



# VALIUM<sup>®</sup>

(brand of diazepam)

## TABLETS

This product information is intended for United States residents and on-screen viewing only.  
Before prescribing, please refer to printed complete product information.

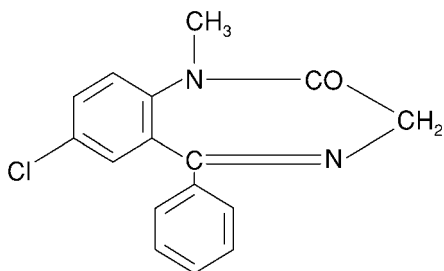
### Complete Product Information

- [DESCRIPTION](#)
- [CLINICAL PHARMACOLOGY](#)
- [INDICATIONS](#)
- [CONTRAINDICATIONS](#)
- [WARNINGS](#)
- [PRECAUTIONS](#)
- [ADVERSE REACTIONS](#)
- [DRUG ABUSE AND DEPENDENCE](#)
- [DOSAGE AND ADMINISTRATION](#)
- [HOW SUPPLIED](#)



**VALIUM®**  
brand of  
diazepam  
**TABLETS**

**DESCRIPTION:** Valium (diazepam) is a benzodiazepine derivative. The chemical name of diazepam is 7-chloro-1,3-dihydro-1-methyl-5-phenyl-2H-1,4-benzodiazepin-2-one. It is a colorless to light yellow crystalline compound, insoluble in water. The empirical formula is  $C_{16}H_{13}ClN_2O$  and the molecular weight is 284.75. The structural formula is as follows:



Valium is available for oral administration as tablets containing 2 mg, 5 mg or 10 mg diazepam. In addition to the active ingredient diazepam, each tablet contains the following inactive ingredients: anhydrous lactose, corn starch, pregelatinized starch and calcium stearate with the following dyes: 5-mg tablets contain FD&C Yellow No. 6 and D&C Yellow No. 10; 10-mg tablets contain FD&C Blue No. 1. Valium 2-mg tablets contain no dye.

**PHARMACOLOGY:** In animals, Valium appears to act on parts of the limbic system, the thalamus and hypothalamus, and induces calming effects. Valium, unlike chlorpromazine and reserpine, has no demonstrable peripheral autonomic blocking action, nor does it produce extrapyramidal side effects; however, animals treated with Valium do have a transient ataxia at higher doses. Valium was found to have transient cardiovascular depressor effects in dogs. Long-term experiments in rats revealed no disturbances of endocrine function.

Oral LD<sub>50</sub> of diazepam is 720 mg/kg in mice and 1240 mg/kg in rats. Intraperitoneal administration of 400 mg/kg to a monkey resulted in death on the sixth day.

*Reproduction Studies:* A series of rat reproduction studies was performed with diazepam in oral doses of 1, 10, 80 and 100 mg/kg. At 100 mg/kg there was a decrease in the number of pregnancies and surviving offspring in these rats. Neonatal survival of rats at doses lower than 100 mg/kg was within normal limits. Several neonates in these rat reproduction studies showed skeletal or other defects. Further studies in rats at doses up to and including 80 mg/kg/day did not reveal teratological effects on the offspring.

## **VALIUM® (diazepam)**

In humans, measurable blood levels of Valium were obtained in maternal and cord blood, indicating placental transfer of the drug.

**INDICATIONS:** Valium is indicated for the management of anxiety disorders or for the short-term relief of the symptoms of anxiety. Anxiety or tension associated with the stress of everyday life usually does not require treatment with an anxiolytic.

In acute alcohol withdrawal, Valium may be useful in the symptomatic relief of acute agitation, tremor, impending or acute delirium tremens and hallucinosis.

Valium is a useful adjunct for the relief of skeletal muscle spasm due to reflex spasm to local pathology (such as inflammation of the muscles or joints, or secondary to trauma); spasticity caused by upper motor neuron disorders (such as cerebral palsy and paraplegia); athetosis; and stiff-man syndrome.

Oral Valium may be used adjunctively in convulsive disorders, although it has not proved useful as the sole therapy.

The effectiveness of Valium in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

**CONTRAINDICATIONS:** Valium is contraindicated in patients with a known hypersensitivity to this drug and, because of lack of sufficient clinical experience, in pediatric patients under 6 months of age. It may be used in patients with open angle glaucoma who are receiving appropriate therapy, but is contraindicated in acute narrow angle glaucoma.

