Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Insomniger 20 mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 10mg of temazepam.

Excipients with known effect:
Each tablet contains 68.69 mg of lactose.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablets

White to pale yellow, round, flat bevelled-edge scored tablets with 9 mm diameter, marked 'T/20' on the scored side, and 'G' on the other.

The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Short-term management of insomnia. Benzodiazepines are only indicated when the disorder is severe, disabling or subjecting the individual to extreme distress.

For premedication prior to minor surgery or other related procedures.

4.2 Posology and method of administration

Posology

Adults including the elderly
Treatment should be started with the lowest recommended dose. The maximum dose should not be exceeded.

Insomnia
Dosage should be checked regularly at the start of treatment in order to decrease, if necessary, the dose or frequency of administration to prevent overdose due to accumulation. Treatment should be as short as possible. Generally the duration of treatment varies from a few days to two weeks with a maximum, including tapering-off, of four weeks. The tapering-off process should be tailored to the individual. In certain cases extension beyond the maximum treatment period may be necessary; if so, it should not take place without re-evaluation of the patient's status.

The product should be taken on retiring or up to 30 minutes before going to bed.

Adults: 10-20 mg. In exceptional circumstances the dose may be increased to 30-40 mg.

Elderly: 10 mg. In exceptional circumstances the dose may be increased to 20 mg.

Premedication
Adults: The usual dose is 20-40 mg, 30 to 60 minutes before procedure.

Elderly: Elderly patients are likely to respond to smaller doses, possibly half the normal adult dose or less.

Patients should be accompanied home when temazepam has been used as a premedicant prior to surgery or other procedures on a day attendance basis.

Paediatric population
The safety and efficacy of temazepamin children and adolescents less than 18 years of age has not been established and as such is not recommended for use.

Patients with hepatic impairment
Patients with impaired liver function should have a reduced dose.

Method of administration
For oral use.

4.3 Contraindications

Hypersensitivity to the active substance, other benzodiazepines or to any of the excipients listed in section 6.1.

- Myasthenia gravis
- Severe respiratory insufficiency
- Sleep apnoea syndrome
- Severe hepatic insufficiency
- Use in children and adolescents.

4.4 Special warnings and precautions for use

Risk from concomitant use of sedative medicines such as benzodiazepines or related drugs
Concomitant use of temazepam and sedative medicines such as benzodiazepines or related drugs may result in sedation, respiratory depression, coma and death. Because of these risks, concomitant prescribing with these sedative medicines should be reserved for patients for whom alternative treatment options are not possible. If a decision is made to prescribe Maneo tablets concomitantly with sedative medicines, the lowest effective dose should be used, and the duration of treatment should be as short as possible.

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

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 with using benzodiazepines. They are more likely to occur in the elderly. Should this occur, use of the drug should be discontinued.

Tolerance
Some loss of efficacy to the hypnotic effect of short-acting benzodiazepines may develop after repeated use for a few weeks.

Amnesia
Benzodiazepines may induce anterograde amnesia at therapeutic dosages, with the risk increasing at high dosages. The condition occurs most often several hours after ingesting the product, and therefore patients should ensure that they will be able to have an uninterrupted sleep of 7 - 8 hours. Amnesia effects may be associated with inappropriate behaviour.

Dependence
Use of benzodiazepines (even at therapeutic doses) may lead to the development of physical and psychological dependence upon these products. 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 or in patients with significant personality disorders.

Once physical dependence has developed, abrupt termination of treatment will be accompanied by withdrawal symptoms. These may consist of headaches, muscle pain, extreme anxiety, tension, depression, restlessness, insomnia, confusion and irritability and sweating. 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, vomiting, 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 hypnotic treatment. It may be accompanied by other reactions including mood changes, anxiety, sleep disturbances and restlessness. These symptoms may be difficult to distinguish from the original symptoms for which the drug was prescribed.

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 and withdrawal
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 the tapering off process. Extension beyond this period 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 minimising anxiety over such symptoms should they occur while the medicinal product is being discontinued.

There are indications that, in the case of benzodiazepines with a short duration of action, withdrawal phenomena can become manifest within the dosage interval, especially when the dosage is high. When benzodiazepines with a long duration 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.

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).

Convulsions/seizures may be more common in patients with pre-existing seizure disorders or who are taking other drugs that lower the convulsive threshold (e.g. tricyclic antidepressants).

