tavapadon (Juvmo™)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO351

Description

Tavapadon (Juvmo) is a dopamine receptor agonist that selectively targets and binds to dopamine D1/D5 receptor subtypes.

Length of Authorization

- Initial: 12 months
- Renewal: 12 months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit*
tavapadon (Juvmo)	Parkinson's disease	Titration pack (0.25 mg and 1 mg)	100 tablets/40 days
		5 mg, 10 mg, and 15 mg tablets	30 tablets/30 days

**See appendix for quantity exceptions when members are already on long-term moderate CYP3A4 inducers. Quantity exceptions beyond 45 mg/day are not allowed.*

Initial Evaluation

~~I.~~ **Tavapadon (Juvmo)** may be considered medically necessary when the following criteria are met:

A. The member has a diagnosis of **Parkinson's Disease (PD); AND**

B. Medication is prescribed by, or in consultation with, a neurologist, or prescriber specializing in the treatment of Parkinson's disease; **AND**

C. Member has experienced inadequate control of Parkinson's disease symptoms on maximum tolerated doses of oral levodopa-based therapy; **OR**

1. Member has a documented contraindication to levodopa-based therapy; **AND**

D. Treatment with at least <u>two</u> of the following have been ineffective or not tolerated with documentation of adherence and history of what defined failure for this member, unless all are contraindicated:

1. Pramipexole or pramipexole ER*
2. Ropinirole or ropinirole ER*
3. Rotigotine patch (Neupro)*; **AND**

E. Treatment with at least <u>two</u> of the following have been ineffective or not tolerated with documentation of adherence and history of what defined failure for this member, unless all are contraindicated:

1. Monoamine oxide –B (MAO-B) inhibitor (e.g., rasagiline, safinamide, selegiline)*
2. Catechol-O-methyl transferase (COMT) inhibitor (e.g., entacapone, opicapone (Ongentys), tolcapone)*
3. Amantadine

*<u>Please note:</u> medications notated with an asterisk may require additional review

II. Tavapadon (Juvmo) is considered investigational when used for all other conditions, including, but not limited to:
   A. Restless leg syndrome (RLS)

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member has exhibited improvement or stability of disease symptoms [e.g., experienced improvement in motor symptoms, reduction in "Off" periods, reduced dose of levodopa, etc.]

Supporting Evidence

I. Motor symptoms in Parkison's disease (PD) impact affect as many as 77% of patients; these include physical, visible signs of PD: resting tremor, muscular rigidity, postural instability. These advance into falls, axial postural deformities, dysphagia, and in advanced disease, these pharyngeal dysfunctions have an increase in aspiration risk and lead to higher numbers of upper respiratory tract infections and pneumonia. Pharmacotherapies for managing the symptoms of PD show the greatest efficacy early in the course of the disease. As symptoms become refractory to standard therapies, levodopa, patients begin experiencing fluctuations in symptoms ("Off" periods) within two years of beginning therapy.
II. Levadopa based regimen (e.g., oral carbidopa/levodopa) is the most effective mainstay for PD motor symptoms. Motor fluctuations, including end-of-dose "wearing off," may be managed by adjusting the dose or timing, reducing dietary protein or taking levodopa on an empty stomach, using longer-acting formulations, treating constipation, or adding dopamine agonist (e.g., pramipexole, ropinirole, or rotigotine), a COMT inhibitor (e.g., entacapone, opicapone, or tolcapone), or MAO-B inhibitors (rasagiline, safinamide, or selegiline) may be needed if adjustments to levodopa for "wearing off" are insufficient or poorly tolerated. While the choice of medication should be personalized for each patient, the primary considerations when adding adjunctive medications are the potential for worsened dyskinesia and nonmotor dopaminergic side effects (e.g., impulse control disorders, orthostatic hypotension, hallucinations, sleep disturbances, etc.).
III. Some patients unresponsive to one dopamine agonist may respond to another, although this effect is unpredictable. Comparative analyses of dopamine agonist formulations found limited evidence that any specific formulation or route of administration is superior.
IV. Dopamine agonists may also be recommended in early Parkinson's disease with minimal motor symptoms (as levodopa-sparing therapy) and as adjunctive therapy to carbidopa/levodopa to improve wearing off effects. For more advanced disease, on-demand agents such as subcutaneous apomorphine (Apokyn) or inhaled levodopa (Inbrija) are indicated to manage sudden or prolonged "Off" episodes. Device-assisted infusions are also available to provide

