## A closer look at GOCOVRI®


# GO

with **all-day** medication coverage

With 1 nightly dose, GOCOVRI is the **only** medication proven to reduce **both** dyskinesia and OFF time for more GOOD ON time, today and tomorrow.

### INDICATIONS

GOCOVRI® is indicated:

- For the treatment of dyskinesia in patients with Parkinson's disease receiving levodopa-based therapy, with or without concomitant dopaminergic medications
- As adjunctive treatment to levodopa/carbidopa in patients with Parkinson's disease experiencing "off" episodes

### IMPORTANT SAFETY INFORMATION

#### CONTRAINDICATIONS

- GOCOVRI is contraindicated in patients with end-stage renal disease (creatinine clearance below 15 mL/min/1.73 $m^2$).

GOCOVRI®
(amantadine) extended release capsules
68.5 mg | 137 mg

**Please see additional Important Safety Information on (page 1) and full Prescribing Information.**

## IMPORTANT SAFETY INFORMATION (CONT'D)
## WARNINGS AND PRECAUTIONS

- **Falling Asleep During Activities of Daily Living and Somnolence:** Patients treated with Parkinson's disease medications have reported falling asleep during activities of daily living. If a patient develops daytime sleepiness during activities that require full attention (e.g., driving a motor vehicle, conversations, eating), GOCOVRI should ordinarily be discontinued, or the patient should be advised not to drive and to avoid other potentially dangerous activities.
- **Suicidality and Depression:** Monitor patients for depression, including suicidal ideation or behavior. Prescribers should consider whether the benefits outweigh the risks of treatment with GOCOVRI in patients with a history of suicidality or depression.
- **Hallucinations/Psychotic Behavior:** Patients with a major psychotic disorder should ordinarily not be treated with GOCOVRI because of the risk of exacerbating psychosis. Observe patients for the occurrence of hallucinations throughout treatment, especially at initiation and after dose increases.
- **Dizziness and Orthostatic Hypotension:** Monitor patients for dizziness and orthostatic hypotension, especially after starting GOCOVRI or increasing the dose. Concomitant use of alcohol when using GOCOVRI is not recommended.
- **Withdrawal-Emergent Hyperpyrexia and Confusion:** Rapid dose reduction or abrupt discontinuation of GOCOVRI may cause an increase in the symptoms of Parkinson's disease or cause delirium, agitation, delusions, hallucinations, paranoid reaction, stupor, anxiety, depression, or slurred speech. Avoid sudden discontinuation of GOCOVRI.
- **Corneal Edema:** Has been reported and onset can occur within a few weeks to several years. Symptoms include sudden onset blurry vision, or progressive vision loss, with or without eye pain. Corneal involvement is usually bilateral. Corneal grafts have been required when not recognized. Permanent damage can occur if amantadine is continued. Ask patients if their vision has changed and obtain ophthalmologic exams to rule out corneal edema if changes occur. If corneal edema occurs, taper and discontinue GOCOVRI. Resolution typically begins within weeks of cessation.
- **Impulse Control/Compulsive Behaviors:** Patients can experience intense urges (e.g., gambling, sexual, money spending, binge eating) and the inability to control them. It is important for prescribers to ask patients or their caregivers about the development of new or increased urges. Consider dose reduction or stopping GOCOVRI.

## ADVERSE REACTIONS

- The most common adverse reactions (>10% and greater than placebo) were hallucination, dizziness, dry mouth, peripheral edema, constipation, falls, and orthostatic hypotension.

**Please see full Prescribing Information.**

# In clinical trials, GOCOVRI® results showed:

**Significant reductions in both dyskinesia and OFF time, leading to increased GOOD ON time throughout the day.[1,2]**

**Durable reductions in motor complications (MDS-UPDRS Part IV) observed out to 2 years.[3,4]**

## THE EFFICACY AND SAFETY PROFILE OF GOCOVRI 274 MG QHS WERE EVALUATED IN RANDOMIZED PLACEBO-CONTROLLED TRIALS[1,2]

| | |
|---|---|
| **Study Designs** | **Study 1:** 24-week study, PD patients* with dyskinesia (N=121)<br>**Study 2:** 12-week study, PD patients* with dyskinesia (N=75) |
| **Outcomes Measured & Results** | **Primary efficacy endpoint:** Change in Unified Dyskinesia Rating Scale (UDysRS†) total score from baseline through Week 12: -17.7 (GOCOVRI) vs -7.6 (placebo) ($P$<0.0001)<br>**Key secondary endpoints:** (from baseline to Week 12)<br>- GOOD ON time‡: 3.8 h increase (GOCOVRI) vs 1.4 h (placebo) ($P$<0.0001)<br>- OFF time: 0.6 h decrease (GOCOVRI) vs 0.4 h *increase* (placebo) ($P$=0.0006) |

Levodopa (LD) and other PD medication dose adjustments were not allowed during the course of either pivotal Phase 3 study. In all, 100% of patients received LD and 68% received concomitant dopaminergic medications with LD.[1,2]

