NEW INDICATION

REXULTI® (brexpiprazole) now indicated for the treatment of agitation associated with Alzheimer's dementia[1*]

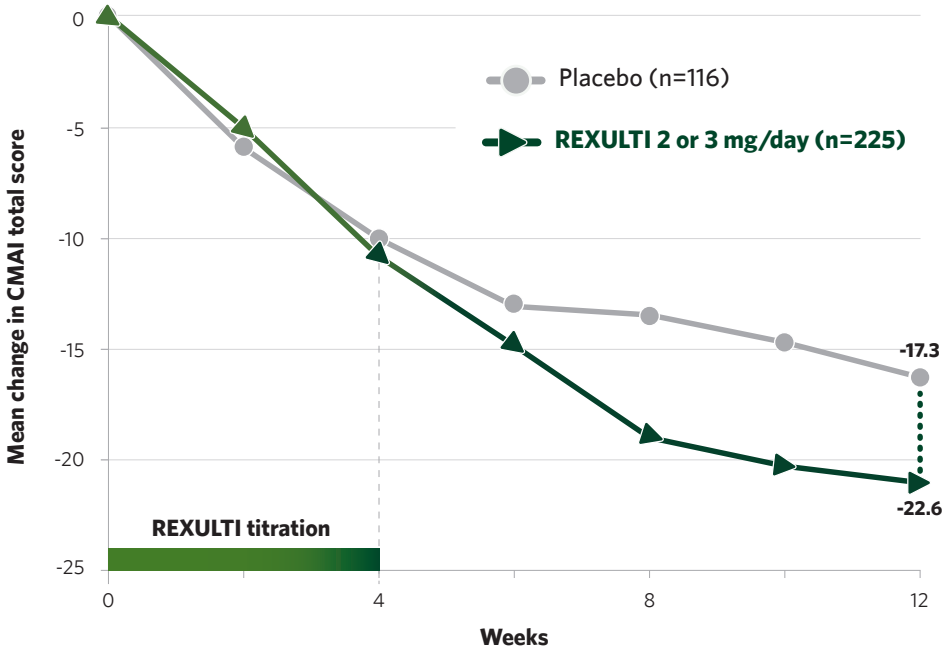
*In patients who are unresponsive to non-pharmacological interventions.[1]

Fictional patient and caregiver.

REXULTI is proven to reduce the frequency of agitation symptoms[2*]

*Patients receiving REXULTI 2 or 3 mg/day experienced a 31% greater reduction from baseline in CMAI total score vs placebo at 12 weeks (p=0.003)[2]

Change from baseline in CMAI total score (Lee *et al.*)[2]



Adapted from Lee D *et al.* 2023.[2]

31%

greater reduction in frequency vs placebo

Treatment difference: -5.3 (p=0.003)

