CANMAT RECOMMENDS **1ST LINE ADJUNCTIVE THERAPY OPTION** BREXPIPRAZOLE

For patients with an inadequate response to antidepressant treatment during the current episode of MDD[1,2*]

Meet Catherine†

"I've felt some relief on my antidepressant, but I still have days when I'm down and anxious due to my depression."

HISTORY

- 34-year-old teacher **diagnosed with MDD**
- Current **episode ongoing for past 6 months,** has missed **multiple social engagements**

TREATMENT

- **Currently on antidepressant treatment**

CURRENT PRESENTATION

- Has **experienced some improvement** with current medication but is frustrated that **it's not providing enough relief**
- Experiences **pervasive sad mood** and **anxious symptoms** with **trouble sleeping** and **sustained fatigue**
- Has difficulty **concentrating** and **remembering** things

DAY-TO-DAY IMPACT

- Catherine's major complaint is **losing her ability to be fully present and engaged** in interacting with her family
- She has **lost all interest** in eating, sex, hobbies, and her daily exercise routine
- Even **simple tasks** that were once easy now **cause her significant distress**

PATIENT GOALS

- **Functional recovery**
- To **enjoy social events**

How would you treat Catherine?

PrREXULTI® is indicated for use as an adjunct to antidepressants for the treatment of major depressive disorder (MDD) in adult patients with an inadequate response to prior antidepressant treatments during the current episode.[3]

Data for REXULTI on the Montgomery-Åsberg Depression Rating Scale (MADRS) and social and family functioning (work/school functioning was not statistically significant) are presented elsewhere in this tool. The effects of REXULTI on decision-making, sleep, fatigue, concentration, memory, libido/intercourse, appetite, hobbies, exercise, performing day-to-day activities and anxiety have not been evaluated as an individual predefined endpoint in prospectively designed, well-controlled randomized trials.

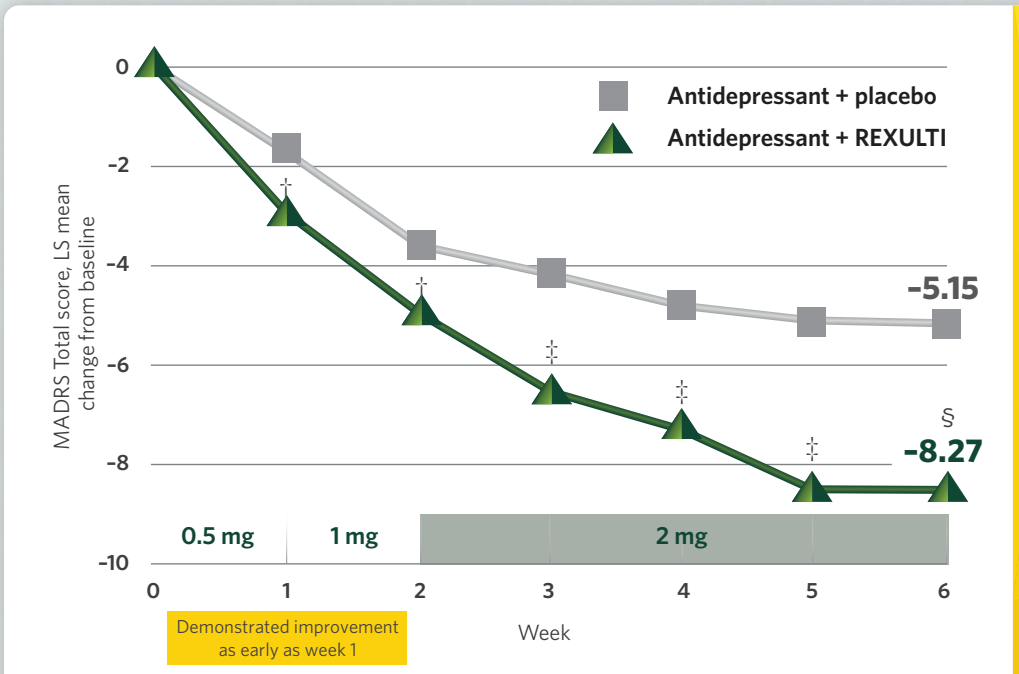
CANMAT: Canadian Network for Mood and Anxiety Treatments.
* See guidelines for complete recommendations.
† Fictional case. May not be representative of the general population.

