SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Tensium/Diazepam 2mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Diazepam BP 2mg

3 PHARMACEUTICAL FORM

Tablet

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Adults

- Short-term use in anxiety or insomnia.
- Adjunct in acute alcohol withdrawal.
- Muscle spasm in association with fibrositis, cervical spondylosis, arthritis and bursitis.
- May be useful in cerebral spasticity in selected cases; as an adjunct to some types of epilepsy e.g. myclonus; and sedative cover for some minor surgical procedures, endoscopy, cardiac catheterisation cardioversion.

Children

- Night terrors and somnambulism.

- May be useful in controlling tension and irritability in cerebral spasticity in selected cases.

Benzodiazepines are only indicated when the order is severe, disabling or subjecting the individual to extreme distress.

The use of benzodiazepines to treat short-term 'mild' anxiety is considered to be inappropriate and unsuitable.

4.2 Posology and method of administration

Route of administration: Oral
Prior to starting treatment with Diazepam, a discussion should be held with patients to put in place a strategy for ending treatment with Diazepam 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. If this medicine is being used for the treatment of epilepsy this medicine should be used for as long as the prescriber considers it necessary.
When treatment is started it may be useful to inform the patient that treatment 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 has been discontinued.

Anxiety

Adults:

The starting dose should be 2 mg 3 times daily increased if necessary to 15 - 30 mg daily, in divided doses adjusted on an individual basis. Treatment should always be as short as possible and should not take place without re-evaluation of the situation.

Elderly and debilitated patients:

Dosage should not exceed half the adult dose. The same applies to patients with impaired liver or renal function and steps should be taken to ensure that there is no accumulation of plasma diazepam in these patients.

Children:

Not recommended.

Insomnia associated with anxiety

Adults:

5-15 mg before at bed time. Treatment should be as short as possible and would normally vary from a few days to two weeks with a maximum, including tapering off of four weeks. Where extension beyond the maximum treatment period may be necessary it should not take place without re-evaluation of the patient's status.

Elderly and debilitated patients:

Dosage should not exceed half the adult dose. The same applies to patients with impaired liver or renal function and steps should be taken to ensure that there is no accumulation of plasma diazepam in these patients.
Children:

Not recommended.
Night terrors and somnambulism

Children:

1 - 5 mg at bedtime
Symptomatic relief of acute alcohol withdrawal

Adults:

5 – 20 mg, repeated if necessary in 2 to 4

hours **Conditions associated with muscle**

spasm

Adults:

2 – 15 mg daily in divided doses, increased if necessary in spastic conditions to 60 mg daily according to response. Cerebral spasticity in selected cases, *child:* 2 – 40 mg in divided doses.
Premedication
Adults:
5 mg on night before minor or dental surgery, then 5 mg 2 hours before

procedure

Elderly and debilitated patients:

Dosage should not exceed half those normally recommended.

4.3 Contraindications

Myasthenia gravis
Hypersensitivity to benzodiazepines
Acute pulmonary insufficiency
Severe respiratory depression
Sleep apnoea syndrome
Severe hepatic insufficiency

4.4 Special warnings and Special precautions for use

Tolerance

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

Drug dependence, tolerance and potential for abuse

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. Dependence may be physical or psychic.
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 Diazepam should be reviewed regularly, with frequent assessments of patients being undertaken during the course of their treatment.

<u>Drug withdrawal syndrome</u>

Prior to starting treatment with Diazepam, 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 Diazepam 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, and for use in epilepsy).
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.
Once physical dependence has developed, abrupt termination of treatment will be accompanied by withdrawal symptoms. These may consist of headache, muscle pain, extreme anxiety, tension, restlessness, confusion, 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 gradually.

Duration of treatment

The duration of treatment should be as short as possible (see Posology) and should not exceed four weeks for insomnia and 8-12 weeks in case of anxiety, 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. Patients should be made aware of the possibility of rebound phenomena, thereby minimising anxiety other symptoms should they occur while the product is being discontinued.
There are indications that, in the case of benzodiazepines with a short duration of action, withdrawal phenomena can become manifest with the dosage interval, especially when the dosage is high.
When diazepam is being used it is important to warn against changing to a benzodiazepine with a short duration of action, as withdrawal symptoms may develop.

Amnesia

Diazepam 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' 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, treatment with the product should be discontinued.
They are more likely to occur in children and the elderly.

