CAPLYTA™ (lumateperone) is indicated for the treatment of schizophrenia in adults.

Important Safety Information

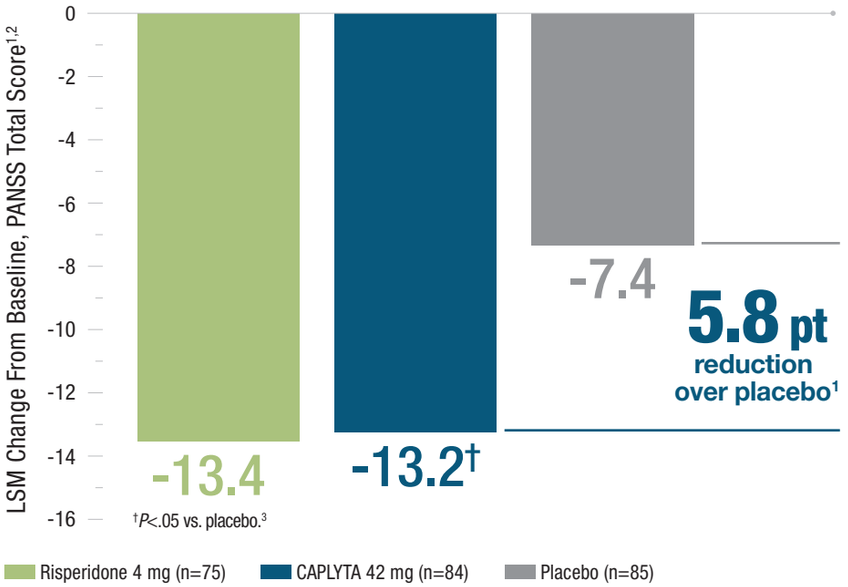
Boxed Warning: Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. CAPLYTA is not approved for the treatment of patients with dementia-related psychosis.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including **Boxed Warning**.

CAPLYTA™
(lumateperone) capsules
42 mg

In 2 clinical trials, CAPLYTA demonstrated statistically superior improvements vs. placebo in symptoms of schizophrenia[1]

Study 1. CAPLYTA Demonstrated Significant Improvements in PANSS (Positive and Negative Syndrome Scale) Total Score[1]*



Baseline PANSS Total Scores: CAPLYTA 42 mg: 88.1; risperidone 4 mg: 86.1; placebo: 86.3.[1,2]

78% greater reduction in PANSS than placebo for CAPLYTA at Day 28[1]

This study was not designed to allow for an efficacy comparison of CAPLYTA and risperidone. Risperidone was included for assay sensitivity.[1,3]

Study 1 randomized 335 patients to either CAPLYTA 42 mg, CAPLYTA 84 mg, active comparator, or placebo in a 1:1:1:1 fashion. Patients were generally moderately to markedly ill. Median age was 42 years (range 20 to 55 years). 17% were female, 19% were Caucasian, and 78% were African American. The treatment effect in the CAPLYTA 84 mg group (vs. placebo) was not statistically significant.[1,3]

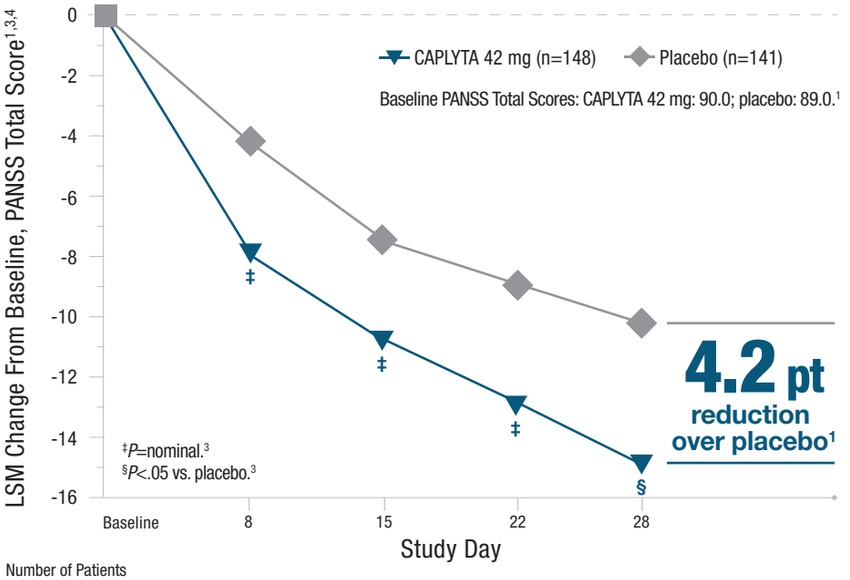
LSM=least squares mean. *Please see page 5 for description of PANSS.