Elderly or debilitated patients and patients with spinal and cerebellar ataxia
Elderly or debilitated patients, as well as patients with spinal and cerebellar ataxia, may be more susceptible to the effects of temazepam. Due to the myorelaxant effect, there is risk of ataxia and confusion with falls and subsequent hip fractures, particularly for older patients when they get up at night. These patients should be monitored frequently and have their dosage adjusted carefully according to patient response (see section 4.2).

Respiratory insufficiency
A lower dose is recommended for patients with chronic respiratory insufficiency due to the risk of respiratory depression. Use of benzodiazepines, including temazepam, may lead to potentially fatal respiratory depression. Temazepam should be used with caution in patients with compromised respiratory function (e.g. chronic obstructive pulmonary disease, sleep apnoea syndrome). Temazepam should not be used in conjunction with drugs which may depress the patient's respiratory function (see section 4.5).

Hepatic or renal impairment
Benzodiazepines are not indicated to treat patients with severe hepatic insufficiency as it may precipitate encephalopathy.

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

Psychoses
Benzodiazepines are not indicated for the primary treatment of psychotic illness.

Depression
Pre-existing depression may be unmasked during benzodiazepine use. Benzodiazepines should not be used alone to treat depression or anxiety associated with depression (suicide may be precipitated in such patients).

Drug and alcohol abuse
Benzodiazepines should be used with extreme caution in patients with a history of alcohol or drug abuse. Abuse has been reported in polydrug abusers.

Other potential causes of insomnia
Insomnia may be a symptom of several other disorders. The possibility should be considered that the complaint may be related to an underlying physical or psychiatric disorder for which there is more specific treatment.

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

4.5 Interaction with other medicinal products and other forms of interactions

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

Not recommended
Concomitant intake with alcohol. The sedative effect may be enhanced when the product is used in combination with alcohol. This affects the ability to drive or use machines.

Take into account
Combination with CNS depressants. Enhancement of the central depressive effect may occur in cases of concomitant use with alcohol, barbiturates, antipsychotics (neuroleptics), hypnotics, anxiolytics/sedatives, antidepressant agents, narcotic analgesics, antiepileptic drugs, anaesthetics, sedative antihistamines, antihypertensives and beta (receptor) blockers. Administration of theophylline or aminophylline may reduce the sedative effects of benzodiazepines, including temazepam. In the case of narcotic analgesics enhancement of the euphoria may also occur leading to an increase in psychological dependence.

When temazepam 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. Concomitant intake with muscle relaxants may increase the relaxant effect of temazepam.

The sedative effect of temazepam may be enhanced when it is taken in combination with disulfiram.

Concomitant use of oral contraceptive steroids may enhance the elimination of temazepam and slightly decrease the drug effect.

Known inhibitors of hepatic enzymes, particularly cytochrome P450 have been shown to reduce the clearance of benzodiazepines and may potentiate their action and known inducers of hepatic enzymes, e.g. rifampicin, may increase the clearance of benzodiazepines.
Temazepam in combination with 4-hydroxybutanoic acid (sodium sorbate) may cause an increased respiratory depression.

4.6 Fertility, pregnancy and lactation

Pregnancy
Insufficient data are available on temazepam to assess its safety during pregnancy. Temazepam is not recommended for administration during pregnancy. Animal studies with benzodiazepines have shown minor effects on the foetus while a few studies have reported late behavioural disturbance in offspring exposed in utero. In humans, umbilical cord blood samples indicate placental transfer of benzodiazepines and their glucuronide metabolites.

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 pregnant or suspects that she is pregnant.

If, for compelling medical reasons, temazepam is administered during the late phase of pregnancy, or during labour, effects on the neonate, such as hypothermia, hypotonia and moderate respiratory depression, can be expected due to the pharmacological action of the product.

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 of developing withdrawal symptoms in the postnatal period.

Breastfeeding
Temazepam may pass into breast milk, consequently its use during breastfeeding is not recommended. Sedation and inability to suckle have occurred in breastfed neonates of lactating mothers taking benzodiazepines. Breastfed infants of lactating mothers should be observed for pharmacological effects (including sedation and irritability).

4.7 Effects on ability to drive and use machines

Not recommended
Sedation, amnesia, impaired concentration and impaired muscle function may adversely affect the ability to drive or to use machines. If insufficient sleep duration occurs, the likelihood of impaired alertness may be increased (see also section 4.5).

