SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Temazepam Tablets 10mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 10mg Temazepam BP.
Excipient with known effect: Lactose monohydrate.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

Temazepam Tablets 10mg are round, white to pale yellow tablets with TEM 10 on one side and plain on the other.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the short-term treatment of insomnia in cases where it is severe, disabling or subjecting the individual to extreme distress, especially for those patients in whom the persistence of a hypnotic effect would be undesirable.

Temazepam is also indicated for pre-operative medication prior to minor surgery or other similar procedures particularly when hospital admission is not essential.

4.2 Posology and method of administration

Posology

Treatment to be given
• under close medical supervision
• at the lowest effective dose
• for the shortest possible duration (not exceeding 4 weeks)
Treatment should be tapered off gradually (see section 4.4)

Extension of use should not take place without further clinical evaluation

Chronic use not recommended (little is known of the long term safety and efficacy: potential for dependence – see section 4.4).

When treatment is started the patient should be informed that
  • treatment will be of limited duration
  • the dosage will be progressively decreased
  • there is the possibility of rebound phenomena

Patients who have received benzodiazepines for a long time may require an extended withdrawal period.

The recommended doses are as follows:

**Insomnia**

*Adults*
10-20 mg at bedtime. A dose of 20mg will be found satisfactory for most patients. In extreme cases this may be increased to 30-40mg in patients who do not respond to the lower dose.

*Elderly or debilitated or those with cerebrovascular disease or hepatic or renal impairment*
5mg at bedtime. This may be increased to 10mg or to 20mg in extreme cases.

**Premedication**

*Adults*
The normal dose is 20-40mg, half an hour to one hour before the procedure. It is recommended that patients should be accompanied home after medication with Temazepam prior to surgical or investigative procedures.

*Elderly and patients suffering from cerebrovascular disease*
Dosage should be reduced to possibly half the normal adult dose (10-20mg, one hour before the procedure). In general hypnotics should be avoided in the elderly as they are at risk of becoming ataxic and confused. This may lead to falls and injury.

*Paediatric population*
Temazepam tablets are not recommended for use in children. The safety and efficacy in children less than 18 years old has not been established.

**Method of administration**
For oral administration.
4.3 Contraindications

- Hypersensitivity to the active substance, benzodiazepines or to any of the excipients listed in section 6.1
- Acute pulmonary insufficiency, severe respiratory depression, sleep apnoea (risk of further respiratory depression) or CNS depression
- Acute narrow angle glaucoma (due to anticholinergic effects of temazepam)
- Phobic or obsessional states; chronic psychosis (paradoxical reactions may occur. Inadequate evidence of safety and efficacy).
- Mild anxiety states
- Severe hepatic insufficiency (may precipitate encephalopathy. Elimination half-life of temazepam may be prolonged)
- Neuromuscular respiratory weakness including myasthenia gravis (condition may be exacerbated)
- Breast-feeding
- Children aged 18 years or under
- Temazepam should not be used alone in depression or anxiety with depression (may precipitate suicide)

4.4 Special warnings and precautions for use

The cause for insomnia should be determined prior to the use of temazepam, and it should not be used for first line treatment of psychotic illness.

Severe anaphylactic and anaphylactoid reactions, including rare fatal cases of anaphylaxis, have been reported in patients receiving temazepam. Cases of angioedema involving the tongue, glottis, or larynx have been reported in patients after taking the first or subsequent doses of sedative-hypnotics, including temazepam.

When temazepam is used for pre-medication, patients should be accompanied home afterwards.

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 for insomnia, including tapering off process. Extension beyond these periods should not take place without re-evaluation of the situation.

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

There are indications that, in the case of benzodiazepines with a short duration of action such as temazepam, withdrawal phenomena can become manifest between doses, especially when the dosage is high.
When benzodiazepines with a long duration of action are being used it is important to warn against changing to a benzodiazepine with a short duration of action, as withdrawal symptoms may develop.