## IMPACT OF GOCOVRI ON MOTOR COMPLICATIONS WAS EVALUATED IN THE LARGEST AND LONGEST-RUNNING (2 YEARS) OPEN-LABEL TRIAL OF AMANTADINE-BASED THERAPY TO DATE[3,4]

| | |
|---|---|
| **Study Design** | Patients (N=223) directly enrolled at completion of GOCOVRI Phase 3 trials (continuing GOCOVRI or previous placebo) or patients enrolled from a broader population representing real-world clinical settings (DBS or amantadine IR):<br>- **CONTINUING GOCOVRI** (n=60)<br>- **PREVIOUS PLACEBO** (n=78)<br>- **DBS** (n=61)<br>- **GAP'** (n=24) → - **AMANTADINE IR§** (n=32)<br>All groups started at a daily GOCOVRI dose of 137 mg during Week 1, then increased to a maintenance dosage of 274 mg from Week 2 to Week 100, and tapered back down to 137 mg for the final week.[3] |
| **Outcomes Measured** | **Primary endpoint:** Evaluating long-term safety and tolerability of GOCOVRI.<br>**Key secondary endpoint:** Change in MDS-UPDRS Part IV measuring motor complications with a higher score indicating an increase in severity (max score of 24).[5] |

Study participants were allowed to change PD medications (including levodopa dose) throughout the trial as needed; however, other amantadine formulations were not permitted.[3]

*Patients who had at least 1 hour of troublesome dyskinesia time during the day and at least mild functional impact because of dyskinesia.[1]

†The Unified Dyskinesia Rating Scale (UDysRS) is a standardized clinical research tool that uses both patient historical and objective measurements to assess presence of dyskinesia and its impact on daily activities. Total scores range from 0 to 104 points, with higher scores indicating more severe dyskinesia.[6]

‡GOOD ON time = ON time without troublesome dyskinesia.

§Previous-amantadine IR subgroup represented patients who were being treated with amantadine IR at the time of enrollment in the present trial and switched directly to open-label GOCOVRI. These patients came from the Participation-Gap (n=8) or the DBS group (n=24).

'Participation-Gap group represented patients who completed double-blind treatment in a GOCOVRI clinical trial (EASED, EASE LID, or EASE LID 3) but did not enroll directly in the present trial.

**Abbreviations:** QHS, once at bedtime; PD, Parkinson's disease; DBS, deep brain stimulation; IR, immediate release; MDS-UPDRS, Movement Disorders Society-Unified Parkinson's Disease Rating Scale.

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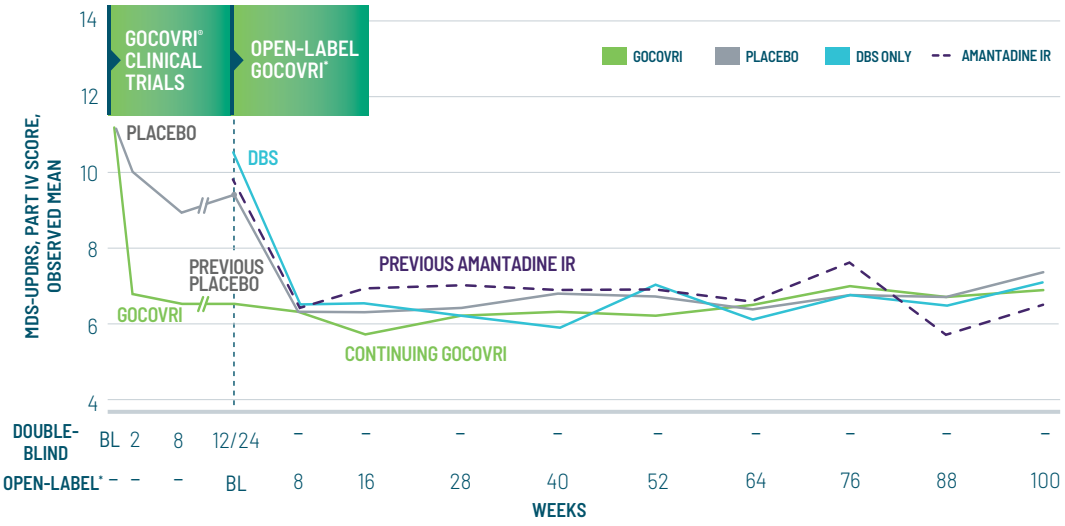
# Long-term results

## Reductions in motor complication scores were maintained for all groups, regardless of previous therapy, for the full 2 years of the OLE, including patients previously on amantadine IR and with DBS.[3,4]




MDS-UPDRS Part IV measures motor complications within the last week, including[5]:

- Time spent with dyskinesia (0–4 pts)
- Functional impact of dyskinesia (0–4 pts)
- Time spent in OFF dystonia (0–4 pts)
- Functional impact of fluctuations (0–4 pts)
- Complexity of motor fluctuations (0–4 pts)
- Painful OFF-state dystonia (0–4 pts)

*Number of patients enrolling directly from the double-blind study were at baseline and at week 100, respectively: continuing GOCOVRI 60, 37; previously on placebo: 78, 42; DBS: 61, 41; previously on amantadine IR: 32, 20. Participation-Gap patients are not summarized here due to small sample size.