continuous exposure to dopaminergic therapy for the treatment of motor fluctuations in advanced disease. These devices include levodopa-carbidopa intestinal gel (LCIG Duopa) administered through a percutaneous gastrojejunostomy tube and continuous subcutaneous infusions (CSIs) with foscarbidopa/foslevodopa (Vyalev) or apomorphine (Onapgo).

V. The 2025 Update on Treatments for Parkinson's Disease Motor Fluctuations – An International Parkinson and Movement Disorder Society (IPMDS) Evidence-Based Medicine Review states levodopa ER, pramipexole IR and ER, ropinirole IR, rotigotine, opicapone, safinamide, and bilateral subthalamic nucleus deep brain stimulation (STN DBS) were assessed as efficacious, and continuous intestinal levodopa infusion, continuous subcutaneous (SC) levodopa, continuous SC apomorphine, ropinirole prolonged release, ropinirole patch, continuous SC apomorphine, entacapone, rasagiline, istradefylline, amantadine controlled release, zonisamide, bilateral globus pallidus (GPi) DBS, and pallidotomy were assessed as likely efficacious for the treatment of motor fluctuations in people with PD who are already being treated with levodopa.

VI. Device-assisted and surgical treatments are also available to improve motor function in selected patients with advanced PD and motor fluctuations, whose condition cannot be further improved by medical therapy. These treatments may include deep brain stimulation (DBS), focused ultrasound therapy (FUS), continuous levodopa-carbidopa intestinal gel (Duopa) infusion, and continuous subcutaneous apomorphine infusion (Apokyn, Kynmobi).

VII. Advanced Parkinson's disease is not well defined in clinical literature; however, advanced PD may be described as the later stages of the disease when symptoms have progressed significantly and impact daily life. Clinical trials often define advanced PD based on the presence of motor fluctuations, emergence of dyskinesia, and/or a certain amount of motor "Off" time in a day and use progression of motor symptoms as a marker. Additional clinical features may include more difficulty with completing activities of daily living, severe motor fluctuations (tremors, rigidity, slow movement, increasing falls, motor "off" time in a day), non-motor symptoms (sleep disturbances, depression, anxiety), and emergence of cognitive decline (confusion, hallucinations, memory loss).

VIII. Tavapadon (Juvmo) is the first selective (non-ergot) D1/D5 dopamine receptor agonist; however, selective D1/D5 partial agonism proposed neuropsychiatric advantage over D2/D3 agonists remains unknown. The efficacy of tavapadon (Juvmo) was established in the TEMPO clinical development program. The expected place in therapy for tavapadon (Juvmo) is as an adjunct to levodopa and as an alternative to other dopamine agonists.

a. The TEMPO-1 and TEMPO-2 trials evaluated tavapadon (Juvmo) vs. placebo in adults with PD not on concomitant levodopa. Across TEMPO-1 and TEMPO-2 clinical trials, 28% of patients on tavapadon (Juvmo) were taking MAO-B inhibitors at baseline. The primary endpoint was change from baseline to week 26 in the combined score of the MDS-UPDRS Parts II and III (reflecting activities of daily living and motor performance) at 26 weeks. Tavapadon (Juvmo) improved motor and activities of daily living scores relative to placebo at 26 weeks in early Parkinson disease. The TEMPO-3 trial evaluated the safety and efficacy of flexible-dose tavapadon (Juvmo) (5-15 mg once daily) or placebo adjunctive to oral levodopa in adults with PD experiencing motor fluctuations. Treatment adding tavapadon (Juvmo) to levodopa increased total daily "On" time

without troublesome dyskinesia by roughly one hour more than placebo and cut "Off" time by about an hour as well. Durability of response was maintained up to 20 months in the long term open-label extension study (TEMPO-4) evaluating rollover participants previously receiving tavapadon in early and advanced PD.

