

Patient leaflet in accordance with Pharmacist's Regulations (Preparations) 1986

The medicine is marketed according to doctor's prescription only.

**Rexulti 0.5 mg, Rexulti 1 mg, Rexulti 2 mg, Rexulti 3 mg, Rexulti 4 mg
film coated tablets**

Composition

Each film coated tablet of Rexulti contains the active ingredient:

Rexulti 0.5 mg: Brexpiprazole 0.5 mg

Rexulti 1 mg: Brexpiprazole 1 mg

Rexulti 2 mg: Brexpiprazole 2 mg

Rexulti 3 mg: Brexpiprazole 3 mg

Rexulti 4 mg: Brexpiprazole 4 mg

Inactive ingredients

See section 6.

- **Read the leaflet carefully until the end before using the medication.** This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or the pharmacist.

- This medicine was prescribed for you. Do not pass it on to others. It may harm them even if their ailment/ medical condition seems similar to yours.

Warning: Increased Mortality in Elderly Patients with Dementia-Related Psychosis and Suicidal Thoughts and Behaviors

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. REXULTI is not approved for the treatment of patient with dementia-related psychosis without agitation associated with dementia due to Alzheimer's disease.

Suicidal Thoughts and Behaviors

Antidepressants increased the risk of suicidal thoughts and behaviors in patients aged 24 years and younger in short-term studies. Monitor closely for clinical worsening and for emergence of suicidal thoughts and behaviors. The safety and effectiveness of REXULTI have not been established in pediatric patients with MDD (major depressive disorder).

1. What is the medicine for?

REXULTI is indicated for:

- As adjunctive therapy to antidepressants for the treatment of major depressive disorder (MDD) in adults .
- For treatment of schizophrenia in adults and pediatric patients ages 13 years and older.
- Treatment of agitation associated with dementia due to Alzheimer's disease

Limitations of Use:

REXULTI is not indicated as an "as needed" treatment for agitation associated with dementia due to Alzheimer's disease

Therapeutic group: atypical antipsychotic drugs

2. Before using the medicine

Do not use the medicine:

- if you are allergic to the active ingredient (bexpiprazole) or to any of the other ingredients of this medicine (listed in section 6).

Reactions have included rash, facial swelling, urticaria, and anaphylaxis.

Special warnings regarding the use of the medicine

Rexulti may cause serious side effects, including:

- **Increased risk of death in elderly people with dementia-related psychosis.**
Medicines like REXULTI can raise the risk of death in elderly people who have lost touch with reality (psychosis) due to confusion and memory loss (dementia). REXULTI is not approved for the treatment of people with dementia-related psychosis without agitation associated with dementia due to Alzheimer's disease (see framed warning at the beginning of the leaflet).
- **Increased risk of suicidal thoughts and actions** (see framed warning at the beginning of the leaflet).

REXULTI and antidepressant medicines may increase suicidal thoughts and actions in some people 24 years of age and younger, **especially within the first few months of treatment or when the dose is changed.**

Depression and other mental illnesses are the most important causes of suicidal thoughts and actions.

- **How to watch and try to prevent suicidal thoughts and actions?**
 - Pay close attention to any changes, especially sudden changes in mood, behaviors, thoughts, or feelings. This is very important when REXULTI or the antidepressant medicine is started or when the dose is changed.
 - Call the doctor right away to report new or sudden changes in mood, behavior, thoughts, or feelings, or if you develop suicidal thoughts or actions.
 - Keep all follow-up visits with your doctor as scheduled. Call the doctor between visits as needed, especially if you have concerns about symptoms.

Call a doctor right away if you or your family member have any of the following symptoms, especially if they are new, worse, or worry you:

- | | |
|--|---|
| ○ thoughts about suicide or dying | ○ attempts to commit suicide |
| ○ new or worsening depression | ○ new or worsening anxiety |
| ○ feeling very agitated or restless | ○ panic attacks |
| ○ trouble sleeping (insomnia) | ○ new or worsening irritability |
| ○ acting aggressive, being angry, or violent | ○ acting on dangerous impulses |
| ○ an extreme increase in activity or talking (mania) | ○ other unusual changes in behavior or mood |

- **Problems controlling your body temperature so that you feel too warm.** Do not become too hot or dehydrated during treatment with Rexulti: Do not exercise too much; In hot weather stay inside in a cool place if possible; Stay out of the sun; Do not wear too much or heavy clothing ; Drink plenty of water.

