Choose PrREXULTI® for your patients with agitation associated with Alzheimer's dementia (AAD)

PrREXULTI® is indicated for the symptomatic management of agitation associated with Alzheimer's dementia in patients with aggressive behaviour, unresponsive to non-pharmacological approaches.[1]

Meet Diane and her caregiver Isabelle*

> ***My mother lives at home with me. Recently, she has started to get more agitated and restless. It is getting increasingly difficult to calm her, so I am open to explore any potential options that might help her.***
>
> ***– Isabelle, daughter.***

PATIENT HISTORY

- 74-year-old female diagnosed with Alzheimer's dementia 3 years ago
- Moved in with her daughter 2 years ago
- Currently on cholinesterase inhibitor treatment
- MMSE score = 21 (consistent with previous visit)

CAREGIVER-REPORTED RECENT SYMPTOMS

- Agitated
- Occasional screaming (aggressive)
- General restlessness (physically non-aggressive)
- Repeatedly asking for attention (verbally agitated)
- Has stopped coming on daily walks at the nearby park

TREATMENT GOALS

- **Help manage agitation symptoms**

How would you treat Diane?

Data for REXULTI on manifestations of agitated behaviours are presented elsewhere in this tool. The effects of REXULTI on functioning and quality of life have not been evaluated as a predefined endpoint in prospectively designed, well-controlled, randomized trials.

MMSE: Mini-Mental State Examination.
* Fictional case. May not be representative of the general population.

PrREXULTI® brexpiprazole tablets

Simple once-daily dosing option for your patients

Recommended dosing titration schedule designed to be easy to follow[1]

1. Initiate with	2. Aim for a recommended target dose of	3. Maximum dose of
		
0.5 mg/day	**2** mg/day	**3** mg/day

Recommended dose titration			
Day	1–7	8–14	15 and thereafter
Dose	**0.5** mg/day	**1** mg/day	**2** mg/day

Adapted from Product Monograph

[Pr]REXULTI® is taken orally, with or without food.

- After at least 14 days at 2 mg once daily, the dose can be increased to the maximum recommended dose of 3 mg daily, if clinically warranted. To minimize the risk of adverse events, the lowest effective dose should be used.
- Physicians are advised to assess the risks and benefits of the use of REXULTI in elderly patients with AAD, taking into account risk predictors for stroke or existing cardiovascular comorbidities in the individual patient.
- Discontinuation should be considered if signs and symptoms of cerebrovascular adverse events occur.

Please consult the Product Monograph for full dosing information.

Clinical use:
PrREXULTI® is not indicated as an as needed (prn) treatment for AAD. It may take up to six to eight weeks after REXULTI initiation to demonstrate significant clinical efficacy.

The efficacy and safety of REXULTI in the treatment of AAD were demonstrated in two 12-week, randomized, double-blind, placebo-controlled, fixed-dose trials in adult patients. When considering the use of REXULTI for the treatment of AAD, clinicians are advised to assess the risks and benefits of the use of REXULTI in elderly patients with AAD keeping in mind the increased risk of mortality in this patient population treated with antipsychotics and the risk predictors for stroke or existing cardiovascular comorbidities.

- Not indicated in pediatric patients <18 years of age 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®'s efficacy profile in AAD was evaluated in three pivotal trials

The efficacy and safety profile of REXULTI was evaluated in three 12-week, randomized, double-blind, placebo-controlled trials (two fixed-dose and one flexible-dose) that enrolled **1,048 patients** presenting symptoms of agitation associated with Alzheimer's dementia (AAD).[1]

Study 11[1,2]

Objective
To assess the efficacy, tolerability and safety profile of REXULTI (fixed-dose 2 or 3 mg/day) in patients with AAD who had specifically met CMAI factor 1.

Select inclusion criteria[1,2]

- Probable Alzheimer's disease diagnosis as per NINCDS-ADRDA Criteria
- MMSE: ≥5 and ≤22
- Total score of ≥4 on the agitation/aggression item of the NPI/NPI-NH
- Exhibited sufficient agitation behaviours at time of entry to warrant use of pharmacotherapy, after excluding other factors
- Met criteria for CMAI Factor 1 Aggressive Behaviours*

A total of **345 patients**

aged 56–90 years old (mean, 74 years old) were enrolled in **Study 11** to receive either REXULTI 2 mg/day or 3 mg/day (n=225), or placebo (n=116).