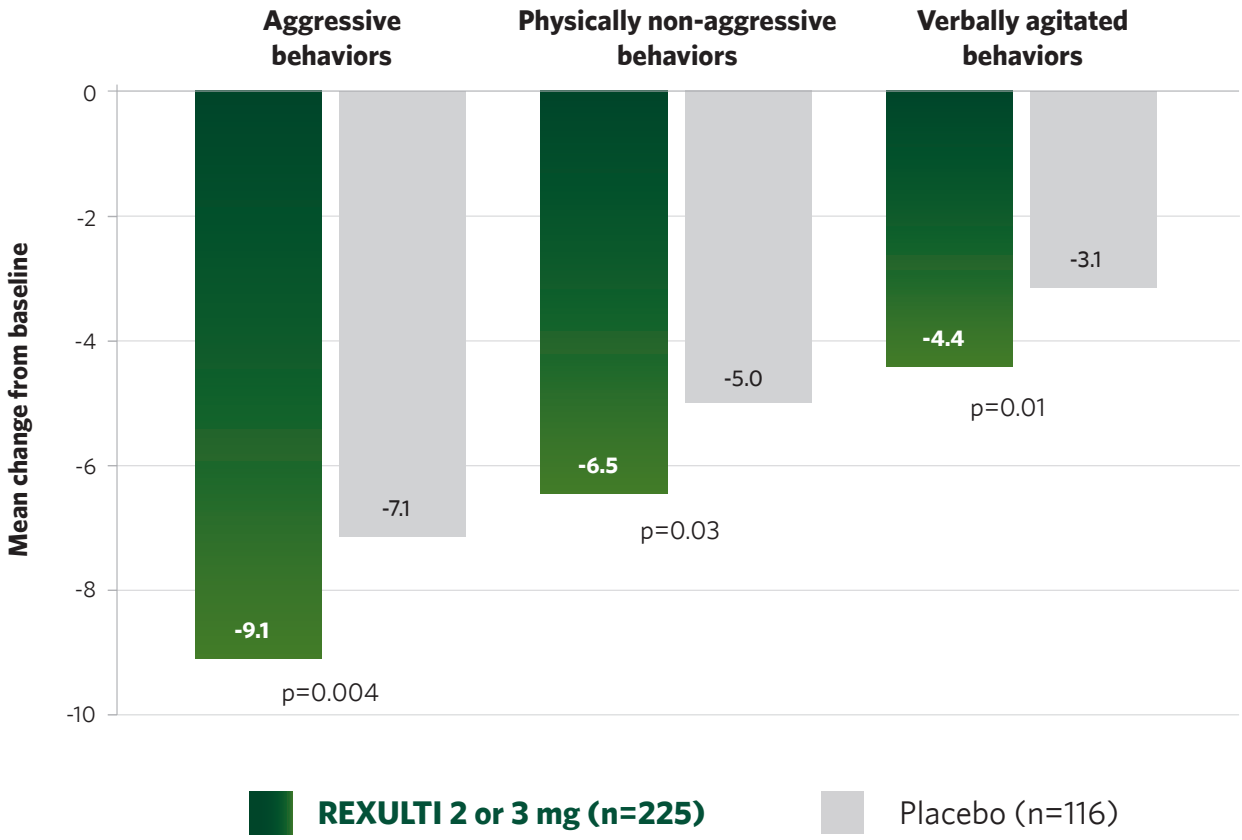
In Grossberg *et al.*, REXULTI 2 mg/day provided a significantly greater mean reduction from baseline in CMAI total score vs placebo at 12 weeks (-21.6 vs -17.8, treatment difference: -3.8; p=0.04)[3]

CMAI, Cohen-Mansfield Agitation Inventory.

REXULTI reduced the frequency of agitation symptoms across CMAI subscales[2*]

*Patients receiving REXULTI 2 or 3 mg/day had a statistically significant reduction from baseline in CMAI subscales at 12 weeks vs placebo (nominal p<0.05)[2]

Mean change in CMAI subscales from baseline (Lee *et al.*)[2†]



[†]In a supplementary analysis to examine the magnitude and direction of CMAI subscale response, Factor 1 (aggressive behaviour), Factor 2 (physically non-aggressive behaviour), and Factor 3 (verbal agitation) scores trended in the same direction with no single factor overly influencing the CMAI total score.

Study design: Two Phase III, 12-week, randomised, double-blind, placebo-controlled fixed-dose studies evaluating frequency of agitation symptoms (CMAI total score) and safety in patients with probable Alzheimer's disease diagnosis as per National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorders Association Criteria, agitation as determined by Neuropsychiatric Inventory – Nursing Home version, Agitation/Aggression domain score ≥4 and Mini-Mental State Examination score ≥5 and ≤22 who exhibit sufficient agitation behaviours at time of entry to warrant use of pharmacotherapy, after excluding other factors. In Lee *et al.* patients also met provisional International Psychogeriatric Association criteria for agitation associated with Alzheimer's dementia and had aggressive agitation at baseline (≥1 CMAI Factor 1 behaviour). In Grossberg *et al.*, patients were randomised 1:1:1 to receive REXULTI 1 mg/day (n=134), REXULTI 2 mg/day (n=138) or placebo (n=131). In Lee *et al.* patients were randomised 2:1 to receive REXULTI 2–3 mg/day (n=228) or placebo (n=117). The primary endpoint in both studies was change in agitation symptom frequency (CMAI total score) from baseline to Week 12.[1-3] The CMAI is a clinically validated scale measuring the frequency of 29 agitated behaviours and is scored by clinicians based on caregiver input.[1]

CMAI, Cohen-Mansfield Agitation Inventory.