Before taking REXULTI, tell your doctor about all of your medical conditions, including if you:

- have or have had heart problems or a stroke
- have or had low or high blood pressure
- have or have had diabetes or high blood sugar or a family history of diabetes or high blood sugar. Your doctor should check your blood sugar before you start Rexulti and during treatment with Rexulti.
- have or have had high levels of total cholesterol, LDL-cholesterol, or triglycerides, or low levels of HDL cholesterol
- have or have had seizures (convulsions)
- have or have had kidney or liver problems
- have or have had a low white blood cell count
- are pregnant or plan to become pregnant. See " Pregnancy and breast-feeding" section below.
- are breastfeeding or plan to breastfeed. See " Pregnancy and breast-feeding" section below.

Children and adolescents:

Schizophrenia

Safety and effectiveness of REXULTI for treatment of schizophrenia have been established in pediatric patients 13 years of age and older.

Major Depressive Disorder

Safety and effectiveness in pediatric patients with major depressive disorder have not been established. Antidepressants increased the risk of suicidal thoughts and behaviors in pediatric patients.

Interactions with other drugs:

If you are taking, or have recently taken, other medicines, including nonprescription medicines and nutritional supplements, tell the doctor or pharmacist.

Use of the medicine and food: REXULTI can be taken with or without food.

Pregnancy and breast-feeding

- Tell your doctor before taking Rexulti, if you are pregnant or plan to become pregnant. REXULTI may harm your unborn baby. Taking REXULTI during your third trimester of pregnancy may cause your baby to have abnormal muscle movements or withdrawal symptoms after birth. Talk to your healthcare provider about the risk to your unborn baby if you take REXULTI during pregnancy.
 - o Tell your healthcare provider if you become pregnant or think you are pregnant during treatment with REXULTI.
- Tell your doctor before taking Rexulti, if you are breastfeeding or plan to breastfeed. It is not known if REXULTI passes into your breast milk. Talk to your doctor about the best way to feed your baby during treatment with REXULTI.

Driving and using machines:

Do not drive a car, operate machinery, or do other dangerous activities until you know how REXULTI affects you. REXULTI may make you feel drowsy.

Important information on some of the ingredients of the medicine:

Rexulti contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, consult with your doctor before taking this medicine.

3. How should you use the medicine?

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure. **The dosage and treatment regimen will be determined by the doctor only.** Rexulti is taken orally, with or without food.

The usual dose is:

Major depressive disorder (MDD) in adults:

The recommended starting Rexulti dosage for the adjunctive treatment of MDD in adults is 0.5 mg or 1 mg once daily.

The doctor may gradually increase the dosage to 2 mg once daily. Dosage increases should occur at weekly intervals based on your response and tolerability. The maximum recommended daily dosage is 3 mg.

Treatment of Schizophrenia (adults and pediatric patients 13 to 17 years):

Adults

The recommended starting Rexulti dosage for the treatment of schizophrenia in adults is 1 mg once daily on Days 1 to 4.

The doctor may gradually increase the dosage to 2 mg once daily on Day 5 through Day 7, then to 4 mg on Day 8 based on your clinical response and tolerability. The recommended target dosage is 2 mg to 4 mg once daily.

Pediatric Patients (13 to 17 years of age)

The recommended starting Rexulti dosage for the treatment of schizophrenia in pediatric patients 13 to 17 years of age is 0.5 mg taken orally once daily on Days 1 to 4. The doctor may gradually increase the dosage to 1 mg once daily on Day 5 through Day 7, then to 2 mg on Day 8 based on the clinical response and tolerability. Weekly dose increases can be made by the doctor in 1 mg increments. A recommended target Rexulti dosage is 2 mg to 4 mg once daily. The maximum recommended daily dosage is 4 mg.

