

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

PrREXULTI® 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).

REXULTI is not to be used if you are elderly and have dementia.

What is REXULTI used for?

REXULTI is used in adults:

- for the treatment of schizophrenia
- along with antidepressant medication for the treatment of major depressive disorder (MDD)

Not all people with these disorders 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

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 not a cure, but it can help manage symptoms in adult patients.

How does REXULTI work?

Antipsychotic medications affect dopamine and serotonin (chemicals found in the brain called

neurotransmitters) that allow for the communication between your nerve cells. Illnesses that affect the brain, like schizophrenia or depression, may be due to certain naturally occurring chemicals (neurotransmitters) in the brain being out of balance. These imbalances may cause some of the symptoms you may be experiencing. Exactly how REXULTI works is not known. However, it seems that REXULTI corrects the balance of dopamine and serotonin in your body.

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, 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 ingredient in the medication.

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
 - 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 drugs.
- have been told you are a “CYP2D6 poor metabolizer”.
- have a tumour in your pituitary gland.
- have or have had involuntary, irregular muscle movements, especially in the face (tardive dyskinesia).
- 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 doctor **right away** if you or those close to you notice these behaviours.

Effects in Newborns: Babies born to mothers taking REXULTI while they are pregnant can

have serious health problems. Sometimes, the problems 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 drugs:

- 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.

Serious Allergic Reaction: REXULTI can cause **serious life-threatening** skin reaction such as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS).

This skin reaction 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:

- fever
- severe rash
- 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 drugs like REXULTI. Symptoms include:

- severe muscle stiffness or inflexibility with high fever,
- rapid or irregular heartbeat,
- sweating,
- state of confusion or reduced consciousness

High Levels of Prolactin: If you have high levels of prolactin (measured with a blood test) 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 make you feel drowsy. Do not drive a car, operate machinery, or do other dangerous activities until you know how REXULTI affects you.

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.

Blood Tests: Your healthcare professional should take blood tests before starting REXULTI. Blood tests will include checking the number of infection-fighting white blood cells, cholesterol levels, blood fat levels and levels of the hormone prolactin. Your doctor should continue to monitor your blood for as long as you are being treated. While you are taking REXULTI your healthcare professional will also check your weight, blood sugar and blood pressure regularly.

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:

- Drugs 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 drug used to treat infections in people with weakened immune systems.
- Drugs used to treat malaria, such as quinine and chloroquine.
- Drugs used to treat fungal infections, such as amphotericin B, itraconazole, fluconazole, voriconazole and ketoconazole.
- Domperidone often used to increase production of breast milk.
- Drugs used to prevent nausea and vomiting, such as ondansetron.
- Chemotherapy drugs used to treat cancer, such as sunitinib, nilotinib, ceritinib, vandetanib, vorinostat and arsenic trioxide.
- Drugs used to treat breathing problems like asthma and COPD, such as salmeterol and formoterol.
- Antidepressant drugs such as bupropion, fluoxetine, citalopram, venlafaxine, amitriptyline, imipramine, maprotiline and paroxetine.
- Drugs used to treat heart problems such as quinidine, procainamide, disopyramide, amiodarone, sotalol, ibutilide, dronedarone, flecainide and propafenone.
- Anti-seizure drugs such as carbamazepine and phenytoin.
- Diuretics or “water pills”.
- Laxatives and enemas.
- Antacid drugs, such as proton pump inhibitors.
- Opioids such as methadone.
- Other antipsychotic drugs such as chlorpromazine, pimozide, haloperidol, droperidol, ziprasidone and risperidone.

- Drugs 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.
- Do not change your dose or stop taking REXULTI without speaking to your healthcare professional.
- REXULTI can be taken with or without food.

Usual adult dose:

Schizophrenia:

Usual starting dose: 1 mg once a day.

Usual dose: 2-4 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.

Overdose:

If you think you have taken too much REXULTI, contact your 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 feel when taking REXULTI. If you experience any side effects not listed here, contact 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)

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, light-headedness, blurred vision, nausea, vomiting, fatigue (may occur when you go from lying or sitting to standing up).	√		
Neuroleptic Malignant Syndrome : Severe muscle stiffness or inflexibility with high fever, rapid or irregular heartbeat, sweating, state of confusion or reduced consciousness			√
Serious Allergic Reactions known as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) (serious skin reaction that may affect more than one or more organs): Fever, severe rash, peeling skin, swollen lymph glands, swelling of your face, 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.			√
Priapism : Long-lasting (greater than 4 hours in duration) and painful erection of the penis			√
New or worsening constipation		√	
Rhabdomyolysis : Very dark (“tea coloured”) urine, muscle tenderness and/or aching			√
UNKNOWN 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, talk to 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.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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