PACKAGE LEAFLET: Information for the patient

AFEBRIL

Rectal solution – 5 mg / 2.5 ml

(Diazepam)

Read all of this leaflet carefully before you start using 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 symptoms are the same as yours.
- If any of the side effects becomes worse or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Afebril is and what it is used for
2. Before you use Afebril
3. How to use Afebril
4. Possible side effects
5. How to store Afebril
6. Further information

1. WHAT AFEBRIL IS AND WHAT IT IS USED FOR

Afebril contains the active substance diazepam. Diazepam is a long-lasting benzodiazepine. It acts as anxiolytic, hypnosedative, myorelaxant and anticonvulsive through specific benzodiazepine receptors by potentiating the GABA–ergic transmission and as a result the central nervous system is inhibited.

Afebril is used in:

- status epilepticus, febrile convulsions, convulsions due to poisoning;
- acute anxiety and agitation.

Afebril rectal solution may be of particular value for the treatment of convulsions in children.

Your doctor may have given you Afebril for another reason. Ask your doctor if you want to know why you were given Afebril.

2. BEFORE YOU USE AFEBRIL

Do not use Afebril if you:

- are hypersensitive to diazepam and benzodiazepines in general;
- are allergic to any of the excipients mentioned at the end of this leaflet (see section 6);
- suffer from unstable myasthenia gravis or neuromuscular respiratory weakness, acute pulmonary insufficiency, sleep apnoea syndrome, severe hepatic impairment.

Take special care with Afebril

Ask your doctor before using Afebril.

It should be used with caution in patients:

- who suffer from porphyria;
- who are elderly, with muscle weakness, with hepatic or renal function impairment, because they are more prone to adverse effects, and may require reduced doses;
- with personality disorders and organic brain changes (particularly in patients with arteriosclerosis);
- who suffer from chronic psychosis, phobia or obsession;
- with a history of alcohol or drug addiction because of the risk of dependence; (diazepam may cause dependence after regular use, even in therapeutic doses for short periods, in this case it should be withdrawn by gradual reduction of the dose).

Taking other medicines

Please tell your doctor or pharmacist if you are taking / using, have taken / used recently or will take / use other drugs including those without a prescription.

It is especially important to tell your doctor if you are taking:

- other drugs that have CNS-depressant properties such as: antidepressants (fluvoxamin), antihistamines, antipsychotics, general and local anaesthetics, hypnotics, sedatives, anxiolytics and analgesics which may enhance the sedative effect of diazepam;

- ACE inhibitors, adrenergic neuron blockers, alpha-blockers, angiotensin-II receptor antagonists, beta-blockers, calcium channel-blockers and antihypertensives (moxonidine, methyldopa) which may enhance the hypotensive effect;
- antiepileptics: phenytoin may reduce diazepam serum levels, whereas sodium valproate may increase serum levels of diazepam;
- antibacterials: rifampicin increases the clearance of diazepam, whereas isoniazide reduces the clearance of diazepam;
- antivirals: ritonavir may increase the sedative effect and cause respiratory depression;
- disulfiram, which inhibits the metabolism of diazepam;
- oral contraceptives: they can slow down the removal of diazepam from the body and increase its effect;
- theophylline: it can weaken the effect of diazepam;
- cimetidine, omeprazole, esomeprazole: inhibit the metabolism of diazepam;
- fluconazole, voriconazole: they can slow down the removal of diazepam from the body and increase its effect.

Taking Afebril with food and drinks

Food does not affect the absorption of Afebril. Patients who use Afebril should also be aware about the simultaneous consumption of alcoholic beverages, because such a combination can enhance the undesirable effects of diazepam, as well as of alcohol.

Pregnancy

It may be used only if there is a clear indication such as seizure control. Your doctor will discuss on the risks and benefits of using this drug during pregnancy.

High doses administered during pregnancy may cause neonatal hypothermia, hypotonia, and respiratory depression.

Tell your doctor or pharmacist if you think you are pregnant or you are planning to get pregnant.

Breastfeeding

Tell your doctor or pharmacist if you are breast-feeding.

Diazepam passes into the breastmilk, therefore it should be avoided during breastfeeding.

Driving and using machines

Patients using Afebril should not engage in activities requiring complete mental alertness, such as the use of dangerous machinery or driving.

Important information about some of the excipients of Afebril

This medicine contains 6 mg benzoic acid and 30 mg sodium benzoate in each plastic vial of 2.5 ml, which are equivalent to 2.4 mg / ml benzoic acid and 12 mg / ml sodium benzoate. Benzoic acid and sodium benzoate may cause allergic reactions and mild local irritations.

