

PRODUCT MONOGRAPH

^{TC} DALMANE[®]

Flurazepam Hydrochloride

Capsules; 15 mg, 30 mg

Hypnotic

Valeant Canada limitée/Limited
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Montreal (Quebec) H4R 2P9

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[®] REGISTERED TRADEMARK
Valeant Canada Ltée/Ltd.

NAME OF DRUG

^{TC} DALMANE[®]

(flurazepam hydrochloride)

HYPNOTIC

ACTIONS AND CLINICAL PHARMACOLOGY

Dalmane[®] (flurazepam hydrochloride), a benzodiazepine derivative, is a hypnotic agent which does not appear to decrease dream time as measured by rapid eye movements (REM). 'Dalmane' decreases sleep latency and number of awakenings for a consequent increase in total sleep time.

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 daytime anxiety (see WARNINGS).

Flurazepam is a benzodiazepine with a long half-life.

Rebound Insomnia

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.

Pharmacokinetics

Following oral administration of 15 mg flurazepam hydrochloride to male and female volunteers, measurable concentrations for the parent compound were not detectable. Flurazepam undergoes rapid and pronounced metabolism to two pharmacologically active metabolites, namely hydroxyethyl flurazepam and flurazepam aldehyde. In healthy volunteers, C_{max} values for the two metabolites were 8.6 and 2.5 ng/mL, respectively. They were reached in an average of 1.0

and 1.2 hours, respectively. The mean elimination half-lives for these two metabolites were less than 2.5 hours.

The final active and principal metabolite, desalkyl flurazepam (DAFLZ), appears in the systemic circulation more slowly, with a mean C_{\max} of 14 ng/mL attained an average of 10.6 hours after dosing. The mean elimination half-life of DAFLZ is approximately 75 hours (range 50 to 100 hours). Therefore, multiple-dose therapy with flurazepam leads to the accumulation of DAFLZ.

The half-life of DAFLZ was found to be longer in elderly males than in young males (160 versus 74 hours, $p < 0.05$), but was similar in elderly and young females (120 versus 90 hours, $p = \text{N.S.}$). DAFLZ was extensively bound to plasma protein. The unbound fraction increased with age regardless of sex.

Following 15 days treatment with 15 mg flurazepam once daily, mean steady-state plasma levels of DAFLZ were higher in elderly than in young men (81 and 53 ng/mL, $p < 0.05$), but were similar in elderly and young women (86 and 85 ng/mL).

More than 50% of the total dose of flurazepam appears in the urine in 24 hours, with eventual urinary excretion accounting for 80% or more of the total dose. The major urinary metabolite is conjugated hydroxyethyl flurazepam. Less than 1% of the dose is excreted in the urine as DAFLZ. Approximately 10% of the total dose of flurazepam appears in the feces.

INDICATIONS AND CLINICAL USE

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.

‘Dalmane’ (flurazepam hydrochloride) 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 awakening.

Treatment with ‘Dalmane’ should usually not exceed 7 to 10 consecutive days. Use for more than 2 to 3 consecutive weeks requires complete re-evaluation of the patient. Prescriptions for ‘Dalmane’ should be written for short-term use (7 to 10 days) and it should not be prescribed in quantities exceeding a one-month supply.

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

CONTRAINDICATIONS

‘Dalmane’ (flurazepam hydrochloride) is contraindicated in patients with known hypersensitivity to benzodiazepines, or any component of its formulation, and in those with severe impairment of respiratory function, e.g., significant sleep apnea syndrome.

'Dalmane' is contraindicated in patients who have myasthenia gravis or severe hepatic insufficiency.

WARNINGS

General: Benzodiazepines should be used with extreme caution in patients with a history of substance or alcohol abuse.

The smallest possible effective dose should be prescribed for elderly patients. Inappropriate, heavy sedation in the elderly, may result in accidental events/falls.

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.

'Dalmane' should be used with caution in patients who in the past manifested paradoxical reactions to alcohol and/or sedative medications.

