PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

# RESTORIL®

Temazepam

Capsule, 15 mg and 30 mg, Oral

USP

Hypnotic

AA Pharma Inc.
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Vaughan, Ontario
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**RECENT MAJOR LABEL CHANGES**

| | |
|---|---|
| 1 Indications, 1.2 Geriatrics | 11/2021 |
| 3 Serious Warnings and Precautions Box | 11/2021 |
| 4 Dosage and Administration, 4.1 Dosing considerations | 11/2021 |
| 7 Warnings and Precautions | 11/2021 |
| 7 Warnings and Precautions, 7.1.4 Geriatrics | 11/2021 |

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**Sections or subsections that are not applicable at the time of authorization are not listed.**

## PART I: HEALTH PROFESSIONAL INFORMATION

## 1 INDICATIONS

RESTORIL (temazepam) is indicated for the symptomatic relief of transient and short-term insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakenings.

The use of hypnotics should be restricted for insomnia where disturbed sleep results in impaired daytime functioning.

### 1.1 Pediatrics

Pediatrics (<18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

### 1.2 Geriatrics

Geriatrics: Evidence from clinical studies and experience suggests that use in the geriatric population is associated with differences in safety or effectiveness.

Long-term use of RESTORIL should be avoided in elderly patients. Enhanced monitoring is recommended (see 7 WARNINGS AND PRECAUTIONS, Falls and Fractures; 4.1 Dosing considerations).

## 2 CONTRAINDICATIONS

RESTORIL is contraindicated in patients:

- with a known hypersensitivity to the drug, to other benzodiazepines or to any component of the drug's formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.
- with myasthenia gravis.
- with sleep apnea syndrome.
- who in the past manifested paradoxical reactions to alcohol and/or sedative medications.

## 3 SERIOUS WARNINGS AND PRECAUTIONS BOX

**Serious Warnings and Precautions**

**Addiction, Abuse and Misuse**

The use of benzodiazepines, including RESTORIL, can lead to abuse, misuse, addiction, physical dependence and withdrawal reactions. Abuse and misuse can result in overdose or death, especially when benzodiazepines are combined with other medicines, such as opioids, alcohol or illicit drugs.

- Assess each patient's risk prior to prescribing RESTORIL
- Monitor all patients regularly for the development of these behaviours or conditions.
- RESTORIL should be stored securely to avoid theft or misuse.

**Withdrawal**

Benzodiazepines, like RESTORIL can produce severe or life-threatening withdrawal symptoms.

- Avoid abrupt discontinuation or rapid dose reduction of RESTORIL.
- Terminate treatment with RESTORIL by gradually tapering the dosage schedule under close monitoring.

(see 7 WARNINGS AND PRECAUTIONS, Dependence/Tolerance)

**Risks from Concomitant use with Opioids**

Concomitant use of RESTORIL and opioids may result in profound sedation, respiratory depression, coma and death (see 7 WARNINGS AND PRECAUTIONS, General, Concomitant use with opioids).

- Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are not possible.
- Limit dosages and durations to the minimum required.
- Follow patients for signs and symptoms of respiratory depression and sedation.

## 4 DOSAGE AND ADMINISTRATION

### 4.1 Dosing Considerations

- Sleep disturbance may be the presenting manifestation of a physical and/or psychiatric disorder. Consequently, a decision to initiate symptomatic treatment of insomnia should only be made after the patient has been carefully evaluated.
- RESTORIL should always be prescribed at the lowest effective dose for the shortest duration possible.
- RESTORIL can produce withdrawal signs and symptoms or rebound phenomena following abrupt discontinuation or rapid dose reduction (see 3 SERIOUS WARNINGS AND PRECAUTIONS BOX, Withdrawal; 7 WARNINGS AND PRECAUTIONS, Dependence/Tolerance). Abrupt discontinuation should be avoided and treatment - even if only of short duration - should be terminated by gradually tapering the dosage schedule under close monitoring.
- Tapering should be tailored to the specific patient. Special attention should be given to patients with a history of seizure.
- If a patient experiences withdrawal signs and symptoms, consider postponing the taper or raising the benzodiazepine to the previous dosage prior to proceeding with a gradual taper.
- Geriatric patients in particular may be more sensitive to benzodiazepines (see 7 WARNINGS AND PRECAUTIONS, Falls and Fractures).
- Long-term use of RESTORIL should be avoided in elderly patients. Enhanced monitoring is recommended.

### 4.2 Recommended Dose and Dosage Adjustment

**Recommended Dose**

**Adults:** the recommended dose of RESTORIL is 30 mg before retiring, 15 mg may be sufficient for some

patients.

**Elderly and/or Debilitated Patients:** the initial dose should not exceed 15 mg before retiring (see 7.1.4 Geriatrics).

**Pediatrics:** RESTORIL is not indicated for children under 18 years of age (see 7.1.3 Pediatrics).

**Dosage Adjustment**

The lowest effective dose of RESTORIL (temazepam) should be used. Treatment with RESTORIL should usually not exceed 7-10 consecutive days. Use for more than 2-3 consecutive weeks requires complete re-evaluation of the patient. Prescriptions for RESTORIL should be written for short-term use (7-10 days) and it should not be prescribed in quantities exceeding a 1-month supply.

An appropriate hypnotic dose should produce the desired hypnotic effect while avoiding oversedation and impairment of performance the next day.

RESTORIL is intended only for short-term use and therefore, should not be prescribed in quantities exceeding those required for that cycle of administration. Prescription should not be renewed without further assessment of the patient's needs.

### 4.4 Administration

Capsules are for oral administration.

### 4.5 Missed Dose

If the patient misses a dose, inform the patient to skip the missed dose and take the next dose at the regular dosing schedule.

## 5 OVERDOSAGE

Manifestations of acute overdosage of RESTORIL, as with other benzodiazepines, can be expected to reflect the increasing CNS effects of the drug and include somnolence, confusion and coma, with reduced or absent reflexes. With large overdoses, respiratory depression, hypotension and finally coma will result. If the patient is conscious, vomiting should be induced mechanically or with emetics (e.g., syrup of ipecac 20 to 30 mL). General supportive measures should be employed.. Maintenance of adequate pulmonary ventilation is essential and fluids should be administered intravenously to encourage diuresis. The use of pressor agents, such as norepinephrine bitartrate or metaraminol, intravenously may be necessary to combat hypotension but only if considered essential. The value of dialysis in emergency therapy for benzodiazepine overdosage has not been determined. If excitation occurs, barbiturates should not be used. It should be borne in mind that multiple agents may have been ingested.

The benzodiazepine antagonist, flumazenil, is a specific antidote in known or suspected benzodiazepine overdose.

