Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Nortem 10mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 10 mg of temazepam

Excipient(s) with known effect
Each tablet contains 140.0 mg lactose.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet.
White to pale yellow, flat bevel edged tablets with a breakline on one side, 5K1 on reverse.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

As a hypnotic for the short-term management of insomnia only when it is severe, disabling or subjecting the individual to extreme distress.

For pre-medication prior to minor surgery or other related procedures.

4.2 Posology and method of administration

Oral.

The treatment period should be of the shortest duration possible. This may vary from a few days to two weeks with a maximum (including tapering off) of four weeks. The dose reduction process should be tailored to the individual. In certain cases extension beyond the maximum treatment period may be necessary; if this is the case 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.

Dosage

Insomnia
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.

Pre-medication: The usual dose is 20 - 40 mg 30 to 60 minutes before the procedure.

Children: Not recommended for use in children.

Treatment should be started with the lowest, recommended dose. The maximum dose should not be exceeded. Patients suffering from renal or hepatic impairment should receive a reduced dose.

4.3 Contraindications

Myasthenia Gravis.

Severe respiratory insufficiency.

Sleep apnoea syndrome.

Severe hepatic insufficiency.

Nortem Tablets are contraindicated in patients with hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

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

Dependence
Use of benzodiazepines may lead to the development of physical and psychic 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 drug and alcohol abuse.

Dependence may lead to withdrawal symptoms, especially if treatment is discontinued abruptly. Therefore, the drug should always be discontinued gradually.

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, restlessness, confusion and 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, and may occur on withdrawal of treatment. It may be accompanied by other reactions including mood changes, anxiety, sleep disturbances and restlessness. Since the risk of withdrawal/ 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 depending on the indication. Treatment should not exceed 4 weeks, including the tapering off period. 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 is aware of the possibility of rebound phenomena, thereby minimising anxiety while the product is being discontinued.

There are indications that, in the case of benzodiazepines with a short elimination half-life, withdrawal phenomena can become manifest within the dosage interval, especially when the dosage is high.

Amnesia
Benzodiazepines may induce anterograde amnesia. The condition occurs most often several hours after ingesting the product and therefore to reduce the risk of this occurring, patients should ensure that they will be able to have an uninterrupted sleep for 7 - 8 hours.

Psychiatric and 'paradoxical' reactions
Reactions like restlessness, agitation, irritability, aggressiveness, delusions, rages, hallucinations, psychoses, inappropriate behaviour are known to occur when using benzodiazepines. Should this occur, use of the product should be discontinued. These are more likely to occur in children and the elderly.

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 with opioids should be reserved for patients for whom alternative treatment options are not 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 (where applicable) to be aware of these symptoms (see section "Interaction with other medicinal products and other forms of interaction").

Specific patient groups

Elderly or debilitated patients may be more susceptible to the effects of benzodiazepines – therefore these patients should be monitored frequently and have their dosage adjusted carefully according to patient response (see section 4.2). Use of benzodiazepines may lead to potentially fatal respiratory depression. A lower dose is therefore recommended for patients with chronic respiratory insufficiency. Benzodiazepines are not indicated to treat patients with severe hepatic insufficiency as it may precipitate encephalopathy.

Temazepam should be used with caution in elderly, due to the risk of sedation and/or musculoskeletal weakness that can promote falls, often with serious consequences in this population.1
Benzodiazepines are not indicated to treat patients with severe hepatic insufficiency as it may precipitate encephalopathy.
Benzodiazepines are not indicated for the primary treatment of psychotic illness. Benzodiazepines should not be used alone to treat depression or anxiety associated with depression (suicide may be precipitated in such patients). Benzodiazepines should also be used with extreme caution in patients with a history of alcohol or drug abuse.

Excipient(s)

Lactose

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

Sodium

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interactions

Not recommended:

Concomitant intake of 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 antipsychotics (neuroleptics), hypnotics, anxiolytics/sedatives, antidepressants, narcotic analgesics, anti-epileptic drugs, anaesthetics and sedative antihistamines.

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

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

Concomitant use of disulfiram may slow down the elimination of temazepam.

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

Compounds which inhibit certain hepatic enzymes (particularly cytochrome P450) may enhance the activity of benzodiazepines and benzodiazepine-like agents.