Important Safety Information (continued)

Contraindications: CAPLYTA is contraindicated in patients with known hypersensitivity to lumateperone or any components of CAPLYTA. Reactions have included pruritus, rash (e.g. allergic dermatitis, papular rash, and generalized rash), and urticaria.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including **Boxed Warning**.

Study 2. Change From Baseline in PANSS Total Score[1,3,4]



Number of Patients					
Placebo	141	141	131	118	109
CAPLYTA 42 mg	148	146	142	134	130

41% greater reduction in PANSS than placebo for CAPLYTA at Day 28[1]

Limitation: The weekly time points prior to Day 28 were not powered for statistical analysis and should be considered descriptive only. Therefore, the results require cautious interpretation and could represent chance findings.[3]

Study 2 randomized 450 patients to either CAPLYTA 28 mg, CAPLYTA 42 mg, or placebo in a 1:1:1 fashion. Patients were generally moderately to markedly ill. Median age was 44 years (range 19 to 60 years). 23% were female, 26% were Caucasian, and 66% were African American. The treatment effect in the CAPLYTA 28 mg group (vs. placebo) was not statistically significant.[1,3]

Important Safety Information (continued)

Warnings & Precautions: Antipsychotic drugs have been reported to cause:

- **Cerebrovascular Adverse Reactions in Elderly Patients with Dementia-Related Psychosis,** including stroke and transient ischemic attack. See **Boxed Warning** on front cover.

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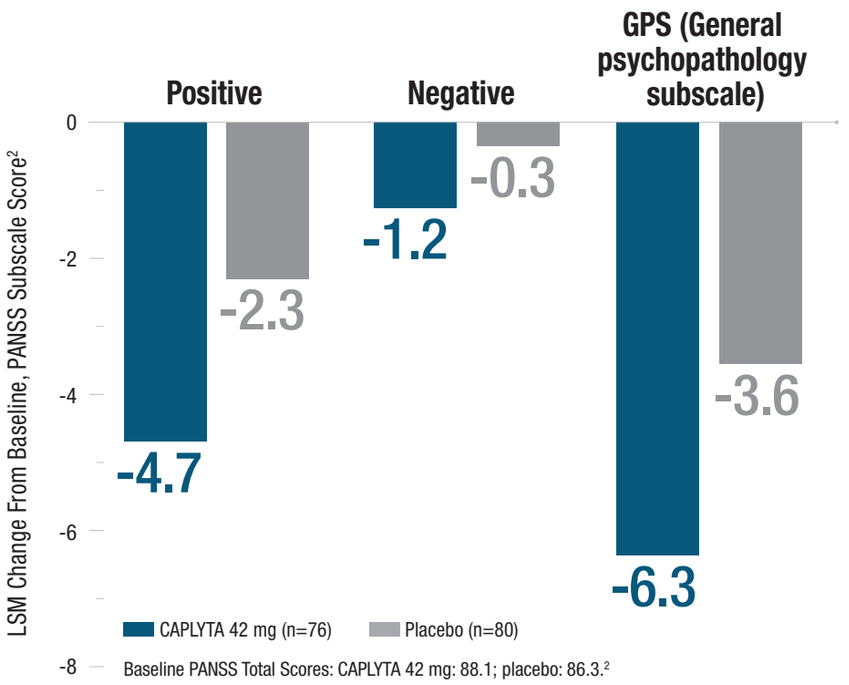
Change in PANSS symptom domains[2]



Baseline PANSS Total Scores: CAPLYTA 42 mg: 88.1; placebo: 86.3.[2]

Limitation: These secondary endpoints were not powered for statistical analysis and should be considered descriptive only. Therefore, the results require cautious interpretation and could represent chance findings.[2]

LSM=least squares mean. See page 2 for study design.