REXULTI has a demonstrated safety profile[1*]

*In three 12-week, placebo-controlled studies.[1]

REXULTI is a psychotropic medication with documented safety in adults up to 90 years old[1]

Adverse reactions in ≥2 patients treated with REXULTI and greater than placebo from three 12-week placebo-controlled trials[1]

System Organ Class MedDRA Preferred Term	REXULTI (mg/day)				Placebo N=388 (%)
	<1 mg N=157 (%)	2 and 3 mg N=366 (%)	0.5–2 mg N=132 (%)	ALL N=655 (%)	
Blood and Lymphatic System Disorders					
Anaemia	2 (1.3)	4 (1.1)	0 (0.0)	6 (0.9)	2 (0.5)
Gastrointestinal Disorders					
Diarrhoea	3 (1.9)	6 (1.6)	4 (3.0)	13 (2.0)	6 (1.5)
Dry Mouth	2 (1.3)	5 (1.4)	2 (1.5)	9 (1.4)	1 (0.3)
Salivary Hypersecretion	1 (0.6)	4 (1.1)	1 (0.8)	6 (0.9)	0 (0.0)
General Disorders and Administration Site Conditions					
Asthenia	3 (1.9)	8 (2.2)	0 (0.0)	11 (1.7)	5 (1.3)
Fatigue	3 (1.9)	3 (0.8)	2 (1.5)	8 (1.2)	1 (0.3)
Pyrexia	1 (0.6)	4 (1.1)	0 (0.0)	5 (0.8)	0 (0.0)
Infections and Infestations					
Bronchitis	0 (0.0)	4 (1.1)	1 (0.8)	5 (0.8)	1 (0.3)
Cystitis	0 (0.0)	3 (0.8)	2 (1.5)	5 (0.8)	1 (0.3)
Pneumonia	2 (1.3)	2 (0.5)	4 (3.0)	8 (1.2)	3 (0.8)
Respiratory Tract Infection Viral	0 (0.0)	1 (0.3)	2 (1.5)	3 (0.5)	0 (0.0)
Urinary Tract Infection	3 (1.9)	12 (3.3)	2 (1.5)	17 (2.6)	6 (1.5)
Investigations					
Blood Creatine Phosphokinase Increased	3 (1.9)	3 (0.8)	3 (2.3)	9 (1.4)	0 (0.0)
Blood Lactate Dehydrogenase Increased	2 (1.3)	0 (0.0)	1 (0.8)	3 (0.5)	0 (0.0)
Blood Pressure Increased	2 (1.3)	5 (1.4)	0 (0.0)	7 (1.1)	2 (0.5)
Electrocardiogram QT Prolonged	4 (2.5)	3 (0.8)	1 (0.8)	8 (1.2)	2 (0.5)
Weight Increased	2 (1.3)	2 (0.5)	3 (2.3)	7 (1.1)	2 (0.5)