As with all patients on CNS depressant drugs, patients should be warned not to drive or operate machinery until it is known that they do not become drowsy or dizzy from temazepam. Drowsiness is most likely to occur after initiation of the use of benzodiazepines and gradually subsides. Driving skills are usually not affected in the morning after taking a 20 mg dose of temazepam in the preceding evening.

4.8 Undesirable effects

The undesirable effects of temazepam are reported by organ system and frequency. The frequencies are represented as follows: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).

The following terminologies have been used to classify the occurrence of adverse reactions, as applicable:

System Organ Class	Frequency	Undesirable effects
Blood and lymphatic system disorders	Rare	• Blood disorders
	Not known	• Thrombocytopenia, agranulocytosis, pancytopenia
Immune system disorders	Not known	• Anaphylactic reaction, anaphylactoid reaction, hypersensitivity
Endocrine disorders	Not known	• Inappropriate antidiuretic hormone secretion (SIADH)
Metabolism and nutrition disorders	Not known	• Hyponatraemia
Psychiatric disorders	Common	• Depression (pre-existing depression may be unmasked during benzodiazepine use)
	Uncommon	• Libido disorder, orgasm abnormal, emotional disorder
	Not known	• Suicide attempt, suicidal ideation

		• Restlessness, agitation, irritability, aggressiveness, delusion, rages, nightmares, hallucinations, hostility, disturbance in sexual arousal, anger, sleep disorder, insomnia, drug dependence, psychotic disorder, psychoses, inappropriate behaviour and other adverse behavioural effects are known to occur when using benzodiazepines. They may be quite severe and are more likely to occur in the elderly (see section 4.4). • Numbed emotions (this phenomenon occurs predominantly at the start of therapy and usually disappears with repeated administration) • Anterograde amnesia may occur using therapeutic dosages, the risk increasing at higher dosages. Amnesic effects may be associated with inappropriate behaviour (see section 4.4).
Nervous system disorders	Very common	• Sedation
	Common	• Ataxia, confusional state, dizziness, drowsiness
	Uncommon	• Slow response to stimuli, disturbance in attention
	Not known	• Coma, extrapyramidal disorder, convulsion, amnesia, tremor, vertigo, dysarthria, drowsiness during the day, reduced alertness, impaired concentration, headache, sleep disturbance/restless sleep. These phenomena occur predominantly at the start of therapy and usually disappear with repeated administration.
Eye disorders	Not known	• Visual impairment, including diplopia and vision blurred (this phenomenon occurs predominantly at the start of therapy and usually disappears with repeated administration)
Vascular disorders	Rare	• Hypotension
	Not known	• Blood pressure decreased
Respiratory, thoracic and mediastinal disorders	Not known	• Respiratory depression, apnoea, sleep apnoea syndrome exacerbated, obstructive pulmonary disease exacerbated (the extent of respiratory depression with benzodiazepines is dose dependent, with more severe depression occurring with high doses)
Gastrointestinal disorders	Uncommon	• Nausea

	Not known	• Dryness of the mouth • Gastrointestinal disturbances • Constipation
Hepatobiliary disorders	Not known	• Jaundice, blood bilirubin increased, transaminases increased, blood alkaline phosphatase increased
Skin and subcutaneous tissue disorders	Not known	• Alopecia, skin reactions
Musculoskeletal and connective tissue disorders	Not known	• Muscle weakness (this phenomenon occurs predominantly at the start of therapy and usually disappears with repeated administration). Due to the myorelaxant effect there is a risk of falls and consequently fractures in the elderly.
Reproductive system and breast disorders	Uncommon	• Erectile dysfunction
General disorders and administration site conditions	Common	• Asthenia, fatigue
	Not known	• Hypothermia, paradoxical drug reaction (anxiety)
Investigations	Rare	• Abnormal liver function tests

Withdrawal reactions
Withdrawal of treatment may be accompanied by mood changes, anxiety, sleep disturbances or restlessness. The risk of withdrawal or rebound phenomena is greater after abrupt discontinuation of treatment. It is recommended that the dosage is decreased gradually.