Important Safety Information (continued)

Warnings & Precautions: Antipsychotic drugs have been reported to cause:

- **Neuroleptic Malignant Syndrome,** which is a potentially fatal reaction. Signs and symptoms include: hyperpyrexia, muscle rigidity, delirium, autonomic instability, elevated creatinine phosphokinase, myoglobinuria (and/or rhabdomyolysis), and acute renal failure. Manage with immediate discontinuation of CAPLYTA and provide intensive symptomatic treatment and monitoring.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including **Boxed Warning**.

The PANSS is a 30-item scale that measures the following symptoms[5]*:

Positive Subscale Symptoms:

- Delusions
- Hallucinations
- Conceptual disorganization
- Excitement
- Grandiosity
- Suspiciousness/persecution
- Hostility

Negative Subscale Symptoms:

- Blunted affect
- Emotional withdrawal
- Poor rapport
- Passive/apathetic social withdrawal
- Difficulty in abstract thinking
- Lack of spontaneity and flow of conversation
- Stereotyped thinking

GPS Symptoms:

- Somatic concern
- Anxiety
- Guilt feelings
- Tension
- Mannerisms and posturing
- Depression
- Motor retardation
- Uncooperativeness
- Unusual thought content
- Disorientation
- Poor attention
- Lack of judgment and insight
- Disturbance of volition
- Poor impulse control
- Preoccupation
- Active social avoidance

*Each item is rated by a clinician on a 7-point scale. A score of 1 indicates the absence of symptoms, and a score of 7 indicates extremely severe symptoms. The PANSS total score may range from 30 to 210, with higher scores reflecting greater overall symptom severity.[1]

Important Safety Information (continued)

Warnings & Precautions: Antipsychotic drugs have been reported to cause:

- **Tardive Dyskinesia,** a syndrome of potentially irreversible, dyskinetic, and involuntary movements which may increase as the duration of treatment and total cumulative dose increases. The syndrome can develop after a relatively brief treatment period, even at low doses. It may also occur after discontinuation of treatment. Given these considerations, CAPLYTA should be prescribed in a manner most likely to reduce the risk of tardive dyskinesia. Discontinue CAPLYTA if clinically appropriate.

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(lumateperone) capsules

CAPLYTA demonstrated safety in over 1700 US adult patients[1]

Most Common Adverse Reactions in 4- to 6-week Inpatient Trials (Morning Dosing)[1,3]*

	CAPLYTA 42 mg (n=406)	Placebo (n=412)
Somnolence/Sedation	24%	10%
Dry mouth	6%	2%

- Somnolence with CAPLYTA was predominantly mild[3]
- There was no single adverse reaction leading to discontinuation that occurred at a rate of >2% in CAPLYTA-treated patients[1]

*Incidence of at least 5% of subjects exposed to CAPLYTA and greater than twice the rate of placebo.[1]

In short-term trials, patients on CAPLYTA experienced

metabolic, EPS, prolactin, and weight changes similar to placebo[1]

- Metabolic changes, including hyperglycemia, diabetes mellitus, dyslipidemia, and weight gain, have been reported with antipsychotic drugs[1]
- Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements, may develop in patients treated with antipsychotic drugs[1]

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including **Boxed Warning**.

Important Safety Information (continued)

Warnings & Precautions: Antipsychotic drugs have been reported to cause:

- **Orthostatic Hypotension and Syncope.** Monitor heart rate and blood pressure and warn patients with known cardiovascular or cerebrovascular disease. Orthostatic vital signs should be monitored in patients who are vulnerable to hypotension.
- **Falls.** CAPLYTA may cause somnolence, postural hypotension, and motor and/or sensory instability, which may lead to falls and, consequently, fractures and other injuries. Assess patients for risk when using CAPLYTA.
- **Seizures.** Use CAPLYTA cautiously in patients with a history of seizures or with conditions that lower seizure threshold.
- **Potential for Cognitive and Motor Impairment.** Advise patients to use caution when operating machinery or motor vehicles until they know how CAPLYTA affects them.

