

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr**REXULTI**[®] **brexpiprazole tablets**

Read this carefully before you start taking **REXULTI** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **REXULTI**.

Serious Warnings and Precautions

REXULTI belongs to a group of medicines called atypical antipsychotics. These medicines have been linked to a higher rate of death when used in elderly patients with dementia (which is the loss of memory and other mental abilities).

What is REXULTI used for?

REXULTI is used to treat symptoms of **schizophrenia** in adults. Not all people with this disorder have the same symptoms. Some of the most common symptoms of schizophrenia may include:

- hallucinations (seeing, feeling, hearing or smelling things that are not there)
- delusions (believing things that are not true)
- paranoia (not trusting others or feeling very suspicious)
- avoiding family members and friends and wanting to be alone
- feeling depressed, anxious or tense

REXULTI is also used in combination with antidepressant medications to treat symptoms of **Major Depressive Disorder (MDD)** in adults. It is prescribed when you do not respond adequately to an antidepressant alone and after you have tried different antidepressant treatments during your current depressive episode. Some of the common symptoms of depression may include:

- feeling sad or hopeless
- loss of interest and enjoyment
- a change in appetite or weight
- difficulty concentrating or sleeping
- feeling tired
- headaches
- unexplained aches and pain

REXULTI is also used to manage **agitation associated with Alzheimer's dementia (AAD)** in adults. It is prescribed when you have aggressive behaviours and do not respond well to other approaches that do not involve medications.

REXULTI is not a cure for your condition, but it can help manage your symptoms and help you feel better.

How does REXULTI work?

Antipsychotic medications affect the chemicals that allow your nerve cells to communicate with each other (neurotransmitters). Illnesses that affect the brain may be due to certain chemicals (dopamine and serotonin) in the brain being out of balance. These imbalances may cause some of the symptoms you may be experiencing. Exactly how REXULTI works is unknown. However, it seems to adjust the balance of these chemicals.

What are the ingredients in REXULTI?

Medicinal ingredient: brexpiprazole

Non-medicinal ingredients: corn starch, ferric oxide red (0.25 mg, 0.5 mg, 3 mg), ferric oxide yellow (0.25 mg, 0.5 mg, 1 mg, 2 mg), ferrousferrous oxide (0.25 mg, 2 mg, 3 mg), hydroxypropyl cellulose, hypromellose, lactose monohydrate, low-substituted hydroxypropyl cellulose, magnesium stearate, microcrystalline cellulose, talc, and titanium dioxide.

REXULTI comes in the following dosage forms:

Tablets: 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg and 4 mg.

Do not use REXULTI if:

- you are allergic (hypersensitive) to brexpiprazole or to any of the other ingredients in REXULTI.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take REXULTI. Talk about any health conditions or problems you may have, including if you:

- have or have a family history of diabetes or high blood sugar.
- have high levels of cholesterol or fats (triglycerides) in your blood.
- have or have had seizures (convulsions).
- have or have had high blood pressure.
- have low blood pressure or get dizzy, especially upon standing, or have a history of fainting.
- have sleep apnea.
- have a history of:
 - stroke
 - mini-stroke
 - blood clot in lungs
 - high cholesterol or
 - high blood pressure

Medicines like REXULTI can raise the risk of stroke/mini-stroke in elderly people who have dementia.

- Have or have a family history of:
 - heart problems
 - a condition called “long QT syndrome” or sudden cardiac death at less than 50 years of age
 - any problems with the way your heart beats
 - heart disease
- are taking any medication that affects how your heart beats.
- have or have had liver or kidney problems.
- have or have had a low levels of white blood cells.
- are at risk for developing blood clots. Risk factors include:
 - having a family history of blood clots