System Organ Class MedDRA Preferred Term	REXULTI (mg/day)				Placebo N=388 (%)
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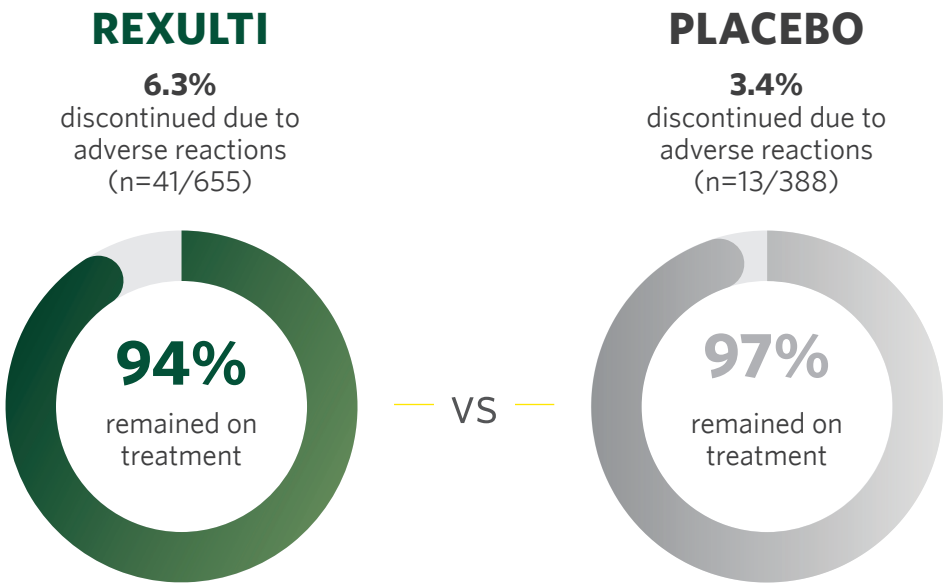
Metabolism and Nutrition Disorders					
Increased Appetite	1 (0.6)	3 (0.8)	3 (2.3)	7 (1.1)	1 (0.3)
Musculoskeletal and Connective Tissue Disorders					
Muscle Spasm	1 (0.6)	2 (0.5)	0 (0.0)	3 (0.5)	0 (0.0)
Nervous System Disorders					
Akathisia	0 (0.0)	2 (0.5)	3 (2.3)	5 (0.8)	1 (0.3)
Extrapyramidal Disorder	1 (0.6)	3 (0.8)	1 (0.8)	5 (0.8)	0 (0.0)
Somnolence	2 (1.3)	12 (3.3)	8 (6.1)	22 (3.4)	7 (1.8)
Psychiatric Disorders					
Confusional State	0 (0.0)	3 (0.8)	0 (0.0)	3 (0.5)	0 (0.0)
Hallucination	0 (0.0)	1 (0.3)	2 (1.5)	3 (0.5)	0 (0.0)
Insomnia	7 (4.5)	12 (3.3)	5 (3.8)	24 (3.7)	11 (2.8)
Psychomotor Retardation	0 (0.0)	3 (0.8)	1 (0.8)	4 (0.6)	0 (0.0)
Respiratory, Thoracic and Mediastinal Disorders					
Epistaxis	1 (0.6)	1 (0.3)	1 (0.8)	3 (0.5)	0 (0.0)
Respiratory Disorder	1 (0.6)	4 (1.1)	0 (0.0)	5 (0.8)	0 (0.0)
Skin and Subcutaneous Tissue Disorders					
Rash	1 (0.6)	2 (0.5)	2 (1.5)	5 (0.8)	0 (0.0)

Adapted from REXULTI Approved Product Information.[1]

REXULTI had similar discontinuation rates due to adverse reactions vs placebo[1*]

*In three 12-week, placebo-controlled studies.[1]



Special warning and precautions for use

Increased mortality in elderly patients with dementia-related psychosis[1]

- Elderly patients with dementia-related psychosis treated with antipsychotic drugs like REXULTI are at an increased risk of death compared to placebo
- In patients with Alzheimer's dementia, REXULTI is only approved for the treatment of agitation and is not approved for the treatment of dementia-related psychosis or agitation due to other conditions (e.g. acute delirium)

QT prolongation[1]

- AAD patients with preexisting QTcF ≥450 msec in men and ≥470 msec in women have not been studied in the REXULTI AAD clinical development program. Any co-medication with the potential to induce QT prolongation was not studied in the AAD clinical development program
- In a study of patients with schizophrenia or schizoaffective disorder, REXULTI did not prolong the QTc interval to any clinically relevant extent at a dose four times the maximum recommended dose for the treatment of AAD

Cardiovascular disorders[1]

- AAD patients with clinically significant pre-existing cardiovascular disorders (including uncontrolled atrial fibrillation, heart failure, or ischaemic heart disease) have not been studied in the REXULTI clinical development program

AAD, agitation associated with Alzheimer's dementia.

REXULTI offers convenient once-daily dosing, with or without food[1]

REXULTI® brexpiprazole tablets

Low starting dose and 2- to 4-week titration schedule[1]

DAYS 1-7	8-14	15-28	29+	
STARTING		RECOMMENDED TARGET	RECOMMENDED TARGET	RECOMMENDED MAXIMUM
0.5 mg/day	**1** mg/day	**2** mg/day	**2** mg/day	OR → If clinically warranted → **3** mg/day

Tablets not to actual size

Dose can be increased to the maximum recommended daily dose of 3 mg/day after at least 28 days, based on clinical response and tolerability[1]

Dose adjustments for REXULTI[1]

Dose adjustments may be needed:

- in patients with hepatic or renal impairment

Administer half the usual dose of REXULTI:

- when taken with strong CYP3A4 inhibitors or strong CYP2D6 inhibitors
- in patients who are known CYP2D6 poor metabolisers

Administer a quarter of the usual dose of REXULTI:

