SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Temazepam Tablets 10mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 10mg Temazepam PhEur

Excipient with known effect
Each 10mg tablet contains 141.10mg lactose PhEur.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

White to pale yellow, circular, flat bevelled-edge uncoated tablets impressed "C" and the identifying letters "ZM" on either side of a central division line on one face and blank on the reverse.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Indicated for:

1) The short-term treatment of insomnia only when it is severe, disabling, or subjecting the individual to extreme stress, especially for those patients in whom the persistence of a hypnotic effect would be undesirable.

2) The premedication before minor surgical and investigative procedures particularly when hospital admission is not essential.

4.2 Posology and method of administration

Posology
Prior to starting treatment with temazepam, a discussion should be held with patients to put in place a strategy for ending treatment with temazepam 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.

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.
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
10-20mg 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 (10-20 mg, 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.

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 temazepam 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 temazepam, 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 temazepam 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.

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 temazepam. 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.

Risk from concomitant use of opioids:
Concomitant use of Temazepam 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 Temazepam with opioids should be reserved for patients for whom alternative treatment options are not possible. If a decision is made to prescribe Temazepam 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).

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).

Temazepam contains lactose:
Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interactions 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).

Opioids
The concomitant use of sedative medicines such as benzodiazepines or related drugs such as Temazepam 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).

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
*P*ossible 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

Pregnancy

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.

Breastfeeding

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, 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.

Psychiatric disorders Drug dependence (see section 4.4). 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.

General disorders and administration site conditions
Drug withdrawal symptoms (see section 4.4)
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

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, 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.

5.1 Pharmacodynamic properties

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

Mechanism of action
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

6.1 List of excipients

Lactose
Magnesium stearate
Maize starch
Povidone
Colloidal silica

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Shelf-life

Two years from the date of manufacture.

Shelf-life after dilution/reconstitution

Not applicable.

Shelf-life after first opening

Not applicable.

6.4 Special precautions for storage

250µm white PVC/60g/m^2 PVdC with 20µm aluminium foil blister packs

Store below 25°C. Store in the original package to protect from moisture. Keep the blister in the outer carton to protect from light.

All other containers

Store below 25°C in a dry place. Protect from light.

6.5 Nature and contents of container

The product containers are rigid injection moulded polypropylene or injection blow-moulded polyethylene containers with snap-on polyethylene lids; in case any supply difficulties should arise the alternative is amber glass containers with screw caps.
The product may also be supplied in blister packs and cartons:
a) Carton: Printed carton manufactured from white folding box board.
b) Blister pack: (i) 250µm white rigid PVC. (ii) Surface printed 20µm hard temper aluminium foil with 5-6g/M² PVC and PVdC compatible heat seal lacquer on the reverse side or:
c) Blister pack: 250µm white PVC/60g/m^2 PVdC with 20µm aluminium foil

Pack sizes: 7s, 21s, 28s, 30s, 50s, 56s, 60s, 84s, 100s, 112s, 250s, 500s, 1000s
Product may also be supplied in bulk packs, for reassembly purposes only, in polybags contained in tins, skillets or polybuckets filled with suitable cushioning material. Bulk packs are included for *temporary* storage of the finished product before final packaging into the proposed marketing containers.
Maximum size of bulk packs: 50,000.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

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

7 MARKETING AUTHORISATION HOLDER

Accord-UK Ltd
(Trading style: Accord)
Whiddon Valley
Barnstaple
Devon
EX32 8NS

8 MARKETING AUTHORISATION NUMBER

PL 00142/0363

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization: 3rd January 1995
Date of latest renewal: 5th October 2005

10 DATE OF REVISION OF THE TEXT

10/03/2026