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Weight change on CAPLYTA in clinical trials

In short-term clinical trials, mean change in body weight from baseline at Day 28 was +3.5 lbs for CAPLYTA 42 mg and +2.9 lbs for placebo[3]

Weight change on CAPLYTA was similar to placebo in short-term trials[3]

In a long-term study of CAPLYTA, patients saw:

-4 lbs (average weight loss) after 6 months[1]

-7 lbs (average weight loss) after 1 year[1]

Important Safety Information (continued)

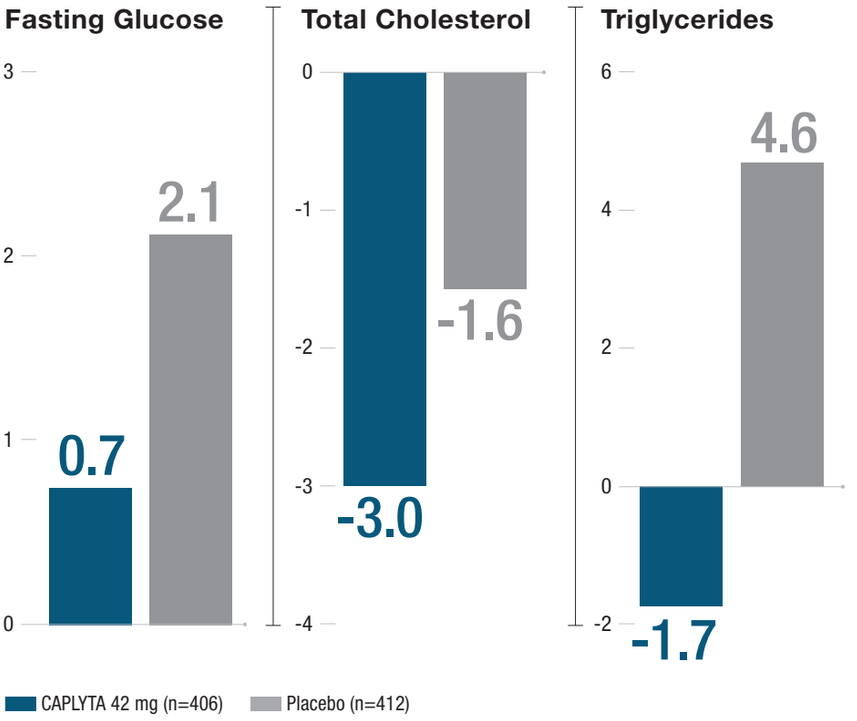
Warnings & Precautions: Antipsychotic drugs have been reported to cause:

- **Leukopenia, Neutropenia, and Agranulocytosis (including fatal cases).** Perform complete blood counts in patients with pre-existing low white blood cell count (WBC) or history of leukopenia or neutropenia. Discontinue CAPLYTA if clinically significant decline in WBC occurs in absence of other causative factors.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including **Boxed Warning**.

CAPLYTA had metabolic effects similar to placebo[1]

Mean Change From Baseline, mg/dL[3]



- CAPLYTA mean change from baseline was similar to placebo in terms of glycemic control, total cholesterol, and triglycerides[1]
- Data were collected in patients with acute schizophrenia over 4-6 weeks[1]

Important Safety Information (continued)

Warnings & Precautions: Antipsychotic drugs have been reported to cause:

- **Metabolic Changes,** including hyperglycemia, diabetes mellitus, dyslipidemia, and weight gain. Hyperglycemia, in some cases extreme and associated with ketoacidosis, hyperosmolar coma or death, has been reported in patients treated with antipsychotics. Measure weight and assess fasting plasma glucose and lipids when initiating CAPLYTA and monitor periodically during long-term treatment.

