SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Oxazepam Tablets 15mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Oxazepam tablets containing oxazepam 15mg.

Oxazepam (INN, BAN) is chemically defined as 7-chloro-1,3-dihydro-3-hydroxy-5-phenyl-2H-1,4-benzodiazepine-2-one.

3 PHARMACEUTICAL FORM

Oxazepam Tablets 15mg are white round tablets, 6.5mm in diameter, having flat faces with bevelled edges. A breakbar on one face and “15” on the other.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Oxazepam is indicated for the short term relief (2-4 weeks) of anxiety that is disabling or subjecting the individual to unacceptable distress, occurring alone or in association with insomnia or short-term psychosomatic, organic and psychotic illness.

The use of benzodiazepines to treat short-term anxiety is considered to be inappropriate.

4.2 Posology and method of administration

Posology

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.

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).

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 Dosage regimes should not exceed beyond 4 weeks and treatment should be withdrawn gradually to minimise possible withdrawal symptoms (See Special Warnings and Precautions for Use).

Please note that in patients with renal or hepatic impairment, lower doses may be sufficient (see Special Warnings and Precautions for Use).

Adults:

- Anxiety – one to two 15mg tablets three (or four) times daily
- Insomnia associated with anxiety – In most cases, 15-25mg dose taken 1 hour before retiring. This may be increased to a maximum of 50mg where necessary

Elderly or patients who are particularly sensitive to the effects of benzodiazepines:

10-20mg three or four times daily

Children:

Oxazepam is not recommended for the treatment of children

Method of Administration

Oral administration

4.3 Contraindications

- Hypersensitivity to benzodiazepines including Oxazepam Tablets or their components
- Chronic psychosis
- Phobic or obsessional states
- Respiratory depression
- Sleep apnoea syndrome
- Myasthenia gravis
- Acute pulmonary insufficiency
- Severe hepatic insufficiency

4.4 Special warnings and precautions for use

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.

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.

If a patient develops withdrawal reactions, consider pausing the taper or increasing the dosage to the previous tapered dosage level.

If women take this drug during pregnancy, there is a risk that their newborn infants will experience neonatal withdrawal syndrome.

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).

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 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.

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).

Special patient groups

Oxazepam is not intended for the primary treatment of psychotic illness or depressive disorders, and should not be used alone to treat depressed patients. The use of benzodiazepines may have a disinhibiting effect and may release suicidal tendencies in depressed patients. Also, pre-existing depression may emerge during benzodiazepine use.

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.

Benzodiazepines are not indicated to treat patients with severe hepatic impairment as they may precipitate encephalopathy, renal impairment, muscle weakness or porphyria

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.

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.

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

4.5 Interaction with other medicinal products and other forms of interaction

The following drug interactions with oxazepam should be considered:

- 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).
- Enhancement of other CNS depressant drugs such as barbiturates, antipsychotics, sedatives/hypnotics, anxiolytics, antidepressants, narcotic analgesics (enhancement of euphoria may also occur, leading

to an increase in psychological dependence), sedative antihistamines, anticonvulsants, anaesthetics, lofexidine, nabilone and tizanidine.

- 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).
- Concomitant use of alcohol is not recommended. The sedative effects may be enhanced when oxazepam is used in combination with alcohol. This will affect the ability to drive or use machines.
- Compounds which inhibit certain hepatic enzymes (particularly cytochrome P450) may enhance the activity of benzodiazepines. To a lesser degree this also applies to benzodiazepines which are metabolised only by conjugation.
- 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.
- Anti-epileptic 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).

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

If the drug is prescribed to a woman of childbearing potential, she should be warned to contact her physician about stopping the drug 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 take 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.

Breastfeeding

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 Interactions).

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

Adverse reactions, when they occur, are usually observed at the beginning of therapy and generally decrease in severity or disappear with continued use or upon decreasing the dose.

Blood and lymphatic disorders	Blood dyscrasias, leucopenia
Psychiatric disorders	Mild drowsiness*, disorientation, dreams, †nightmares, lethargy, amnesia (see below), mild excitatory effects with stimulation of affect**, numbed emotions, reduced alertness, †restlessness, †agitation, †irritability, †delusions, †rages, †psychoses, †inappropriate behaviour, behavioural adverse effects including paradoxical †aggressive outbursts,

	excitement, †hallucinations, confusion, drug dependence (see section 4.4), uncovering of depression with suicidal tendencies.***
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, gastrointestinal disorders
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).
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 † = more likely to occur in children and the elderly	

Amnesia

Anterograde amnesia may occur using therapeutic dosages, the risk increasing at higher dosages and may lead to the patient exhibiting inappropriate behaviour.

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 is increased with higher doses and/or longer use; it is also greater in patients with a history of alcoholism or drug abuse, or in patients with significant personality disorders. (see Special Warnings and Precautions for Use)

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.

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 or search for ‘MHRA Yellow Card’ in the Google Play or Apple App Store.

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- Insomnia associated with anxiety – In most cases, 15-25mg dose taken 1 hour before retiring. This may be increased to a maximum of 50mg where necessary

Elderly or patients who are particularly sensitive to the effects of benzodiazepines:

10-20mg three or four times daily

Children:

Oxazepam is not recommended for the treatment of children

Method of Administration

Oral administration

4.3 Contraindications

- Hypersensitivity to benzodiazepines including Oxazepam Tablets or their components
- Chronic psychosis
- Phobic or obsessional states
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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.