Pregnancy: The use of 'Dalmane' (flurazepam hydrochloride) 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 'Dalmane' is prescribed to women 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 might be pregnant.

Memory disturbance: Anterograde amnesia of varying severity has been reported following therapeutic doses of benzodiazepines. The event is rare with 'Dalmane'. 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 benzodiazepines, 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 'Dalmane' 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.

Abnormal thinking and psychotic behavioural changes have been reported to occur in association with the use of benzodiazepines including ‘Dalmane’, 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 depressants (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.

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.

Anxiety, Restlessness: An increase in daytime anxiety and/or restlessness has been observed during treatment with short half-life benzodiazepines although the syndrome can apply on occasion to drugs with longer elimination half-lives as well. Flurazepam has a long half-life.

Depression: Caution should be exercised if ‘Dalmane’ 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.

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 ‘Dalmane’. 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 ‘Dalmane’ appears to increase the risk of such behaviours, as does the use of ‘Dalmane’ at doses exceeding the maximum recommended dose. ‘Dalmane’ is not to be taken with alcohol. Caution is needed with concomitant use of other CNS depressant drugs. Due to the risk to the patient and the community, discontinuation of ‘Dalmane’ should be strongly considered for patients who report any such sleep-related behaviours.

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 ‘Dalmane’. 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 'Dalmane' should not be rechallenged with the drug.

PRECAUTIONS

Drug Interactions: 'Dalmane' (flurazepam hydrochloride) may produce additive CNS depressant effects when co-administered with alcohol, sedative antihistamines, narcotic analgesics, anticonvulsants, or psychotropic medications which themselves can produce CNS depression.

Compounds which inhibit certain hepatic enzymes (particularly cytochrome P450) may enhance the activity of benzodiazepines. Examples include cimetidine or erythromycin.

Drug Abuse, Dependence and Withdrawal: Withdrawal symptoms, similar in character to those noted with barbiturates and alcohol (convulsions, tremor, abdominal and muscle cramps, vomiting, sweating, dysphoria, perceptual disturbances and insomnia) have occurred following abrupt discontinuations of benzodiazepines, and may follow the discontinuation of 'Dalmane'. The more severe symptoms are usually associated with higher dosages and longer usage, although patients given therapeutic dosages for as few as 1 to 2 weeks can also have withdrawal symptoms including daytime anxiety between nightly doses. Consequently, abrupt discontinuation should be avoided and a gradual dosage tapering schedule is recommended in any patient taking more than the lowest dose for more than a few weeks. The recommendation for tapering is particularly important in patients with a history of seizures.

The risk of dependence is increased in patients with a history of alcoholism, drug abuse, or in patients with marked personality disorders. Caution must be exercised in administering 'Dalmane' to these individuals.

As with all hypnotics, repeat prescriptions should be limited to those who are under medical supervision.

Patients with Specific Conditions: 'Dalmane' should be given with caution to patients with impaired hepatic or renal function, or severe pulmonary insufficiency. Respiratory depression has been reported in patients with compromised respiratory function.

Patients Requiring Mental Alertness: Because of 'Dalmane'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 'Dalmane' and alcohol or CNS-depressant drugs.

Use in Pregnancy: For teratogenic effects see WARNINGS. 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.

Use in Nursing Mothers: The safety of ‘Dalmane’ during lactation has not been established. Therefore, its use during nursing is not recommended.

Use in Children: The safety and effectiveness of ‘Dalmane’ in children below the age of 15 have not been established.

Use in the Elderly: Elderly patients are especially susceptible to dose-related adverse effects, such as drowsiness, dizziness, or impaired coordination. Inappropriate, heavy sedation may result in accidental events/falls. Therefore, the lowest possible dose (15 mg) should be used in these subjects.

Laboratory Tests: Should ‘Dalmane’ be used repeatedly, periodic blood counts, liver, and kidney function tests should be performed.

