Patient Package Insert in Accordance With the Pharmacists' Regulations (Preparations) – 1986

This medicine is dispensed with a doctor's prescription only

Bondormin

Tablets

Active ingredient:
Each tablet contains Brotizolam 0.25 mg
For the list of the additional ingredients, see section 6.
See also 'Important information about some of the medicine's ingredients' in section 2.

Read this entire leaflet carefully before using the medicine.
This leaflet contains concise information about the medicine. If you have any further questions, please refer to the doctor or pharmacist.
This medicine has been prescribed for treatment for you. Do not pass it on to others under any circumstance. It may harm them, even if you think their medical condition is similar to yours.

Introduction to the patient leaflet for benzodiazepines
This medicine belongs to the benzodiazepine group which has special properties requiring extreme caution while using it.
Close medical monitoring is very important when taking this medicine.
When taking this medicine, be sure to contact the doctor after 2 weeks, since the treatment is intended for short time periods only.
Prolonged use of the medicine may cause the effect of the medicine to be lessened.
Prolonged use may cause a severe effect of dependence, making it difficult for the patient to stop taking the medicine and therefore you should stop taking the medicine gradually, as instructed by the doctor.
Uncontrolled discontinuation of treatment may be accompanied by withdrawal symptoms such as: tension, irritability, confusion, tremor, insomnia, abdominal pain, vomiting, nausea, sweating, convulsions, muscle pains and spasms.
See 'If you stop taking the medicine' in section 3.
Sometimes, prolonged use of the medicine may cause changes in behavioral patterns and disturbing thoughts.
Particularly for elderly care is recommended when walking, since the medicine impairs alertness and sometimes coordination of body movements, therefore there is concern of stumbling or falling.

Taking this medicine along with medicines from the opioid group, other medicines that depress the central nervous system (including drugs) or alcohol, may cause a feeling of profound drowsiness, breathing difficulties (respiratory depression), coma, and death.

1. What is the medicine intended for?

Bondormin is a medicine intended for the treatment of sleep problems.

Therapeutic group: benzodiazepines
The medicine does not treat the cause of the sleep disturbances.

2. Before using the medicine

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient, to other benzodiazepines, or to any of the other ingredients the medicine contains (for the list of the other ingredients, see section 6).
- You are pregnant or breastfeeding.
- You suffer from severe respiratory insufficiency, sleep apnea syndrome (breathing pauses during sleep), severe liver insufficiency, myasthenia gravis which is a disease manifested in muscle weakness, or if you suffer or have suffered in the past from dependence on medicines, illicit drugs or alcohol.
- You suffer from intoxication from alcohol, sleeping pills, opioid painkillers, or psychiatric medicines (such as antipsychotic medicines, antidepressants, lithium).
- Do not use the medicine in children and adolescents under the age of 18.

Special warnings regarding the use of the medicine:
Before treatment with Bondormin, tell the doctor if:

- You abuse or have abused in the past alcohol, illicit drugs and medicines.
- If you are already being treated with Bondormin.
- If you suffer or have suffered in the past from impaired function of: the respiratory system, the liver. In these cases, the doctor may recommend a reduced dosage.
- If you suffer or have suffered in the past from depression or suicidal thoughts.
- If you are sensitive to any food or medicine.

Additional warnings

- Prolonged use may cause physical and psychological dependence! The risk of dependence on the medicine increases with the dose increase and treatment duration . Therefore, the doctor will direct you to use the medicine for as short a period as possible and may also perform periodical monitoring. Psychological dependence can be recognized when you reach a point where you do not want to stop using the medicine. If a physical dependency on the medicine exists, sudden discontinuation will be accompanied by withdrawal symptoms (see the 'If you stop taking the medicine' section). The risk of developing dependence is also higher in patients who abuse or have abused in the past medicines or alcohol (see 'If you stop taking the medicine' in section 3).
- Your memory may be impaired during the treatment with the medicine. This effect usually occurs several hours after taking the medicine. Contact the doctor if you experience this effect.
- If you suffer from psychosis (a serious psychiatric illness that affects behavior and self-control), Bondormin is not suitable for you.
- If you suffer from severe depression or anxiety with episodes of severe depression, treatment with Bondormin may increase the risk of developing self-harming or suicidal thoughts. Consult your doctor before treatment with the medicine. Your doctor will closely monitor you during the treatment with Bondormin. Whenever these thoughts arise, contact your doctor or go to the hospital immediately.
- Do not use this medicine frequently or for a long period without consulting your doctor.
- Taking the medicine daily for several weeks may decrease the effectiveness of the medicine.
- Bondormin has a muscle relaxation effect, which may increase the risk of falls. Use with caution in the elderly.