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|---|
| For management of a suspected drug overdose, contact your regional poison control centre. |

## 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

**Table 1 – Dosage Forms, Strengths, Composition and Packaging**

| Route of Administration | Dosage Form / Strength/Composition | Non-medicinal Ingredients |
|---|---|---|
| oral | Capsules 15 mg, 30 mg | Ammonium hydroxide, croscarmellose sodium, D&C Red No. 28, FD&C Blue No. 1, FD&C Red No. 40, gelatin, lactose anhydrous, magnesium stearate, microcrystalline cellulose, propylene glycol, red iron oxide (15 mg capsules only), shellac glaze, simethicone, sodium lauryl sulfate, talc, and titanium dioxide |

**RESTORIL 15mg:** Hard gelatin capsule with pink opaque body and maroon opaque cap imprinted 'TM 15' in white ink, filled with white powder. 15 mg temazepam. Available in bottles of 100.

**RESTORIL 30mg:** Hard gelatin capsule with light blue opaque body and maroon opaque cap, imprinted 'TM 30' in white ink, filled with white powder. 30 mg temazepam. Available in bottles of 100.

## 7 WARNINGS AND PRECAUTIONS

Please see 3 SERIOUS WARNINGS AND PRECAUTIONS BOX.

### General

The failure of insomnia to remit after 7-10 days of treatment may indicate the presence of a primary psychiatric and/or medical illness or the presence of sleep state misperception.

Worsening of insomnia or the emergence of new abnormalities of thinking or behaviour may be the consequence of an unrecognized psychiatric or physical disorder. These have also been reported to occur in association with the use of drugs that act at the benzodiazepine receptors.

**Concomitant use with opioids**: Concomitant use of benzodiazepines, including RESTORIL, and opioids may result in profound sedation, respiratory depression, coma, and death. Because of these risks, reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are not possible (see 3 SERIOUS WARNINGS AND PRECAUTIONS BOX, Risks from Concomitant use with Opioids; 9.1 Serious Drug Interactions).

Observational studies have demonstrated that concomitant use of opioid analgesics and benzodiazepines increases the risk of drug-related mortality compared to use of opioid analgesics alone. Because of similar pharmacological properties, it is reasonable to expect similar risk with the concomitant use of other CNS depressant drugs with benzodiazepines.

If a decision is made to prescribe RESTORIL concomitantly with opioids, prescribe the lowest effective dosages and minimum durations of concomitant use. In patients already receiving an opioid analgesic, prescribe a lower initial dose of RESTORIL than indicated, and titrate based on clinical response. If an opioid analgesic is initiated in a patient already taking RESTORIL, prescribe a lower initial dose of the opioid analgesic and titrate based on clinical response. Follow patients closely for signs and symptoms of respiratory depression and sedation (see 5 OVERDOSAGE).

Advise both patients and caregivers about the risks of respiratory depression and sedation when RESTORIL is used with opioids.

Advise patients not to drive or operate heavy machinery until the effects of concomitant use of the

opioid have been determined.

**Potentiation of Drug Effects:** RESTORIL may potentiate the effects of other central nervous system depressant drugs such as alcohol, barbiturates, non-barbiturate hypnotics, antihistamines, narcotics, antipsychotic and antidepressant drugs, and anticonvulsants. Therefore, different benzodiazepines should usually not be used simultaneously and careful consideration should be given if other CNS depressants are administered in combination with RESTORIL. Patients should be advised against the simultaneous use of other CNS depressant drugs and should be cautioned not to take alcohol because of the potentiation of effects that might occur (see 9.4 Drug-Drug Interactions).

**Dependence/Tolerance**

Use of benzodiazepines, such as RESTORIL, can lead to abuse, misuse, addiction, physical dependence (including tolerance) and withdrawal reactions. Abuse and misuse can result in overdose or death, especially when benzodiazepines are combined with other medicines, such as opioids, alcohol, or illicit drugs.

The risk of dependence increases with higher doses and longer term use but can occur with short-term use at recommended therapeutic doses. The risk of dependence is greater in patients with a history of psychiatric disorders and/or substance (including alcohol) use disorder.

- Discuss the risks of treatment with RESTORIL with the patient, considering alternative (including non-drug) treatment options.
- Carefully evaluate each patient's risk of abuse, misuse and addiction, considering their medical condition and concomitant drug use, prior to prescribing RESTORIL. In individuals prone to substance use disorder, RESTORIL should only be administered if deemed medically necessary, employing extreme caution and close supervision.
- RESTORIL should always be prescribed at the lowest effective dose for the shortest duration possible.
- All patients receiving benzodiazepines should be routinely monitored for signs and symptoms of misuse and abuse. If a substance use disorder is suspected, evaluate the patient and refer them for substance abuse treatment, as appropriate.

**Withdrawal:** Benzodiazepines, such as RESTORIL, can produce withdrawal signs and symptoms, ranging from mild to severe and even life threatening, following abrupt discontinuation or rapid dose reduction. Other factors that may precipitate withdrawal are switching from a long-acting to a short-acting benzodiazepine, decreasing blood levels of the drug or administration of an antagonist. The risk of withdrawal is higher with higher dosages and/or prolonged use, but can occur with short-term use at recommended therapeutic doses.

The onset of withdrawal signs and symptoms can range from hours to weeks following drug cessation and occur even with tapered dosage. Some symptoms can persist for months. Since symptoms are often similar to those for which the patient is being treated, it may be difficult to distinguish from a relapse of the patient's condition.

Severe or life-threatening signs and symptoms of withdrawal include catatonia, delirium tremens, depression, dissociative effects (e.g. hallucinations), mania, psychosis, seizures (including status epilepticus) and suicidal ideation and behaviour.

Other withdrawal signs and symptoms include abdominal cramps, cognitive impairment, diarrhea, dysphoria, extreme anxiety or panic attacks, headache, hypersensitivity to light, noise and physical

contact, insomnia, irritability, muscle pain or stiffness, paresthesia, restlessness, sweating, tension, tremors and vomiting. There is also a possibility of rebound anxiety or rebound insomnia.

- Abrupt discontinuation should be avoided and treatment - even if only of short duration - should be terminated by gradually tapering the dosage schedule under close monitoring.
- Tapering should be tailored to the specific patient. Special attention should be given to patients with a history of seizure.
- If a patient experiences withdrawal symptoms, consider postponing the taper or raising the benzodiazepine to the previous dosage prior to proceeding with a gradual taper.
- Inform patients of risk of discontinuing abruptly, reducing dosage rapidly or switching medications.
- Stress the importance of consulting with their health care professional in order to discontinue safely.
- Patients experiencing withdrawal symptoms should seek immediate medical attention.