**Tolerance**
Limits of tolerance in patients with organic cerebral changes (particularly arteriosclerosis) or cardiorespiratory insufficiency may be very wide; care must be taken in adapting the dosage with such patients. Loss of efficacy to the hypnotic effects may develop after repeated use for a few weeks. Care should be taken in patients with chronic renal or hepatic disease (elimination half-life of temazepam may be prolonged). Sedatives given to patients with cirrhosis may precipitate encephalopathy. Alcohol should be avoided during treatment with temazepam (additive CNS depression).

**Dependence**
The risk of dependence (physical or psychological) increases with dose and duration of treatment and is greater in patients with a history of alcohol or drug abuse, or in patients with a marked personality disorder. Therefore

- regular monitoring of such patients is essential
- routine repeat prescriptions should be avoided
- treatment should be withdrawn gradually

**Withdrawal effects**
If physical dependence has developed, abrupt termination of treatment results in withdrawal symptoms. These include headache, muscle pain, extreme anxiety, tension, restlessness, confusion and irritability, sleep disturbance, diarrhoea and mood changes. In severe cases the following may occur: a feeling of unreality or of being separated from the body, depersonalisation, hyperacusis, confusional states, numbness and tingling of the extremities, hypersensitivity to light, noise and physical contact, psychotic manifestations including hallucinations or epileptic seizures. Withdrawal symptoms will be worse in patients who have been dependent on alcohol or other narcotic drugs in the past, but can occur following abrupt cessation of treatment in patients receiving normal therapeutic doses for a short period of time.

**Rebound symptoms**
Symptoms including insomnia and anxiety may occur on withdrawal of treatment. It may be accompanied by other reactions including mood changes, anxiety or sleep disturbances and restlessness. As this is greater after abrupt discontinuation, the dose should be decreased gradually (see section 4.2).

**Amnesia**
Anterograde amnesia may occur, most often several hours after ingestion. To reduce the risk, patients should ensure that they will be able to have an uninterrupted sleep of 7-8 hours (see also section 4.8). Insufficient sleep may adversely affect the ability to drive/operate machinery etc. (see section 4.7).

**Bereavement/loss**
Psychological adjustment may be inhibited by benzodiazepines

**Psychiatric and `paradoxical` reactions**

Reactions such as restlessness, agitation, irritability, aggressiveness, excitement, confusion, delusions, rage, nightmares, hallucinations, psychoses, inappropriate behaviour and other adverse behavioural effects can occur. These reactions are more likely in children and the elderly, and extreme caution should be used in prescribing benzodiazepines to patients with personality disorders. Should they occur, treatment should be discontinued.

Complex sleep behaviour-related events such as “sleep driving” (i.e. driving while not fully awake after ingestion of a sedative-hypnotic, with amnesia for the event) have been reported in patients who are not fully awake after taking a sedative-hypnotic, including triazolam. These events can occur with sedative-hypnotics, including temazepam, alone at therapeutic doses. The use of alcohol and other CNS depressants with sedative-hypnotics appears to increase the risk of such behaviours, as does the use of sedative-hypnotics at doses exceeding the maximum recommended dose. Due to the risk to the patient and the community, discontinuation of sedative-hypnotics should be strongly considered for patients who report such events.

**Specific patient groups**

*Patients with depression*

Temazepam should not be used alone to treat depression or anxiety associated with depression as suicide may be precipitated in such patients.

*Patients with a history of alcohol & drug abuse*

Temazepam should be used with extreme caution in patients with a history of alcohol or drug abuse (risk of abuse/dependence).

*Patients with phobias and/or chronic psychoses*

Temazepam is not recommended (inadequate evidence of efficacy and safety)

*Pregnant women*

Avoid regular use in pregnant women (risk of neonatal withdrawal symptoms); use only if clear indication such as seizure control (high doses during late pregnancy or labour may cause neonatal hypothermia, hypotonia and respiratory depression) (see also section 4.6).