- when taken with the concurrent use of both strong/moderate CYP2D6 inhibitors and strong/moderate CYP3A4 inhibitors
- in patients who are known CYP2D6 poor metabolisers taking strong/moderate CYP3A4 inhibitors

Administer double the usual dose over 1 to 2 weeks:

- when administering with strong CYP3A4 inducers

REXULTI now indicated for the treatment of agitation associated with Alzheimer's dementia[1*]

*In patients who are unresponsive to non-pharmacological interventions.[1]

↓31%

Proven to reduce the frequency of agitation symptoms[2†]

†Patients receiving REXULTI 2 or 3 mg/day experienced a 31% greater reduction from baseline in CMAI total score vs placebo at 12 weeks (p=0.003).[2]

Demonstrated safety profile with comparable discontinuation rates vs placebo[1‡]

‡In three 12-week, placebo-controlled studies. Discontinuation rates for REXULTI and placebo were (6.3% vs 3.4%).[1]

1.

Convenient once-daily dosing[1]

CMAI, Cohen-Mansfield Agitation Inventory.

PBS Information: Authority Required (STREAMLINED) for the treatment of schizophrenia. Code: 4246
This product is not listed on the PBS for the treatment of agitation associated with Alzheimer's dementia.

Please review the REXULTI Approved Product Information before prescribing. Product Information is available by scanning the QR code or calling Lundbeck on 1300 721 277.

Scan for PI

Minimum Product Information: Rexulti® (brexpiprazole). **Indications:** Treatment of adult patients with schizophrenia. Treatment of adult patients with agitation associated with Alzheimer's dementia (AAD), who are unresponsive to non-pharmacological interventions. **Contraindication**s: Hypersensitivity to brexpiprazole or any of the tablet excipients. **Precautions:** Elderly patients with dementia-related psychosis; suicidality; tardive dyskinesia; neuroleptic malignant syndrome; seizure; cerebrovascular events; hyperglycaemia; diabetes mellitus; orthostatic hypotension; cardiovascular disease, cerebrovascular disease or conditions predisposing to hypotension; venous thromboembolism; body temperature regulation; dysphagia; leucopenia, neutropenia, agranulocytosis; potential impairment of cognitive and motor skills; impulse control disorders; sleep apnoea; lactose containing, avoid in patients with galactose intolerance and glucose-galactose malabsorption; concomitant medical illness; pregnancy (Category C), congenital anomalies, neonatal effects; avoid breastfeeding; children <18 years; CNS disorders other than Alzheimer's Dementia (AD), QT prolongation, Cardiovascular disorders. **Interactions:** Dosage adjustment is recommended for co-administered strong CYP2D6 or CYP3A4 inhibitors (e.g. quinidine or ketoconazole) strong CYP3A4 inducers (e.g. rifampicin) see Approved PI. **Adverse Effects:** For schizophrenia there are no adverse reactions meeting the very common criteria from clinical trials. Common: diarrhoea; dyspepsia, toothache, weight increase, decreased appetite, blood creatinine phosphokinase increase, back pain, pain in extremity, muscle spasm, muscle pain, akathisia, tremor, sedation, pruritus. For AAD, common adverse events include: diarrhoea, dry mouth, asthenia, fatigue, pneumonia, urinary tract infection, blood creatine phosphokinase increased, blood pressure increased, electrocardiogram qt prolonged, weight increased, increased appetite, somnolence, insomnia. For further details on all adverse reactions see Approved PI. **Dosage & Administration:** To be taken with or without food. For schizophrenia the recommended starting dose is 1 mg once daily on Days 1–4. Titrate to 2 mg on Day 5 and to 4 mg on Day 8. Recommended target dose is 2 mg to 4 mg once daily. For AAD, the recommended starting dose is 0.5 mg once daily on Days 1–7. Titrate to 1 mg on Days 8 and to 2mg on Day 15. The recommended target dosage range is 2 mg to 3 mg once daily. Consult Approved PI for dosage adjustments for patients with renal or hepatic impairment.**Date of PI update:** 1 October 2024.

References: 1. REXULTI Approved Product Information. **2.** Lee D *et al. JAMA Neurol* 2023; 80(12): 1307–16. **3.** Grossberg GT *et al. Am J Geriatr Psychiatry* 2020; 28(4): 383–400.

Otsuka Lundbeck

REXULTI® brexpiprazole tablets