ADVERSE EFFECTS

The most common adverse reactions reported with ‘Dalmane’ (flurazepam hydrochloride) are dizziness, drowsiness, lightheadedness, and ataxia. These adverse effects are particularly common in elderly and debilitated patients (See PRECAUTIONS). Severe sedation, lethargy, disorientation, and coma, probably indicative of drug intolerance or overdosage, have been reported.

Isolated instances of headache, heartburn, upset stomach, nausea, vomiting, amnesia, constipation, diarrhea, gastrointestinal pain, nervousness, apprehension, irritability, weakness, palpitations, chest pains, and genito-urinary complaints have been reported. However, in controlled studies, these appeared as often or more often with placebo than with the active drug.

There have also been rare occurrences of leukopenia, granulocytopenia, sweating, flushes, difficulty in focusing, blurred vision, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, nightmares, numbed emotions, reduced alertness, changes in libido, inappropriate behaviour and elevated SGOT, SGPT, total and direct bilirubins, and alkaline phosphatase. Paradoxical reactions such as excitement, stimulation, agitation, aggressiveness, rages, psychoses and hyperactivity have also been reported in rare instances when using drugs that act at the benzodiazepine receptors.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Manifestations of ‘Dalmane’ overdosage include somnolence, confusion and coma. Respiration, pulse and blood pressure should be monitored as in all cases of drug overdosage. General supportive measures should be employed, along with immediate gastric lavage. Intravenous fluids should be administered and an adequate airway maintained. Hypotension and CNS depression may be combated by judicious use of appropriate therapeutic agents. The value of

dialysis has not been determined. If excitation occurs in patients following 'Dalmane' overdose, barbiturates should not be used.

As with the management of intentional overdose with any drug, it should be borne in mind that multiple agents may have been ingested. The benzodiazepine antagonist, flumazenil ('Anexate') is a specific antidote in known or suspected benzodiazepine overdose. (For conditions of use see 'Anexate' Product Monograph.)

DOSAGE AND ADMINISTRATION

The lowest effective dose of 'Dalmane' (flurazepam hydrochloride) should be used. Treatment with 'Dalmane' should be as short as possible, and should usually not exceed 7-10 consecutive days. Use for more than 2-3 consecutive weeks requires complete re-evaluation of the patient.

Dosage should be individualized for maximal beneficial effects.

Adults: The usual adult dosage is 30 mg before retiring. In some patients, 15 mg may suffice.

Elderly and/or Debilitated Patients: It is recommended that therapy be initiated with 15 mg until individual responses are determined.

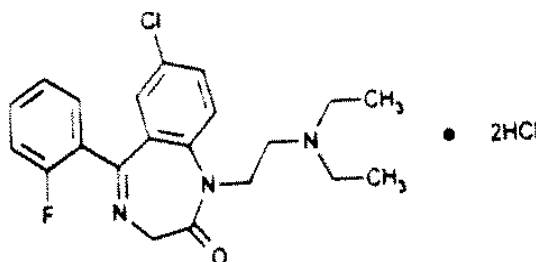
PHARMACEUTICAL INFORMATION

i) Drug Substance

Proper Name: Flurazepam Hydrochloride

Chemical Name: 7-chloro-1-[2(diethylamino)ethyl]-5-(0-fluorophenyl)-1, 3-dihydro-2H-1, 4-benzodiazepin-2-one-dihydrochloride

Structural Formula:



Molecular Formula: $C_{21}H_{23}ClFN_3O \cdot 2HCl$

Molecular Weight: 460.81

Description: Flurazepam hydrochloride is an off-white to yellow, crystalline powder. It is odourless, or has a slight odour, and its solutions are acid to litmus. Melts at about 212°C with decomposition. Freely soluble in water and in alcohol; slightly soluble in isopropyl alcohol and in chloroform.

ii) Composition

Each 'Dalmane' capsule contains either 15 or 30 mg of flurazepam hydrochloride, lactose, cornstarch, talc (15mg), magnesium stearate, gelatin, D&C yellow #10, FD&C yellow #6, titanium dioxide, FD&C blue #1 (30mg), FD&C red #40, D & C red #28 (15 mg).

iii) Stability and Storage Recommendations

Keep in a tightly closed, light-resistant container. Store at 15-30°C.