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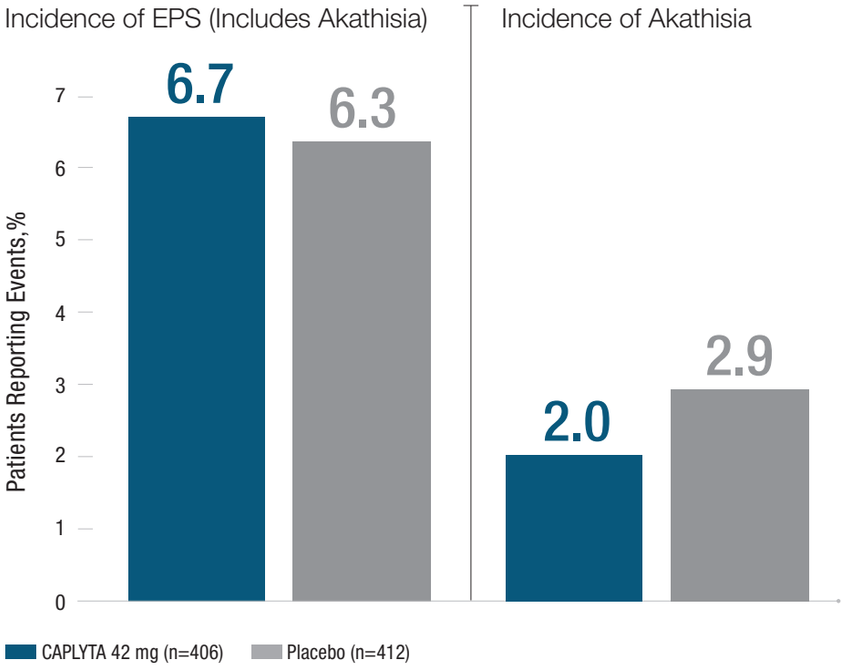
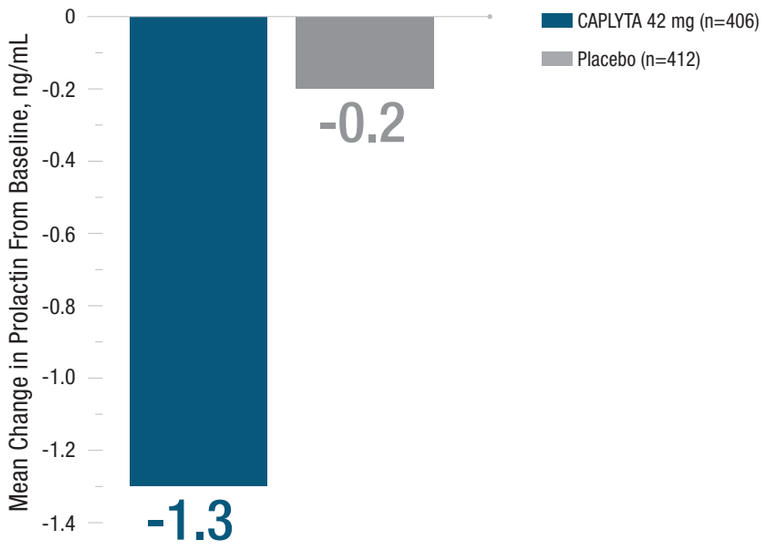
EPS profile was similar to placebo[1,3]

Incidence of EPS* and Akathisia in Acute Trials[1,3]



*EPS (extrapyramidal symptoms) include akathisia, extrapyramidal disorder, muscle spasms, restlessness, musculoskeletal stiffness, dyskinesia, dystonia, muscle twitching, tardive dyskinesia, tremor, drooling, and involuntary muscle contractions.[1]

Prolactin levels were similar to placebo[3]



Important Safety Information (continued)

Warnings & Precautions: Antipsychotic drugs have been reported to cause:

- **Tardive Dyskinesia,** a syndrome of potentially irreversible, dyskinetic, and involuntary movements which may increase as the duration of treatment and total cumulative dose increases. The syndrome can develop after a relatively brief treatment period, even at low doses. It may also occur after discontinuation of treatment. Given these considerations, CAPLYTA should be prescribed in a manner most likely to reduce the risk of tardive dyskinesia. Discontinue CAPLYTA if clinically appropriate.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including **Boxed Warning**.