**WARNINGS:** Valium is not of value in the treatment of psychotic patients and should not be employed in lieu of appropriate treatment. As is true of most preparations containing CNS-acting drugs, patients receiving Valium should be cautioned against engaging in hazardous occupations requiring complete mental alertness such as operating machinery or driving a motor vehicle.

As with other agents which have anticonvulsant activity, when Valium is used as an adjunct in treating convulsive disorders, the possibility of an increase in the frequency and/or severity of grand mal seizures may require an increase in the dosage of standard anticonvulsant medication. Abrupt withdrawal of Valium in such cases may also be associated with a temporary increase in the frequency and/or severity of seizures.

Since Valium has a central nervous system depressant effect, patients should be advised against the simultaneous ingestion of alcohol and other CNS-depressant drugs during Valium therapy.

***Usage in Pregnancy:*** An increased risk of congenital malformations associated with the use of minor tranquilizers (diazepam, meprobamate and chlordiazepoxide) during the first trimester of pregnancy has been suggested in several studies. Because use of these drugs is rarely a matter of urgency, their use during this period should almost always be avoided. The possibility that a woman of childbearing

## VALIUM<sup>®</sup> (diazepam)

**potential may be pregnant at the time of institution of therapy should be considered. Patients should be advised that if they become pregnant during therapy or intend to become pregnant they should communicate with their physicians about the desirability of discontinuing the drug.**

*Management of Overdosage:* Manifestations of Valium overdose include somnolence, confusion, coma and diminished reflexes. Respiration, pulse and blood pressure should be monitored, as in all cases of drug overdose, although, in general, these effects have been minimal following overdose. General supportive measures should be employed, along with immediate gastric lavage. Intravenous fluids should be administered and an adequate airway maintained. Hypotension may be combated by the use of Levophed<sup>®\*</sup> (levarterenol) or Aramine<sup>®†</sup> (metaraminol). Dialysis is of limited value. As with the management of intentional overdose with any drug, it should be borne in mind that multiple agents may have been ingested.

Flumazenil, a specific benzodiazepine-receptor antagonist, is indicated for the complete or partial reversal of the sedative effects of benzodiazepines and may be used in situations when an overdose with a benzodiazepine is known or suspected. Prior to the administration of flumazenil, necessary measures should be instituted to secure airway, ventilation and intravenous access. Flumazenil is intended as an adjunct to, not as a substitute for, proper management of benzodiazepine overdose. Patients treated with flumazenil should be monitored for re sedation, respiratory depression and other residual benzodiazepine effects for an appropriate period after treatment. **The prescriber should be aware of a risk of seizure in association with flumazenil treatment, particularly in long-term benzodiazepine users and in cyclic antidepressant overdose.** The complete flumazenil package insert, including CONTRAINDICATIONS, WARNINGS and PRECAUTIONS, should be consulted prior to use.

Withdrawal symptoms of the barbiturate type have occurred after the discontinuation of benzodiazepines. (See DRUG ABUSE AND DEPENDENCE section.)

**PRECAUTIONS:** If Valium is to be combined with other psychotropic agents or anticonvulsant drugs, careful consideration should be given to the pharmacology of the agents to be employed—particularly with known compounds which may potentiate the action of Valium, such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants. The usual precautions are indicated for severely depressed patients or those in whom there is any evidence of latent depression; particularly the recognition that suicidal tendencies may be present and protective measures may be necessary. The usual precautions in treating patients with impaired renal or hepatic function should be observed.

In elderly and debilitated patients, it is recommended that the dosage be limited to the smallest effective amount to preclude the development of ataxia or oversedation (2 mg to 2½ mg once or twice daily, initially, to be increased gradually as needed and tolerated).

The clearance of Valium and certain other benzodiazepines can be delayed in association with Tagamet (cimetidine) administration. The clinical significance of this is unclear.

## **VALIUM® (diazepam)**

*Information for Patients:* To assure the safe and effective use of benzodiazepines, patients should be informed that, since benzodiazepines may produce psychological and physical dependence, it is advisable that they consult with their physician before either increasing the dose or abruptly discontinuing this drug.

*Pediatric Use:* Safety and effectiveness in pediatric patients below the age of 6 months have not been established.