DOSAGE FORMS

Availability: 'Dalmane' 15 mg capsule: each No.2 hard gelatin capsules, ivory opaque body and medium orange opaque cap, imprinted "Dalmane 15" on body and with the "ICN" logo on the cap contains 15 mg of Flurazepam Hydrochloride.

'Dalmane' 30 mg capsule: each No.2 hard gelatin capsules, ivory opaque body and red opaque cap, imprinted "Dalmane 30" on body and with the "ICN" logo on the cap contains 30 mg of Flurazepam Hydrochloride.

Both strengths (15 and 30 mg) are available in bottles of 100 capsules.

PHARMACOLOGY

In animals, flurazepam hydrochloride has been demonstrated to produce sedative, anticonvulsant, taming, and muscle relaxant effects. At high doses, flurazepam hydrochloride exhibited sedative effects in rats (36 mg/kg), as well as a depressant effect on behaviour in squirrel monkeys (40 mg/kg). Some cardiovascular depressant effects were also observed, but were largely attributed to the central nervous system depressant effects of high doses.

Flurazepam and its metabolites bind with high affinity to mouse brain membranes. In vitro specific binding affinities (K_i) for flurazepam, hydroxyethyl-flurazepam, flurazepam aldehyde and desalkyl-flurazepam were 10.7, 16.2, 10.6, and 0.85 nM, respectively. Flurazepam hydrochloride is rapidly absorbed from the gastrointestinal tract and is rapidly metabolized. Studies in rats with ^{14}C -labelled flurazepam hydrochloride indicated that the drug is widely distributed throughout body tissues with no excessive accumulation of drug or metabolite in any one tissue.

TOXICOLOGY

The oral LD₅₀ was 870 mg/kg in mice, 1,232 mg/kg in rats and 568 mg/kg in rabbits. Chronic toxicity studies for one year indicated that the tolerated dose is 80 mg/kg/day in the rat and 10 mg/kg/day in the dog.

Effects on Reproduction: A two-cycle reproductive study in rats was carried out at doses of 5 and 50 mg/kg/day of flurazepam hydrochloride. There were no significant teratogenic or other adverse effects related to the drug. In the second series of rat reproductive studies, doses of 3 and 20 mg/kg/day of flurazepam hydrochloride did not induce changes in fertility and general reproductive performance. There were no significant teratogenic effects related to the drug or adverse effects in the perinatal and postnatal study. In another reproductive study in rats at doses of 10, 20, 40 and 80 mg/kg/day, no adverse effects on reproduction and no significant teratological changes were noted.

In rabbits, two sets of teratogenic studies were done. In the first, flurazepam hydrochloride was administered in doses of 5 and 20 mg/kg/day. Twenty-three live litters were obtained in this study. One animal which received 20 mg/kg/day had a litter of nine viable but deformed fetuses. In the second study, the dose of flurazepam hydrochloride was increased to 40 mg/kg/day without the occurrence of abnormalities in all eleven litters. In both studies, there were no significant differences between the control and treated groups in maternal weight, body weight of viable fetuses, fetal body weight and litter size.

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PART III: CONSUMER INFORMATION

TM DALMANE[®]

Flurazepam hydrochloride capsules

This leaflet is part III of a three-part "Product Monograph" published when 'Dalmane' was approved for sale in Canada and is designed specifically for Consumers. Please read this information before you start to take your medicine. Keep this leaflet until you have finished all your tablets, as you may need to read it again. This leaflet should not replace a discussion between you and your doctor about the risks and benefits of 'Dalmane'. This leaflet is a summary and will not tell you everything about 'Dalmane'. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION**What the medication is used for:**

'Dalmane' is intended to help you sleep if you have transient and short-term insomnia. Symptoms of insomnia include difficulty falling asleep and/or waking up often during the night or too early in the morning.