(see 3 SERIOUS WARNINGS AND PRECAUTIONS BOX, Addiction, Abuse and Misuse; 3 SERIOUS WARNINGS AND PRECAUTIONS BOX, Withdrawal; 4.1 Dosing Considerations)

**Driving and Operating Machinery**

Because of RESTORIL's CNS depressant effect, patients receiving the drug should be cautioned against engaging in hazardous occupations requiring complete mental alertness such as operating machinery or driving a motor vehicle. For the same reason, patients should be warned against the concomitant ingestion of RESTORIL and alcohol or CNS depressant drugs.

**Falls and Fractures**

There have been reports of falls and fractures among benzodiazepine users due to adverse reactions such as sedation, dizziness and ataxia. The risk is increased in those taking concomitant sedatives (including alcoholic beverages), the elderly or debilitated patients.

**Hepatic/Biliary/Pancreatic**

Temazepam is O-conjugated in the liver. Hence, RESTORIL should be given with caution to patients with impaired hepatic function.

**Immune**

**Severe Anaphylactic and Anaphylactoid Reactions:** Rare 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 RESTORIL. Some patients have had additional symptoms such as dyspnea, throat closing or nausea and vomiting that suggest anaphylaxis. Some patients have required medical therapy in the emergency department. If angioedema involves the throat, glottis or larynx, airway obstruction may occur and be fatal. Patients who develop angioedema after treatment with RESTORIL should not be rechallenged with the drug.

**Neurologic**

**Memory disturbance:** Anterograde amnesia of varying severity has been reported following therapeutic doses of benzodiazepines. The event is rare with RESTORIL. Anterograde amnesia is a dose-related phenomenon and elderly subjects may be at particular risk. Cases of transient global amnesia

and "traveller's amnesia" have also been reported in association with benzodiazepines, the latter in individuals who have taken the drug, often in the middle of the night, to induce sleep while travelling.

Transient global amnesia and traveller's amnesia are unpredictable and not necessarily dose-related phenomena. Patients should be warned not to take RESTORIL under circumstances in which a full night's sleep and clearance of the drug from the body are not possible before they need again to resume full activity.

**Psychiatric**

**Abnormal thinking and psychotic behavioural changes** have been reported to occur in association with the use of benzodiazepines including RESTORIL, although rarely. Some of the changes may be characterized by decreased inhibition, e.g., aggressiveness or extroversion that seem excessive, similar to that seen with alcohol and other CNS depressant (e.g., sedative/hypnotics). Particular caution is warranted in patients with a history of violent behaviour and a history of unusual reactions to sedatives including alcohol and the benzodiazepines. Psychotic behavioural changes that have been reported with benzodiazepines include bizarre behaviour, hallucinations, and depersonalization. Abnormal behaviours associated with the use of benzodiazepines have been reported more with chronic use and/or high doses but they may occur during the acute, maintenance or withdrawal phases of treatment.

It can rarely be determined with certainty whether a particular instance of abnormal behaviours listed above is drug-induced, spontaneous in origin, or a result of an underlying psychiatric disorder. Nevertheless, the emergence of any new behavioural sign or symptom of concern requires careful and immediate evaluation.

**Anxiety/Restlessness:** An increase in daytime anxiety and/or restlessness have been observed during treatment with RESTORIL. This may be a manifestation of inter dose withdrawal due to the short elimination half-life of the drug.

**Complex Sleep-Related Behaviours:** Complex sleep-related behaviours 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 have taken RESTORIL. Other potentially dangerous behaviours have been reported in patients who got out of bed after taking a sedative-hypnotic and were not fully awake, including preparing and eating food, making phone calls, leaving the house, etc. As with “sleep-driving”, patients usually do not remember these events. The use of alcohol and other CNS-depressants with RESTORIL appears to increase the risk of such behaviours, as does the use of RESTORIL at doses exceeding the maximum recommended dose. RESTORIL is not to be taken with alcohol (see 9.3 Drug-Behavioural Interactions). Caution is needed with concomitant use of other CNS depressant drugs (see 9.4 Drug-Drug Interactions). Due to the risk to the patient and the community, discontinuation of RESTORIL should be strongly considered for patients who report any such complex sleep-related behaviours.

**Confusion:** The benzodiazepines affect mental efficiency, e.g., concentration, attention and vigilance. The risk of confusion is greater in the elderly and in patients with cerebral impairment.

**Depression:** Caution should be exercised if RESTORIL is prescribed to patients with signs or symptoms of depression that could be intensified by hypnotic drugs. The potential for self-harm (e.g., intentional overdose) is high in patients with depression and thus, the least amount of drug that is feasible should be available to them at any one time.

RESTORIL should be used with caution in severely depressed patients or those in whom there is any evidence of latent depression; it should be recognized that suicidal tendencies may be present and protective measures may be necessary.

**Rebound Insomnia:** A transient syndrome, known as "rebound insomnia", whereby the symptoms that led to treatment with a benzodiazepine recur in an enhanced form, may occur on withdrawal of hypnotic treatment.

**Renal**

Temazepam is primarily excreted by the kidney. Hence, RESTORIL should be given with caution to patients with impaired renal function.

**Reproductive Health: Female and Male Potential**

- **Fertility**

The clinical data for the effect of RESTORIL on fertility is not available.

- **Teratogenic Risk**

There are no adequate and well-controlled studies of RESTORIL in pregnant women. Animal studies with other anxiolytic-sedative agents have suggested increased risk of congenital malformations (see 7.1.1 Pregnant women; 16 NON-CLINICAL TOXICOLOGY, Reproductive and Developmental **Toxicology**).

**Respiratory**

RESTORIL should be given with caution to patients with severe pulmonary insufficiency: respiratory depression has been reported in patients with compromised respiratory function.

### 7.1 Special Populations

#### 7.1.1 Pregnant Women

The use of RESTORIL during pregnancy is not recommended.

Benzodiazepines may cause fetal damage when administered during pregnancy. During the first trimester of pregnancy, several studies have suggested an increased risk of congenital malformations associated with the use of benzodiazepines. During the last weeks of pregnancy, ingestion of therapeutic doses of a benzodiazepine hypnotic has resulted in neonatal CNS depression due to transplacental distribution.

If the drug is prescribed to a woman of childbearing potential, the patient should be warned of the potential risk to a fetus and advised to consult her physician regarding the discontinuation of the drug if she intends to become pregnant or suspects that she is pregnant.

