SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Oxazepam 10 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 10mg of Oxazepam

Excipient with known effect: Each tablet contains 100 mg of lactose

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

White round flat tablet with a score line on one side and coded OXA 10 on the other side.

The score line is not intended for breaking the tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Oxazepam is recommended for short term use of approximately 2-4 weeks. As with all benzodiazepines, doctors should be aware that long term use may lead to dependence and withdrawal symptoms in certain patients.

Oxazepam is indicated for the short-term treatment of anxiety that is disabling or subjecting the individual to unacceptable distress, occurring alone or in association with psychosomatic, organic or psychotic illness.

4.2 Posology and method of administration

Posology

Prior to starting treatment with oxazepam, a discussion should be held with patients to put in place a strategy for ending treatment with oxazepam in order to minimise the risk of dependence, addiction and drug withdrawal syndrome (see section 4.4).
Treatment should be given for the shortest possible duration.

Dosage and duration of therapy should be individualised and all patients receiving oxazepam should be carefully monitored and re-evaluated before any extension of the treatment 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dosage regimes should not exceed beyond 4 weeks, including the period of tapering off and treatment should always be withdrawn gradually to minimise possible withdrawal symptoms (see section 4.4).

Please note that in patients with renal or hepatic impairment, lower doses may be sufficient (see section 4.4).

Adults:
Anxiety
15 -30mg three or four times daily.

Insomnia associated with anxiety:
Generally 15-25mg one hour before retiring. This may be increased to a maximum of 50mg when necessary.

Elderly patients and those who are particularly sensitive to benzodiazepines:
10-20mg three or four times a day.

Paediatric population:
Not recommended for children.

Method of administration
For oral administration.

4.3 Contraindications

- Hypersensitivity to benzodiazepines or to any excipients listed in section 6.1.
- For phobic or obsessional states.
- For the treatment of chronic psychosis.
- In acute pulmonary insufficiency.
- Respiratory depression.
- In patients with myasthenia gravis.
- In patients with sleep apnoea syndrome.
- In severe hepatic insufficiency.

4.4 Special warnings and precautions for use

Patients should be advised that since their tolerance for alcohol and other CNS depressants will be diminished in the presence of oxazepam, these substances should either be avoided or taken in reduced dosage.

Drug dependence, tolerance and potential for abuse

Drug addiction comprises behavioural, cognitive and physiological phenomena that may include a strong desire to take the drug, difficulties in controlling drug use and possible tolerance or physical dependence. Physical dependence is a state that develops as a result of physiological adaptation in response to repeated drug use, which manifests as withdrawal signs and symptoms after abrupt discontinuation or a significant dose reduction of a drug. Addiction and dependence are related but distinct presentations and in discussing these themes, terminology that apportion blame to the individual should be avoided.

For all patients, prolonged use of this product may lead to drug dependence and addiction but can occur with short-term use at recommended therapeutic doses. The risks are increased in individuals with current or past history of substance misuse disorder (including alcohol misuse) or mental health disorder (e.g., major depression).

Additional support and monitoring may be necessary when prescribing for patients at risk of drug misuse.

A comprehensive patient history should be taken to document concomitant medications, including over-the-counter medicines and medicines obtained on-line, and past and present medical and psychiatric conditions.

Patients may find that treatment is less effective with chronic use and express a need to increase the dose to obtain the same level of symptom control as initially experienced. Patients may also supplement their treatment with additional medications to achieve the same effect. These could be signs that the patient is developing tolerance. The risks of developing tolerance should be explained to the patient.

Overuse or misuse may result in overdose and/or death. It is important that patients only use medicines that are prescribed for them at the dose they have been prescribed and do not give this medicine to anyone else.

Patients should be closely monitored for signs of misuse, abuse, or addiction.

The clinical need for treatment with oxazepam should be reviewed regularly, with frequent assessments of patients being undertaken during the course of their treatment.

Falls

Due to the potential adverse reactions including ataxia, muscle weakness, dizziness, drowsiness and fatigue (see section 4.8), Benzodiazepines may be associated with an increased risk of falling especially in elderly patients. As a result, caution should be exercised particularly when getting up at night. The elderly should receive a reduced dose (see section 4.2).

Duration of treatment
The duration of treatment should be as short as possible (see section 4.2) depending on the indication, but should not exceed 4 weeks, 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.

Drug withdrawal syndrome
Prior to starting treatment with oxazepam, a discussion should be held with patients to explain the risk of dependence, addiction, and drug withdrawal syndrome. A withdrawal strategy for ending treatment with oxazepam should also be put in place with the patient before starting treatment (there may be exceptions to this in specific clinical situations such as symptom management in end of life palliative care).

Drug withdrawal syndrome may occur upon abrupt cessation of therapy or dose reduction. When a patient no longer requires therapy, it is advisable to taper the dose gradually to minimise symptoms of withdrawal. Tapering from a high dose may take in excess of weeks or months. Patients should be informed of this when the medication is first prescribed.