Study endpoints[1,2]

Primary endpoint

- Change from baseline in the CMAI score at week 12

Key secondary endpoint

- Change from baseline in the CGI-S Scale score at week 12

CGI-S: Clinical Global Impression Severity; CMAI: Cohen-Mansfield Agitation Inventory; MMSE: Mini-Mental State Examination; NINCDS-ADRDA: National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association; NPI/NPI-NH: Neuropsychiatric Inventory/Neuropsychiatric Inventory Nursing Home.

* To meet this criterion, one of the following must be displayed: 1) ≥1 aggressive behaviours occurring several times per week, or 2) ≥2 aggressive behaviours occurring once or twice per week, or 3) ≥3 aggressive behaviours occurring less than once per week.

Cohen-Mansfield Agitation Inventory (CMAI) scale

The **CMAI scale** is a clinician-rated questionnaire consisting of 29 items, which assess the frequency of manifestations of agitated behaviours in elderly patients, based on caregiver input.[1]

Agitated behaviours can be grouped into three specific factors:

Factor 1: Aggressive behaviour (item examples)

- Screaming
- Kicking
- Throwing things
- Pushing
- Scratching
- Hurting self or others
- Cursing or verbal aggression

Factor 2: Physically non-aggressive behaviour (item examples)

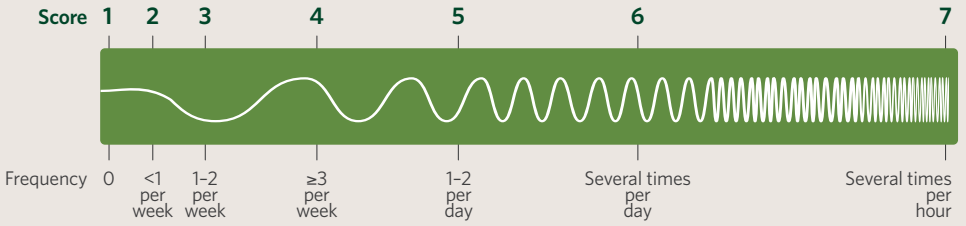
- Performing repetitive mannerisms
- General restlessness
- Pacing, aimless wandering

Factor 3: Verbally agitated behaviour (item examples)

- Complaining
- Repetitive sentences or questions
- Constant unwarranted requests for attention or help

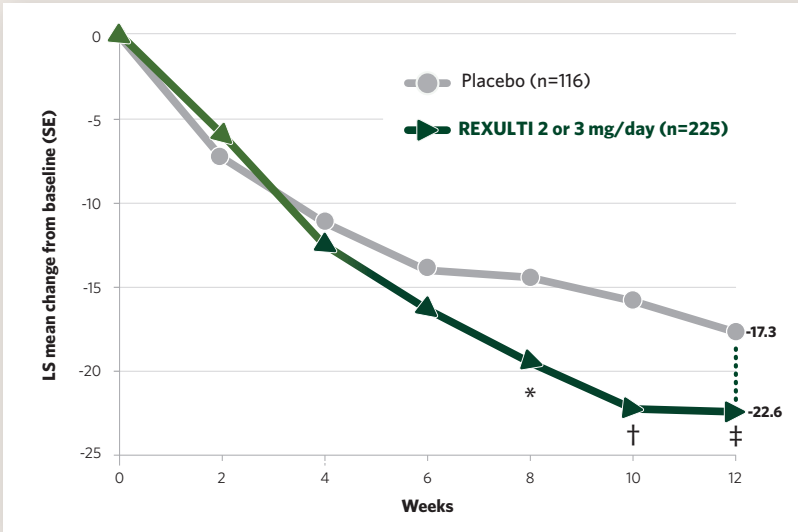
Scoring the CMAI

- Each of these 29 agitated behaviours is rated on a scale of 1 (never) to 7 (very frequent agitated behaviours) over the last 2 weeks[3]
- The sum of each agitated behaviour's frequency scores creates a CMAI total score ranging from 29 (best) to 203 (worst)
- A negative change in score indicates improvement



Improvement in the frequency of manifestations of agitation symptoms observed at week 12, as measured by the CMAI

Demonstrated improvement in CMAI Total score at week 12[1,2]



31% GREATER RELATIVE REDUCTION
vs. placebo (LSMD -5.3; 95% CI: -8.8, -1.9; *p*=0.0026)

Baseline CMAI total scores: REXULTI 80.6, placebo 79.2
* $p<0.01$; nominal p values with no adjustment for multiplicity.
† $p=0.001$; nominal p values with no adjustment for multiplicity.
‡ $p=0.001$.

