

 PACKAGE LEAFLET:
Information for the patient

DIAZEPAM

Tablets - 5 mg
Solution for injection - 10 mg/2 ml
(Diazepam)

Read this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Diazepam is and what it is used for
2. Before you take Diazepam
3. How to take Diazepam
4. Possible side effects
5. How to store Diazepam
6. Other information

1. WHAT DIAZEPAM IS AND WHAT IT IS USED FOR

Diazepam is a long - acting benzodiazepinic preparation. It exerts an anxiolytic, hypno - sedative (hypnotic and sedative), muscle relaxant and anticonvulsant action through the specific benzodiazepinic receptors, the major part of which are found in the limbic system, hypothalamus, cerebellum and corpus striatum. These receptors and the gamma - aminobutyric acid (GABA) receptors form an anatomical and functional unit. After diazepam is bound with a receptor, then the GABA transmission and the central nervous system inhibition is potentiated. The consequences are manifested with an anticonvulsant and muscle relaxant action. The stimulatory action of serotonin, noradrenaline and acetylcholine neurotransmitters is reduced, because of the increased action of GABA and as a consequence, the anxiolytic, hypnotic and sedative action of diazepam is potentiated.

Diazepam is used as follows:

Tablets: anxiety conditions, insomnia, muscle spasms, acute alcohol withdrawal syndrome.

Solution for injection: severe anxiety conditions, symptoms of the acute alcohol withdrawal syndrome (delirium tremens), status epilepticus, muscle spasms, tetanus, premedication in anaesthesia. Your doctor may have given Diazepam to you for another purpose. Ask your doctor if you want to know why Diazepam has been given to you.

2. BEFORE YOU TAKE DIAZEPAM

Diazepam should not be used:

- if you are allergic to diazepam and to the benzodiazepines in general;
- if you are allergic to any of the excipients mentioned at the end of this leaflet;
- if you have severe episodes of chronic hypercapnia;
- in acute respiratory failure;
- in severe hepatic failure;
- in sleep apnea syndrome;
- in chronic psychosis;
- in phobic or obsessive conditions;
- in closed angle glaucoma;
- in Myasthenia gravis;
- in children aged less than 6 months;
- during breast - feeding;
- during concomitant use of ketoconazole and itraconazole (because of the inhibition of cytochrome P450 3A).

Diazepam should not be used alone in the treatment of depression and anxiety associated with depression.

Because of benzyl alcohol content, the solution for injection Diazepam should not be used in children less than 3 years old. If you think that you have any of the above-mentioned conditions, do not take the medicine. Talk first to your doctor and follow the given advices.

Take special care with Diazepam

Inform your doctor if you:

- are allergic to other drugs;
- are old or debilitated;
- have hepatic or renal impairment;
- have muscle weakness;
- have personality disorders;
- have arteriosclerosis in the brain;
- suffer of cardiorespiratory failure, because a further respiratory deterioration may happen, but however it should be noted that in some patients the sedative effect may help them by reducing the strain of breathing;
- have a history of drug or alcohol abuse, because of the risk of dependence.

Avoid prolonged use and abrupt withdrawal of Diazepam.

Taking other medicines

Inform your doctor or pharmacist if you are taking or you have been taking recently other drugs, including those without a prescription, such as:

- other central nervous system depressants, like: alcohol, sedatives, neuroleptics, antidepressants, antihistaminics, general anaesthetics, hypnotics and analgesics, because they potentiate the effect of diazepam;
- cimetidine, because it inhibits the metabolism of diazepam and of the benzodiazepines in general;
- omeprazole, because it inhibits the metabolism of diazepam (increase of the plasmatic concentration);
- isoniazide, because it reduces the clearance of diazepam;
- phenytoin, because it reduces the plasmatic levels of diazepam;
- valproic acid, because it increases the plasmatic levels of diazepam;
- rifampicin, because it causes a marked increase of the metabolism and/or of the clearance of diazepam;
- ketoconazole and itraconazole (because of the inhibition of cytochrome P450 3A).