- being over the age of 65
- smoking
- being overweight
- having a recent major surgery (such as hip or knee replacement)
- not being able to move due to air travel or other reasons
- taking oral birth control (“The Pill”)
- are dehydrated or suffer from excessive vomiting, diarrhea, or sweating.
- have a history of drug abuse or addiction.
- drink alcohol or use recreational drugs.
- have had problems tolerating the recommended doses of some medicines.
- have been told you are a “CYP2D6 poor metabolizer”.
- have a tumor in your pituitary gland.
- have or have had involuntary, irregular muscle movements, especially in the face (tardive dyskinesia).
- have Parkinson’s disease or dementia with Lewy bodies (DLB).
- have a problem with the movement of your gut (paralytic ileus), a narrowing or blockage of your gut or other serious gut problem.
- are elderly and have dementia (loss of memory and other abilities).
- have one of the following rare hereditary diseases because lactose is a non-medicinal ingredient in REXULTI:
 - Galactose intolerance
 - Lapp lactase deficiency
 - Glucose-galactose malabsorption
- are pregnant or plan to become pregnant. It is not known if REXULTI may harm your unborn baby. Using REXULTI in the last trimester of pregnancy may cause muscle movement problems, medicine withdrawal symptoms, or both of these in your newborn. If you become pregnant while taking REXULTI, contact your healthcare professional immediately.
- are breastfeeding or plan to breastfeed. It is not known if REXULTI passes into your breast milk. You and your healthcare professional should decide if you will take REXULTI or breastfeed.

Other warnings you should know about:

Thoughts of Suicide and Worsening of your Depression or Other Mental Illnesses: You may sometimes have thoughts of harming or killing yourself if you are:

- depressed and/or
- have other mental illnesses

Since medicines like REXULTI take time to work, usually about two weeks but sometimes longer, these thoughts occur more often when you first start treatment.

If you have thoughts of harming or killing yourself at any time, contact your healthcare professional or go to a hospital **right away**. You may find it helpful to tell a relative or close friend that you are depressed or have other mental illnesses. Ask them to read this leaflet. You might ask them to tell you if they:

- think your depression or mental illness is getting worse, or
- if they are worried about changes in your behaviour.

Impulse Behaviours: The following behaviours may occur in some people who take REXULTI:

- hypersexuality (uncontrollable and/or inappropriate sexual behaviour)
- an urge to gamble, spend money, binge eat, other urges or the development of new or increased urge

Tell your healthcare professional **right away** if you or those close to you notice these behaviours.

Effects in Newborns: In some cases, babies born to mothers taking REXULTI during pregnancy have symptoms that are severe and require the newborn to be hospitalized. Sometimes, the symptoms may get better on their own. Be prepared to get immediate medical help for your baby if they:

- have trouble breathing
- are overly sleepy
- have muscle stiffness or floppy muscles (like a rag doll)
- are shaking
- are having trouble feeding

Falls: The following symptoms have been reported with the use of antipsychotic medications:

- feeling sleepy,
- a fall in blood pressure when you stand up from sitting or lying down,
- vision or speech problems

This can lead to falls that may cause fractures or other fall-related injuries. Certain medications, diseases or conditions can make this worse.

Severe Skin Reactions: Severe skin reactions such as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), Stevens-Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN), and Acute Generalized Exanthematous Pustulosis (AGEP) that can be serious or life-threatening have been reported in very rare cases with atypical antipsychotics.

These skin reactions can spread to your mouth, lips, face, hands, trunk (torso), arms and legs. Contact your healthcare professional **right away** if you or the patient you are caring for experiences any of the following symptoms at any time during treatment with REXULTI:

- fever
- severe rash
- blisters or peeling skin
- swelling of the face
- swollen lymph glands
- flu-like feeling
- yellow skin or eyes
- shortness of breath
- swelling of the legs
- dry cough
- chest pain or discomfort
- feeling thirsty
- urinating less often, less urine or dark urine

Neuroleptic Malignant Syndrome (NMS): NMS is potentially a life-threatening condition that has been reported with the use of antipsychotic medications like REXULTI. Symptoms include:

- severe muscle stiffness or inflexibility with high fever,
- rapid or irregular heartbeat,

- sweating,
- state of confusion or reduced consciousness

Increased Levels of Prolactin: REXULTI can raise your levels of a hormone called “prolactin”. This is measured with a blood test. Symptoms may include:

- In men:
 - swelling in the breast
 - difficulty in getting or maintaining an erection or other sexual dysfunction
- In women:
 - discomfort in the breasts
 - leaking of milk from the breasts (even if not pregnant)
 - missing your menstrual period or other problems with your cycle

If you have high levels of prolactin and a condition called hypogonadism you may be at an increased risk of breaking a bone due to osteoporosis. This occurs in both men and women.