4.6 Fertility, pregnancy and lactation

Insufficient data are available on temazepam to assess its safety during pregnancy and lactation. Temazepam is not recommended for administration during 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 treatment if she intends to become or suspects that she is pregnant.

Administration of the medicinal product during the last trimester of pregnancy or during labour is only allowed on strict medical indication as, due to the pharmacological action of the product, effects on the neonate such as hypothermia, hypotonia and moderate respiratory depression, can be expected.

Moreover, infants born to mothers who took benzodiazepines chronically during the latter stages of pregnancy may have developed physical dependence. Most benzodiazepines will be excreted into breast milk, although to a variable extent. Breast-feeding is therefore not recommended whilst taking this product.

4.7 Effects on ability to drive and use machines

Not recommended: The temazepam is sedating especially with concomitant use of alcohol. This affects the ability to drive or use machines.

Sedation, amnesia, impaired concentration and impaired muscle function may adversely affect the ability to drive our use machines. If insufficient sleep duration occurs, the likelihood of impaired alertness may be increased. Patients affected by drowsiness while taking benzodiazepines should not drive or operate machinery. Drowsiness is most likely to occur after initiation of the use of benzodiazepines and gradually subsides. The driving skills are usually not affected in the morning after taking 20 mg dose of temazepam in the preceding evening.

4.8 Undesirable effects

Psychiatric disorders
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 high dosages. Amnesic effects may be associated with inappropriate behaviour. (See Section 4.4).

Changes in libido have been reported occasionally.
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. These reactions are more likely to occur in children and the elderly. Should this occur, use of the product should be discontinued. (See Section 4.4).

Nervous system disorders
Drowsiness during the day, reduced alertness, impaired concentration, fatigue, headache, dizziness, ataxia, and restless sleep. These phenomena occur predominantly at the start of therapy and usually disappear with repeated administration.

Eye disorders
Double vision, (this phenomenon occurs predominantly at the start of therapy and usually disappears with repeated administration).

Gastrointestinal disorders
Dryness of the mouth or gastro-intestinal disturbances have been reported occasionally.

Skin and subcutaneous tissue disorders
Skin reactions have been reported occasionally.
Musculoskeletal, connective tissue and bone disorders.
Muscle weakness (this phenomenon occurs predominantly at the start of therapy and usually disappears with repeated administration). Due to the myorelaxant effect the risk of falls and consequently of hip fractures in elderly patients is increased.

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

The use of benzodiazepines may lead to the development of physical and psychic dependence. Once physical dependence has occurred, abrupt termination of treatment will be accompanied by withdrawal symptoms. These include headaches, muscle pain, extreme anxiety, tension, restlessness, confusion and irritability. In severe cases symptoms may include derealisation, depersonalisation, hyperacusis, numbness and tingling of extremities, hypersensitivity to light, noise and physical contact, hallucinations or epileptic seizures. (See Section 4.4).

Reporting of side effects

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, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@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).

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 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. The value of dialysis has not been determined for temazepam.

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.

Overdose of benzodiazepines is usually manifested by degrees of central nervous system depression ranging from drowsiness to coma. In mild cases, symptoms include drowsiness, mental confusion and lethargy. In some serious cases, symptoms may include ataxia, hypotonia, hypotension, respiratory depression, rarely coma and very rarely death.

Flumazenil may be used as an antidote.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: NO5CD07
Pharmacotherapeutic Group: Benzodiazepine derivatives.

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

5.2 Pharmacokinetic properties

Absorption
Pharmacokinetic studies have shown that temazepam is well absorbed (90-100%) and the first pass effect is slight (at 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.

Metabolism
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 of 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 level 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
Cellulose microcrystalline
Titanium dioxide E171
Croscarmellose sodium
Magnesium Stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25ºC. Store in the original package in order to protect from light.

6.5 Nature and contents of container

PVdC coated PVC film with hard temper aluminium foil blister strips in packs of 28 tablets.

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

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

7 MARKETING AUTHORISATION HOLDER

Teva B.V.
Swensweg 5
2031GA Haarlem
Netherlands

8 MARKETING AUTHORISATION NUMBER

PA1986/085/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 13 December 2008

10 DATE OF REVISION OF THE TEXT

January 2022