These drugs may be affected by Diazepam or may affect the way it acts, therefore during their concomitant use a change of the dosage of Diazepam may be needed. Your doctor or pharmacist will advise you.

Taking Diazepam with food and drinks

Food does not influence diazepam absorption. Patients who use Diazepam should be conscient also about the concomitant consume of alcoholic beverages, because such combination may potentiate the undesirable effects of diazepam, and of alcohol also.

Pregnancy

Inform your doctor or pharmacist if you are pregnant or if you are planning to become pregnant. Your doctor or pharmacist will discuss on the risks and benefits of the administration of this drug during pregnancy. The use of diazepam during pregnancy should be made only if it is indispensable, very carefully even in this case, and only after the possible risk for the fetus with the benefits of taking it during pregnancy are evaluated.

Breast - feeding

Inform your doctor or pharmacist if you are breast - feeding, because Diazepam administration during this period is contraindicated. The doctor or pharmacist will discuss on the risks and benefits of the administration of this drug if you are breast - feeding or you are planning to do this.

Driving and using machines

Patients who use Diazepam should be warned not to be involved in jobs requiring mental alertness, such as using hazardous machinery, or driving.

Important information about some of the excipients of Diazepam

Diazepam tablets contain lactose. If you have been told by your doctor that you have intolerance to some sugars, talk to your doctor before taking this medicine.

Diazepam - solution for injection contains:

- 40 mg / 2 ml benzyl alcohol. Benzyl alcohol may cause toxic reactions and allergic reactions in infants and children up to 3 years old, therefore this drug should not be used in these ages. Talk to your doctor or pharmacist if you have problems with the liver or kidneys, or if you are pregnant or breast - feeding because high volumes may cause toxicity;
- ethanol (alcohol). Ethanol is harmful for people who suffer from alcoholism. It should be taken into consideration in pregnant women or who are breast - feeding, children and patients at high risk, like those with liver disease or epilepsy.

3. HOW TO TAKE DIAZEPAM

Always take Diazepam as your doctor has told you. You should check with your doctor or pharmacist if you are not sure. If you feel that the effects of Diazepam are too strong or too weak, talk to your doctor or pharmacist. Your doctor may ask you to take Diazepam for a longer period. Ask your doctor for advice if you are not sure for how long to take it.

The tablets should be swallowed with at least a glass of water. You are advised not to take alcoholic beverages with this drug.

Tablets:

By mouth: To get the optimal effect, the dose should be carefully individualised. A practical overview for the dosage of diazepam that is taken by mouth, is given as follows:

Adults:

- Anxiety conditions: 2 mg, 3 times daily up to a maximal dose of 15
- 30 mg daily, in divided doses.
- Insomnia: 5 mg - 10 mg at bedtime.
- Acute alcohol withdrawal syndrome: 10 mg, 3 times daily in the first 24 hours and then 5 mg, 3 times daily.
- Muscle spasms: 2 mg - 15 mg daily, in divided doses.

Elderly: 2.5 mg, 1 - 2 times daily.

Children over 6 months of age: 0.1 - 0.3 mg/kg.

Solution for injection:

By injection: In acute conditions the dosage may be repeated after an hour, although a usual interval is considered that of 4 hours. In elderly and debilitated patients and when other sedatives are also used, lower doses should be used (2 to 5 mg), and also a slow increase of the dose.

Injection routes: The injections of diazepam should not be mixed or diluted with any other drug, in the same syringe. Intramuscular: The drug is injected deep in the muscle. In the vein: The drug should be injected slowly in the vein, by using a large vein and continuing for at least 1 minute for every 5 mg.

Perfusions: The content of one ampoule of diazepam is diluted with 250 ml of glucose solution 5 % or 10 % or sodium chloride solution 0.9 % and is carefully mixed.