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CAPLYTA had a favorable metabolic and endocrine profile with long-term use[3]

Metabolic and Endocrine Parameters in a Long-Term Trial[3]

Mean Change From Baseline

	Day 300*
Blood Glucose	
Glucose (mg/dL)	+3.0 (n=172)
Insulin (mcIU/mL)	+1.0 (n=168)
Lipids (mg/dL)	
LDL	-7.6 (n=167)
HDL	-1.4 (n=172)
Total Cholesterol	-9.6 (n=172)
Triglycerides	-2.5 (n=172)
Prolactin (ng/mL)	
Prolactin	-4.9 (n=171)

Changes in Weight in Short- and Long-Term Trials[3]

Weight (lbs)	Short-term trials†	Day 175*	Day 350*
CAPLYTA 42 mg	+3.5 (n=388)	-4.2 (n=328)	-7.2 (n=107)
Placebo	+2.9 (n=412)	N/A	N/A

- Antipsychotic drugs have been reported to cause weight gain. Measure weight when initiating CAPLYTA and monitor periodically during long-term treatment[1]

*Study Design: Open-label study of 603 stable outpatients with schizophrenia who discontinued their current antipsychotic treatment and started CAPLYTA 42 mg with no dose titration. Assessment of safety, tolerability, and efficacy were conducted at baseline and were measured at Day 8, 15, 25, and approximately every 25 days thereafter, for up to 1 year. The primary objective was to evaluate the safety and tolerability of CAPLYTA.[3]

†Data reported from 4- to 6-week placebo-controlled studies.[1]

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including **Boxed Warning**.

With CAPLYTA, your patient is on the right dose, right from the start[1]

Not actual size.

Convenient, 42 mg once-daily dose[1]

- Administered with food
- Avoid:
  - Concomitant use with CYP3A4 inducers, moderate or strong CYP3A4 inhibitors and UGT inhibitors
  - In patients with moderate to severe hepatic impairment

No dose titration required[1]

Important Safety Information (continued)

Warnings & Precautions: Antipsychotic drugs have been reported to cause:

- **Body Temperature Dysregulation.** Use CAPLYTA with caution in patients who may experience conditions that may increase core body temperature such as strenuous exercise, extreme heat, dehydration, or concomitant anticholinergics.
- **Dysphagia.** Use CAPLYTA with caution in patients at risk for aspiration.

CAPLYTA™
(lumateperone) capsules

Clinical pharmacology of CAPLYTA

The antipsychotic activity of CAPLYTA is thought to be mediated through a combination of antagonism of serotonin 5-HT_{2A} receptors and postsynaptic antagonism of dopamine D_2 receptors[1]

CAPLYTA simultaneously has:

Affinity at 5-HT_{2A} approximately 60 times higher than at dopamine D_2[1,3*]

- High 5-HT_{2A}/D_2 occupancy ratio allows for lower amounts of dopamine D_2 antagonism at therapeutic doses[6]

A moderate binding affinity for dopamine D_1 and SERT[1]

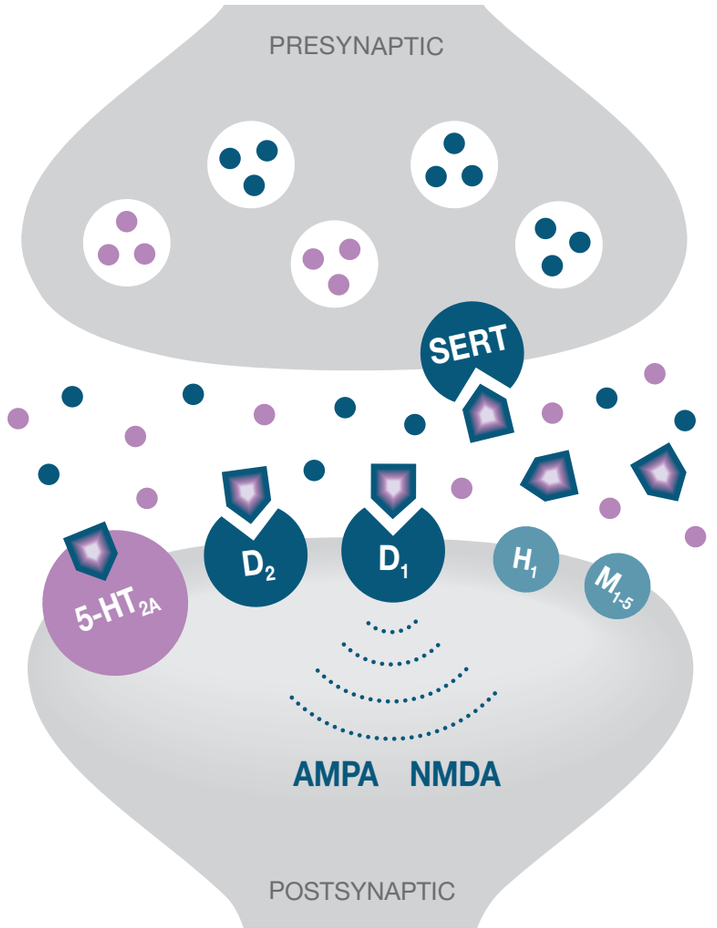
A low binding affinity for off-target receptors like muscarinic and histaminergic receptors[1]