Treatment with 'Dalmane' should usually not go on for more than 7-10 days and should be restricted for insomnia where disturbed sleep results in impaired daytime functioning. 'Dalmane' does not treat the underlying cause of your insomnia.

What it does:

'Dalmane' is one of several benzodiazepine sleeping pills that have generally similar properties such as a calming effect.

If you are prescribed one of these medications, you should consider both their benefits and risks. Important risks and limitations include the following:

- you may become dependent on the medication,
- the medication may affect your mental alertness or memory, particularly when not taken as prescribed.

(see "WARNINGS AND PRECAUTIONS")

When it should not be used:

Do not take 'Dalmane' if you have:

- known allergy to flurazepam or other benzodiazepines, or any of the ingredients 'Dalmane' contains (see "What the nonmedicinal ingredients are")
- severe lung or respiratory disease, including sleep apnea
- myasthenia gravis, a chronic disease characterized by weakness of the skeletal muscles
- a severe liver condition

What the medicinal ingredient is:

Flurazepam hydrochloride

What the nonmedicinal ingredients are:

Non-medicinal ingredients are cornstarch, D&C red #28 (15 mg), D&C yellow #10, FD&C blue #1 (30mg), FD&C red #40, FD&C yellow #6, gelatin, lactose, magnesium stearate, talc (15mg), titanium dioxide.

What dosage forms it comes in:

'Dalmane' is available in 15 mg or 30 mg capsules for oral administration.

WARNINGS AND PRECAUTIONS**Complex sleep-related behaviours**

There have been reports of people getting out of bed while not fully awake after taking 'Dalmane' and doing activities that they did not know they were doing. The next morning, they did not remember doing those activities. This unusual behaviour is more likely to occur when 'Dalmane' is taken with alcohol or other drugs that can make you sleepy such as those for the treatment of depression or anxiety. The activities you may do in these situations can put you and people around you in danger. Reported activities included driving a car ("sleep-driving"), leaving the house, making and eating food, talking on the phone, etc.

Important:

1. Do not take more 'Dalmane' than prescribed.
2. Do not take 'Dalmane' if you drink alcohol.
3. Talk to your doctor about all of your medicines, including over-the-counter medicines and herbal products. Your doctor will tell you if you can take 'Dalmane' with your other medicines.
4. You and people close to you should watch for the type of unusual behaviour described above. If you find out that you have done *any* such activities for which you have no memory you should call your doctor immediately.

Mental Alertness: 'Dalmane' may affect your ability to be alert. DO NOT DRIVE A CAR or operate potentially dangerous machinery until you experience how this drug will affect you.

Memory Problems: All benzodiazepine sleeping pills can cause a special type of memory loss (amnesia); you may not recall events that occurred during some period of time, usually several hours, after taking the drug. This lapse is usually not a problem, because the person taking the sleeping pill intends to be asleep during this critical period of time. But it can be a problem if you take the medication to induce sleep while travelling, such as during an airplane flight, because you may wake up before the effect of the drug is gone. This has been called "traveller's amnesia". DO NOT TAKE 'Dalmane' when a full night's sleep is not possible before you would again need to be active and functional; e.g., an overnight flight of less than 8 hours. Memory lapses may occur in such situations. Your body needs time to eliminate the medication from your system.

Tolerance/Withdrawal Symptoms: After nightly use for more than a few weeks benzodiazepines may lose some of their effectiveness. You may also develop a degree of dependence.

“Withdrawal” effects can occur when patients stop taking benzodiazepine sleeping pills. The effects may occur following use for only a week or two but may be more common and severe after long periods of continuous use. For example, you may experience an increase in sleep difficulties (rebound insomnia) and/or increased daytime anxiety (rebound anxiety) for one or two days after discontinuing ‘Dalmane’.

Other withdrawal symptoms following abrupt stopping of sleeping pills may range from unpleasant feelings to a major withdrawal syndrome that may include abdominal and muscle cramps, vomiting, sweating, tremor, and rarely, convulsions. The severe symptoms are uncommon.