Non-teratogenic effects: a child born to a mother who is on benzodiazepines may be at risk for withdrawal symptoms from the drug during the postnatal period. Also, neonatal flaccidity has been reported in an infant born to a mother who had been receiving benzodiazepines.

### 7.1.2 Breast-feeding

It is not known whether or not RESTORIL is excreted in human milk. Therefore, it should not be given to breast-feeding mothers.

### 7.1.3 Pediatrics

Pediatrics (<18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

### 7.1.4 Geriatrics

Debilitated patients, or those with organic brain syndrome, are prone to CNS depression after even low doses of benzodiazepines and may experience paradoxical reactions to these drugs. Therefore, RESTORIL should be used only at the lowest possible dose and adjusted when necessary under careful observation, depending on the response of the patient.

Long-term use of RESTORIL should be avoided in elderly or debilitated patients who may be more sensitive to benzodiazepines. There is an increased risk of cognitive impairment, delirium, falls, fractures, hospitalizations and motor vehicle accidents in these users. Enhanced monitoring is recommended in this population.

## 8 ADVERSE REACTIONS

### 8.1 Adverse Reaction Overview

In clinical trials, drowsiness, dizziness, and confusion occurred at a higher incidence in RESTORIL-treated patients as compared with placebo-treated patients.

Ataxia has been reported with an incidence of 0.5 - 0.9 % in clinical trials.

There have been reports of falls and fractures in benzodiazepine users due to adverse reactions such as sedation, dizziness and ataxia (See 7 WARNINGS AND PRECAUTIONS, Falls and Fractures).

### 8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials; therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

During controlled clinical trials in which 1076 patients received RESTORIL at bedtime, the Adverse Events occurring in 1% or more of patients are listed below.

**Table 2 - Treatment Emergent Adverse Events Incidence in Insomnia Placebo-Controlled Studies**

| | RESTORIL n = 1076 (%) | Placebo n = 783 (%) |
|---|---|---|
| **Gastrointestinal Disorders** | | |
| Nausea | 3.1 | 3.8 |
| Dry mouth | 1.7 | 2.2 |
| Diarrhea | 1.7 | 1.1 |
| Abdominal discomfort | 1.5 | 1.9 |
| **General Disorders** | | |
| Fatigue | 4.8 | 4.7 |
| Lethargy | 4.5 | 3.4 |
| Hangover | 2.5 | 1.1 |
| Weakness | 1.4 | 0.9 |
| **Nervous System Disorders** | | |
| Drowsiness | 9.1 | 5.6 |
| Headache | 8.5 | 9.1 |
| Dizziness | 4.5 | 3.3 |
| Blurred Vision | 1.3 | 1.3 |
| Vertigo | 1.2 | 0.8 |
| **Psychiatric Disorders** | | |
| Nervousness | 4.6 | 8.2 |
| Anxiety | 2.0 | 1.5 |
| Depression | 1.7 | 1.8 |
| Euphoria | 1.5 | 0.4 |
| Confusion | 1.3 | 0.5 |
| Nightmares | 1.2 | 1.7 |

### 8.3 Less Common Clinical Trial Adverse Reactions

The following adverse events have been reported with an incidence of 0.5 - 0.9%:

Cardiac Disorders*:* dyspnea, palpitations.

Eye disorders: burning eyes.

Gastrointestinal disorders: vomiting.

Metabolism and nutrition disorders: anorexia.

Musculoskeletal and connective tissue disorder: backache.

Nervous system disorders: ataxia, equilibrium loss, tremor, increased dreaming.

Skin and subcutaneous tissue disorders: hyperhidrosis.

The following adverse events have been reported with an incidence of less than 0.5%:

Eye disorders: horizontal nystagmus.

Nervous system disorders: restlessness, overstimulation, agitation.

Psychiatric disorders: amnesia, hallucinations

### 8.5 Post-Market Adverse Reactions

**Injury, Poisoning and Procedural Complications**

There have been reports of falls and fractures in benzodiazepine users due to adverse reactions such as sedation, dizziness and ataxia. The risk is increased in those taking concomitant sedatives (including alcoholic beverages), the elderly and debilitated patients.

**Dependence/Withdrawal**

Development of physical dependence and withdrawal following discontinuation of therapy has been observed with benzodiazepines such as RESTORIL. Severe and life-threatening symptoms have been reported (see 3 SERIOUS WARNINGS AND PRECAUTIONS BOX, Addiction, Abuse and Misuse; 7 WARNINGS AND PRECAUTIONS, Dependence/Tolerance).

## 9 DRUG INTERACTIONS

### 9.1 Serious Drug Interactions

**Serious Drug Interactions**

Concomitant use of RESTORIL and opioids may result in profound sedation, respiratory depression, coma and death.

- Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are not possible.
- Limit dosages and durations to the minimum required.
- Follow patients for signs and symptoms of respiratory depression and sedation.

(see 7 WARNINGS AND PRECAUTIONS, General, Concomitant use with opioids)

### 9.2 Drug Interactions Overview

RESTORIL may produce additive CNS depressant effects when co-administered with alcohol, sedative antihistamines, anticonvulsants, or psychotropic medications which themselves can produce CNS depression. (see 9.3 Drug-Behavioural Interactions; 9.4 Drug-Drug Interactions)

The activity of benzodiazepines, including RESTORIL, may be enhanced by compounds which inhibit certain hepatic enzymes such as cytochrome P450 enzymes. (see 9.4 Drug-Drug Interactions)

### 9.3 Drug-Behavioural Interactions

RESTORIL may produce additive CNS depressant effects when co-administered with alcohol. Patients should be cautioned not to take alcohol because of the potentiation of effects that might occur.

### 9.4 Drug-Drug Interactions

**CNS depressant drugs:** RESTORIL may potentiate the effects of other central nervous system depressant drugs such as alcohol, barbiturates, non-barbiturate hypnotics, antihistamines, narcotics, antipsychotic and antidepressant drugs, and anticonvulsants. Therefore, different benzodiazepines should usually not be used simultaneously and careful consideration should be given if other CNS depressants are administered in combination with RESTORIL. Patients should be advised against the simultaneous use of other CNS depressant drugs because of the potentiation of effects that might occur.

**Cytochrome P450:** Compounds, which inhibit certain hepatic enzymes (particularly cytochrome P450), may enhance the activity of benzodiazepines, including RESTORIL. Examples include cimetidine or erythromycin.

**Opioids:** Due to additive CNS depressant effect, the concomitant use of benzodiazepines, including RESTORIL, and opioids increases the risk of profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate. Limit dosages and durations of concomitant use of benzodiazepines and opioids to the minimum required. Follow patients closely for respiratory depression and sedation (see 3 SERIOUS WARNINGS AND PRECAUTIONS BOX, Risks from Concomitant use with Opioids; 7 WARNINGS AND PRECAUTIONS, General, Concomitant use with opioids).