Pr REXULTI® brexpiprazole tablets

An adjunctive treatment for MDD with demonstrated efficacy

PrREXULTI® efficacy was evaluated across multiple 6-week clinical trials, which included over 1800 patients who fulfilled the DSM-IV-TR criteria for MDD with or without symptoms of anxiety and with demonstrated inadequate response to 1–3 prior antidepressants in the current episode and an inadequate response during the prospective antidepressant trial phase.[3]

Improved depression symptoms, as measured by MADRS at week 6 (clinician-rated)[3,4]*



62%
(-3.12 points, *p*=0.0001)
greater reduction for patients treated with antidepressant + REXULTI vs. antidepressant + placebo at week 6

Baseline MADRS Total score, antidepressant + placebo: 27.14, n=191; antidepressant + REXULTI: 26.61, n=187
† $p<0.01$; ‡ $p<0.001$; § $p=0.0001$

Adapted from Product Monograph and Thase *et al.* (incl. Supplementary Material)

COVERED by most public formularies and private insurance plans in Canada[5–13]¶

DSM-IV-TR: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision; MADRS: Montgomery-Åsberg Depression Rating Scale (a 10-item physician-administered questionnaire rating patients' symptoms of apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts and suicidal thoughts, on a scale from 0 to 6 with higher values reflecting more severe symptoms); SDS: Sheehan Disability Scale.

* Results from a phase 3, 6-week, randomized, double-blind, placebo-controlled fixed-dose trial in adult patients who fulfilled the DSM-IV-TR criteria for MDD, with or without symptoms of anxiety, had an inadequate response to 1–3 prior antidepressant treatment(s) in current episode and an inadequate response during 8 weeks of prospective antidepressant treatment. Patients remained on background antidepressant treatment and were randomized to receive adjunct placebo (n=191) or adjunct REXULTI (0.5 mg/day for week 1, 1 mg/day for week 2, 2 mg/day for week 3 onwards; n=187).

¶ REXULTI is eligible by Non-Insured Health Benefits, Correctional Service Canada and Veterans Affairs Canada as a general benefit, and for formulary coverage in the following provinces and territories: Alberta (regular benefit); Ontario (general benefit); Manitoba, Newfoundland and Labrador, and Northwest Territories (open benefit).

Demonstrated SDS domain results at week 6[3*]

As measured by the SDS, a 3-item self-rated instrument used to assess functional impairment in three domains, with higher values reflecting greater impairment:[3,14]

- **Work/School**
- **Social life**
- **Family life**

In trial 4 (PYXIS), the SDS Mean score showed statistically significant greater improvement with antidepressant + [Pr]REXULTI® 2 mg/day than with antidepressant + placebo (-1.35 vs. -0.91, $p<0.05$; key secondary endpoint).

The social life and family life domains showed statistically significant improvement for patients taking antidepressant + REXULTI 2 mg/day vs. antidepressant + placebo ($p<0.05$), while the work/school domain did not.

SDS domains	Antidepressant + REXULTI	Antidepressant + placebo	*P* value
Work/School	-1.09	-0.90	0.4771
Social life	-1.54	-1.04	0.0323
Family life	-1.33	-0.73	0.0129

Adapted from Thase *et al.* Supplementary Material

Clinical use:
When considering the use of REXULTI as adjunctive treatment in MDD, clinicians must take into account the safety concerns associated with antipsychotic drugs, a class of drugs to which REXULTI belongs. Safety concerns of this class include: weight gain; hyperlipidemia; hyperglycemia; tardive dyskinesia; and neuroleptic malignant syndrome. REXULTI should only be prescribed in patients with MDD by clinicians who are aware of the importance and are experienced in the early detection and management of the safety issues associated with this class of drugs.

The efficacy and safety of REXULTI in the adjunctive treatment of MDD were demonstrated in 6-week, double-blind, placebo-controlled trials in adult patients. Therefore, the required length of adjunctive treatment with REXULTI is not known. When prescribed as an adjunct to antidepressants in the treatment of MDD, REXULTI should be used for the shortest period of time that is clinically indicated. It is not known whether efficacy in adjunct treatment is due to REXULTI alone or from combined treatment with an antidepressant.

- The safety and efficacy of REXULTI have not been systematically evaluated in MDD patients ≥65 years of age. Use caution when treating geriatric patients.
- REXULTI is not indicated in pediatric patients (<18 years) and its use is not recommended in this population.