IX. The safety profile of tavapadon (Juvmo) in the TEMPO studies was consistent throughout the clinical program, where most AEs were nonserious, mild or moderate in severity. The incidence of adverse events in tavapadon (Juvmo) group was highest during the titration phase than during the dose adjustment or maintenance phases. Rates of discontinuation due to AEs were higher for tavapadon (Juvmo) across trials, with the most common reason being due to AE. Treatment-emergent adverse events led to early study discontinuation in 22-30% of patients treated with tavapadon (Juvmo) and in 9-19% of those treated with placebo. This appears to be similar to the discontinuation rates of available dopamine agonist therapy, with reports of up to 44% of patients discontinuing dopamine agonist treatment within the first two months of initiating dopamine agonists compared to levodopa (Frazer et al. 2022). The most common reported AE (> 5%): tavapadon (Juvmo) versus placebo (without concomitant levodopa) were nausea (27% vs. 2%), headache (17% vs. 5%), dizziness (14% vs. 4%), fatigue (10% vs 3%), dysgeusia (8% vs 0%), vomiting (7% vs <1%), dry mouth (5% vs <1%), and anxiety (5% vs 2%). Tavapadon (Juvmo) with concomitant oral levodopa versus placebo and oral levodopa: nausea (14% vs 4%), dyskinesia (10% vs 2%), dizziness (8% vs 3%), headache (7% vs. 3%), hallucinations (7% vs 1%), and orthostatic hypotension (6% vs 1%).
    a. Adverse events of special interest:
        i. Tavapadon (Juvmo) without concomitant levodopa: Incidence rates of somnolence were similar between tavapadon (Juvmo) and placebo groups (3.2% vs 3.7%). Impulse control disorders and dyskinesia were reported in 1% and 0.6% of participants receiving tavapadon (Juvmo) vs 0% in placebo.
        ii. Tavapadon (Juvmo) with concomitant oral levodopa: Incidence rates of somnolence were similar between tavapadon (Juvmo)+levodopa and placebo+levodopa groups (5.2% vs 4.3%). Impulse control disorders and dyskinesia were reported in 2% tavapadon (Juvmo)+levodopa vs 1% in placebo+ levodopa. Dyskinesia was reported in 10% of participants receiving tavapadon (Juvmo)+levodopa vs 2% in placebo.

X. The label does not carry contraindications for use; however, the warnings and precautions of the label are consistent with other dopamine agonists on the market. The warnings and precautions section of the tavapadon (Juvmo) label includes hypotension/orthostatic hypotension, impulse control/compulsive behaviors, and hallucinations and psychotic-like behavior, based on the side effect profile reported in the TEMPO clinical program. In absence of tavapadon demonstrating superior efficacy over comparable alternatives and high cost, trials of cost-effective dopaminergic agonist treatment options and guideline directed PD therapies are available and should be considered prior to coverage.

XI. Tavapadon (Juvmo) has clinically significant drug-drug interactions with CYP3A inhibitors and inducers. The tavapadon (Juvmo) label includes a statement on avoiding concomitant use of strong or moderate CYP3A inhibitors during titration. Dose modification may be necessary for

patients initiating a strong or moderate CYP3A4 inhibitor for patients already established on tavapadon (Juvmo) maintenance (5-15mg daily). Examples of strong or moderate CYP3A inhibitors include clarithromycin, itraconazole, ketoconazole, and other medications that substantially inhibit CYP3A metabolism. For members already receiving maintenance therapy, tavapadon (Juvmo) dosing frequency must be reduced when a strong or moderate CYP3A inhibitor is initiated (e.g., 5 mg once daily reduced to 5 mg every 7 days with a strong CYP3A inhibitor or every 3 days with a moderate CYP3A inhibitor). Conversely, strong CYP3A inducers (e.g., rifampin, carbamazepine, phenytoin, St. John's wort) should be avoided during both titration and maintenance therapy because they can substantially reduce tavapadon (Juvmo) exposure and may compromise efficacy. Long-term use of moderate CYP3A inducers may require modified titration and increased dosing frequency per prescribing information. Therefore, quantity exceptions beyond the maximum recommended maintenance dose of 15 mg daily will be reviewed on a case-by-case basis and may be considered only when medically necessary to manage clinically significant CYP3A-mediated drug interactions.