If you are taking, or have recently taken any other medicines, including non-prescription medicines and nutritional supplements, please tell your doctor or pharmacist. Especially inform your doctor or pharmacist if you are taking the following medicines (it should be noted that the following list indicates

the active ingredients in the medicines. If you are not sure whether you are using one of these medicines, please consult with your doctor or pharmacist):

- Medicines that affect the central nervous system (e.g. sedatives, sleeping pills, antidepressants or antianxiety medicines, antipsychotic medicines, medicines for treatment of epilepsy, certain antihistamines, anesthetics, narcotic painkillers) - use of these medicines during treatment with Bondormin could lead to increased suppression of the central nervous system.
- Opioids (strong painkillers, drug substitution medicines, and certain cough medicines) - simultaneous use with Bondormin increases the risk of drowsiness, breathing difficulties (respiratory depression), coma and even death. Therefore prescribing opioids with Bondormin should be considered only when no other treatment options exist. If your doctor instructs you to take Bondormin together with opioids, he might limit the dosage and duration of the treatment. Tell the doctor if you are taking opioid-containing medicines and closely follow the doctor's recommendations. If you observe any of the symptoms, refer to the doctor immediately.
- Strong painkillers from the opioid group - simultaneous use with Bondormin can increase the feeling of euphoria and accelerate dependence.
- Muscle relaxants - concomitant use with Bondormin, may increase the muscle relaxing effect.
- Medicines for treatment of diabetes and high blood pressure, medicines for treatment of heart problems (e.g. digoxin), hormones - caution should be exercised when these medicines are used concomitantly with Bondormin since there may be an interaction.
- The following medicines may cause an increase in the effect of Bondormin: antifungals from the azole group(e.g. itraconazole, ketoconazole), antibiotics from the macrolide group(e.g. clarithromycin, erythromycin), protease inhibitors (e.g. indinavir, nelfinavir, ritonavir), cimetidine, astemizole, immunosuppressants (e.g. ciclosporin, sirolimus, tacrolimus), calcium channel blockers, anti-malaria medicines such as mefloquine and halofantrine, midazolam, pimozide, sildenafil, medicines to lower cholesterol from the statins group (e.g. atorvastatin, lovastatin, simvastatin), steroids (e.g. ethinylestradiol), tamoxifen, terfenadine.
- The following medicines may cause a decrease in the effect of Bondormin: carbamazepine, efavirenz, St. John's wort (Hypericum), nevirapine, phenobarbital, phenytoin, primidone, rifabutin, rifampicin.

Use of this medicine and food:

- Take the medicine on an empty stomach.
- Do not drink grapefruit juice during the treatment.

Use of the medicine and alcohol consumption: Do not drink wine or alcoholic beverages during the treatment period with the medicine. Use of alcohol during the treatment with Bondormin can cause sedation, fatigue, and difficulty concentrating.

Pregnancy, breastfeeding and fertility:

Do not use the medicine if you are pregnant or breastfeeding.

Babies born to mothers who took benzodiazepines for a long time during the pregnancy may develop physical dependence. These children had withdrawal symptoms in the period after birth. In addition, in high dosages in advanced stages of pregnancy and close to childbirth, may cause respiratory depression in the newborn. There is a low chance of impaired development of the fetus when benzodiazepines are used in early pregnancy stages.

If you are pregnant, planning to become pregnant, or suspect you are pregnant, refer to your doctor.

There is no clinical information on the effects of the medicine on fertility.

Driving and use of machinery:

This medicine can affect the ability to react, even when used according to the doctor’s instructions, and can therefore impair the ability to drive and to use machinery. Use of the medicine may impair alertness, the ability to concentrate and muscle functioning (especially with an insufficient amount of sleep, if used

concomitantly with medicines that depress the central nervous system or concomitantly with alcohol). If you feel symptoms such as those listed above, do not drive or operate machinery. In any case, employ caution in driving a vehicle, operating dangerous machinery and in any activity requiring alertness.

Use in children and adolescents: This medicine is not intended for children and adolescents under the age of 18 (efficacy and safety have not been investigated for this population group).

Use in the elderly, in debilitated patients, patients with impaired liver function or patients with respiratory failure: this group may be more sensitive to the effects of the medicine, and therefore it should be used cautiously and with a reduced dosage. The effects of the medicine, particularly in the elderly, include increased risk of falling as a result of muscle relaxation (see 'Introduction').

Important information about some of the medicine's ingredients:
Bondormin contains lactose. If you are sensitive to lactose, inform the doctor before taking this medicine.

3. How to use this medicine?

Always use according to the doctor's instructions. Check with your doctor or pharmacist if you are not sure.
The dosage and manner of treatment will be determined by the doctor only.
The standard dosage is usually: half a tablet up to one tablet (as decided by the doctor), before going to sleep.

Under no circumstance should you exceed the recommended dose.
There is no information on crushing or chewing the tablets. Swallow the medicine with water or gradually dissolve under the tongue. The medicine should be taken on an empty stomach.
The tablet may be halved according to the scored line.
make sure to get at least 7 hours of sleep after taking the medicine, in order to function properly after waking up (see also 'Driving and use of machinery' section).

If you accidentally took a higher dosage: if you took an overdose or if a child has accidentally swallowed the medicine, proceed immediately to a hospital emergency room and bring the package of the medicine with you.
Symptoms of an overdose may include drowsiness, confusion, fatigue. In severe cases, impaired coordination, reduction in muscle tone, low blood pressure, respiratory depression, coma (rare), and death (very rare) may occur.