Recommended Dosage for Agitation Associated with Dementia Due to Alzheimer's Disease

The recommended starting REXULTI dosage for the treatment of agitation associated with dementia due to Alzheimer's disease is 0.5 mg taken once daily on Days 1 to 7. The doctor may gradually increase the dosage on Days 8 through 14 to 1 mg once daily, and on Day 15 to 2 mg once daily. The recommended target dose is 2 mg once daily. The dosage can be increased to the maximum recommended daily dosage of 3 mg once daily after at least 14 days, based on clinical response and tolerability.

Take Rexulti exactly as your doctor tells you to take it. Do not change the dose or stop taking Rexulti yourself.

Do not exceed the recommended dosage.

- Do not divide the tablet. The tablets do not have a score/dividing line and therefore the tablets cannot be split into equal doses.

- **If you have accidentally taken a higher dosage**, you should refer to your doctor or go to the nearest hospital emergency room. If a child has accidentally swallowed the medicine, proceed immediately to a doctor or to the emergency room of a hospital and bring the package of the medicine with you.

- If you have forgotten to take the medicine

You should not miss a dose of Rexulti. If you miss a dose, take the missed dose as soon as you remember. If you are close to your next dose, just skip the missed dose and take your next dose at your regular time. Do not take 2 doses of Rexulti at the same time. If you are not sure about your dosing, call your doctor.

- You should complete the treatment as recommended by the doctor. Even if there is an improvement in your health, do not stop the treatment without first talking to your doctor.

Stopping an antidepressant medicine suddenly can cause other symptoms.

- **Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.**

- **If you have any further questions on the use of this medicine, ask your doctor or pharmacist.**

4. Side effects

As with all medicines, the use of Rexulti may cause side effects in some users. Do not be

alarmed at reading the list of side effects. You may not suffer from any of them.

Rexulti may cause serious side effects, including:

- **See section 2 of this leaflet.**
- **Cerebrovascular problems, including stroke, in elderly people with dementia-related psychosis that can lead to death.** REXULTI is not approved for the treatment of patients with dementia-related psychosis without agitation associated with dementia due to Alzheimer's disease.
- **Neuroleptic Malignant Syndrome (NMS):** is a **serious condition that can lead to death.** Call your doctor or go to the nearest hospital emergency room right away if you have some or all of the following signs and symptoms of NMS: high fever; changes in your breathing, pulse, heart rate, and blood pressure; stiff muscles; confusion; increased sweating
- **Uncontrolled body movements (tardive dyskinesia).** Rexulti may cause movements that you cannot control in your face, tongue, or other body parts. Tardive dyskinesia may not go away, even if you stop taking Rexulti. Tardive dyskinesia may also start after you stop taking Rexulti.
- **Unusual and uncontrollable (compulsive) urges.** Some people taking Rexulti have had strong unusual urges, to gamble and gambling that cannot be controlled (compulsive gambling). Other compulsive urges include sexual urges, shopping, and eating or binge eating. If you or your family members notice that you are having new or unusual strong urges or behaviors, talk to your doctor.
- **Low white blood cell count.** Your doctor may do blood tests during the first few months of treatment with Rexulti.
- **Decreased blood pressure (orthostatic hypotension) and fainting.** You may feel dizzy, lightheaded or pass out (faint) when you rise too quickly from a sitting or lying position.
- **Falls.** Rexulti may make you sleepy or dizzy, may cause a decrease in your blood pressure when changing position (orthostatic hypotension), and can slow your thinking and motor skills which may lead to falls that can cause fractures or other injuries.
- **Seizures (convulsions).**
- **Problems controlling your body temperature so that you feel too warm.**
See section 2 of this leaflet.
- **Difficulty swallowing** that can cause food or liquid to get into your lungs.
- **Sleepiness, drowsiness, feeling tired, difficulty thinking and doing normal activities.**

Problems with your metabolism such as:

- **High blood sugar (hyperglycemia) and diabetes.** Increases in blood sugar can happen in some people who take Rexulti. Extremely high blood sugar can lead to coma or death. Your doctor should check your blood sugar before you start, or soon after you start Rexulti and then regularly during long term treatment with Rexulti.