### 9.5 Drug-Food Interactions

Interactions with food have not been established.

### 9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

### 9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

## 10 CLINICAL PHARMACOLOGY

### 10.1 Mechanism of Action

RESTORIL is a benzodiazepine with hypnotic properties.

Benzodiazepines act as depressants of the central nervous system (CNS). It is believed that benzodiazepines enhance or facilitate the effects of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA).

Benzodiazepines act as agonists at the benzodiazepine receptors sites. The benzodiazepine-GABA receptor-chloride ionophore complex functions mainly in the gating of the chloride channel. Benzodiazepines are thought to produce their pharmacological effects by facilitating GABA-mediated transmission in the CNS, which reportedly increase the frequency of the chloride channel opening.

In sleep laboratory studies, the effect of temazepam 15 mg and 30 mg, was compared to placebo over a two week period. There was a linear dose-response improvement in total sleep time and sleep latency with significant drug-placebo differences occurring for total sleep time at both doses, and for sleep latency at the higher dose. REM sleep was essentially unchanged and slow wave sleep was decreased.

In the sleep laboratory studies, no measurable effects on daytime alertness or performance occurred following RESTORIL treatment or during the withdrawal period, even though a transient sleep disturbance in some sleep parameters was observed following the withdrawal of the higher doses.

The duration of hypnotic effect and the profile of unwanted effects may be influenced by the alpha (distribution) and beta (elimination) half-lives of the administered drug and any active metabolites formed. When half-lives are long, the drug or metabolite may accumulate during periods of nightly administration and be associated with impairments of cognitive and motor performance during waking

hours. If half-lives are short, the drug and metabolites will be cleared before the next dose is ingested, and carry-over effects related to sedation or CNS depression should be minimal or absent. However, during nightly use and for an extended period, pharmacodynamic tolerance or adaptation to some effects of benzodiazepine hypnotics may develop.

If the drug has a very short elimination half-life, it is possible that a relative deficiency (i.e., in relation to the receptor site) may occur at some point in the interval between each night's use. This sequence of events may account for two clinical findings reported to occur after several weeks of nightly use of rapidly eliminated benzodiazepine hypnotics: 1) increased wakefulness during the last third of the night and 2) the appearance of increased day-time anxiety (see 7 WARNINGS AND PRECAUTIONS, Psychiatric, Anxiety/Restlessness).

### 10.2 Pharmacodynamics

In animals, temazepam produces sedative and muscle relaxant effects. At higher doses it has some cardiovascular depressant effects. In unanesthetized rabbits and dogs, temazepam caused slight but significant decreases in blood pressure at oral doses from 5 to 20 mg/kg.

Temazepam decreases spontaneous activity at doses of 2.5 to 5 mg/kg p.o. in the mouse, 20 mg/kg p.o. in the rat and at 10 mg/kg p.o. in the dog. It produces ataxia in the mouse and rat at 10 mg/kg p.o. and in the dog at 20 mg/kg p.o. Loss of righting reflex occurs in mouse and rat at 40 mg/kg p.o. and muscle tone is decreased in the mouse at 10 to 40 mg/kg p.o. and in the rat and dog at 20 mg/kg p.o. Ptosis, myosis and piloerection occur in the mouse at 2.5 to 5 mg/kg p.o., in the rat at 10 to 20 mg/kg p.o., and in the dog bradycardia occurs at 20 to 40 mg/kg and photophobia at 80 mg/kg p.o.

Temazepam potentiates the sleep-enhancing effects of hexobarbitone, induces sleep in cebus monkeys at the minimum effective dose of 3.75 mg/kg p.o. and blocks the lingomandibular reflex in cats at the dose of 0.1 to 1.0 mg/kg i.v. Temazepam also blocks pentylenetetrazol-induced convulsions in mice at the dose of 0.23 mg/kg p.o.

### 10.3 Pharmacokinetics

**Absorption**

Orally administered temazepam is well absorbed in man. Oral administration of 15 to 45 mg temazepam in man resulted in rapid absorption with significant blood levels achieved in 30 minutes and peak levels at 2-3 hours.

**Distribution**

Approximately 96% of unchanged drug is bound to plasma protein. In a multiple dose study, steady-state was approximated after the second daily dose with no evidence of accumulation after 5 consecutive daily doses of 30 mg temazepam. Steady-state plasma levels at 2.5 hours were 382 $\forall$ 192 ng/mL.

**Metabolism**

In a single and multiple dose absorption, distribution, metabolism and excretion (ADME) study, using $^{3}H$ labelled drug, RESTORIL was found to have minimal (8%) first-pass metabolism. There were no active metabolites formed and the only significant metabolite present in blood was the O-conjugate. The inactive O-conjugate metabolite was formed with a half-life of 10 hours and excreted with a half-life of approximately 2 hours. Thus, O-conjugation is the rate limiting step in the biodispositon.

At the dose of 30 mg once a day for 8 weeks, no evidence of enzyme induction was found in man.

**Elimination**

Drug levels in blood declined in a biphasic manner with a short half-life ranging from 0.4 to 0.6 hours and a terminal half-life from 3.5 to 18 hours (mean 9 hours). Twenty-four hours after a single oral dose of temazepam approximately 80% - 90% of the drug was recovered in urine, primarily as the O-conjugate. Because RESTORIL is eliminated by O-conjugation, minimal accumulation occurs. Total recovery from feces and urine in single- and multiple-dose studies was approximately 95%, with only 3-13% of the radioactivity detectable in feces. Less than 1% of the dose was excreted as unchanged drug or N-desmethyltemazepam. A dose-proportional relationship has been established for the area under the plasma concentration/time curve over the 15-30 mg dose range.

## 11 STORAGE, STABILITY AND DISPOSAL

Store at room temperature 15°C - 25°C, in well-closed, light-resistant containers.

RESTORIL should never be disposed of in household trash. Disposal via a pharmacy take back program is recommended.

