Doctor Leaflet

1. NAME OF THE MEDICINAL PRODUCT

VABEN TABLETS

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 10mg Oxazepam

3. PHARMACEUTICAL FORM

White tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Anxiolytic.

4.2 Posology and method of administration

Posology

Tablets for oral administration.

All patients taking oxazepam should be carefully monitored and routine repeat prescriptions be avoided. Patients who have received benzodiazepines for a long time may require an extended withdrawal period. Long-term chronic use is not recommended.

As an anxiolytic, the lowest effective dose should be employed, for the shortest time possible; dosage regimes should not exceed beyond 4 weeks and treatment should always be gradually withdrawn.

Adults:

Anxiety 10-30mg three or four times a day.

Elderly patients and those who are particularly sensitive to benzodiazepines: initial dosage 10 mg three times daily. If necessary, increase cautiously to 15 mg three or four times daily.

Children: Not recommended for children.

4.3 Contraindications

Known hypersensitivity to benzodiazepines or any other ingredient in the tablet**;** phobic or obsessional states; chronic psychosis; respiratory depression, acute pulmonary insufficiency; myasthenia gravis; sleep apnoea syndrome; severe hepatic insufficiency.

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

4.4 Special warnings and precautions for use

Tolerance

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

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 or drug abuse.

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 and irritability. In severe cases the following symptoms may occur: derealisation, depersonalisation, hyperacusis, numbness and tingling of the extremities, hypersensitivity to light, noise and physical contact, hallucinations or epileptic seizures.

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 is decreased.

Duration of treatment

The duration of treatment should be as short as possible (see Posology) depending on the indication, but should not exceed 4 weeks for insomnia and eight to twelve weeks in case of anxiety, including tapering off process. Extension beyond these periods should not take place without reevaluation 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 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 an uninterrupted sleep of 7-8 hours (see also Undesirable Effects).

Psychiatric and paradoxical reaction

Reactions like restlessness, agitation, irritability, aggressiveness, delusion, rages, nightmares, hallucinations, psychoses, inappropriate behavior and other adverse behavioral 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.

Specific patient groups

Benzodiazepines should not be given to children without careful assessment of the need to do so; the duration of treatment must be kept to a minimum. Elderly should be given a reduced dose (see Posology). A lower dose is also recommended for patients with chronic respiratory insufficiency due to the risk of respiratory depression. Benzodiazepines are not indicated to treat patients with severe hepatic insufficiency as they may precipitate encephalopathy, renal impairment, muscle weakness or porphyria.

Benzodiazepines are not recommended for the primary treatment of psychotic illness or marked personality disorder.

Benzodiazepines should not be used alone to treat depression or anxiety associated with depression (suicide may be precipitated in such patients).

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

4.5 Interaction with other medicinal products and other forms of interaction

The following drug interactions with oxazepam should be considered:

• Enhancement of other CNS depressant drugs such as antipsychotics, narcotic analgesics (enhancement of euphoria may also occur, leading to an increase in psychic dependence), antidepressants, hypnotics, anaesthetics, sedative antihistamines, lofexidine, nabilone and tizanidine.

• Oestrogen-containing contraceptives (concurrent use may cause a decrease in plasma levels of oxazepam).

• Antibacterials (Rifampicin may increase the metabolism of oxazepam).

• Antivirals (concurrent use of zidovudine with benzodiazepines may decrease Zidovudine clearance. Ritonavir may inhibit benzodiazepine hepatic metabolism).

• Antiepileptic drugs (concurrent use of phenytoin may cause oxazepam serum levels to fall. Side effects may be more evident with hydantoins or barbiturates).

• Alcohol (concomitant intake with alcohol is not recommended. The sedative effects may be enhanced when oxazepam is used in combination with alcohol. This affects the ability to drive or use machines.)

• Antihypertensives (enhanced hypotensive effects. Enhances sedative effect with alpha blockers or moxonidine)

• Dopaminergics (concurrent use with benzodiazepines may decrease the therapeutic effects of levodopa).

• Baclofen (enhanced sedative effect).

• Probenecid (may increase effects and possibility of excessive sedation).

4.6 Pregnancy and lactation

If the product is prescribed to a woman of childbearing potential, she should be warned to contact her physician regarding discontinuance of the product if she intends to become or suspects that she is pregnant.

If, for compelling medical reasons, the product is administered during the late phase of pregnancy, or during labour at high doses, effects on the neonate, such as hypothermia, hypotonia and moderate respiratory depression, can be expected, due to the pharmacological action of the compound.

