

Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

The medicine is dispensed with a doctor's prescription only

Assival 2 mg Tablets

Composition:
Each tablet contains:
Diazepam 2 mg

Assival 5 mg Tablets

Composition:
Each tablet contains:
Diazepam 5 mg

Assival 10 mg Tablets

Composition:
Each tablet contains:
Diazepam 10 mg

For information about inactive ingredients and allergens, see section 2. Important information about some of this medicine's ingredients, and section 6. Additional information.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

Introduction

This medicine belongs to a group called benzodiazepines, which has special properties that require extreme caution when used.

- Close medical follow-up is very important when taking this medicine.
- When you take this medicine, be sure to contact your doctor after 2-4 weeks, as the treatment is only intended for short periods of time.
- Prolonged use of this medicine may cause it to be less effective.
- This use may lead to a serious side effect of dependence, where it will be difficult for the patient to stop taking the medicine.
- Uncontrolled discontinuation of treatment is accompanied by withdrawal symptoms such as tension, nervousness, confusion, tremors, insomnia, abdominal pain, nausea, vomiting, sweating, spasms.
- At times, prolonged use of this medicine may cause changes in behavioral patterns and intrusive thoughts.
- Particularly in the elderly, be careful when walking, as the medicine inhibits alertness and at times coordination of body movements, and therefore there is a concern of slips and falls.

Taking this medicine along with opioids, other central nervous system depressants (including drugs) or alcohol may cause a sense of deep drowsiness, difficulty breathing (hypoventilation), coma and death.

1. What is this medicine intended for?

Assival is intended for the treatment of tension, anxiety, agitation due to acute alcohol withdrawal, adjunct for the relief of skeletal muscle spasm, convulsive disorders.

Therapeutic group: Benzodiazepines.

This medicine is not generally intended for children.

This medicine should be used for as short a time as possible and for no more than four weeks. If used for a long time without a break, there is a risk of becoming dependent or of having problems when you stop the treatment.

When taking this medicine, there is a risk of dependence (a need to keep taking the medicine). The risk increases with the dose and length of treatment. The risk is greater if you have a history of alcohol or drug abuse.

2. Before using the medicine

Do not use this medicine if:

- You are **sensitive (allergic)** to the active ingredient or other benzodiazepine medicines or to any of the other ingredients in this medicine (see section 6 - Additional information).
- You have **breathing problems**, which may be severe, including slow and/or shallow breathing.
- You suffer from **depression** (with or without anxiety) or hyperactivity.
- You have a **phobia** (a fear of particular object or situation) or other mental illness.
- You have **severe myasthenia gravis** (a condition which causes muscles to weaken and tire easily).
- You suffer from **sleep apnea** (a sleep disorder where you have abnormal pauses in breathing during sleep).
- You have **severe liver disorders**.
- You have **porphyria** (an inherited condition causing skin blisters, abdominal pain and brain or nervous system disorders).
- You are **planning a pregnancy** or are **pregnant** (see below under "Pregnancy and breastfeeding").

Special warnings about using this medicine

Before using Assival, tell your doctor if:

- You have a history of **alcoholism or drug abuse** • You have problems with your **heart and lungs** or have **severe kidney failure** • You have someone **close to you** who has recently died • You have **low blood levels** of a protein called albumin
- You have a **personality disorder** • You have a poor blood supply to the brain (**arteriosclerosis**) • You are **elderly**. Assival tablets can cause confusion and have effects on muscles causing falls and injuries • You have **breathing difficulties** • You **smoke** • You suffer from **depression** • You have **suicidal thoughts** • You have **epilepsy** or a history of **seizures**.

Other considerations

- **Mental side effects** – tell your doctor if you experience side effects such as agitation, hyperactivity, restlessness, aggressiveness, nightmares or hallucinations. These side effects are more likely to occur in children or the elderly.
- **Amnesia** (total or partial memory loss) – you could experience amnesia when taking this medicine. Amnesia is more likely to occur when taking high doses of Assival.
- **Dependence** – when taking this medicine there is a risk of dependence, which increases with the dose and length of the treatment period and also in patients with a history of alcohol and drug abuse. Therefore, you should take Assival for as short a time as possible.
- **Tolerance** – if after a few weeks you notice that the medicine is not working as well as it did when first starting treatment, you should consult with your doctor.
- **Withdrawal** – treatment should be gradually withdrawn. Withdrawal symptoms occur with Assival even when normal doses are given for short periods of time. See section 3 under "Stopping use of Assival and withdrawal symptoms".