Most serious warnings and precautions:
Increased mortality in elderly patients with dementia: Elderly patients with dementia treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Analyses of 13 placebo-controlled trials with various atypical antipsychotics (modal duration of 10 weeks) in these patients showed a mean 1.6-fold increase in the death rate in the drug-treated patients. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature.

Other relevant warnings and precautions:
- Body temperature regulation
- Risk of falls and somnolence
- Contains lactose
- Orthostatic hypotension
- Risk of QT prolongation
- Evaluate patients for a history of drug abuse
- Driving and operating machinery
- Reports of hyperglycemia and diabetic ketoacidosis
- Weight gain
- Dyslipidemia
- Hyperprolactinemia
- Priapism
- Risk of leukopenia/neutropenia
- Venous thromboembolism
- Serious hypersensitivity reactions
- Neuroleptic malignant syndrome
- Tardive dyskinesia
- Risk of seizures/convulsions
- Risk of suicide
- Risk of impulse-control disorders/compulsive behaviours
- Severe cutaneous adverse reactions
- Dysphagia
- Should not be used during pregnancy or breast-feeding
- Caution when used in geriatric patient populations due to potential increased risk of cerebrovascular adverse events, including fatalities
- Monitoring and laboratory tests: blood glucose, fasting lipid profile and body weight, complete blood count (CBC), white blood cell (WBC) and differential counts, prolactin and blood pressure, should be monitored at baseline and periodically throughout treatment

For more information:
Please consult the Product Monograph at www.rexultimonograph.ca for important information relating to adverse reactions, drug interactions, and dosing information, which have not been discussed in this piece. The Product Monograph is also available by calling us at **1-877-341-9245**.

Pr REXULTI® brexpiprazole tablets

Simple once-daily dosing options for your patients

Recommended dosing with a flexible titration schedule in MDD[3]

Option A

1. Initiate with

0.5 mg/day

1 week

1 mg/day

1 week

2. Achieve recommended target dose/ Maximum dose of

2 mg/day

Option B

1. Initiate with

1 mg/day

1 week

2. Achieve recommended target dose/ Maximum dose of

2 mg/day

Adapted from Product Monograph

PrREXULTI® is taken orally, with or without food.

- No additional benefit was demonstrated at doses greater than 2 mg/day.
- Dosage increases should occur at weekly intervals based on the patient's clinical response and tolerability. Periodically reassess to determine the continued need and appropriate dose for treatment.
- The required length of adjunctive treatment with REXULTI is unknown. When prescribed as an adjunct to antidepressants in the treatment of MDD, REXULTI should be used for the shortest period of time that is clinically indicated.

Please consult the Product Monograph for full dosing information.

Consider adding REXULTI for your patients with MDD who are facing an inadequate response to their antidepressant and request samples today!

References: 1. Lam RW, Kennedy SH, Adams C, *et al.* Canadian Network for Mood and Anxiety Treatments (CANMAT) 2023 Update on Clinical Guidelines for Management of Major Depressive Disorder in Adults. *Can J Psychiatry.* 2024;69(9):641-6871-47. **2.** CANMAT. Data on File. CANMAT Letter to PAAB. **3.** REXULTI Product Monograph. Otsuka Pharmaceutical Co., Ltd. **4.** Thase ME, Youakim JM, Skuban A, et al. Efficacy and safety of adjunctive brexpiprazole 2 mg in major depressive disorder: A phase 3, randomized, placebo-controlled study in patients with inadequate response to antidepressants. *J Clin Psychiatry.* 2015;76(9):1224–1231. **5.** REXULTI. Data on File. Private coverage plan. **6.** Alberta Health. Drug benefit list. April 1, 2021. **7.** Manitoba Pharmacare. Formulary Search Results. December 1, 2021. **8.** Ontario Drug Benefit. Formulary. February 26, 2021. **9.** Data on File. Otsuka Pharmaceutical Co., Ltd. 2019. NIHB coverage. **10.** Newfoundland and Labrador. Benefit List update. May 12, 2022. **11.** Correctional Service Canada. Data on File. August 2019. **12.** Veterans Affairs Canada. Formulary Search Results. November 2, 2021. **13.** Northwest Territories. Data on File, NWT. November 17, 2020. **14.** Sheehan DV. Sheehan Disability Scale (SDS) – Overview. 1983.

Otsuka Lundbeck

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REVIEWED BY PAAB

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