## 12 SPECIAL HANDLING INSTRUCTIONS

None

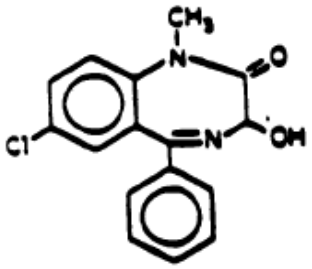
## PART II: SCIENTIFIC INFORMATION

## 13 PHARMACEUTICAL INFORMATION

**Drug Substance**

| | |
|---|---|
| Proper name: | temazepam |
| Chemical name: | 7-Chloro-1,3-dihydro-3-hydroxy-1-methyl-5-phenyl-2*H*-1,4-benzodiazepin-2-one |
| Molecular formula and molecular mass: | $C_{16}H_{13}ClN_2O_2$ and 300.74 |

Structural formula:




| | |
|---|---|
| Physicochemical properties: | A white or almost white odourless, crystalline powder. Practically insoluble in water; sparingly soluble in alcohol; freely soluble in chloroform. Melting point 156°C to 162°C. |

## 14 CLINICAL TRIALS

The clinical trial data on which the original indication was authorized is not available.

## 15 MICROBIOLOGY

No microbiological information is required for this drug product.

## 16 NON-CLINICAL TOXICOLOGY

**General Toxicology:** In the acute toxicity studies the following $LD_{50}$ for temazepam were determined:

**Table 3 – Acute $LD_{50}$ of temazepam**

| SPECIES | SEX | ROUTES | $LD_{50}$ mg/kg |
|---|---|---|---|
| Mouse | M & F | Oral | 1963 (1813-2126) |
| Mouse | M | Oral | 980 ( 860-1117) |
| Mouse | M & F | i.p. | 1050 ( 967-1140) |
| Mouse | M | i.p. | 485 ( 411- 572) |

| SPECIES | SEX | ROUTES | $LD_{50}$ mg/kg |
|---|---|---|---|
| Rat | M & F | Oral | 1823 (1639-2027) |
| Rat | M | Oral | 2800 (2059-3808) |
| Rat | M & F | i.p. | 617 ( 551- 690) |
| Rat | M | i.p. | 670 ( 626- 717) |
| Rabbit | M & F | Oral | ∃2400 |
| Dog | M & F | Oral | ∃1600 |

Overt sedation was prominent in all acute tests and ataxia and decreased locomotion were observed in some tests.

Subacute toxicity experiments lasting from 6 to 13 weeks were conducted in rats (9-250 mg/kg/day p.o.) and dogs (80-200 mg/kg/day p.o.). In the rat changes in hepatic function were seen at the doses over 100 mg/kg/day.

In subacute studies in dogs treatment-related symptoms included decreased locomotion, sedation, abdominal distension and weight loss. Sporadic hyperexcitability was seen in some animals. Chronic toxicity studies of 6 to 12 months were performed in rats (10-160 mg/kg/day p.o.) and dogs (5-120 mg/kg/day p.o.). In the rat the major finding was a liver weight increase at high doses and minimal hepatic lipidosis at the mid and high doses. Dogs at the higher doses employed exhibited slight lethargy.

Two series of 18 month studies were performed in mice at doses from 11-158 mg/kg/day. In one study there was a 4% increase over controls in hepatocellular adenomas in female mice. This incidence is within that found in control groups for the species studied.

**Reproductive and Developmental Toxicology:** Rats (25-840 mg/kg/day) and rabbits (5-60 mg/kg/day) were utilized to assess potential reproductive and teratologic effects. Two segment II type studies in rats provided evidence of the possible increased incidence of fetal resorptions, at doses of 30-120 mg/kg. In perinatal and postnatal studies in rats at doses of 60 and 120 mg/kg/day, resulted in increasing nursling mortality. There were minimal untoward effects on the newborn survival rate. Two segment II type studies in rabbits produced no evidence of potential teratologic effects.

## PATIENT MEDICATION INFORMATION

**READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE**

**RESTORIL®**

**Temazepam Capsules**

Read this carefully before you start taking **RESTORIL** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **RESTORIL**.

**Serious Warnings and Precautions**

**<u>Addiction, Abuse and Misuse</u>: Even if you take RESTORIL exactly as you were told to, you are at risk for abuse, misuse, addiction, physical dependence and withdrawal. Abuse and misuse can result in overdose or death, especially if you take RESTORIL with:**

- **opioids,**
- **alcohol, or**
- **illicit drugs.**

**Your healthcare professional should:**

- **talk to you about the risks of treatment with RESTORIL as well as other treatment (including non-drug) options.**
- **assess your risk for these behaviours before prescribing RESTORIL.**
- **monitor you while you are taking RESTORIL for the signs and symptoms of misuse and abuse. If you feel like you are craving RESTORIL, or not using it as directed, talk to your healthcare professional right away.**

**Store RESTORIL in a secure place to avoid theft or misuse.**

**Withdrawal: If you suddenly stop taking RESTORIL, lower your dose too fast, or switch to another medication, you can experience severe or life-threatening withdrawal symptoms (see Other warnings you should know about).**

- **Always contact your healthcare professional before stopping, or lowering your dose of RESTORIL or changing your medicine.**

**RESTORIL with Opioids: Taking RESTORIL with opioid medicines can cause:**

- **severe drowsiness,**
- **decreased awareness,**
- **breathing problems,**
- **coma, or**
- **death.**

**What is RESTORIL used for?**

RESTORIL is used in adults to treat short-term (usually not more than 7-10 days) insomnia. This is a sleep disorder that makes it hard to fall asleep, hard to stay asleep, or causes you to wake up too early. RESTORIL should be only be used when the effects of insomnia affect your daytime activities.

If you are 65 years or older, talk to your healthcare professional before starting RESTORIL. RESTORIL may not be an effective treatment for you and you may be more sensitive to experiencing side effects.

**How does RESTORIL work?**

RESTORIL belongs to a group of medicines called benzodiazepine sleeping pills. It works in your brain to decrease the time required to fall asleep and increase the total sleep time.

**What are the ingredients in RESTORIL?**

Medicinal ingredient: Temazepam.

Non-medicinal ingredients: Ammonium hydroxide, croscarmellose sodium, D&C Red No. 28, FD&C Blue No. 1, FD&C Red No. 40, gelatin, lactose anhydrous, magnesium stearate, microcrystalline cellulose, propylene glycol, red iron oxide (15 mg capsules only), shellac glaze, simethicone, sodium lauryl sulfate, talc, and titanium dioxide.

**RESTORIL comes in the following dosage forms:**

Capsules: 15 mg and 30 mg of temazepam.

**Do not use RESTORIL if:**

- you are allergic to benzodiazepines, such as temazepam, or to any ingredient in RESTORIL.
- you have a chronic disease characterized by weakness of the skeletal muscles (myasthenia gravis).
- you have a sleep disorder which causes pauses in breathing or shallow breathing while sleeping (sleep apnea).
- you have a past history of unexpected reactions to alcohol or sedative medications. This can include irritability, aggression, hallucinations, etc.