Call your doctor if you have any of these symptoms of high blood sugar during treatment with Rexulti: feel very thirsty; feel very hungry; feel sick to your stomach; need to urinate more than usual; feel weak or tired; feel confused, or your breath smells fruity.

- **Increased fat levels (cholesterol and triglycerides) in your blood.** Your doctor should check the fat levels in your blood before you start, or soon after you start REXULTI, and then periodically during treatment with Rexulti.

- **Weight gain:** You and your doctor should check your weight before you start and often during treatment with Rexulti.

Other side effects- frequencies are according to the clinical trials frequencies

Common side effects – appearing in 1-10 out of 100 users

- Constipation, fatigue, nasopharyngitis, , blood cortisol decreased, increased appetite, sense of restlessness such as feeling like you need to move constantly (akathisia), headache, somnolence, tremor, dizziness, anxiety, restlessness, dyspepsia, diarrhea, blood creatine phosphokinase increased, sedation

Other side effects reported with frequency higher than 1%:

Vision blurred, nausea, dry mouth, salivary hypersecretion, abdominal pain, flatulence, urinary tract infection, blood prolactin increased, myalgia, abnormal dreams, insomnia, increased sweating (hyperhidrosis).

Additional possible side effects with frequency not yet determined

- Dystonia (spasm of the neck muscles, and sometimes tightness of the throat, swallowing difficulty, difficulty breathing, and protrusion of the tongue) may occur in susceptible individuals during the first few days of treatment.

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

Reporting of side effects

Side effects can be reported to the Ministry of Health by clicking on the link "Adverse Drug Reactions Report" that appears on the home page of the Ministry of Health web site (www.health.gov.il), which leads to an online form for reporting side effects. Alternatively you can use the following link: <https://sideeffects.health.gov.il/>

5. How should the medicine be stored?

Avoid poisoning! This medicine and all other medicines should be stored in a closed place out of the reach and sight of children and/or infants in order to avoid poisoning.

Do not induce vomiting unless explicitly instructed by a doctor to do so. Do not use this medicine after the expiry date (exp.date) that appears on the package.

The expiry date refers to the last day of that month.

Storage conditions: Store below 30°C, in the original package in order to protect from light and moisture.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use or expired. These measures will help protect the environment.

6. Additional information

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

lactose monohydrate, corn starch, low-substituted hydroxypropyl cellulose, microcrystalline cellulose,; Colorants - Rexulti 0.5 mg- OPADRY 03A430000 Orange, Rexulti 1 mg- OPADRY 03A420002 Yellow, Rexulti 2 mg- OPADRY 03A410000 Green, Rexulti 3 mg- OPADRY 03A400000 Purple, Rexulti 4 mg- OPADRY 03A480004 White; hydroxypropyl cellulose, magnesium stearate.

- What does the medicine look like and contents of the pack:

Rexulti 0.5 mg: light orange, round, shallow convex; bevel-edged tablet, marked with “BRX” and “0.5”, 7 tablets in package.

Rexulti 1 mg: light yellow, round, shallow convex; bevel-edged tablet, marked with “BRX” and “1”, 28 tablets in package.

Rexulti 2 mg: light green, round, shallow convex; bevel-edged tablet, marked with “BRX” and “2”, 28 tablets in package.

Rexulti 3 mg: light purple, round, shallow convex; bevel-edged tablet, marked with “BRX” and “3”, 28 tablets in package.

Rexulti 4 mg: white, round, shallow convex; bevel-edged tablet, marked with “BRX” and “4”, 28 tablets in package.

License Holder: Lundbeck Israel Ltd., 11 Galgaley Haplada, P.O.B. 13105, Herzliya 4672211

Manufacturer: H. Lundbeck A/S, Ottiliavej 9, DK-2500 Valby, Denmark.

Registration numbers of the medicine in the Ministry of Health registry:

Rexulti 0.5 mg: 163-39-35733

Rexulti 1 mg: 163-40-35734

Rexulti 2 mg: 163-41-35735

Rexulti 3 mg: 163-42-35736

Rexulti 4 mg: 163-43-35737

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