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.

If a patient develops withdrawal reactions, consider pausing the taper or increasing the dosage to the previous tapered dosage level.

If women take this drug during pregnancy, there is a risk that their newborn infants will experience neonatal withdrawal syndrome.

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).

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 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.

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).

Special patient groups

Oxazepam is not intended for the primary treatment of psychotic illness or depressive disorders, and should not be used alone to treat depressed patients. The use of benzodiazepines may have a disinhibiting effect and may release suicidal tendencies in depressed patients. Also, pre-existing depression may emerge during benzodiazepine use.

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.

Benzodiazepines are not indicated to treat patients with severe hepatic impairment as they may precipitate encephalopathy, renal impairment, muscle weakness or porphyria

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.

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.

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

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The following drug interactions with oxazepam should be considered:

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- Enhancement of other CNS depressant drugs such as barbiturates, antipsychotics, sedatives/hypnotics, anxiolytics, antidepressants, narcotic analgesics (enhancement of euphoria may also occur, leading to an increase in psychological dependence), sedative antihistamines, anticonvulsants, anaesthetics, lofexidine, nabilone and tizanidine.
- 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).
- Concomitant use of alcohol is not recommended. The sedative effects may be enhanced when oxazepam is used in combination with alcohol. This will affect the ability to drive or use machines.
- Compounds which inhibit certain hepatic enzymes (particularly cytochrome P450) may enhance the activity of benzodiazepines. To a lesser degree this also applies to benzodiazepines which are metabolised only by conjugation.
- 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.

- Anti-epileptic 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).

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

If the drug is prescribed to a woman of childbearing potential, she should be warned to contact her physician about stopping the drug 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 take 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.

Breastfeeding

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 Interactions).

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

Adverse reactions, when they occur, are usually observed at the beginning of therapy and generally decrease in severity or disappear with continued use or upon decreasing the dose.

Blood and lymphatic disorders	Blood dyscrasias, leucopenia
Psychiatric disorders	Mild drowsiness*, disorientation, dreams, †nightmares, lethargy, amnesia (see below), mild excitatory effects with stimulation of affect**, numbed emotions, reduced alertness, †restlessness, †agitation, †irritability, †delusions, †rages, †psychoses, †inappropriate behaviour, behavioural adverse effects including paradoxical †aggressive outbursts, excitement, †hallucinations, confusion, drug dependence (see section 4.4), uncovering of depression with suicidal tendencies.***
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, gastrointestinal disorders
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).
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
† = more likely to occur in children and the elderly

Amnesia

Anterograde amnesia may occur using therapeutic dosages, the risk increasing at higher dosages and may lead to the patient exhibiting inappropriate behaviour.

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 is increased with higher doses and/or longer use; it is also greater in patients with a history of alcoholism or drug abuse, or in patients with significant personality disorders. (see Special Warnings and Precautions for Use)

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.

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 or search for ‘MHRA Yellow Card’ in the Google Play or Apple App Store.

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, dysarthria, nystagmus and lethargy. In more serious cases, symptoms may include ataxia, hypotension, hypotonia, 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).

Following overdose with oral benzodiazepines, induced vomiting and/or gastric lavage should be undertaken (if ingestion was recent). Alternatively (if there is no advantage in emptying the stomach), activated charcoal may be effective in reducing absorption (50mg for adults and 10-15mg 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 vital signs including respiratory and cardiovascular functions in extensive care. Supported 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 (Anaxate), a benzodiazepine antagonist, is available however should rarely be required. It has a short half-life (about an hour). Flumazenil is NOT TO BE USED IN A MIXED OVERDOSE OR AS A "DIAGNOSTIC" TEST.

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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: N05B A

Oxazepam is a benzodiazepine with anxiolytic, sedative and hypnotic properties and possibly muscle relaxant and anticonvulsant characteristics. It acts by potentiation of the inhibitory effect of gamma-aminobutyrate by binding to specific sites of the brain stem reticular formation and other parts of the CMS.

5.2 Pharmacokinetic properties

Oxazepam is rapidly and almost completely absorbed from the gastrointestinal tract and is highly protein bound (approx.. 90%). Peak serum levels are reached in 1-5 hours and it has been reported to have a half-life of 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.

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 LD_{50} 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 (hydrous), maize starch and magnesium stearate.

6.2 Incompatibilities

None known

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store in a dry place below 25°C.

6.5 Nature and contents of container

1. Blister packs of PVC backed by hard tempered aluminium foil of 28, 30, 56, 60 or 100 tablets.

2. Securitainers of 28, 30, 56, 60 or 500 tablets.

6.6 Special precautions for disposal

Not applicable

7. MARKETING AUTHORISATION HOLDER

Genus Pharmaceuticals Holdings Limited
T/A Genus Pharmaceuticals
Linthwaite,
Huddersfield,
HD7 5QH, UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 17225/0015

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

01/10/1999 / 06/03/2003

10 DATE OF REVISION OF THE TEXT

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7. MARKETING AUTHORISATION HOLDER

Genus Pharmaceuticals Holdings Limited (trading as ‘STADA’)
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Huddersfield,
HD7 5QH,
UK

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01/10/1999 / 06/03/2003

10 DATE OF REVISION OF THE TEXT

19/03/2026