Valium® Tablets
Diazepam

Tranquilizer and anxiolytic

Composition
Each tablet contains:
Diazepam (USP) ...2mg
Each tablet contains:
Diazepam (USP) ...5mg
Each tablet contains:
Diazepam (USP)...10mg

Properties and effects
Diazepam is a member of the group of benzodiazepine tranquilizers, which exert anxiolytic, sedative, muscle-relaxant and anticonvulsant effects. This is now known to be the result of facilitating the action of γ-aminobutyric acid (GABA), the most important inhibitory neurotransmitter in the brain.

Pharmacokinetics
Diazepam is rapidly and completely absorbed from the digestive tract, peak plasma concentrations appearing 30-90 minutes after oral intake. On intramuscular injection, absorption is also complete, though not always more rapid than with oral administration.
The elimination curve of diazepam is biphasic, an initial rapid and extensive distribution phase with a half-life of up to 3 hours being followed by a prolonged terminal elimination phase (half-life up to 48 hours). Diazepam is metabolized to the pharmacologically active nordiazepam ($t^1/_2\beta$=96 hours), hydroxy-diazepam and to oxazepam. Diazepam and its metabolites are highly bound to plasma proteins (diazepam: 98%). They are excreted mainly (about 70%) in the urine in the form of free of (predominantly) conjugated metabolites.
The elimination half-life may be prolonged in the newborn, the elderly and patients with liver or kidney disease, and it should be noted that the plasma concentration may take correspondingly longer to reach the steady state. Diazepam and its metabolites cross the blood-brain and placental barriers. They are also found in breast milk in concentrations approximately one tenth those in the maternal plasma.

Indications
Valium is indicated for the symptomatic relief of anxiety, agitation and tension due to psychoneurotic states and transient situational disturbances. It can also be useful adjunctively in major mental and organic disorders. Anxiety as the main target symptom may be expressed by manifest anxious mood or apprehensive behaviour and/or by functional, automatic or motor equivalents such as palpitation, sweating, insomnia, tremor, restlessness, etc.
Valium is a useful adjunct for the relief of reflex muscle spasm due to local trauma (injury, inflammation). It can also be used to combat spasticity arising from damage to spinal and supraspinal interneurons such as cerebral palsy and paraplegia, as well as in athetosis and stiff-man syndrome.

Dosage and administration
Standard dosage
For optimal effect, the dosage should be carefully individualized. The usual daily doses given below will meet the needs of most patients, though there will be cases requiring higher doses.
Usual adult dosage for oral administration: depending on severity of symptoms, 5–20 mg daily. The single oral dose should not normally exceed 10 mg. The tablets should be taken at a time that meets the needs of the patient in question – usually the evening is the most suitable time.
In acute cases or life-threatening situations, or when the response to enteral administration is insufficient, higher doses may, where appropriate, be given by *parenteral route*.
Duration of treatment: The usual long-term treatment of anxiety with Valium may last, depending on the type of condition and on the causal factors involved, as long as several weeks. After about six weeks' treatment, no further improvement of the patient's anxious state is to be expected; further treatment may be regarded purely as maintenance therapy. During prolonged maintenance therapy, drug-free periods should be introduced at regular intervals to assess the need for continuation.
Treatment with Valium should not be stopped abruptly, however, the dosage should be gradually tapered off.
The effectiveness of long-term treatment (i.e. more than six months) with Valium has not been assessed by systematic clinical studies.

Special dosage instructions
Elderly
Dosage for elderly patients: Elderly patients should be given a reduced dose. These patients should be checked regularly at the start of treatment in order to minimize the dosage and/or the frequency of administration to prevent overdose due to accumulation.
Children
Children's dosage: 0.1-0.3 mg/kg bodyweight daily. Benzodiazepines should not be given to children without careful assessment of the indication; the duration of treatment must be kept to a minimum.

Impaired hepatic function
Patients with impaired hepatic function should be given a reduced dose.

Contraindications
Valium is contraindicated in patients with:
- A known history of hypersensitivity to benzodiazepines
- Severe respiratory insufficiency
- Severe hepatic insufficiency
- Sleep apnea syndrome
- Myasthenia gravis
- Dependence on other substances including alcohol. An exception to the latter is the management of acute withdrawal reactions.

Benzodiazepines are not recommended for the primary treatment of psychotic illness.
Benzodiazepines should not be used alone to treat depression or anxiety associated with depression as suicide may occur in such patients.

Precautions
Benzodiazepines should be used with extreme caution in patients with a history of alcohol or drug abuse.
A lower dose is recommended for patients with chronic respiratory insufficiency, due to the risk of respiratory depression.

Tolerance
Some loss of response to the effects of benzodiazepines may develop after repeated use of Valium for a prolonged time.

Dependence
Use of benzodiazepines and benzodiazepine-like agents may lead to the development of physical and psychological dependence. The risk of dependence increases with dose and duration of treatment; it is also greater in predisposed patients with a history of alcohol or drug abuse.

Withdrawal
Once physical dependence has developed, abrupt termination of treatment will be accompanied by withdrawal symptoms.

These may consist of headache, muscle pain, extreme anxiety, tension, restlessness, confusion and irritability. In severe cases, the following symptoms may occur: derealization, depersonalization, hyperacusis, numbness and tingling of the extremities, hypersensitivity to light, noise and physical contact, hallucinations or epileptic seizures.