Driving and Using Machines: REXULTI may change (reduce) your judgement, thinking or motor skills, and make you feel sleepy. Do not drive a car, operate machinery, or do other dangerous activities until you know how REXULTI affects you.

Hypotension (low blood pressure): Some people may faint, or get lightheaded and dizzy, especially when getting up from a lying or sitting position. This is more likely to happen if you are elderly and also at the start of treatment or when you increase the dose. This will usually pass on its own but if it does not, tell your healthcare professional.

Dehydration and Overheating: It is important not to become too hot or dehydrated while you are taking 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 clothing or heavy clothing.
- Drink plenty of water.

Check-ups and testing: Your healthcare professional may do check-ups and tests before you start REXULTI and during your treatment. These may include:

- blood tests to monitor your:
 - blood sugar levels.
 - complete blood cell count. This test measures the number and quality of red blood cells, white blood cells and platelets.
 - blood fat levels, including cholesterol and triglycerides (types of fat).
 - levels of the hormone prolactin.
- blood pressure checks to monitor any changes.
- body weight checks to monitor any weight gain.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with REXULTI:

- Medicines used to treat HIV infection and AIDS, such as indinavir, lopinavir/ritonavir, nelfinavir, ritonavir and saquinavir.

- Antibiotics used to treat bacterial infections, such as erythromycin, clarithromycin, azithromycin, tacrolimus, moxifloxacin, levofloxacin, ciprofloxacin and rifampin.
- Pentamidine, an antimicrobial medicine used to treat infections in people with weakened immune systems.
- Medicines used to treat malaria, such as quinine and chloroquine.
- Medicines used to treat fungal infections, such as amphotericin B, itraconazole, fluconazole, voriconazole and ketoconazole.
- Domperidone often used to increase production of breast milk.
- Medicines used to prevent nausea and vomiting, such as ondansetron.
- Chemotherapy medicines used to treat cancer, such as sunitinib, nilotinib, ceritinib, vandetanib, vorinostat and arsenic trioxide.
- Medicines used to treat breathing problems like asthma and COPD, such as salmeterol and formoterol.
- Antidepressant medicines such as bupropion, fluoxetine, citalopram, venlafaxine, amitriptyline, imipramine, maprotiline and paroxetine.
- Medicines used to treat heart problems such as quinidine, procainamide, disopyramide, amiodarone, sotalol, ibutilide, dronedarone, flecainide and propafenone.
- Anti-seizure medicines such as carbamazepine and phenytoin.
- Diuretics or “water pills” used to help rid your body of salt and water.
- Laxatives and enemas used to help relieve and prevent constipation.
- Antacid medicines, such as proton pump inhibitors.
- Opioids used to relieve pain such as methadone.
- Other antipsychotic medicines such as chlorpromazine, pimozide, haloperidol, droperidol, ziprasidone and risperidone.
- Medicines used to lower blood pressure.
- St John’s wort, an herbal product used to treat depression.
- Alcohol. You should not drink alcohol with taking REXULTI.
- Grapefruit or grapefruit juice. Do not eat grapefruit or drink grapefruit juice while taking REXULTI.

How to take REXULTI:

- Take REXULTI exactly as your healthcare professional tells you to take it.
- Your healthcare professional has decided on the best dosage for you depending on your overall health and other medications you are taking. Your healthcare professional may change your dose depending on how you respond.
- When you start your treatment with REXULTI, your healthcare professional will gradually increase your dose. Carefully follow their instructions.
- Even if you feel better, do NOT change your dose or stop taking REXULTI without speaking to your healthcare professional first.
- Take REXULTI once a day, with or without food.

Usual dose:

Adults:

- **Schizophrenia:**
Usual starting dose: 1 mg once a day.
Usual dose: 2 - 4 mg once a day.
Maximum dose: 4 mg once a day.

- **Major Depressive Disorder (MDD):**
Usual starting dose: 0.5 mg or 1 mg once a day.
Usual dose: 2 mg once a day.
Maximum dose: 2 mg once a day.
- **Agitation associated with Alzheimer's dementia (AAD):**
Usual starting dose: 0.5 mg once a day.
Usual dose: 2 mg once a day. If it is right for you, your healthcare professional may increase your dose to 3 mg once a day.
Maximum dose: 3 mg once a day.