Moreover, infants born to mothers who took benzodiazepines chronically during the latter stages of pregnancy may have developed physical dependence and may be at some risk for developing withdrawal symptoms in the postnatal period.

Since benzodiazepines are found in the breast milk, benzodiazepines should not be given to breast feeding mothers.

4.7 Effects on ability to drive and use machines

Sedation, amnesia and impaired muscular function may adversely affect the ability to drive or use machines. If insufficient sleep occurs, the likelihood of impaired alertness may be increased (see also Interactions).

4.8 Undesirable effects

When used at the appropriate recommended dosage for short term treatment of anxiety the dependence potential of oxazepam is low. However, the risk of dependence increases with higher doses and longer-term use and is further increased in patients with a history of alcoholism, drug abuse or in patients with marked personality disorders.

Transient mild drowsiness and lightheadedness is commonly seen in the first few days of therapy. If this becomes troublesome dosage should be reduced. Dizziness, ataxia, vertigo, headache and syncope have been reported with or without drowsiness. Occasionally hypotension has occurred. Blurred vision, disorientation, dreams and fever have also occurred. Mild excitatory effects with stimulation of affect has been reported in psychiatric patients and usually occur within the first few weeks of therapy.

Other adverse effects which have been rarely reported include minor diffuse skin rashes (morbilliform, urticarial and macropapular), altered libido, nausea, lethargy, oedema, slurred speech, tremor, blood dyscrasias, increased liver enzymes, jaundice and leucopenia, amnesia, muscle weakness, salivation changes, G.I disturbances, dysarthria, incontinence and urinary retention.

Behavioural adverse effects include paradoxical aggressive outbursts, excitement, hallucinations, confusion and the uncovering of depression with suicidal tendencies. Extreme caution should therefore be exercised in prescribing benzodiazepines to patients with personality disorders.

As with all benzodiazepines, withdrawal may be associated with physiological and psychological symptoms including depression, persistent tinnitus, involuntary movements, paraesthesia, perceptual changes, confusion, convulsions, muscle cramps, abdominal cramps and vomiting.

Symptoms such as anxiety, depression, headache, insomnia, tension and sweating have been reported following abrupt discontinuation of benzodiazepines and these symptoms may be difficult to distinguish from the original symptoms of anxiety.

4.9 Overdose

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, ataxia, dysarthia, nystagmus and lethargy, in more serious cases, symptoms may include hypotension, respiratory depression and rarely coma.

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 may have been taken.

Following overdose with oral benzodiazepines activated charcoal should be considered to reduce absorption. 50g for adults and 10-15g for children if they have taken more than 1mg/kg within 1 hour, provided they are not too drowsy. Special attention should be paid to respiatory and cardiovascular functions in intensive care. Supportive measures are indicated depending on the patients clinical state**.** The patient is likely to sleep and therefore a clear airway should be maintained.

Flumazenil (Anexate), a benzodiazepine antagonist, is available but should rarely be required. It has a short half-life (about an hour). Flumazenil is **NOT TO BE USED IN MIXED OVERDOSE OR AS A "DIAGNOSTIC" TEST**

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code:N05B A

Oxazepam is a benzodiazepine with anxiolytic, sedative, muscle relaxant and amnesic properties.

Oxazepam is a sedative and anxiolytic acting by potentiation of the inhibitory effect of gamma-aminobutyrate by binding to specific receptor sites of the brain stem reticular formation and other parts of the CNS.

5.2 Pharmacokinetic properties

Oxazepam is rapidly and almost completely absorbed from the GI tract and is highly protein bound (approximately 90%). It has been reported to have a half-life ranging from about 6-20 hours. It is the ultimate pharmacologically active metabolite of diazepam and is itself largely metabolised to the inactive glucuronide. Peak serum levels are reached in 1-5 hours**.**

Oxazepam crosses the placental barrier and is excreted in breast milk; lethargy and weight loss may occur in breast fed infants.

5.3 Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose, corn starch, povidone, magnesium stearate.

6.2 Incompatibilities

None known.

6.3 Special precautions for storage

Store below 25°C

6.4 Nature of container

PVC/Aluminium blister pack, 30 tablets.

7. Registration holder:

Rafa Laboratories Ltd., P.O.Box 405, Jerusalem 91003.

Registration number: 220621031

The format of this leaflet was determined by the Ministry of Health that checked and approved its content in January 2012.