This medicine contains 50 mg benzyl alcohol in each plastic vial of 2.5 ml, which is equivalent to 20 mg / ml benzyl alcohol. Benzyl alcohol may cause allergic reactions and mild local irritations.

This medicine contains 1000 mg propylene glycol in each plastic vial of 2.5 ml, which is equivalent to 400 mg / ml propylene glycol.

3. HOW TO USE AFEBRIL

Always use Afebril exactly as your doctor has told you. If you are not sure, talk to your doctor or pharmacist.

Afebril solution is administered rectally.

The patient should be in the lateral position. Use firm pressure with the thumb and two other fingers to empty the content. To avoid suction, maintain pressure until it is withdrawn from the rectum. Press together the patient's buttocks for a short time until the solution is completely absorbed.

Afebril rectal solution should not be used in children under 1 year.

Dosage is as follows:

- For status epilepticus, febrile convulsions, convulsions due to poisoning:

500 micrograms/kg for adults and children over 10 kg, repeated every 12 hours if necessary.

- For acute anxiety and agitation:

500 micrograms/kg repeated after 12 hours if necessary. It is not recommended for children.

Elderly and debilitated patients should be given not more than one half the usual adult dose.

Dosage reduction may also be required in patients with hepatic or renal impairment.

If you use more Afebril than you should

If you use more Afebril than you should, or if the children have been taking this medicine by accident, please contact your doctor, the hospital or call the emergency to get an opinion of the risk and advice on the action to be taken.

Symptoms

Impairment of consciousness is fairly rapid in poisoning by benzodiazepines. Deep coma or other manifestations of severe depression of brainstem vital functions are rare; more common is a sleep-like state. Since tolerance to benzodiazepines develops rapidly, consciousness is often regained while drug concentrations in the blood are higher than those which induced coma. Anxiety and insomnia can occur during recovery from acute overdosage, while a full-blown withdrawal syndrome, possibly with major convulsions, can occur in patients who have previously been chronic users.

Treatment

The treatment of benzodiazepine overdosage is generally symptomatic and supportive. The specific benzodiazepine antagonist, flumazenil, is rarely required and can be hazardous, particularly in mixed overdoses involving tricyclic antidepressants or in benzodiazepine-dependent patients. Flumazenil should be used only by highly qualified doctors.

If you forget to use Afebril

If you forget a dose, use the next dose when it is the normal time to use it.
Do not use a double dose to make up for the forgotten dose.
If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Afebril can cause side effects, although not everybody gets them.
The most common side effects are: drowsiness, tiredness, muscle weakness, and fatigue.
Less frequent are: confusion, gastrointestinal disturbances, skin reactions, depression, headache, hypotension, urinary retention, slurred speech, changes in salivation, tremor, vertigo, blurred vision, respiratory depression, changes in libido.

In rare cases jaundice, blood disorders, and hypersensitivity reactions have been observed. Paradoxical reactions such as instant excitement, anxiety, sleep disorders, aggressiveness were observed.

Dependence: symptoms of benzodiazepine dependence include: anxiety, depression, impaired concentration, insomnia, headache, dizziness, tinnitus, loss of appetite, tremor, perspiration, irritability, perceptual disturbances (such as hypersensitivity to physical, auditory, and visual stimuli), abnormal taste, nausea, vomiting, abdominal cramps, palpitations, tachycardia, mild systolic hypertension and orthostatic hypotension. Rare and more serious symptoms include: paranoid psychosis, convulsions, hallucinations, and a state resembling delirium tremens, sleep disorders.

If you notice any of these side effects or any side effect not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE AFEBRIL

Keep out of the reach and sight of children.
Do not use Afebril after the expiry date which is stated on the package.
Do not store above 25°C.
Store in the original package to protect it from the impact of external factors.

6. FURTHER INFORMATION

What Afebril – rectal solution contains

The active substance is diazepam.
Every rectal solution 2.5 ml contains 5 mg diazepam.
The excipients are: ethanol 96%, propylene glycol, benzyl alcohol, benzoic acid, sodium benzoate, hydroxypropyl cellulose, sodium hydroxide solution, purified water.

Content of the pack

The form of the packaging is box with 5 rectal solutions of 2.5 ml.

Marketing Authorisation Holder (MAH) and Manufacturer:

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Tirana, Albania.

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