The reduction schedule for a patient should be tailored to the individual and should be modified to allow intolerable withdrawal symptoms to improve before making the next reduction. If using a published withdrawal schedule, apply it flexibly to accommodate the person’s preferences, changes to their circumstances and the response to dose reductions.

Suggest a slow stepwise rate of reduction proportionate to the existing dose, so that decrements become smaller as the dose is lowered, unless clinical risk is such that rapid withdrawal is needed.

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.

Risk from concomitant use of opioids
Concomitant use of oxazepam 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

oxazepam with opioids should be reserved for patients for whom alternative treatment options are not possible. If a decision is made to prescribe oxazepam concomitantly with opioids, the lowest effective dose should be used, and the duration of treatment should be as short as possible (see also general dose recommendation in section 4.2).

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 caregivers (where applicable) to be aware of these symptoms (see section 4.5).

Amnesia
Benzodiazepines may induce anterograde amnesia. This condition usually occurs several hours after ingestion therefore patients should ensure that they will be able to have a period of uninterrupted sleep which is sufficient to allow dissipation of drug effect (e.g. 7-8 hours) wherever possible.

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 section 4.2). 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). Also, pre-existing depression may emerge during benzodiazepine use.

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

Caution should be used in the treatment of patients with acute narrow-angle glaucoma.

Patients with impaired renal or hepatic function should be monitored frequently and have their dosage adjusted carefully according to response. Lower doses may be sufficient in these patients. The same precautions apply

to elderly or debilitated patients and patients with chronic respiratory insufficiency.

Some patients taking benzodiazepines have developed a blood dyscrasia, and some have had elevations in liver enzymes. Periodic haematologic and liver-function assessments are recommended where repeated courses of treatment are considered clinically necessary.

Although hypotension has occurred only rarely, benzodiazepines should be administered with caution to patients in whom a drop in blood pressure might lead to cardiovascular or cerebrovascular complications. This is particularly important in elderly patients.

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

4.5 Interaction with other medicinal products and other forms of interaction

The following drug interactions with oxazepam should be considered:

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

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

Opioids
The concomitant use of sedative medicines such as benzodiazepines or related drugs such as oxazepam with opioids increases the risk of sedation, respiratory depression, coma and death because of additive CNS depressant effect. The dosage and duration of concomitant use should be limited (see section 4.4).

Muscle Relaxants
When taken with muscle relaxants, the overall muscle-relaxing effect may be increased (accumulative) therefore caution is advised, especially in elderly patients and at higher doses (risk of falling, see Section 4.4).

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). The clinical significance of these interactions has yet to be established.

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

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).

Compounds which inhibit certain hepatic enzymes (particularly cytochrome P450) may enhance the activity of benzodiazepines. To a lesser degree this also applies to benzodiazepines that are metabolised only by conjugation.

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.

Pregnancy
Benzodiazepines should not be used during pregnancy, especially during the first and last trimesters. Benzodiazepines may cause foetal damage when administered to pregnant women.
There is a possibility that infants born to mothers who took benzodiazepines chronically during the later stages of pregnancy may develop physical dependence. The infant may also develop withdrawal symptoms during the postnatal period such as hypoactivity, hypotonia, hypothermia, respiratory depression, apnoea, feeding problems, and impaired metabolic response to cold stress.

Breast-feeding
The concentration of oxazepam and its conjugate in human breast milk is approximately 10% of the plasma level. Therefore, oxazepam should not be administered to breast-feeding mothers.

4.7 Effects on ability to drive and use machines

Sedation, amnesia, dizziness 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 section 4.5).

This medicine can impair cognitive function and can affect a patient's ability to drive safely. This class of medicine is in the list of drugs included in regulations under 5a of the Road Traffic Act 1988. When prescribing this medicine, patients should be told:

- The medicine is likely to affect your ability to drive
- Do not drive until you know how the medicine affects you
- It is an offence to drive while under the influence of this medicine
- However, you would not be committing an offence (called 'statutory defence') if:
  - The medicine has been prescribed to treat a medical or dental problem and
  - You have taken it according to the instructions given by the prescriber and in the information provided with the medicine and
  - It was not affecting your ability to drive safely

4.8 Undesirable effects

Blood and lymphatic system disorders

Blood dyscrasias, leucopenia

Psychiatric disorders

Drug dependence (see section 4.4, and also see below), mild drowsiness*, disorientation, dreams, †nightmares, lethargy, amnesia (see below), mild excitatory effects with stimulation of effect**, numbed emotions, reduced alertness, †restlessness, †agitation, †irritability, †delusions, †rages, †psychoses, †inappropriate behaviour, behavioural adverse effects including paradoxical †aggressive outbursts, excitement, †hallucinations, confusion, uncovering of depression with suicidal tendencies***.

†These are more likely to occur in children and the elderly.

Nervous system disorders
Dizziness, light-headedness*, ataxia, vertigo, headache, syncope, slurred speech, tremor, dysarthria.

