pregnant now, are planning to become pregnant or if you are breast-feeding (see also the sections on 'Pregnancy' and 'Breast-feeding' for more information).

Warnings and precautions

Talk to your doctor or pharmacist before taking TRIKA if you:

- Have ever felt so depressed that you have thought about taking your own life.

- Have ever suffered any mental illness that required hospital treatment.

- Have problems with your lungs, kidneys or liver.

- Have abused drugs or alcohol in the past or find it difficult to stop taking medicines, drinking or taking drugs. Your doctor may want to give you special help when you need to stop taking these tablets.

- Have been prescribed medicines for severe anxiety before, because your body can quickly become used to this type of medicine so that it no longer helps you

Benzodiazepines and related products should be used with caution in elderly, due to the risk of sedation and / or musculoskeletal weakness that can promote falls, often with serious consequences in this population.

Children and adolescents

Do not give this medicine to children and adolescents below the age of 18 years because safety and efficacy have not been established.

Other medicines and TRIKA

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, especially medicines listed below, as the effect of TRIKA or the other medicine may change when taken at the same time:

- Any other medicines to treat anxiety or depression or to help you sleep (e.g. nefazodone, fluvoxamine, fluoxetine).

- Some strong pain killers (e.g. opioids such as - morphine, codeine or propoxyphene).

- Antipsychotic medicines used to treat mental illnesses like schizophrenia.

- Medicines to treat epilepsy.

- Antihistamines for relief of allergies.

- Medicines for treating fungal infections (e.g. ketoconazole).

- Oral contraceptives (‘the pill’).

- Certain antibiotics (e.g. erythromycin).

- Cimetidine (for treating stomach ulcers).

- Diltiazem (used for angina and high blood pressure).

- Digoxin (used to treat various heart conditions).

- Ritonavir or other similar medicines used for treating HIV.

If you are going to have an operation where you will be given a general anaesthetic, tell your doctor or anaesthetist that you are taking TRIKA.

Concomitant use of TRIKA and opioids (strong pain killers, medicines for substitution therapy and some cough medicines) increases the risk of drowsiness, difficulties in

breathing (respiratory depression), coma and may be life-threatening. Because of this, concomitant use should only be considered when other treatment options are not possible. However, if your doctor does prescribe TRIKA together with opioids the dosage and duration of concomitant treatment should be limited by your doctor. Please tell your doctor about all opioid medicines you are taking, and follow your doctor's dosage recommendation closely. It could be helpful to inform friends or relatives to be aware of sign and symptoms stated above. Contact your doctor when experiencing such symptoms

TRIKA with food, drink and alcohol

It is important not to drink any alcohol while you are taking TRIKA, as alcohol increases the effects of the medicine.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Do not breast-feed while taking TRIKA, as the drug may pass into breast milk.

Driving and using machines

TRIKA can make you feel sleepy or woozy and make you lose concentration so it is very important you do not operate machinery until you know how the tablets affect you.

TRIKA can affect your ability to drive as it may make you sleepy or dizzy.

9.3. How to take TRIKA Tablets?

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Your doctor will tell you how many tablets to take and when to take them. This information is also on the label of the carton the tablets come in.

Do not take your tablets with an alcoholic drink.

The recommended dose is:

Adults

You will usually start by taking one 250 microgram or one 500 microgram tablet three times a day. This gives a total dose of 750 micrograms to 1500 micrograms each day.

If clinically required, your doctor may increase your medicine in small increments. Where the dose does need to be increased, it is usual to increase the night time dose first, before the daytime doses to make sure you are more alert during the day. If you start to get side effects the doctor may lower your dose.

The elderly

If you are an older patient or you have for example kidney or liver problems and you need a lower dose you will normally start on a dose of 250 micrograms two or three times a day. This dose may be slowly increased if needed and if you do not get any side effects.

Use in children and adolescents

Alprazolam is not recommended for children and adolescents under the age of 18 years.

Route and/or method of administration

For oral use.

Duration of treatment

TRIKA tablets are only used for short-term treatment (not more than 12 weeks). You will not normally be given a prescription for more than 4 weeks and you will be regularly reviewed by your doctor during this time. A decreased effect of the drug may develop if used for more than a few weeks.

If you take more TRIKA than you should

It is important that you do not take more tablets than you are told to. If you do accidentally take too many tablets you may experience drowsiness, confusion, feeling cold, slurred speech, drop in blood pressure and difficulty breathing. If you do accidentally take too many tablets, seek medical attention straight away.

If you forget to take TRIKA

If you forget to take a dose, take it as soon as you remember unless it is time for your next dose.

Do not take a double dose to make up for a missed dose.

If you stop taking TRIKA

Always see your doctor before you stop taking TRIKA tablets as the dose needs to be reduced gradually. If you stop taking the tablets or reduce the dose suddenly you can get 'rebound' effects which might cause you to become temporarily more anxious or restless or to have difficulty sleeping. These symptoms will go away as your body re-adjusts. If you are worried, your doctor can tell you more about this.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

9.4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everyone gets them.

Reasons for stopping TRIKA treatment immediately

If you get any of these symptoms see your doctor straight away as treatment will need to be discontinued. Your doctor will then advise how treatment will be stopped.