Dependence/Abuse: All benzodiazepine sleeping pills can cause dependence (addiction) especially when used regularly for more than a few weeks, or at higher doses. Some people develop a need to continue taking these drugs, either at the prescribed dose or at higher doses not only for continued therapeutic effect, but also to avoid withdrawal symptoms or to achieve non-therapeutic effects.

Individuals who depend, or have depended at any time in the past, on alcohol or other drugs may be at particular risk of becoming dependent on drugs of this class. But **ALL PEOPLE ARE AT SOME RISK**. Consider this matter before you take these medications beyond a few weeks.

Mental and Behavioural Changes: A variety of abnormal thinking and behaviour changes may occur when you use benzodiazepine sleeping pills. Some of these changes include aggressiveness and extroversion which seem out of character. Other changes, although rare, can be more unusual and extreme such as confusion, strange behaviour, restlessness, illusions, hallucinations, feeling like you are not yourself, worsening insomnia and worsening depression, including suicidal thinking.

It is rarely clear whether such symptoms are caused by the medication, or by an illness that was present before the medication was used, or are simply spontaneous happenings. If you develop any unusual disturbing thoughts or behaviour while using ‘Dalmane’, discuss the matter immediately with your doctor.

Worsening of Side Effects

DO NOT CONSUME ALCOHOL WHILE TAKING ‘Dalmane’. Some medicines may also worsen side effects that some patients experience with ‘Dalmane’ (see “INTERACTIONS WITH THIS MEDICATION”).

Elderly: An increased risk of falls and fractures has been reported in elderly people who take benzodiazepines such as ‘Dalmane’.

Effects on Pregnancy: Certain benzodiazepine sleeping pills have been linked to birth defects when taken during the early months of pregnancy. In addition, benzodiazepine sleeping pills taken during the last weeks of pregnancy have been known to sedate the baby and may also cause withdrawal symptoms after birth. **DO NOT TAKE ‘Dalmane’** at any time during pregnancy.

BEFORE you use ‘Dalmane’ talk to your doctor or pharmacist if:

- You have a lung disease or breathing problems.
- You have liver or kidney condition.
- You have a history of depression and/or suicide thoughts or attempts.
- You have had unexpected reactions to alcohol or sedative medications in the past, such as irritability, aggression, hallucinations, etc.
- You have a history of drug or alcohol abuse or addiction.
- You are planning to become pregnant, you are pregnant, or you become pregnant while taking this medication.
- You are breastfeeding.
- You consume alcohol.
- You are taking other medicines, including drugs you can buy without a prescription.
- You have lactose intolerance.

INTERACTIONS WITH THIS MEDICATION

‘Dalmane’ may produce more pronounced side effects when co-administered with alcohol, other tranquilizers or sleeping pills, sedative antihistamines, narcotic analgesics, anticonvulsants, antipsychotics and antidepressants or other psychotropic medications which themselves can make you sleepy.

Compounds which inhibit certain hepatic enzymes (particularly cytochrome P450) may enhance the activity of benzodiazepines. Examples include cimetidine or erythromycin.

Do not take ‘Dalmane’ if you drink alcohol. **DO NOT USE ‘Dalmane’** along with other medications without first discussing this with your doctor.

PROPER USE OF THIS MEDICATION

Benzodiazepine sleeping pills are effective medications and are relatively free of serious problems when used for the short-term management of insomnia. Insomnia may last only for a short time and may respond to brief treatment. The risks and benefits of prolonged use should be discussed with your doctor.

Usual dose:

‘Dalmane’ is a prescription medication intended to help you sleep. Follow your doctor’s advice about how to take ‘Dalmane’, when to take it, and how long to take it.

Adults: The recommended dose is 30 mg just before bedtime, although some patients may require only 15 mg.

Elderly and/or Debilitated Patients should start with 15 mg just before bedtime.

DO NOT TAKE ‘Dalmane’ if it is not prescribed for you.

DO NOT TAKE ‘Dalmane’ for more than 7 to 10 days without first consulting your doctor. If you still have problems sleeping after you finish your capsules, contact your doctor again.