Adapted from Product Monograph and Lee *et al.* 2023

Demonstrated improvement in CGI-S score at week 12 (secondary endpoint)[1,2]

REXULTI 2 or 3 mg/day **was statistically significantly superior to placebo** in improving agitation symptoms at week 12 (LSMD −0.27, $p=0.0078$).

CGI-S: Clinical Global Impression Severity; CMAI: Cohen-Mansfield Agitation Inventory; LS: least squares; LSMD: least-squares mean difference; SE: standard error.

Demonstrated safety profile

Safety and tolerability profile

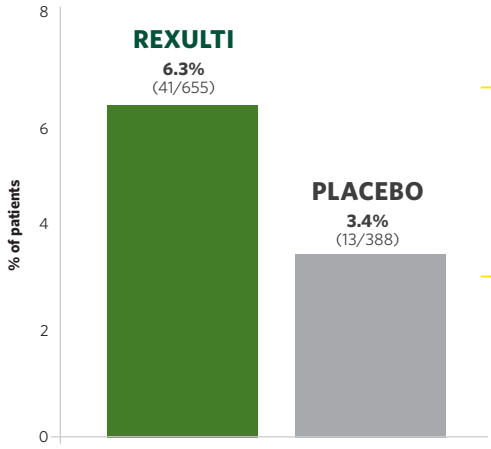
TEAEs with incidence of ≥2% in any PrREXULTI® dose group (0.5 to 3 mg) and greater than placebo group in 12-week, placebo-controlled, fixed-dose and flexible-dose trials[1]

	REXULTI (mg/day)						
	≤1 mg (n=157)	2 mg (n=213)	3 mg (n=153)	2 and 3 mg (n=366)	0.5–2 mg (n=132)	**All doses** (n=655)	**Placebo** (n=388)
Somnolence	**1%**	**3%**	**3%**	**3%**	**6%**	**3%**	**2%**
Dizziness	**<1%**	**4%**	**3%**	**4%**	**5%**	**3%**	**3%**
Insomnia	**5%**	**4%**	**2%**	**3%**	**4%**	**4%**	**3%**
Nasopharyngitis	**3%**	**2%**	**3%**	**3%**	**3%**	**3%**	**3%**
Urinary tract infection	**2%**	**3%**	**3%**	**3%**	**2%**	**3%**	**2%**

Adapted from Product Monograph

Most treatment-emergent adverse events (TEAEs) were mild or moderate in severity. None of the adverse events reported in the 12-week trials met the criteria of most common adverse event (incidence of ≥5% in the REXULTI [all brexpiprazole] group and at least twice the rate of placebo).

Discontinuation rates due to adverse events



<7% of patients discontinued treatment due to adverse events, whether treated with REXULTI or placebo

Consider PrREXULTI®

DEMONSTRATED REDUCTION IN THE FREQUENCY OF MANIFESTATIONS OF AGITATION SYMPTOMS

Significantly **greater reduction in LSMD from baseline in the CMAI Total score** was observed in REXULTI 2 or 3 mg/day compared to placebo at week 12.[1,2]

DEMONSTRATED SAFETY PROFILE

- Most adverse events were mild or moderate in severity[1]
  - TEAEs with incidence of ≥2% in any REXULTI dose group (0.5 to 3 mg, ≥2%; N=655) were nasopharyngitis, urinary tract infection, dizziness, somnolence and insomnia.
- **<7%** of patients discontinued treatment due to adverse events
  - Discontinuation rates due to adverse reactions were 6.3% (41/655) with REXULTI and 3.4% (13/388) with placebo.

CMAI: Cohen-Mansfield Agitation Inventory; LSMD: least-squares mean difference; TEAEs: treatment-emergent adverse events.

STUDIED IN >1,000 PATIENTS

REXULTI was studied in three phase 3 pivotal trials which enrolled 1,048 patients with dementia due to Alzheimer's disease.[1,2]

SIMPLE ONCE-DAILY DOSING

1 X DAILY

- REXULTI is taken once daily with or without food[1]
- Clear titration schedule initiating with 0.5 mg, titrating to 1 mg, then aiming for a target dose of 2 mg/day
- Maximum dose of 3 mg/day

References: 1. REXULTI Product Monograph. Otsuka Pharmaceutical Co., Ltd. **2.** Lee D, Slomkowski M, Hefting N, *et al*. Brexpiprazole for the treatment of agitation in Alzheimer dementia: a randomized clinical trial. *JAMA Neurol*. 2023;80(12):1307–1316. **3.** Interior Health. Cohen-Mansfield Agitation Inventory (CMAI). Accessed January 4, 2024.

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REVIEWED BY PAAB

PrREXULTI® brexpiprazole tablets