The mechanism of action of CAPLYTA in schizophrenia is unknown.[1]

Elevated levels of dopamine D_2 receptor occupancy are known to be associated with increases in EPS and prolactin.[6]

*5-HT_{2A} (k_i=0.48 nM); D_2 (k_i=47 nM); human recombinant receptor expressed in HEK-293 cells. Observed values may vary.[3]

MOA Visualization



The binding of CAPLYTA to the D_1 receptor may contribute to indirect activation of the AMPA and NMDA receptors[7]

Important Safety Information (continued)

Drug Interactions: Avoid concomitant use with CYP3A4 inducers, moderate or strong CYP3A4 inhibitors and UGT inhibitors.

Special Populations: Neonates exposed to antipsychotic drugs during the third trimester of pregnancy are at risk for extrapyramidal and/or withdrawal symptoms following delivery. Breastfeeding is not recommended. Avoid use in patients with moderate or severe hepatic impairment.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including **Boxed Warning**.

Important Safety Information (continued)

Adverse Reactions: The most common adverse reactions in clinical trials with CAPLYTA vs. placebo were somnolence/sedation (24% vs. 10%) and dry mouth (6% vs. 2%).

CAPLYTA™
(lumateperone) capsules

LYTAlink™

Help your patients start and stay on CAPLYTA

Intra-Cellular Therapies is committed to supporting you and your patients

Savings card

Eligible, commercially insured patients may **pay as little as $0 for their first fill** and **$15 for subsequent fills** of CAPLYTA.

How to access the savings card:

- Provide your patients with the savings card
- Patients can text "CAPLYTA" to 26789 to receive the Copay eCard on their phones through the **CAPLYTA text message program**. Patients can also sign up for text messages about copay savings and refill reminders. Patients can opt out of this program at any time
- Patients can download the copay card at www.CAPLYTA.com

Prior authorization support

You can visit www.covermymeds.com to initiate the prior authorization process for both commercially and government-insured patients.

1-866-452-5017 or live chat at www.covermymeds.com
(M-F: 8:00AM-11:00PM ET, Sat: 8:00AM-6:00PM ET)

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including **Boxed Warning**.

Medicare Part D/low-income subsidy patients[8,9]

Your Medicare Part D patients with a low-income subsidy (LIS) may be able to receive help with prescription costs through Medicare. This program is also known as **Extra Help**.

Medicare Part D patients are automatically enrolled in Extra Help if they are:

- Dual eligible: receive both Medicare and Medicaid, or are older than 65 years and on Medicaid
- Receiving Supplemental Security Income
- Members of a Medicare Savings Program

Patients who are enrolled in Extra Help pay a maximum of $8.95 for brand name prescriptions[10]

- Medicare beneficiaries receiving LIS get assistance in paying for their Part D monthly premium, annual deductible, coinsurance, and copayments. Also, individuals enrolled in the Extra Help program do not have a gap in prescription drug coverage, also known as the coverage gap, or the Medicare "donut hole"[8]

PROGRAM TERMS, CONDITIONS, AND ELIGIBILITY CRITERIA: This offer is valid for eligible new or existing patients who are filling a prescription for CAPLYTA. Eligible patients must be at least 18 years old and less than 65 years old, residents of the U.S., excluding Puerto Rico, and have a valid prescription for CAPLYTA for a Food & Drug Administration–approved indication. This Co-Pay Program is valid ONLY for patients with commercial insurance and NOT valid for prescriptions reimbursed under Medicaid, a Medicare drug benefit plan, TRICARE, or other federal or state health programs. Offer is not valid for cash paying patients and is only good at participating retail pharmacies. Offer is not transferable, is not insurance, has no cash value, and may not be used in combination with other offers. Void if prohibited by law, taxed, or restricted.