Drug interactions:

If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist. Particularly if you are taking:

- **Sodium oxybate** (used to prevent episodes of sudden onset of sleep (narcolepsy) with muscle weakness).
 - **Antidepressants** (e.g. fluvoxamine, fluoxetine).
 - **Antipsychotics** such as clozapine (to treat mental problems).
 - **Antihistamines** (to treat allergies).
 - **General anesthetics**.
 - **Sedatives** (used to give calming effects).
 - **Hypnotics** (to help you sleep).
 - **Erythromycin** (an antibiotic).
 - **Muscle relaxants** (e.g. suxamethonium, tubocurarin).
 - Some **strong pain killers** such as **morphine** (opioids) may give you a heightened sense of wellbeing when taken with Assival, which can increase your desire to continue taking these medicines (dependency) or can make you very sleepy.
 - Barbiturates such as **phenobarbital** (to treat epilepsy and mental disorders).
 - **Medicines to lower high blood pressure, diuretics, nitrates** (for heart conditions) as these could lower your blood pressure too much.
 - **Antacids** (reduce stomach acid) may slow down absorption of Assival in the body.
- Taking these medicines with Assival could affect your mental status, make you very sleepy and suppress your breathing and blood pressure.
- **Disulfiram** (to treat alcohol addiction). Taking this medicine with Assival could make you very sleepy and can cause Assival to be removed from the body more slowly than usual.
 - **Medicines for epilepsy**, e.g. phenobarbital, phenytoin and carbamazepine, sodium valproate (Assival can affect the blood levels of these medicines). Assival can furthermore affect how phenytoin works.
 - **Theophylline** (to treat asthma and other breathing disorders). It can weaken the effect of Assival, because it can cause Assival to be removed from the body more quickly than usual.
 - **Cimetidine, omeprazole or esomeprazole** (stomach acid reducing medicines), as these can cause Assival to be removed from the body more slowly than usual.
 - **Rifampicin**, to treat infections (an antibiotic) as this can cause Assival to be removed from the body more quickly than usual. The effect of Assival can be weakened.
 - **Hypericum perforatum** (St. John's wort, an herbal remedy).
 - **Amrenavir, atazanavir, ritonavir, delavirdine, efavirenz, indinavir, nelfinavir, zidovudine, saquinavir** (antivirals), **fluconazole, itraconazole, ketoconazole or voriconazole** (anti-fungal medicines) as these can cause Assival to be removed from the body more slowly than usual and therefore increase the risk of side effects. They can make you feel sleepy for longer or cause difficulty breathing.
 - **Isoniazid** (used to treat tuberculosis), as it can cause Assival to be removed from the body more slowly than usual.
 - **Oral contraceptives**, as they can slow down the removal of Assival from the body and increase its effect. Breakthrough bleeding can occur when taking Assival and oral contraceptives together, but the contraceptive protection is not reduced.
 - **Cisapride** (used to treat stomach problems), as it can cause Assival to be removed from the body more slowly than usual.
 - **Corticosteroids** (medicines used to treat inflammation in the body) as they can weaken the effect of Assival.
 - **Levodopa** (used to treat Parkinson's disease). Assival can reduce the effect of levodopa.
 - **Valproic acid** (used to treat epilepsy and mental disorders) as it can slow down the removal of Assival from the body and increase its effect.
 - **Ketamine** (an anesthetic) as Assival increases the effect of ketamine.
 - **Lofexidine** (to help relieve symptoms when you stop taking opioids).
 - **Nabilone** (to treat nausea and vomiting).
 - **Alpha blockers, beta blockers or moxonidine** (to lower high blood pressure).

Concomitant use of Assival and opioids (strong pain killers, medicines for substitution therapy and some cough medicines) increases the risk of deep drowsiness, difficulties in breathing (respiratory depression), coma and may be life threatening. Because of this, concomitant use should only be considered when other treatment options are not possible. However, if your doctor does prescribe Assival together with opioids, the dose and duration of concomitant treatment should be limited by your doctor. Please tell your doctor about all opioid medicines you are taking, and follow your doctor's dose recommendation closely. It could be helpful to inform friends or relatives to be aware of the signs and symptoms stated above. Contact your doctor when experiencing such symptoms.