Eye disorders
Blurred vision, double vision.

Vascular disorders
Hypotension.

Gastrointestinal disorders

Nausea, salivation changes, gastro-intestinal disturbances.

Hepatobiliary disorders
Increased liver enzymes, jaundice.

Skin and subcutaneous tissue disorders
Minor diffuse skin rashes (morbilliform, urticarial and maculopapular).

Musculoskeletal and connective tissue disorders
Muscle weakness.

Renal and urinary disorders
Incontinence, urinary retention.

Reproductive system and breast disorders
Altered libido.

General disorders and administration site conditions
Fever, oedema, fatigue.

Drug withdrawal symptoms (see 4.4 Special warnings and precautions):
Symptoms reported following discontinuation of benzodiazepines include headaches, muscle pain, anxiety, tension, depression, insomnia, restlessness, confusion, irritability, sweating, and the occurrence of “rebound” phenomena whereby the symptoms that led to treatment with benzodiazepines recur in an enhanced form. These symptoms may be difficult to distinguish from the original symptoms for which the drug was prescribed.

In severe cases the following symptoms may occur: derealisation; depersonalisation; hyperacusis; tinnitus; numbness and tingling of the extremities; hypersensitivity to light, noise, and physical contact; involuntary movements; hyperreflexia, tremor, nausea, vomiting; diarrhoea, abdominal cramps, loss of appetite, agitation, palpitations, tachycardia, panic attacks, vertigo, short-term memory loss, hallucinations/delirium; catatonia; hyperthermia, convulsions. Convulsions may be more common in patients with pre-existing seizure disorders or who are taking other drugs that lower the convulsive threshold such as antidepressants.

Injury, poisoning and procedural complications
Fall.

* Commonly seen in the first few days of therapy. If this becomes troublesome dosage should be reduced.
** Reported in psychiatric patients and usually occur within the first few weeks of therapy.
*** Extreme caution should therefore be exercised in prescribing benzodiazepines to patients with personality disorders.

Amnesia

Anterograde amnesia may occur using therapeutic dosages, the risk increasing at higher dosages. Amnesic effects may be associated with inappropriate behaviour (see section 4.4).

Dependence
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 (see section 4.4).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard.

4.9 Overdose

Patients should be informed of the signs and symptoms of overdose and to ensure that family and friends are also aware of these signs and to seek immediate medical help if they occur.

Overdose of benzodiazepines, induced vomiting and/or gastric lavage should be undertaken (if ingestion was recent). Alternatively (if there is no advantage in emptying the stomach), 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 respiratory and cardiovascular functions in intensive care. Supportive measures are indicated depending on the patient's clinical state. The patient is likely to sleep and therefore a clear airway should be maintained.

Hypotension, though unlikely, may be controlled with noradrenaline. The dialysability of oxazepam is minimal.

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

Pharmacotherapeutic group: Oxazepam is a benzodiazepine tranquilliser. It is used in the short-term treatment of anxiety.

ATC Code: N05BA

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 metabolised by a simple one-step process to a pharmacologically inert compound, 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

Acute oral LD50 in mice is greater than 5000 mg/kg.

Fatty metamorphosis of the liver has been noted in six-week toxicity studies in rats given this product at 0.5% of the diet. Such accumulations of fat are considered reversible, since no liver necrosis or fibrosis is seen.

In vitro mutagenicity reports on Oxazepam are inconclusive.

In a carcinogenicity study, oxazepam was administered with diet to rats for two years. Male rats receiving 30 times the maximum human dose showed a statistical increase, when compared to controls, in benign thyroid follicular cell tumours, testicular interstitial cell adenomas, and prostatic adenomas. An earlier published study reported that mice fed dietary dosages of 35 or 100 times the human daily dose of oxazepam for 9 months developed a dose-related increase in liver adenomas. In an independent analysis of some of the microscopic slides from this mouse study, several of these tumours were

classified as liver carcinomas. At this time, there is no evidence that clinical use of oxazepam is associated with tumours.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose
Maize Starch
Pregelatinised Maize Starch
Magnesium Stearate

6.2 Incompatibilities

None known.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store in a cool dry place. Store in the original container in order to protect from light.

6.5 Nature and contents of container

A polypropylene tubular container with a tamper-evident tear strip in pack sizes of: 7, 14, 21, 28, 30, 50, 56, 60, 84, 90, 100, 112, 120, 250, 500 and 1000 tablets or PVdC coated PVC/Aluminium blisters (40g/m^2 PVdC on 250µ PVC/25µm Al) in pack sizes of: 7, 14, 21, 28, 30, 50, 56, 60, 84, 90, 100, 112 and 120 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Tillomed Laboratories Limited
220 Butterfield
Great Marlings
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LU2 8DL
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 11311/0526

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization: 22/10/1979
Date of latest renewal: 16/12/2008

10 DATE OF REVISION OF THE TEXT

23/12/2025