Specific Patient Groups

Diazepam is not recommended for the primary treatment of psychotic illness.
Diazepam should not be used alone to treat depression or anxiety associated with depression because suicide may be precipitated in such patients.
Diazepam should be used with extreme caution in patients with a history of alcohol or drug abuse.
Not for use in phobic or obsessional states (inadequate evidence of efficiency and safety).
Diazepam should not be given to children without careful assessment, and the duration of treatment must be kept to the minimum. The 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.

4.5 Interaction with other medicinal products and other forms of interaction

Not recommended: Concomitant intake with alcohol
Diazepam should not be used together with alcohol as this may enhance the sedative effects and affect the ability to drive or operate machinery.

Take into account: Combination with CNS depressants
Enhancement of the central depressive effect may occur if diazepam is combined with centrally acting drugs such as neuroleptics, tranquillisers, antidepressants, hypnotics, analgesics, anaesthetics and sedative antihistamines. The elderly may require special supervision.

When diazepam is used in conjunction with anti-epileptic drugs, side effects and toxicity may be more evident, particularly with hydantoins or barbiturates or combinations including them. This requires extra care in adjusting dosage in the initial stages of treatment.

In the case of narcotic analgesics enhancement of the euphoria may also occur leading to an increase in psychic dependence.

Compounds that 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.

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 breast milk, benzodiazepines should not be given to breast-feeding mothers.

4.7 Effects on ability to drive and use machines

Diazepam can impair cognitive function and can affect a patient's ability to drive or to use machines 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

If insufficient sleep duration occurs, the likelihood of impaired alertness may be increased (see also Interactions).

4.8 Undesirable effects

Common adverse effects include drowsiness, sedation, unsteadiness and ataxia; these are dose related and may persist into the following day even after a single dose. The elderly are particularly sensitive to the effects of central depressant drugs and may experience confusion, especially if organic brain changes are present; the dosage of diazepam should not exceed one-half that recommended for other adults.

Other adverse effects are rare and include numbed emotions, reduced alertness, fatigue, headache, dizziness, muscle weakness, vertigo, hypotension, gastrointestinal upsets, skin rashes, visual disturbances, changes in libido and urinary retention. Isolated cases of blood dyscrasias and jaundice have also been reported.

Amnesia

Anterograde amnesia may occur using therapeutic dosages, the risk increasing at higher dosages. Amnestic effects may be associated with inappropriate behaviour. (See warnings and precautions).

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 benzodiazepinelike agents. They may be quite severe with this product. They are more likely to occur in children and the elderly.

Drug dependence (see section 4.4)

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

General disorders and administration site conditions:

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 [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.
As with other benzodiazepines, overdosage 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, vomiting, should be induced (within one hour) if the patient is conscious or gastric lavage is 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 is usually manifested by varying degrees of depression of the central nervous system, ranging from drowsiness to coma. Symptoms in mild cases 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 Pharmacodynamic properties

Diazepam binds to receptors in various regions of the brain, such as the spinal cord, the brain stem, cerebellum, limbic system, and cerebral cortex.

Diazepam blocks EEG arousal from stimulation of the brain stem reticular formation. It acts as a CNS depressant on spinal reflexes and it also depresses the duration of the electrical after-discharge in the limbic system.

Diazepam is an anxiolytic; it is a sedative and a hypnotic. Diazepam is a muscle relaxant. Diazepam in standard doses causes a slight decrease in respiratory rate, blood pressure and left ventricular stroke work.

5.2 Pharmacokinetic properties

Oral absorption	100%.
Presystemic metabolism	insignificant
Plasma half-life	range 20-100h mean 30h
Volume of distribution	1.1l.kg
Plasma protein binding	98-99%

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose
Maize starch
Starch, Pregelatinised
Magnesium stearate

6.2 Incompatibilities

None known.

6.3 Shelf life

36 months for containers.

6.4 Special precautions for storage

Store below 25°C in a dry place.
Protect from light.
Keep container well closed.

6.5 Nature and contents of container

High density polystyrene containers with polythene lids and/or polypropyline containers with polythene lids and polyurethane or polythene inserts.
Pack sizes: 50, 100, 500, 1000.

6.6 Special precautions for disposal

No special instructions

7 MARKETING AUTHORISATION HOLDER

Chelonia Healthcare Limited
11 Boumpoulinas Street,
3rd floor, 1060 Nicosia
Cyprus

8 MARKETING AUTHORISATION NUMBER(S)

PL 33414/0035

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

28/10/1983

10 DATE OF REVISION OF THE TEXT

26/01/2026