Adults:

- Severe anxiety conditions: 5 - 10 mg in the vein or in the muscle; if necessary repeat after 4 hours.
- Symptoms of acute alcohol withdrawal syndrome (delirium tremens): 10 - 20 mg in the vein or in the muscle; if necessary repeat a dose of 5 - 10 mg every 4 hours.
- Status epilepticus: 0.15 - 0.25 mg/kg body weight, slowly in the vein or in the muscle, that is repeated after 30 - 60 minutes or it is used in infusion; the maximal dose for 24 hours is 3 mg/kg body weight.
- Muscle spasms: 10 - 20 mg in the vein or in the muscle, 1 - 2 times daily.
- Tetanus: 0.1 - 0.3 mg/kg body weight slowly in the vein, with an interval of 1 to 4 hours or 3 - 4 mg/kg body weight with infusion within 24 hours.
- Premedication in anaesthesia: 10 - 20 mg, 1 hour before the intervention.

Ask your doctor for the use of Diazepam - solution for injection in children.

For injections into the vein should not be selected very small veins; injections in the arteries or the extravasation should be absolutely avoided.

If you take more Diazepam

If you take more Diazepam than you should, or if the children have taken this medicine incorrectly, please contact your doctor or call the hospital or emergency to get an opinion for the risk and an advice for the actions to be taken.

The possible risk of physical dependence to diazepam is very low in patients who take the recommended doses.

If you forget to take Diazepam

If you forget a dose (or more doses), take the next dose when it is time to take it usually.

Do not take a double dose (or higher) to make up for a forgotten dose (doses).

If you stop taking Diazepam

Diazepam should not be used for a long time and then discontinued immediately, because undesirable effects may appear to you.

If you have further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

All medicines may cause side effects. Sometimes they are serious, most of times not. Do not get alarmed by this list of possible side effects. None of them may appear to you.

Inform your doctor if any of the following side effects bothers you:

- the most usual are: fatigue, weariness, muscle weakness and ataxia;
- more rare are: confusion, constipation, depression, diplopia, dysarthria, headache, hypotension, respiratory depression, urinary retention and incontinence, slurred speech, tremor, dizziness, blurred vision, changes of the libido, salivary changes, amnesia;
- rarely is observed increase of transaminases and alkaline phosphatases, and also jaundice appearance;
- paradoxical reactions are observed, like: immediate excitation, anxiety, sleep disorders and hallucinations; when these reactions appear, treatment with diazepam should be immediately discontinued;
- excitement, tremor and in rare cases convulsions from the abrupt discontinuance of the treatment, because after a long-term treatment, it may cause potentiation of the symptoms that are controlled by it, although the possible physical dependence to diazepam in patients who take the recommended doses is very small (in these cases it is advised the gradual reduction of the dose);
- after a rapid injection into the vein, thrombosis of the veins, phlebitis, local irritation, vomiting and more rarely vascular changes may occur.

If you notice side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

5. HOW TO STORE DIAZEPAM

Keep away from children.

Do not use Diazepam after the expiry date which is stated on the package.

Store below 25°C.

Store in the original packaging to protect it from light.

6. OTHER INFORMATION

What Diazepam contains

The active substance is diazepam.

Each tablet contains 5 mg diazepam.

The other excipients are: lactose, microcrystalline cellulose, talc, magnesium stearate.

Each ampoule 2 ml contains 10 mg diazepam (5 mg / ml).

The other excipients are: propylene glycol, ethyl alcohol, benzyl alcohol, hydrochloric acid (may be added for pH adjustment) and water for injection.

Content of the pack:

Tablets: carton box with 30 tablets.

Solution for injection: carton box with 10 ampoules 2 ml and carton box with 100 ampoules 2 ml (hospital use).

Explanatory of the illustration icons on the packaging:

 Ask your doctor or pharmacist.

 Contents.  Warning.

 Solution for injection - Ampoules  Tablet shape.

Marketing Authorisation Holder and Manufacturer:

 **PROFARMA Sh.a.**
Rruga "Myslym Keta"
Tel./Fax: 00 355 4 23 89 602
Tirana - ALBANIA

This leaflet was last revised in June 2015.

 SPECIFICATION

 CROPPING AREA 15 X 25 cm

PAY ATTENTION, all the layers are visible. If you have to print this document please check or uncheck the specific layers.