The lowest effective dose should be used.
DO NOT INCREASE THE PRESCRIBED DOSE.

Do not take ‘Dalmane’ if you drink alcohol.

Do not take ‘Dalmane’ when a full night’s sleep is not possible before you would again need to be active and functional.

Do not drive a car or operate potentially dangerous machinery until you experience how ‘Dalmane’ will affect you the next day.

‘Dalmane’ is not for use in children under 18 years of age.

Overdose:

Manifestations of flurazepam hydrochloride overdosage include somnolence, confusion and coma.

Contact your doctor, regional Poison Control Centre or pharmacist immediately if you suspect you have taken an overdose or someone else accidentally takes your ‘Dalmane’. If you are unable to contact them, go to a hospital emergency department for medical help, even though you may not feel sick. Show your doctor your bottle of capsules.

Missed Dose:

If you forget to take ‘Dalmane’ capsules, do not take a double dose to make up for the forgotten individual dose. Take the next dose at the usual time.

Elderly patients are especially susceptible to side effects. Excessive drowsiness in the elderly may result in falls and fractures.

Rare cases of severe allergic reactions have been reported. Symptoms may include swelling of the tongue or throat, trouble breathing, and nausea and vomiting. Get emergency medical help if you get these symptoms after taking ‘Dalmane’.

Withdrawal-related side effects: See “WARNINGS AND PRECAUTIONS, **Tolerance/Withdrawal Symptoms**”.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Seek urgent medical attention
		Only if severe	In all cases	
Rare	Unexpected reactions such as excitement, agitation, hyperactivity, hallucination, worsened insomnia, aggressiveness, irritability, rages, psychoses, and violent behaviour		✓	
	Severe allergic reactions (swelling of the tongue or throat, trouble breathing, nausea and vomiting)			✓
	Depressed mood; thoughts of death or suicide		✓	
Very rare	Somnambulism (sleepwalking) – getting out of bed while not fully awake and do activities you do not remember the day after		✓	

This is not a complete list of side effects. For any unexpected effects while taking ‘Dalmane’, contact your doctor or pharmacist.

HOW TO STORE IT

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Common Side Effects

Benzodiazepine sleeping pills may cause drowsiness, dizziness, light-headedness, and difficulty with coordination. Users must be cautious about engaging in hazardous activities requiring complete mental alertness, e.g., operating machinery or driving a motor vehicle.

DO NOT drink alcohol while using ‘Dalmane’. DO NOT USE benzodiazepine sleeping pills along with other medications without first discussing this with your doctor.

How sleepy you are the day after you use one of these sleeping pills depends on your individual response and on how quickly your body gets rid of the medication. The larger the dose, the more likely that you will experience drowsiness, etc., the next day. For this reason, it is important that you use the lowest dose possible that will still help you sleep at night. Benzodiazepines which are eliminated rapidly tend to cause less drowsiness the next day, but may cause withdrawal problems the day after use.

Store at controlled room temperature (15-30°C) in tightly closed, light resistant container.

Keep out of reach of children.

REPORTING SUSPECTED SIDE EFFECTS

To monitor drug safety, Health Canada through the Canada Vigilance Program collects information on serious and unexpected side effects of drugs. If you suspect you have had a serious or unexpected reaction to this drug you may notify Canada Vigilance:

By toll-free telephone: 866-234-2345
By toll-free fax: 866-678-6789
Online: www.healthcanada.gc.ca/medeffect
By email: CanadaVigilance@hc-sc.gc.ca

By regular mail:
Canada Vigilance National Office
Marketed Health Products Safety and
Effectiveness Information Bureau
Marketed Health Products Directorate
Health Products and Food Branch
Health Canada
Tunney's Pasture, AL 0701C
Ottawa ON K1A 0K9

NOTE: Should you require information related to the management of the side effect, please contact your health care provider before notifying Canada Vigilance. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found by contacting the sponsor, Valeant Canada, at:
1-800-361-4261.

This leaflet was prepared by Valeant Canada limitée/Limited

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