All participants are responsible for reporting the receipt of all Program benefits as required by their insurance provider. No party may seek reimbursement for all or any of the benefit received through this Program. ITCI reserves the right to rescind, revoke or amend the Program without notice at any time. Additional eligibility criteria apply. See full terms and conditions at www.caplyta.com/cost-savings

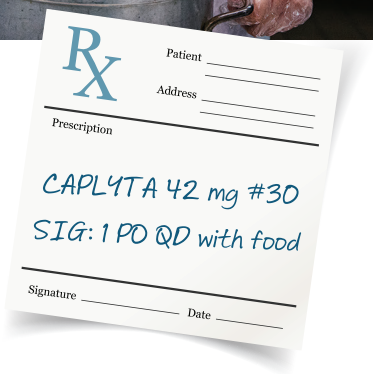
CAPLYTA™
(lumateperone) capsules

CAPLYTA FOR SCHIZOPHRENIA IN ADULTS

Choose CAPLYTA

to help control your patients' symptoms with low rates of side effects[1]

- In clinical trials, the most common adverse reactions were somnolence/sedation (24%) and dry mouth (6%)[1]



CAPLYTA 42 mg offers convenient, titration-free, once-daily dosing with food[1]

- Avoid:
  - Concomitant use of CAPLYTA with CYP3A4 inducers and moderate or strong CYP3A4 inhibitors and UGT inhibitors
  - Use of CAPLYTA in patients with moderate or severe hepatic impairment

Important Safety Information

Boxed Warning: Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. CAPLYTA is not approved for the treatment of patients with dementia-related psychosis.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including **Boxed Warning**.

References: 1. CAPLYTA prescribing information, 2019. **2.** Lieberman JA, Davis RE, Correll CU, et al. ITI-007 for the treatment of schizophrenia: a 4-week randomized, double-blind, controlled trial. *Biol Psychiatry*. 2016;79(12):952-961. **3.** Data on File. 2019. **4.** Correll CU, Davis RE, Weingart M, et al. Efficacy and safety of lumateperone for treatment of schizophrenia: a randomized clinical trial. *JAMA Psychiatry*. Published online January 08, 2020. **5.** Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr Bull*. 1987;13(2):261-276. **6.** Davis RE, Correll CU. CAPLYTA in the treatment of schizophrenia: from novel pharmacology to clinical outcomes. *Expert Rev Neurother*. 2016;6(16):601-614. **7.** Kumar B, Kuhad A, Kuhad A. Lumateperone: a new treatment approach for neuropsychiatric disorders. *Drugs Today (Barc)*. 2018;54(12):713-719. **8.** eHealth Medicare. Low-income subsidy—Medicare Extra Help Program. Accessed February 13, 2020. https://www.ehealthmedicare.com/medicarepart-d-articles/low-income-subsidy-medicare-extra-help-program. **9.** Centers for Medicare and Medicaid Services. Medicare Prescription Drug Benefit Manual: Chapter 13-Premium and cost-sharing subsidies for low-income individuals. Updated July 29, 2011. Accessed February 13, 2020. http://www.cms.gov/Regulations-and-Guidance/Guidance/Transmittals/Downloads/Chapter13.pdf. **10.** Medicare & Medicaid Services. Announcement of Calendar Year (CY) 2020 Medicare Advantage capitation rates and Medicare Advantage and Part D payment policies and final call letter. Published April 1, 2019. Accessed February 13, 2020. https://www.cms.gov/Medicare/Health-Plans/MedicareAdvtgSpecRateStats/Downloads/Announcement2020.pdf.

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