### 4.5 Interaction with other medicinal products and other forms of interaction

**Not recommended**

*Alcohol:* Temazepam should not be used together with alcohol (enhanced sedative effects: effect the ability to drive or operate machinery).

*Sodium oxybate:* avoid concomitant use (enhanced effects of sodium oxybate).

**Take into account**
Centrally acting drugs: Enhancement of the central depressive effect may occur if temazepam is combined with drugs such as neuroleptics, antipsychotics, tranquillisers, anxiolytics/sedatives, anti-epileptic products, narcotic analgesics, antidepressants, MAOIs, hypnotics, analgesics, anaesthetics, barbiturates and sedative antihistamines. The elderly may require special supervision.

Antiepileptic drugs: When used concurrently, side effects and toxicity may be more evident, particularly with hydantoins (e.g. phenytoin) and/or barbiturates. This requires extra care in adjusting dosage in the initial stages of treatment.

Narcotic analgesics: Enhancement of the euphoria may lead to increased psychological dependence.

Other drugs enhancing the sedative effect of Temazepam: cisapride, lofexidine, nabilone, disulfiram and the muscle-relaxants baclofen and tizanidine.

Compound that affect hepatic enzymes (particularly cytochrome P450):
- inhibitors (e.g. cimetidine; ritonavir; fluvoxamine) reduce clearance and may potentiate the action of benzodiazepines
- inducers (e.g. rifampicin) may increase clearance of benzodiazepines

Antihypertensives, vasodilators & diuretics: Enhanced hypotensive effect with ACE-inhibitors, alpha-blockers, angiotensin-II receptor antagonists, calcium channel blockers adrenergic neurone blockers, beta-blockers, moxonidine, nitrates, hydralazine, minoxidil, sodium nitroprusside and diuretics

Dopaminergics: possible antagonism of the effect of levodopa.

Theophylline: possible reduced effects of temazepam

Antivirals: concurrent use of zidovudine with benzodiazepines may decrease zidovudine clearance. Ritonavir may inhibit benzodiazepine hepatic metabolism.

Clozapine: reports of cardiorespiratory collapse. Also increase in hypersalivation with both drugs.

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 Fertility, pregnancy and lactation

The safety of temazepam has not been evaluated in humans and therefore its use should be avoided, especially in the first and third trimester.
Avoid regular use (risk of neonatal withdrawal symptoms); use only if clear indication such as seizure control (high doses during late pregnancy or labour may cause neonatal hypothermia, hypotonia and respiratory depression)

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

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.

Patients should be advised that sedation, amnesia, impaired concentration, dizziness, blurred vision and impaired muscular function may occur and that, if affected, they should not drive or to use machines, or take part in other activities where this would put themselves or others at risk. If insufficient sleep duration occurs, the likelihood of impaired alertness may be increased. Concurrent medication may increase these effects (see section 4.5).

4.8 Undesirable effects

At the start of treatment patients may suffer from drowsiness and light-headedness the next day; confusion and ataxia (especially in the elderly);
amnesia may occur and dependence. Reduced alertness, dizziness, fatigue, muscle weakness, numbed emotions, double vision, respiratory depression or slurred speech. These will normally disappear with continued treatment.

More rarely, headache, vertigo, hypotension, salivation changes, visual disturbances, dysarthria, tremor, incontinence, urinary retention, blood disorders, jaundice, vivid dreams/nightmares, restless sleep, palpitations, change in libido, skin reactions, sedation, impaired muscular function, dry mouth and gastrointestinal disturbances may occur.

Severe anaphylactic and anaphylactoid reactions, including rare fatal cases of anaphylaxis, have been reported in patients receiving temazepam.

Pre-existing depression may be unmasked during treatment with temazepam.

Blood dyscrasias and increased liver enzymes have also been reported to occur occasionally. If any of these effects do occur, treatment should be discontinued.