**To help avoid side effects and ensure proper use, talk to your healthcare professional before you take RESTORIL. Talk about any health conditions or problems you may have, including if you:**

- have ever had a problem with:
  - substance use, including prescribed or illegal drugs, or
  - alcohol.
- have ever had seizures or convulsions (violent uncontrollable shaking of the body with or without loss of consciousness).
- have lung or breathing problems.
- have liver problems.

- have kidney problems.
- have signs of depression or a history of depression.
- have a history of suicide thoughts or attempts.
- have a history of violent behaviours.
- have had an unexpected reaction to sedative medications in the past (e.g., such as irritability, aggression, hallucinations, etc.).
- are pregnant or planning to become pregnant. RESTORIL may harm your baby and is therefore not recommended for use during pregnancy.
- are breastfeeding or planning to breastfeed. RESTORIL is not recommended for use during breastfeeding.
- drink or plan to drink alcohol. Do not drink alcohol while you take RESTORIL.
- are taking other medications, including over-the-counter medications, opioids, sedatives, central nervous system (CNS) depressants (slows down brain activity), and other benzodiazepines.
- are taking illicit drugs.
- are unable to digest lactose, a milk sugar (lactose intolerance). Lactose is a component of RESTORIL.
- are 65 years of age or older.
- have a condition that causes weakness or frailty.
- have impaired thinking, confusion or any other type of brain damage.
- have or have had a psychological disorder.

**Other warnings you should know about:**

**Sleep-Related Behaviours:** Treatment with RESTORIL can cause potentially dangerous sleeping-related behaviours such as getting out of bed while not fully awake after taking RESTORIL and doing activities that you do not know you are doing. If this happens, you may not remember doing these activities when you wake up. These unusual behaviours are more likely to occur when RESTORIL is taken with alcohol or other drugs that can make you sleepy (e.g., medicines used to treat depression or anxiety). If you drink alcohol, do not take RESTORIL The activities you may do in these situations can put you and people around you in danger. This can include driving a car (“sleep-driving”), leaving the house, making and eating food, and talking on the phone.

You and people close to you should watch out for unusual types of behavior when you are asleep. If you find out that you have done any such activities for which you have no memory, you should call your healthcare professional immediately.

**Memory Problems:** RESTORIL can cause a type of memory loss known as amnesia. This is characterized by having difficulty recalling events that recently occurred, usually several hours after taking the medication. If you intend to take RESTORIL before sleeping, this is usually not a problem. However, if you take RESTORIL to induce sleep while travelling, such as during an airplane flight, you may wake up to memory lapse caused by the drug. This has been called “traveller's amnesia” and can be a problem. Therefore, DO NOT TAKE RESTORIL when a full night's sleep is not possible before you need to be active and functional (e.g., an overnight flight of less than 8 hours). Your body needs time to eliminate the medication from your system.

**Tolerance:** In general, RESTORIL should not be taken longer than 7-10 days. The longer you use RESTORIL, the less effective it may become.

**Withdrawal**: If you suddenly stop your treatment, lower your dose too fast, or switch to another medication, you can experience withdrawal symptoms that can range from mild symptoms to severe or life threatening. Some of your withdrawal symptoms can last for months after you stop RESTORIL.

Your risk of going through withdrawal is higher if you are taking RESTORIL for a long time or at high doses. However, symptoms can still occur if you are taking RESTORIL as directed for a short period of time or slowly reducing the dose.

The symptoms of withdrawal often resemble the condition that you are being treated for. After stopping your treatment, it may be hard to tell if you are experiencing withdrawal or a return of your condition (relapse).

Tell your healthcare professional **right away** if you experience any symptoms of withdrawal after changing or stopping your treatment.

Severe symptoms of withdrawal include:

- feeling like you cannot move or respond (catatonia);
- severe confusion, shivering, irregular heartrate and excessive sweating (delirium tremens);
- feeling depressed;
- feeling disconnected from reality (dissociation);
- seeing or hearing things that are not there (hallucinations);
- overactive behavior and thoughts (mania);
- believing in things that are not true (psychosis);
- convulsions (seizures), including some that do not stop;
- thoughts or actions of suicide.

For other symptoms of withdrawal, see the **Serious side effects and what to do about them** table (below).

To reduce your chances of going through withdrawal:

- always contact your healthcare professional before stopping or reducing your dose of RESTORIL or changing medications;
- always follow your healthcare professional's instructions on how to reduce your dose carefully and safely;
- tell your healthcare professional **right away** if you experience any unusual symptoms after changing or stopping your treatment.

**RESTORIL with Opioids:** Taking RESTORIL with opioid medicines can cause severe drowsiness and breathing problems.

Tell your healthcare professional if you:

- are taking opioid medicines,
- are prescribed an opioid medicine after you start taking RESTORIL.

**Driving and Using Machines:** Do NOT drive or operate heavy machinery or do tasks that require special attention while taking RESTORIL. This is especially important if you are taking other depressants like an opioid medicine.

**Falls and Fractures:** Benzodiazepines like RESTORIL can cause you to feel sleepy, dizzy and affect your balance. This increases your risks of falling, which can cause fractures or other fall related-injuries, especially if you:

- take other sedatives,
- consume alcohol,
- are elderly, or
- have a condition that causes weakness or frailty.

**Mental and Behavioural Changes:** A variety of abnormal thinking and behaviour changes may occur when you take benzodiazepine sleeping pills, such as RESTORIL. Some of these changes include aggressiveness and extroversion that seem out of character confusion, strange behaviour, anxiety, restlessness, hallucinations, feeling like you are not yourself, worsening insomnia or depression, and suicidal thoughts. It is hard to determine if these symptoms are caused by the medication, by an illness that was present before the medication was used, or are natural. If you develop any unusual thoughts or behaviour while using RESTORIL, tell your healthcare professional right away.

**Worsening of Side Effects:** Do not consume alcohol while taking RESTORIL. Your symptoms of insomnia may worsen with RESTORIL, especially if you are also taking other similar medications.

**Severe Allergic Reaction:** In rare cases, RESTORIL has caused severe allergic reactions including anaphylaxis, which can be life-threatening. The symptoms of a severe allergic reaction include angioedema of the tongue or throat (swelling of tissues under the skin), shortness of breath, throat closing, nausea or vomiting. Angioedema can lead to a blocked airway and can be life-threatening. If you develop angioedema or you notice signs of a severe allergic reaction after taking RESTORIL, you should stop taking RESTORIL and tell your healthcare professional right away.

**Elderly:** If you are 65 years of age or older and take benzodiazepines including RESTORIL, you are at a higher risk of falls and fractures.