Use (even at therapeutic doses) of benzodiazepines may lead to the development of physical and psychological dependence. Once physical dependence has occurred, abrupt termination of treatment will be accompanied by withdrawal symptoms or rebound phenomenon. These include headaches, muscle pain, extreme anxiety, tension, restlessness, confusion and irritability. In severe cases symptoms may include derealisation, depersonalization, hyperacusis, numbness and tingling of extremities, hypersensitivity to light, noise and physical contact, hallucinations or epileptic seizures (see section 4.4).

Abuse has also been reported.

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 HPRA Pharmacovigilance, Website: www.hpra.ie

4.9 Overdose

As with other benzodiazepines, overdose should not present a threat to life unless combined with other CNS depressants (including alcohol).

However, in post-marketing experience, overdose with temazepam has occurred predominantly in combination with alcohol and/or other drugs. Therefore, in the management of overdose with any medicinal product, it should be borne in mind that multiple agents may have been taken.
When there is a risk of aspiration, induction of emesis is not recommended.
Gastric lavage may be indicated if performed soon after ingestion or in symptomatic patients.

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.
3-OH benzodiazepines are, as a rule, not dialysable and their metabolites (glucuronides) only dialysable with difficulty. The value of dialysis has not been determined for temazepam.
Overdosage 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 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. Flumazenil product information should be consulted prior to temazepam use.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Temazepam is a benzodiazepine: it has anxiolytic, sedative and hypnotic characteristics as well as possible muscle relaxant and anticonvulsant characteristics.

5.2 Pharmacokinetic properties

Absorption
Pharmacokinetic studies have shown that temazepam is well absorbed (90 - 100%) and the first pass effect is slight (about 5%). The time to reach peak plasma levels is usually about 50 minutes when given orally. Maximum plasma levels observed after doses of 20 mg are 660 - 1100 ng/ml. With multiple dosing steady state is obtained by the third day and there is little or no accumulation of parent drug or metabolites.

Distribution
The volume of distribution is 1.3 to 1.5 l/kg body weight, for the unbound fraction 43 - 68 l/kg. Approximately 96% of unchanged drug is bound to plasma proteins.

Biotransformation
Temazepam is metabolised principally in the liver where most of the unchanged drug is directly conjugated to the glucuronide and excreted in the urine. Less than 5% of the drug is demethylated to oxazepam and eliminated as the glucuronide. The glucuronides of temazepam have no demonstrable CNS activity.

Elimination
Temazepam is rapidly eliminated, most studies showing an elimination half life in the range 7 - 11 hours (mean 8 hours). Following a single dose, 80% of the dose appears in the urine, mostly as the conjugates and 12% of the dose appears in the faeces. Less than 2% of the dose is excreted unchanged in the urine.

Elimination in reduced renal function
In established renal insufficiency the metabolic clearance of temazepam as well as the plasma levels of the non-protein bound temazepam remain within the normal range. The elimination half life for temazepam glucuronide is however increased by which this inactive metabolite accumulates. As stated under "Overdose" it is unlikely that temazepam may be significantly removed by dialysis.

5.3 Preclinical safety data

The acute LD_{50} dose for temazepam in mice has been determined as 85 mg/kg after intraperitoneal administration and 2600 mg/kg after oral administration. Repeated dose toxicity studies lasting up to six months did not reveal specific organ toxicity in mice, rats or dogs. A slight increase in the incidence of liver adenomas was found in female mice given 160 mg/kg temazepam in the diet for 18 months. Temazepam did not produce DNA strand breaks in the rat livers.
No animal data is available on teratogenic effects of temazepam.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Maize starch
Gelatin

Talc
Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Amber glass bottle 2 years
Blister pack 2 years
Polypropylene containers 3 years

6.4 Special precautions for storage

Store below 25°C.

Bottles: Keep the container tightly closed andreplace the cap immediately after use in order to protect from moisture.

Blisters: Store in the original package in order toprotect from moisture.

6.5 Nature and contents of container

7, 10, 14, 28, 30, 56, 60, 84, 90, 100 250, 500 tablets are presented in amber glass bottles with tamper-evident polyethylene lid or equivalent, polypropylene containers with polyethylene lid, or PVC/PVdC/Al blister packs.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

McDermott Laboratories Ltd., T/A Gerard Laboratories
35/36 Baldoyle Industrial Estate
Grange Road
Dublin 13
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0577/225/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

First date of authorisation: 25 July 1997

Date of last renewal: 25 July 2007

10 DATE OF REVISION OF THE TEXT

February 2022