**ADVERSE REACTIONS:** Side effects most commonly reported were drowsiness, fatigue and ataxia. Infrequently encountered were confusion, constipation, depression, diplopia, dysarthria, headache, hypotension, incontinence, jaundice, changes in libido, nausea, changes in salivation, skin rash, slurred speech, tremor, urinary retention, vertigo and blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances and stimulation have been reported; should these occur, use of the drug should be discontinued.

Because of isolated reports of neutropenia and jaundice, periodic blood counts and liver function tests are advisable during long-term therapy. Minor changes in EEG patterns, usually low-voltage fast activity, have been observed in patients during and after Valium therapy and are of no known significance.

**DRUG ABUSE AND DEPENDENCE:** Withdrawal symptoms, similar in character to those noted with barbiturates and alcohol (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating), have occurred following abrupt discontinuance of diazepam. The more severe withdrawal symptoms have usually been limited to those patients who had received excessive doses over an extended period of time. Generally milder withdrawal symptoms (eg, dysphoria and insomnia) have been reported following abrupt discontinuance of benzodiazepines taken continuously at therapeutic levels for several months. Consequently, after extended therapy, abrupt discontinuation should generally be avoided and a gradual dosage tapering schedule followed. Addiction-prone individuals (such as drug addicts or alcoholics) should be under careful surveillance when receiving diazepam or other psychotropic agents because of the predisposition of such patients to habituation and dependence.

**DOSAGE AND ADMINISTRATION:** Dosage should be individualized for maximum beneficial effect. While the usual daily dosages given below will meet the needs of most patients, there will be some who may require higher doses. In such cases dosage should be increased cautiously to avoid adverse effects.

### *ADULTS:*

### *USUAL DAILY DOSE*

*Management of Anxiety Disorders and Relief of Symptoms of Anxiety.*

Depending upon severity of symptoms—2 mg to 10 mg, 2 to 4 times daily

*Symptomatic Relief in Acute Alcohol Withdrawal.*

10 mg, 3 or 4 times during the first 24 hours, reducing to 5 mg, 3 or 4 times daily as needed

## VALIUM® (diazepam)

*Adjunctively for Relief of Skeletal Muscle Spasm.* 2 mg to 10 mg, 3 or 4 times daily

*Adjunctively in Convulsive Disorders.* 2 mg to 10 mg, 2 to 4 times daily

*Geriatric Patients, or in the presence of debilitating disease.* 2 mg to 2½ mg, 1 or 2 times daily initially; increase gradually as needed and tolerated

### *PEDIATRIC PATIENTS:*

Because of varied responses to CNS-acting drugs, initiate therapy with lowest dose and increase as required. Not for use in pediatric patients under 6 months. 1 mg to 2½ mg, 3 or 4 times daily initially; increase gradually as needed and tolerated

**HOW SUPPLIED:** For oral administration, Valium is supplied as round, flat-faced scored tablets with V-shaped perforation and beveled edges. Valium is available as follows: 2 mg, white — bottles of 100 (NDC 0140-0004-01) and 500 (NDC 0140-0004-14); 5 mg, yellow — bottles of 100 (NDC 0140-0005-01) and 500 (NDC 0140-0005-14); 10 mg, blue — bottles of 100 (NDC 0140-0006-01) and 500 (NDC 0140-0006-14).

Engraved on tablets:

2 mg—2 VALIUM® (front)  
ROCHE (twice on scored side) <ILLUSTRATION OF 2 mg TABLETS>

5 mg—5 VALIUM® (front)  
ROCHE (twice on scored side) <ILLUSTRATION OF 5 mg TABLETS>

10 mg—10 VALIUM® (front)  
ROCHE (twice on scored side) <ILLUSTRATION OF 10 mg TABLETS>

**Storage:** Store at room temperature 59° to 86°F (15° to 30°C). Dispense in tight, light-resistant containers as defined in USP/NF.

\*Levophed is a registered trademark of Abbott Laboratories.

†Aramine is a registered trademark of MERCK & CO., INC.

**VALIUM<sup>®</sup> (diazepam)**

Distributed by:



**Pharmaceuticals**

Roche Laboratories Inc.  
340 Kingsland Street  
Nutley, New Jersey 07110-1199

**for Roche Products Inc.**

26467475-0300

Revised: March 2000

Printed in USA

Copyright © 1987-2000 by Roche Products Inc. All rights reserved.