Using this medicine and alcohol consumption

Do not drink alcohol while taking Assival. Alcohol may increase the sedative effects of Assival and make you very sleepy.

Using this medicine and food
Grapefruit juice may increase the amount of Assival in your blood. If you are elderly, suffer from cirrhosis or any of the conditions listed in section 2, drinking grapefruit juice could possibly increase the sedative effects of Assival, and you should speak to your doctor or pharmacist.

Drinks containing caffeine may reduce the effect of the medicine.

Pregnancy, breastfeeding and fertility.

Do not take Assival if you are pregnant, might be pregnant or breastfeeding. If you and your doctor decide that you should take this medicine towards the end of your pregnancy (or during labor) this may harm your baby. The baby may have a low temperature, be listless, have breathing problems or difficulty in feeding. Also, if you take this medicine regularly during your pregnancy, your baby may develop withdrawal symptoms. If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines

Assival can make you sleepy, forgetful, have poor coordination along with other side effects that can affect everyday activities (see section 4 - "side effects"). You should not drive or operate dangerous machines or take part in activities, which when under the influence of Assival, could put you or others at risk.

This medicine can affect your ability to drive as it may make you sleepy or dizzy. Do not drive while taking this medicine until you know how Assival affects you. Consult your doctor or pharmacist if you are not sure whether it is safe for you to drive while taking this medicine.

Important information about some of this medicine's ingredients

Assival 2 mg, 5 mg and 10 mg contain lactose. If you have been told that you have intolerance (sensitivity) to some sugars, consult your doctor before taking this medicine. Assival 5 mg contain FD&C Yellow No. 6 (E110), which may cause allergic reactions.

3. How to use this medicine?

Always use according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine. Only your doctor will determine your dose and how you should take this medicine.

Do not exceed the recommended dose.

This medicine is not generally intended for children.

Elderly or frail

If you are elderly or frail, you are likely to be more sensitive to the effects of Assival, such as confusion, and your doctor will prescribe you much lower doses. The dose should not be more than half the adult dose.

Kidney or liver impairment

If you have liver or kidney problems, you may also be given a lower dose.

Directions for use

There is no information about crushing and chewing.

You may split the tablet (2 mg, 5 mg and 10 mg) on the score line.

Swallow the medicine with water.

If you have accidentally used a higher dose

If you (or someone else) swallow a lot of tablets at the same time, or you think a child may have accidentally swallowed some medicine, contact your doctor or nearest hospital emergency room immediately. Signs of an overdose include clumsiness and loss of coordination, feeling sleepy or deep sleep, speech problems, irregular or slow heartbeat, uncontrolled eye movement, muscle weakness or excitement. An extreme overdose may lead to coma (unroutable unconsciousness), reflex problems and breathing difficulties.

If you forget to take the medicine

Do not take a double dose to make up for the forgotten dose. If you forget to take a dose, take it as soon as you remember it and then take the next dose at the right time. Adhere to the treatment as recommended by your doctor.

Stopping use of Assival and withdrawal effects

This medicine should not be stopped suddenly; keep taking it until your doctor tells you how to reduce the dose gradually. If you stop taking the tablets suddenly, you may experience the following side effects:

- **Depression** • **Nervousness** • **Difficulty sleeping** • **Restlessness** • **Sweating** • **Upset stomach/diarrhea** • The symptoms you are being treated for can come back worse than before.
- You may also experience mood changes, anxiety, restlessness and changes in sleep patterns. These effects may occur even after taking low doses for a short period of time. If you stop taking the medicine suddenly after being treated with high doses of Assival, you may experience confusion, hallucinations, shaking, faster heartbeat or fits. Withdrawal may also cause unusual behavior, including aggressive outbursts, excitement or depression with suicidal thoughts or actions.

Do not take medicines in the dark! Check the label and dose every time you take medicine. Wear glasses if you need them. If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. Side effects

Like with all medicines, using Assival may cause side effects in some users. Do not be alarmed by this list of side effects. You may not experience any of them. Consult your doctor if you notice any of the following side effects or any other effect that does not appear here:

Some side effects can be serious and may require immediate medical treatment:

Uncommon side effects (occur in up to 1 in 100 patients)

- Respiratory depression (very slow and/or shallow breathing).

Rare side effects (occur in up to 1 in 1,000 patients)

- Respiratory arrest (cessation of breathing) • Unconsciousness • Jaundice (yellowing of your skin or the white of your eyes).