Overdose:

If you think you, or a person you are caring for, have taken too much REXULTI, contact a healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

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 healthcare professional.

What are possible side effects from using REXULTI?

These are not all the possible side effects you may have when taking REXULTI. If you experience any side effects not listed here, tell your healthcare professional.

Side effects may include:

- diarrhea, constipation
- indigestion, stomach pain
- dry mouth
- weight gain, increased appetite
- dizziness
- difficulty staying still or restlessness
- shakiness (tremor)
- back pain, muscle pain
- sleepiness, drowsiness, fatigue, weakness, sleep disturbances (insomnia)
- anxiety
- headache
- nasopharyngitis (common cold like symptoms)
- rash
- sleep apnea (a sleep disorder where your breathing is interrupted during sleep)
- sleep walking and eating while asleep (sleep-related eating disorders)
- bladder infection

| Serious side effects and what to do about them | | | |
|--|--------------------------------------|--------------|---|
| Symptom / effect | Talk to your healthcare professional | | Stop taking drug and get immediate medical help |
| | Only if severe | In all cases | |
| UNCOMMON | | | |
| Allergic Reaction: Difficulty swallowing or breathing, wheezing; feeling sick to your stomach and throwing up; hives or rash; swelling of the face, lips, tongue or throat | | | √ |
| Tardive Dyskinesia: Muscle twitching or unusual/abnormal movement of the face or tongue or other parts of your body | | √ | |
| Stroke and Transient Ischemic Attacks: Sudden weakness or numbness of the face, arms, or legs, especially if only on one side of the body; sudden confusion, difficulty speaking or understanding others; sudden difficulty in walking or loss of balance or coordination; suddenly feeling dizzy or sudden severe headache with no known cause | | | √ |
| Seizure (fits): Loss of consciousness with uncontrollable shaking | | | √ |
| Blood Clots: Swelling, pain and redness in an arm or leg that is warm to touch. You may develop sudden chest pain, difficulty breathing and heart palpitations | | √ | |
| Hyperglycemia (high blood sugar): Increased thirst, frequent urination, dry skin, headache, blurred vision and fatigue | √ | | |
| Leukopenia (decreased white blood cells): Infections, fatigue, fever, aches, pains, and flu-like symptoms | | √ | |
| Dysphagia: Tightness of the throat, difficulty swallowing or breathing which may lead to choking | | √ | |
| Hypotension (low blood pressure): Dizziness, fainting, lightheadedness, blurred vision, nausea, vomiting, fatigue (may occur when you go from lying or sitting to standing up) | √ | | |

| Serious side effects and what to do about them | | | |
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| Symptom / effect | Talk to your healthcare professional | | Stop taking drug and get immediate medical help |
| | Only if severe | In all cases | |
| Neuroleptic Malignant Syndrome (NMS): Severe muscle stiffness or inflexibility with high fever, rapid or irregular heartbeat, sweating, state of confusion or reduced consciousness | | | √ |
| Priapism: Long-lasting (greater than 4 hours in duration) and painful erection of the penis | | | √ |
| New or worsening constipation | | √ | |
| Rhabdomyolysis (breakdown of damaged muscle): Very dark (“tea coloured”) urine, muscle tenderness and/or aching | | | √ |
| VERY RARE | | | |
| Severe Skin Reactions: Fever, severe rash, swollen lymph glands, flu-like feeling, blisters and peeling skin that may start in and around the mouth, nose, eyes and genitals and spread to other areas of the body, swelling of the face and/or legs, yellow skin or eyes, shortness of breath, dry cough, chest pain or discomfort, feeling thirsty, urinating less often, less urine or dark urine | | | √ |
| UNKNOWN FREQUENCY | | | |
| Thoughts of death or suicide | | | √ |

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Store REXULTI at room temperature, between 15 and 30°C.
- Keep out of reach and sight of children.

If you want more information about REXULTI:

- Talk to your healthcare professional.
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website www.otsukacanada.com, or by calling 1-877-341-9245.

This leaflet was prepared by Otsuka Pharmaceutical Co., Ltd.

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