**Study Limitation:** This study's real-world design permitted treatment with an adjustment of concomitant PD treatments. The lack of a blinded control group reduced the certainty that study findings were due to GOCOVRI. **No formal comparisons can be made between GOCOVRI and other treatment regimens.**[3]

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# All-day medication coverage

## GOCOVRI® has a PK profile that uniquely combines delayed-release and extended-release amantadine.[7]

A SINGLE BEDTIME DOSE OF GOCOVRI DELIVERS HIGH MORNING LEVELS BEFORE THE FIRST LEVODOPA DOSE AND DECREASES IN THE LAST HOURS OF THE DAY[7]


**Amantadine is thought to reduce glutamate hyperactivity by blocking the glutamate NMDA receptor. GOCOVRI is the only amantadine product that is designed to provide a high plasma concentration in the morning to reduce glutamate hyperactivity before the first dose of levodopa.**[1]

There are no head-to-head studies in patients with PD comparing the safety and efficacy of GOCOVRI to that of amantadine IR.

PK data do not provide evidence of clinical safety or efficacy.

These simulated data are derived from a steady-state PK study using the 137 mg QHS dose of GOCOVRI and amantadine IR 81 mg BID.[7]

**GOCOVRI is not interchangeable with other amantadine immediate- or extended-release products.**[1]

**Abbreviations:** BID, twice daily; NMDA, N-methyl-D-aspartate; PK, pharmacokinetic.

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# GO get started

## A convenient, single nightly dose provides all-day medication coverage[1]

**GOCOVRI is available at 2 starting dose strengths for flexible dosing based on your patient's needs.**

### ACHIEVE THE RECOMMENDED DOSE IN JUST 1 WEEK.

| STARTING DOSE - WEEK 1 | TREATMENT DOSE - AFTER WEEK 1 |
|---|---|
|  **137 mg QHS**[2] (CrCl ≥ 60 mL/min/1.73 m$^2$) |  **274 mg QHS**[2] (CrCl ≥ 60 mL/min/1.73 m$^2$) |

**RENAL CONSIDERATIONS:** Since many patients with PD are elderly and more likely to have decreased renal function, a lower starting dose should be considered.*

| STARTING DOSE - WEEK 1 | TREATMENT DOSE - AFTER WEEK 1 |
|---|---|
|  **Starting dose, moderate and severe impairment 68.5 mg QHS**[2] (CrCl = 15-59 mL/min/1.73 m$^2$) |  **Maximum dose, moderate impairment 137 mg QHS**[2] (CrCl = 30-59 mL/min/1.73 m$^2$)<br>  **Maximum dose, severe impairment 68.5 mg QHS**[2] (CrCl = 15-29 mL/min/1.73 m$^2$) |

*Please see full Prescribing Information for additional dosing information for patients with renal impairment.

## Support to help your patients get started and stay on GOCOVRI

### SAMPLES

Samples are available to provide to your patients to determine if GOCOVRI is the next right step in their treatment regimen.†

### $20 CO-PAY

Commercially insured patients who participate in the GOCOVRI Assistance Program pay $20 per prescription‡ until the maximum annual benefit is reached.

†Patients may either participate in the free-trial program or the in-office sample program, but not both.
‡This offer is valid only for patients who have commercial (non-government-funded) insurance and must meet eligibility requirements. See full Terms & Conditions at GocovriHCP.com/terms-and-conditions.

**Abbreviation:** CrCl, creatinine clearance.

**1.** GOCOVRI. Package Insert. Adamas Pharma, LLC. **2.** Elmer LW, Juncos JL, Singer C, et al. Pooled analyses of phase III studies of ADS-5102 (amantadine) extended-release capsules for dyskinesia in Parkinson's disease. *CNS Drugs*. 2018;32(4):387-398. doi:10.1007/s40263-018-0498-4 **3.** Tanner CM, Pahwa R, Hauser RA, et al. EASE LID 2: a 2-year open-label trial of Gocovri (amantadine) extended release for dyskinesia in Parkinson's disease. *J Parkinsons Dis*. 2020;10(2):543-558. doi:10.3233/JPD-191841 **4.** Isaacson SH, Fahn S, Pahwa R, et al. Parkinson's patients with dyskinesia switched from immediate release amantadine to open-label ADS-5102. *Mov Disord Clin Pract*. 2018;5(2):183-190. doi:10.1002/mdc3.12595 **5.** Goetz CG, Tilley BD, Shaftman SR, et al. Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): scale presentation and clinimetric testing results. *Mov Disord*. 2008;23(15):2129-2170. doi:10.1002/mds.22340 **6.** Goetz CG, Nutt JG, Stebbins GT. The Unified Dyskinesia Rating Scale: presentation and clinimetric profile. *Mov Disord*. 2008;23(16):2398-2403. doi:10.1002/mds.22341 **7.** Hauser RA, Pahwa R, Wargin WA, et al. Pharmacokinetics of ADS-5102 (amantadine) extended release capsules administered once daily at bedtime for the treatment of dyskinesia. *Clin Pharmacokinet*. 2019;58(1):77-88. doi:10.1007/s40262-018-0663-4

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