Rebound anxiety
A transient syndrome whereby the symptoms that led to treatment with Valium recur in an enhanced form. This may occur on withdrawal of treatment. It may be accompanied by other reactions including mood changes, anxiety and restlessness.
Since the risk of withdrawal phenomena and rebound phenomena is greater after abrupt discontinuation of treatment, it is recommended that the dosage be decreased gradually.

Amnesia
It should be borne in mind that benzodiazepines may induce anterograde amnesia. Anterograde amnesia may occur using therapeutic dosages, the risk increasing at higher dosages. Amnestic effects may be associated with inappropriate behaviour.
Psychiatric and 'paradoxical' reactions
Paradoxical reactions such as restlessness, agitation, irritability, aggressiveness, delusion, rages, nightmares, hallucinations, psychoses, inappropriate behaviour and other adverse behavioural effects are known to occur when using benzodiazepines. Should this occur, the use of the drug should be discontinued. They are more likely to occur in children and in the elderly.
Sedation, amnesia, impaired concentration and impaired muscle function may adversely affect the ability to drive or operate machinery.

Pregnancy, nursing mothers
The safety of diazepam for use in human pregnancy has not been established. An increased risk of congenital malformation associated with the use of benzodiazepines during the first trimester of pregnancy has been suggested. Review of spontaneously reported adverse drug events shows no greater incidence than would be anticipated from a similar untreated population.
Benzodiazepines should be avoided during pregnancy unless there is no safer alternative. Before administering Valium during pregnancy, especially during the first trimester, possible Risks for the fetus should – as with any other drug – be weighed against the expected therapeutic benefit for the mother.
Continuous administration of benzodiazepines during pregnancy may give rise to hypotension, reduced respiratory function and hypothermia in the newborn child. Withdrawal symptoms in newborn infants have occasionally been reported with this class of drugs. Special care must be taken when Valium is used during labour and delivery, as high single doses may produce irregularities in the fetal heart rate and hypotonia, poor sucking, hypothermia and moderate respiratory depression in the neonate. With newborn infants it must be remembered that the enzyme system involved in the breakdown of the drug is not yet fully developed (especially in premature infants).
Diazepam passes into breast milk. Breast-feeding is therefore not recommended in patients receiving Valium.

Undesirable effects
The most commonly reported undesirable effects are fatigue, drowsiness and muscle weakness. These phenomena occur predominantly at the start of therapy and usually disappear with prolonged administration. The following may also occcur: ataxia, confusion, constipation, depression, diplopia, dysarthria, gastrointestinal disturbances, headache, hypotension, incontinence, increase or decrease in libido, nausea, dry mouth or hypersalivation, skin reactions, slurred speech, tremor, urinary retention, dizziness and blurred vision; very rarely, elevated transaminases and alkaline phosphatase as well as cases of jaundice have been reported occasionally.
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Chronic use (even at therapeutic doses) may lead to the development of physical dependence: discontinuation of the therapy may result in withdrawal or rebound phenomena.
Abuse of benzodiazepines has been reported.

Interactions
If Valium is to be combined with other centrally acting agents, such as antipsychotics, anxiolytics/sedatives, antidepressants, hypnotics, anticonvulsants, narcotic analgesics, anesthetics and sedative antihistamines, it should be borne in mind that their effects may potentiate or be potentiated by the action of Valium.
Concomitant use with alcohol is not recommended due to enhancement of the sedative effect.
There is a potentially relevant interaction between diazepam and compounds which inhibit certain hepatic enzymes (particularly cytochrome P450 III A). Data indicate that these compounds influence the pharmacokinetics of diazepam and may lead to increased and prolonged sedation. At present this reaction is known to occur with cimetidine, ketoconazole, fluvoxamine, fluoxetine and omeprazole.
There have also been reports that the metabolic elimination of phenytoin is affected by diazepam. On the other hand, there is no known interference with commonly used antidiabetic, anticoagulant or diuretic substances. Cisapride may lead to a temporary increase in the sedative effects of orally administered benzodiazepines due to faster absorption.

Overdosage
Symptoms
Overdose of benzodiazepines is usually manifested by central nervous system depression ranging from drowsiness to coma. In mild cases, symptoms include drowsiness, mental confusion and lethargy. In more serious cases, symptoms may include ataxia, hypotonia, hypotension, respiratory depression, coma (rarely) and death (very rarely). However, overdose should not present a threat to life unless combined with other CNS depressants (including alcohol).
Treatment
In the management of overdose with any medicinal product, it should be borne in mind that multiple agents may have been taken. Following overdose with oral benzodiazepines, vomiting should be induced (within1 hour) if the patient is conscious or gastric lavage undertaken with the airway protected if the patient is unconscious. If there is no advantage in emptying the stomach, activated charcoal should be given to reduce absorption. Special attention should be paid to respiratory and cardiac function in intensive care. Flumazenil may be useful as an antagonist. Caution should be observed in the use of flumazenil in epileptics treated with benzodiazepines.

Stability
See expiry on the pack.

Packs

Tablets (scored) 2 mg (white)	30's
Tablets (scored) 5 mg (yellow)	30's
Tablets (scored) 10 mg (light-blue)	30's

INSTRUCTIONS:
Keep all medicines out of the reach of children.
Protect from light, heat and moisture.
Store below 30ºC.
To be sold on prescription of a registered medical practitioner only.

ہدایات:
تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔
روشنی، گرمی اور نمی سے محفوظ رکھیں۔
۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے پر فروخت کی جائے۔

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Martin Dow