If you stop taking the medicine: even if your condition improves, do not stop the treatment with the medicine suddenly without consulting your doctor. This instruction is particularly important for a medicine such as Bondormin (see 'Introduction').

- Sometimes after discontinuation of the medicine, there may initially be a rebound or worsening of the sleep problems and also in rare cases restlessness, mood changes, anxiety and tension. The risk of this is higher when the treatment is stopped suddenly or the dosage is reduced suddenly.
- There may also be withdrawal symptoms after sudden discontinuation of the medicine (particularly if dependence on the medicine has developed), such as: headache, muscle pain, extreme anxiety, tension, sleep problems, restlessness, confusion, irritability. In severe cases, there may be an erroneous perception of reality, personality changes, lack of sensation and tingling sensation in the arms and/or legs, hypersensitivity to light, sounds and touch; hallucinations and epileptic fits. These effects can occur even several days after discontinuing the medicine. Please consult the doctor if you experience these withdrawal symptoms.

Therefore, the doctor will reduce the dosage of the medicine gradually at the end of the treatment. The dose reduction will be adjusted for the patient individually, as it depends on several factors (for instance the duration of treatment and the daily dose). Please consult your doctor how to reduce the dose.
Do not take medicines in the dark! Check the label and the dose <u>each time</u> you take a medicine. Wear glasses if you need them.
If you have further questions concerning the use of the medicine, consult the doctor or pharmacist.

4. Side effects

As with any medicine, use of Bondormin may cause side effects in some users. If side effects occur or if the side effects persist or are bothersome or get worse, please consult your doctor. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Contact your doctor immediately if any of the following side effects occur:

- Paradoxical reactions such as: restlessness, agitation, irritability, anger, aggression, increased insomnia, nightmares, hallucinations, psychoses, changes in behavior patterns including inappropriate conduct, confusion and frenzy (delirium) (uncommon side effects). These reactions may occur during the treatment with benzodiazepines and particularly in the elderly.

Other Side Effects:

Common side effects (appear in 1-10 users out of 100): headache, spinning sensation, disturbances of the digestive system.
Uncommon side effects (appear in 1-10 users out of 1,000): nightmares, depression, mood changes, anxiety, dependency on the medicine, emotional disturbances, behavioral changes, agitation, changes in libido, dizziness, sedation, fatigue, lack of coordination and impaired coordination of body movements (ataxia), memory disorders, dementia, mental and psychomotor impairment, visual disturbances (e.g. double vision), liver disorders (e.g. jaundice and changes in values in liver function tests), dry mouth, skin reactions, muscle weakness, withdrawal symptoms and rebound or worsening of the sleep problems after stopping the medicine, drowsiness (during the day), irritability, increase in risk of accidents and falls.
Rare side effects (appear in 1-10 users out of 10,000): confusion, restlessness, decrease in alertness and preparedness.

If a side effect appears, if one of the side effects worsens, or if you suffer from a side effect not mentioned in the leaflet, consult with the doctor.

- The following side effects may occur, especially at the start of the treatment: drowsiness on the following day, emotional flattening, reduction in alertness and preparedness, confusion, fatigue, dizziness, headache, muscle weakness, lack of coordination and impaired coordination of body movements (ataxia), visual disturbances (double vision). These symptoms usually decrease during the treatment.
- Because of the muscle relaxant effect of Bondormin, caution must be exercised, especially in the elderly (risk of falling).
- Cases of benzodiazepine abuse have been reported.
- Withdrawal symptoms - physical and psychological dependence may develop during the treatment. Sudden discontinuation of the treatment can cause certain symptoms (see 'If you stop taking the medicine' in Section 3).
- Depression that existed before the treatment with Bondormin may be revealed during the treatment.

Side effects may be reported to the Ministry of Health by clicking on the link "Report on side effects following medicinal treatment" on the homepage of the Ministry of Health website (www.health.gov.il) which leads to an online form for reporting side effects, or by entering the link:
https://sideeffects.health.gov.il/

5. How to store the medicine?

- Avoid poisoning! This medicine, and any other medicine, must be stored in a closed place out of the reach and sight of children and/or infants, to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) stated on the package. The expiry date refers to the last day of that month.
- Storage conditions: store below 25°C.

6. Additional information

In addition to the active ingredient, the tablets also contain the following ingredients:
Lactose, corn starch, cellulose microcrystalline, sodium starch glycolate, magnesium stearate

Each tablet contains about 82 mg lactose.

What does the medicine look like and what does the package contain?
Round white tablets with a score line, in blister packs of 10 or 20 tablets per box. Not all package sizes may be marketed.

Registration Holder: Rafa Laboratories Ltd., PO Box 405, Jerusalem 9100301

Medicine registration number. in the National Medicine Registry of the Ministry of Health: 120 37 26021 12.
This leaflet was revised in April 2023 according to MOH's guidelines.

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