Very rare side effects (occur in up to 1 in 10,000 patients)

- Anaphylaxis (severe allergic reaction) with symptoms such as sudden wheezing, swelling of your lips, tongue and throat or body, rash, fainting or difficulties to swallow.

Other side effects:

Very common side effects (occur in more than 1 in 10 patients)

- Drowsiness.

Common side effects (occur in up to 1 in 10 patients)

- Fatigue • Withdrawal symptoms (for possible symptoms, please see "Stopping use of Assival and withdrawal effects" in section 3) • Confusion • Loss of coordination of muscle movements (ataxia) and other movement disorders, tremor.

Uncommon side effects (occur in up to 1 in 100 patients)

- Muscle weakness • Memory loss • Difficulty in concentrating • Balance disorders • Dizziness • Headache • Slurred speech • Stomach and intestinal problems such as nausea, vomiting, constipation, diarrhea • Increased salivation • Allergic skin reactions in the form of itching, skin redness and swelling and skin rash.

Rare side effects (occur in up to 1 in 1,000 patients)

- Mental side effects such as excitation, agitation, restlessness, irritability, aggressiveness, memory loss, inappropriate behavior, delusion, rages, psychoses, nightmares or hallucinations. These side effects may appear or become serious. These side effects are more likely to occur in the elderly. Consult your doctor • Decreased alertness • Depression • Emotional withdrawal • Insomnia (problems sleeping) • Heart problems such as slow heartbeat (bradycardia), heart failure and cessation of heartbeat (cardiac arrest) • Low blood pressure, fainting (syncope) • Increased mucus in the lungs • Dry mouth • Increased appetite • Changes in certain liver enzymes as seen in blood tests • Difficulty urinating, loss of bladder control (leakage of urine) • Breast enlargement in men • Impotence, changes in sexual drive (libido) • Blood disorders (you may develop sore throats, nose bleeds or infections).

Very rare side effects (occur in up to 1 in 10,000 patients)

- Low levels of white blood cells (leukopenia) • Higher level of a certain enzyme in the blood (transaminase).

Side effects of unknown frequency (the frequency of these effects has not been established yet):

- Blurred vision, double vision and involuntary eye movements (these side effects disappear after you have stopped taking Assival).

Withdrawal symptoms: See section 3 under "Stopping use of Assival and withdrawal symptoms".

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor or pharmacist.

Report side effects

You can report side effects to the Ministry of Health by following the link "Reporting Side Effects of Drug Treatment" on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link: <https://sideeffects.health.gov.il>

5. How to store the medicine?

- Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.
- **Store the medicine in a dry place, below 25°C.**
- Do not throw away medicines via wastewater or household waste. Ask the pharmacist how to throw away medicines that you no longer use. These measures will help protect the environment.

6. Additional information

In addition to the active ingredient, this medicine also contains:

Assival 2 mg: Lactose Monohydrate, Starch, Microcrystalline Cellulose, Povidone, Magnesium Stearate, Esmal Sprayng.

Assival 5 mg: Lactose Monohydrate, Starch, Microcrystalline Cellulose, Povidone, Magnesium Stearate, Esmal Sprayng, D&C Yellow No.10 Aluminum Lake, FD&C Yellow No.6 Aluminum Lake (E110).

Assival 10 mg: Microcrystalline Cellulose, Lactose Spray Dried, Esmal Sprayng, Magnesium Stearate, FD&C Blue No.2 Lake.

What the medicine looks like and the size of the pack

Assival 2 mg: White, round flat tablet with beveled edges, scored in half on one side, engraved "TEVA" on the other.

Each pack contains 30 or 1000 tablets in a blister pack.

Assival 5 mg: Yellow, round flat tablet with beveled edges, scored in half on one side, engraved "TEVA" on the other.

Each pack contains 30 or 1000 tablets in a blister pack.

Assival 10 mg: Light blue, round flat tablet with beveled edges, scored in half on one side, engraved "TEVA" on the other.

Each pack contains 30 tablets in a blister pack.

Not all pack sizes may be marketed.

Manufacturer and registration holder's name and address

Teva Pharmaceutical Industries Ltd., P.O.Box 3190, Petah-Tiqva.

The leaflet was revised in November 2020.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:

2 mg: 014.90.24264, 5 mg: 014.61.24381, 10 mg: 058.48.21634

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