Other effects, including delusions, psychoses, hallucinations, psychoses, irritability and restlessness, agitation, aggressiveness, nightmares and rages or other inappropriate behaviour and other adverse behavioural effects have also been reported to occur. They are more likely to occur in children and the elderly. If any of these effects occur, treatment should be discontinued.

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

Withdrawal effects on abrupt cessation of treatment – Depression, anxiety, headache, dizziness, impaired concentration, tinnitus, loss of appetite, tremor, perceptual disturbances, nausea, vomiting, abdominal cramps, palpitations, mild systolic hypertension, tachycardia, orthostatic hypotension, photophobia, hyperacusis, confusion, tension, nervousness, rebound insomnia, irritability, sweating and diarrhoea have been reported following abrupt cessation of treatment. In rare cases, withdrawal following excessive dosages may produce confusional states, psychotic manifestations and convulsions. Broken sleep with vivid dreams may persist for some weeks after withdrawal.

**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

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.

Symptoms
Benzodiazepines commonly cause drowsiness, ataxia, dysarthria and nystagmus. Coma, hypotension and respiratory depression occasionally occur but are seldom serious if these drugs are taken alone. Coma usually lasts a few hours but in the elderly may be more protracted and cyclical. Respiratory depression is more serious in those with severe obstructive airways disease. Patients who are asymptomatic at 4 hours are unlikely to develop symptoms.

Management
Following overdose with oral benzodiazepines, vomiting should be induced (within one hour) if the patient is conscious or gastric lavage undertaken with the airway protected if the patient is unconscious. If there is no advantage in emptying the stomach, activated charcoal should be given to reduce absorption. Special attention should be paid to respiratory and cardiovascular functions in intensive care.

Following overdose with oral benzodiazepines activated charcoal should be given 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.

Flumazenil may be useful as an antidote providing the overdose is not with mixed drugs.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: hypnotics and sedatives, benzodiazepine derivatives, ATC code: N05C D07.

Temazepam is known to have hypnotic/sedative and anxiolytic properties. It therefore results in anxiolysis, muscle relaxation and central nervous system sedation. It has been suggested that a close molecular association between the sites and action for gamma-aminobutyric acid (GABA) and benzodiazepines and potentiation of GABA may be responsible for these effects.

Other neurotransmitters may also be affected.
5.2 Pharmacokinetic properties

Absorption
Temazepam is readily absorbed from the gastro-intestinal tract, although the exact rate of absorption depends on the formulation. Peak plasma levels are reached within 50 minutes if given orally, with multidosing steady state reached by the third day.

Distribution
It is about 96% bound to plasma protein. Temazepam is also found in breast milk in small amounts and may exert its effects on the infant.

Biotransformation
Temazepam is mainly metabolised in the liver with a terminal half-life of between 8 and 15 hours. This half-life depends on time of dose (morning administration has longer half-life than evening) and age of patient (elderly patients experience a longer half-life).

Elimination
80% is excreted in the urine in the form of its inactive glucuronide conjugate together with small amounts of the demethylated derivative, Oxazepam, also in conjugated form. Only approximately 12% appears in the faeces.

5.3 Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1. List of Excipients

Lactose monohydrate, maize starch, pregelled starch, sodium starch glycollate, microcrystalline cellulose and magnesium stearate.

6.2. Incompatibilities

Not known.

6.3. Shelf Life

24 months.

6.4. Special Precautions for Storage
Store at or below 25°C in a dry place. Protect from light.

6.5 Nature and contents of container

Packs of 28, 30, 56, 60, 84, 100, 168, 200, 250 and 500 tablets. Polypropylene containers with polyethylene tamper evident security closure.

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

Sandoz Limited
Frimley Business Park,
Frimley,
Camberley,
Surrey,
GU16 7SR,
United Kingdom.

8. MARKETING AUTHORISATION NUMBER(S)

PL 4416/0269

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

3 February 1997

10 DATE OF REVISION OF THE TEXT

14/02/2016