- Very occasionally treatment with TRIKA can cause serious behavioral or psychiatric effects - for example agitation, restlessness, aggressiveness, irritability, violent anger, false beliefs, nightmares and hallucinations or other inappropriate behavior.

- Sudden wheeziness, difficulty in swallowing or breathing, swelling of eyelids, face or lips, rash or itching (especially affecting the whole body).

Reasons for seeing your doctor straight away

Tell your doctor straight away if you get the following symptoms as your dose or treatment might need to be changed:

- Memory loss (amnesia).

- Yellowing of the skin and whites of the eyes (jaundice).

Dependence and withdrawal symptoms

It is possible to become dependent on medicines like TRIKA while you are taking them which increases the likelihood of getting withdrawal symptoms when you stop treatment.

Withdrawal symptoms are more common if you:

- stop treatment suddenly

- have been taking high doses

- have been taking this medicine for long time

- have a history of alcohol or drug abuse.

This can cause effects such as headaches, muscle pain, extreme anxiety, tension, restlessness, confusion, mood changes, difficulty sleeping and irritability.

In severe cases of withdrawal, you can also get the following symptoms: nausea (feeling sick), vomiting, sweating, stomach cramps, muscle cramps, a feeling of unreality or detachment, being unusually sensitive to sound, light or physical contact, numbness and tingling of the feet and hands, hallucinations (seeing or hearing things which are not there while you are awake), tremor or epileptic fits.

Other side effects that may occur are:

Very common: may affect more than 1 in 10 people

- Depression

- Sleepiness and drowsiness

- Jerky, uncoordinated movements

- Inability to remember bits of information

- Slurred speech

- Dizziness, light-headedness

- Headaches

- Constipation

- Dry mouth

- Tiredness

- Irritability

Common: may affect up to 1 in 10 people

- Loss of appetite

- Confusion and disorientation
- Increased sex drive (men and women) and erectile dysfunction
- Nervousness or feeling anxious or agitated
- Insomnia (inability to sleep or disturbed sleep)
- Problems with balance, and unsteadiness (similar to feeling drunk) especially during the day
- Loss of alertness or concentration
- Inability to stay awake, feeling sluggish
- Shakiness or trembling
- Double or blurred vision
- Feeling sick
- Skin reactions
- Change in your weight

Uncommon: may affect up to 1 in 100 people

- Feeling elated or over-excited, which causes unusual behavior
- Hallucination (seeing or hearing things that do not exist)
- Feeling agitated or angry
- Incontinence
- Cramping pain in the lower back and thighs, which may indicate menstrual disorder
- Muscle spasms or weakness

Not known: frequency cannot be estimated from available data

- In women, irregular periods or production of too much prolactin (the hormone that stimulates milk production)
- Feeling hostile or aggressive
- Abnormal thoughts
- Twisting or jerking movements
- Being hyperactive
- Stomach upsets
- Problems with liver function (this shows up in blood tests), inflammation of the liver (hepatitis)
- Imbalance to part of nervous system. Symptoms may include: fast heart beat and unstable blood pressure (feeling dizzy, light-headed or faint)
- Serious allergic reaction which causes swelling of the face or throat
- Swelling of the ankles, feet or fingers

- Skin reaction caused by sensitivity to sunlight

- Difficulty urinating or bladder control problems

- Increased pressure in the eyes, which can also affect your vision

Reporting of side effects

If you get any 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 directly via any point of contact of Torrent Pharma available at: https://www.torrentpharma.com/index.php/site/info/adverse_event_reporting.

By reporting side effects, you can help provide more information on the safety of this medicine.

9.5. How to store TRIKA.

Store in a cool, dry & dark place. Keep all medicines out of reach of children.

9. 6. Contents of the pack and other information

What TRIKA Looks like and contents of the pack

TRIKA 0.25, 0.5, 1 contains active substance

Alprazolam **TRIKA 0.25**

Other Inactive ingredients are Lactose Monohydrate, Lake of Brilliant Blue, Povidone K-30, Docusate Sodium, Isopropyl Alcohol, Colloidal Silicon Dioxide, Talc, Sodium Starch Glycolate, Magnesium Stearate.

TRIKA 0.5

Other Inactive ingredients are Lactose Monohydrate, Povidone K-30, Docusate Sodium, Colour Erythrosine Supra FCF, Isopropyl Alcohol, Colloidal Silicon Dioxide, Talc, Sodium Starch Glycolate, Magnesium Stearate.

TRIKA 1

Other Inactive ingredients are Lactose Monohydrate, Povidone K-30, Docusate Sodium, Isopropyl Alcohol, Colloidal Silicon Dioxide, Talc, Sodium Starch Glycolate, Magnesium Stearate

10. Details of manufacturer

TORRENT PHARMACEUTICALS LTD.

32 No. Middle Camp, NH-10,

East District, Gangtok, Sikkim-737 135.

Or

Uni Medicolabs

25 & 26, Pharmacity, Selaqui,

Dehradun, Uttarakhand.

11. Details of permission or licence number with date

Mfg Lic No.: M/563/2010 issued on 06.12.2021

OR

Mfg Licence No.: 29/UA/2018 issued on 19.11.2020

12. Date of revision

Aug-2022

MARKETED BY

Torrent Pharmaceuticals Ltd.

IN/ TRIKA 0.25, 0.5 and 1mg/Aug 2022 /02/PI