**Pregnancy:** Benzodiazepines, such as RESTORIL, may harm your unborn baby (e.g., birth defects) if you are pregnant. This risk is higher during the first trimester or last weeks of pregnancy. If you are able to get pregnant, want to be or think you are pregnant, there are specific risks you should discuss with your healthcare professional.

**Monitoring and Testing:** If you are prescribed RESTORIL, your healthcare professional may conduct blood tests to assess your health. Your healthcare professional will interpret your results and may adjust or stop your dose of RESTORIL.

**Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.**

**The following may interact with RESTORIL:**

**Serious Drug Interactions**

**Taking RESTORIL and opioids may cause:**

- **severe drowsiness,**
- **trouble breathing,**
- **coma,**
- **death.**

- alcohol. Do not take RESTORIL if you drink alcohol;
- barbiturates, used to relax the body and help with sleeping;
- other hypnotics that are used to help with sleeping;
  antihistamines that are used to treat allergies;
- medicines used to treat mental health disorders (e.g., antipsychotics and psychotropic medications);
- antidepressants used to treat depression;
- anticonvulsants used to prevent or treat seizures;
- other benzodiazepines typically used to treat anxiety, insomnia, and seizures;
- sedatives;
- medicines that inhibit certain liver enzymes, particularly cytochrome P450 (e.g., cimetidine and erythromycin). If you are unsure, talk to your healthcare professional.

Do not use RESTORIL along with other medications without first discussing this with your healthcare professional.

**How to take RESTORIL:**

- Take RESTORIL by mouth just before going to bed. Do not take RESTORIL if a full night's sleep is not possible before you need to become active and functional again.
- Do not consume any alcohol while taking RESTORIL.

**Usual dose:**

- Take RESTORIL exactly as prescribed by your healthcare professional. They will determine the right dose and the length of RESTORIL for you. This will depend on your age, current health, and if you take certain other medications.
- Your healthcare professional will also monitor how RESTORIL is working for you, especially at the start of your treatment. They may adjust your dose to ensure that the lowest effective dose is prescribed.
- Your healthcare professional will tell you when and how to stop taking the medicine. Always follow your healthcare professional's instructions on how to lower your dose carefully and safely to avoid experiencing withdrawal symptoms.

**Overdose:**

If you think you, or a person you are caring for, have taken too much RESTORIL, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

**Missed Dose:**

If you forget or miss a dose of RESTORIL, do not take the missed dose. Instead, take the next scheduled dose at the usual time. Do not try to make up for the missed dose by taking a double dose.

**What are possible side effects from using RESTORIL?**

These are not all the possible side effects you may have when taking RESTORIL. If you experience any side effects not listed here, tell your healthcare professional.

**Side effects of RESTORIL may include:**

Common (may affect up to 1 in 10 people):

- abdominal discomfort,
- blurred vision,
- dizziness,
- drowsiness,
- dry mouth,
- euphoria,
- falls and fractures,
- fatigue,
- hangover,
- lack of energy,
- nervousness,
- nightmares,
- vertigo,
- weakness.

Uncommon (may affect up to 1 in 100 people):

- anorexia,
- backache,
- burning eyes,
- increased dreaming,
- palpitations (heartbeats that become more noticeable),
- sensory overload (overstimulation),
- tremor,
- uncontrolled and rapid side to side eye movements (horizontal nystagmus).

| Serious side effects and what to do about them | | | |
|---|---|---|---|
| **Symptom / effect** | **Talk to your healthcare professional** | | **Stop taking drug and get immediate medical help** |
| | **Only if severe** | **In all cases** | |
| **COMMON** | | | |
| **Depression** (sad mood that won't go away): difficulty sleeping, sleeping too much, changes in appetite or weight, feelings of worthlessness, guilt, regret, helplessness, hopelessness, withdrawal from social situations, family, gatherings and activities with friends, thoughts of death or suicide, or reduced libido (sex drive). | | ✓ | |
| **UNCOMMON** | | | |
| **Amnesia** (a type of memory loss): difficulty recalling events that recently happened. | | ✓ | |
| **RARE** | | | |
| **Severe allergic reactions:** swelling of the tongue or throat, trouble breathing, sudden wheeziness, chest pain or tightness, shortness of breath, throat closing, nausea, or vomiting. | | | ✓ |
| **Mental and behavioural changes:** excitement, agitation, hyperactivity, hallucination, worsened insomnia, aggressiveness, irritability, rages, psychoses, and violent behaviour. | | ✓ | |
| **Somnambulism** (sleepwalking): getting out of bed while not fully awake and do activities you do not remember the day after, or sleep driving. | | ✓ | |
| **UNKNOWN FREQUENCY** | | | |
| **Overdose:** extreme sleepiness, confusion, slurred speech, slow reflexes, slow shallow breathing, coma, loss of balance and coordination, uncontrolled rolling of the eyes, and low blood pressure. | | | ✓ |

| Serious side effects and what to do about them | | | |
|---|---|---|---|
| **Symptom / effect** | **Talk to your healthcare professional** | | **Stop taking drug and get immediate medical help** |
| | **Only if severe** | **In all cases** | |
| **Respiratory depression:** slow, shallow or weak breathing. | | | ✓ |
| **Withdrawal:**<br>**Severe symptoms include:**<br>**Catatonia:** feeling like you cannot move or respond.<br>**Delirium tremens:** severe confusion, shivering, irregular heartrate and excessive sweating.<br>**Feeling depressed**<br>**Dissociation**: feeling disconnected from reality.<br>**Hallucinations:** seeing or hearing things that are not there.<br>**Mania**: overactive behaviour and thoughts.<br>**Psychosis:** believing in things that are not true.<br>**Convulsions:** (seizures – including some that do not stop): loss of consciousness with uncontrollable shaking.<br>**Thoughts or actions of suicide**<br>**Other symptoms include:**<br>Stomach cramps; trouble remembering or concentrating; diarrhea; feeling uneasy or restless; severe anxiety or panic-attacks; headache; sensitivity to light, noise or physical contact; shaking; vomiting; trouble sleeping; feeling irritable; muscle pain or stiffness; a burning or prickling feeling in the hands, arms, legs or feet; sweating. | | ✓ | |

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

**Reporting Side Effects**

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

*NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.*

**Storage:**

Store RESTORIL capsules at room temperature (15°C to 25°C) in well-closed, light-resistant containers.

RESTORIL should never be thrown into household trash. It should be returned to a pharmacy for proper disposal.

Keep out of reach and sight of children.

**If you want more information about RESTORIL:**

- Talk to your healthcare professional
- Find the full Product Monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website (https://www.aapharma.ca/en/products), or by calling 1-877-998-9097.

This leaflet was prepared by AA Pharma Inc.

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