XII. There is moderate confidence in the quality of evidence given the statistically significant results of the TEMPO-program, reporting tavapadon (Juvmo) improved motor symptoms and activities of daily living in early PD and as an adjunct to levodopa in PD. The primary endpoints were validated and tavapadon (Juvmo) achieved clinically meaningful changes in motor improvements as well as clinically meaningful improvement in good “On” time without troublesome dyskinesia. The efficacy results of tavapadon (Juvmo) appear similar to other dopamine agonists. However, indirect comparison is difficult due to due to variable outcome methodologies across studies. Trial limitations include lack of active comparators.

XIII. The Institute for Clinical and Economic Review (ICER) published evidence report on tavapadon (Juvmo) and treatment for PD found tavapadon (Juvmo) to be comparable to currently available treatments and concluded therapy is not cost effective when compared to key alternatives. Key findings noted, “…while tavapadon provides some relief from key symptoms, benefits were similar to those of older, generic drugs, and discontinuation from tavapadon due to adverse events was relatively high. The combination of modest benefit and uncertainties around discontinuation raise important questions about tavapadon’s long-term value.”.

Investigational or Not Medically Necessary Uses

I. Tavapadon (Juvmo) has not been FDA-approved or sufficiently studied for safety and efficacy for other conditions or settings.
   A. Restless leg syndrome
      i. Several dopamine agonists agents are also FDA-approved to treat restless legs syndrome (RLS), in which patients experience irrepressible sensations in the legs or arms while sitting or lying still. Despite having a similar mechanism of action, there is inadequate evidence to support the use of tavapadon (Juvmo) in RLS treatment.

Appendix

II. Tavapadon (Juvmo) titration starts at 0.25 mg once daily and advances stepwise to the 5 mg maintenance dose on day 41, with a dedicated titration pack recommended. The dose may be increased in 5 mg increments approximately every 15 days to a maximum of 15 mg once daily. If possible, dose optimization to the next highest dose is encouraged.

III. Table 1: Initiating tavapadon (Juvmo) titration and maintenance when on long-term moderate CYP3A4 inducers

Dosage Form	Quantity Limit
Titration pack (0.25 mg and 1 mg)	200 tablets/40 days
5 mg, 10 mg, and 15 mg tablets	90 tablets/30 days

IV. Table 2: Parkinson's Disease therapies (referenced in this policy)

Drug	Route
Levodopa-based therapies	carbidopa/levodopa IR (Sinemet, Dhivy) carbidopa/levodopa ER (Sinemet CR, Rytary, Crexont) levodopa inhalation powder (Inbrija) carbidopa tab (Lodosyn) carbidopa and levodopa enteral suspension (Duopa) foscarbidopa/foslevodopa (Vyalev)
Dopamine agonists	rotigotine transdermal system (Neupro) ropinirole (IR, ER) pramipexole (IR, ER)
COMT inhibitors	entacapone (Comtan) tolcapone (Tasmar) opicapone (Ongentys) carbidopa/entacapone/levodopa (Stalevo)
MAO-inhibitors	rasagiline (Azilect) selegiline (Zelapar) safinamide (Xadago)
Drugs with other mechanisms of action	amantadine (available IR, ER, oral solution) amantadine ER (Gocovri)

References

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Related Policies

Policies listed below may be related to the current policy. Related policies are identified based on similar indications, similar mechanisms of action, and/or if a drug in this policy is also referenced in the related policy.

Policy Name	Disease state
pimavanserin (Nuplazid) Policy	Parkinson’s disease psychosis
istradefylline (Nourianz) Policy	Parkinson’s disease
levodopa (Inbrija) Policy	Parkinson’s disease
apomorphine (Apokyn, Kynmobi) Policy	Parkinson’s disease
Foscarbidopa/foslevodopa (Vyalev)	Parkinson’s disease

Policy Implementation/Updates

Action and Summary of Changes	Date
Policy created	11/2026