Drug Use Research & Management Program
Oregon State University, 500 Summer Street NE, E35
Salem, Oregon 97301-1079
Phone 503-947-5220 | **Fax** 503-947-1119

Drug Use Evaluation: Modafinil and Armodafinil

Plain Language Summary:

- Medicines called stimulants can help people who are very sleepy stay awake and alert. Examples of stimulants used for this purpose include modafinil and armodafinil.
- These medicines are prescribed for conditions like narcolepsy, which causes excessive daytime sleepiness and sudden sleep attacks. They can also be used in addition to other therapy for people with other health issues that can cause extreme tiredness. Examples of these conditions include cancer, depression, or obstructive sleep apnea.
- Providers must send the Oregon Health Authority (OHA) information to document why they are prescribing modafinil or armodafinil before the Oregon Health Plan (OHP) will pay for the medicine. This process is called prior authorization (PA).
- In an evaluation of this policy, we found that most members who were prescribed modafinil or armodafinil did not have claims paid by OHP (63%). About 14% of members had paid claims for modafinil or armodafinil, and prior authorization was denied in 23% of patients. About 26% of people had claims for a different type of stimulant.
- The most common reasons that the Oregon Health Plan did not pay for stimulants were:
    - No documentation of extreme tiredness before starting the medicine or symptom improvement after starting the medicine,
    - No documentation that the member had seen an expert who specialized in their condition, and
    - Prescription of a stimulant for a condition that is not covered by the Oregon Health Plan.
- We recommend that the Oregon Health Plan update their policy to automatically approve modafinil and armodafinil for people with narcolepsy because there is strong evidence to support use of these medicines as an initial treatment option.

Research Questions:

- For members starting treatment with modafinil or armodafinil, what proportion of members ultimately get a paid claim for the requested drug?
- How many members with a denied claim for modafinil or armodafinil have subsequent paid claims for a different stimulant?
- What types of stimulants are subsequently prescribed for members with denied claims for modafinil or armodafinil?
- Are there subgroups of members (e.g., based on diagnoses or denial reason) who are more likely to have subsequent paid claims for a different therapy?

Conclusions:

- Current prior authorization criteria for modafinil and armodafinil provide coverage for excessive sleepiness related to narcolepsy, obstructive sleep apnea (OSA), cancer, depression, and multiple sclerosis.
- Guidelines updated in 2021 from the American Academy of Sleep Medicine recommend either modafinil or armodafinil for narcolepsy, idiopathic hypersomnia, and for fatigue secondary to Lewy body dementia, Parkinson's disease, traumatic brain injury, myotonic dystrophy, or multiple sclerosis.[1] These stimulants are also recommended as adjunct treatments to positive airway pressure in obstructive sleep apnea (OSA)[2] and as an adjunct to antidepressants in people with treatment-resistant depression.[3]

Author: Sarah Servid, PharmD August 2025

- In an evaluation of this policy, 63% of members with an initial denied claim for modafinil or armodafinil did not have subsequent paid claims for any type of simulant or narcolepsy drug. About 14% of members had subsequent paid claims for modafinil or armodafinil (compared to 9% in the baseline period), and 23% of members had denied PAs. The most common reasons for denied PA requests included inadequate documentation for fatigue severity, no documentation of consultation with a relevant specialist, and unfunded diagnosis. About 26% of people had paid claims for a different type of stimulant indicated for attention deficit hyperactivity disorder (ADHD; compared to 19% in the baseline period).
- About 22% of members with denied claims were prescribed more than one tablet per day and 17% of denied PA requests appear to be for doses higher than recommended in the FDA-labeling. There is limited evidence to support improved efficacy of modafinil above 200 mg daily,[4] but also insufficient direct comparative evidence to show that higher doses of modafinil are less safe than other stimulants or other drugs for narcolepsy. All stimulants have similar warnings and precautions for cardiovascular adverse effects, psychiatric adverse events, and abuse or misuse.[4-8]
- The most common stimulants prescribed in the 6 months following a denied claim for modafinil or armodafinil were mixed amphetamine salts (17%), modafinil or armodafinil (14%), methylphenidate (9%), and lisdexamfetamine (3%).
- The proportion of people who switched from modafinil or armodafinil to an ADHD stimulant was generally small but occurred more commonly in people who had denials for modafinil or armodafinil. In people without ADHD stimulant claims in the baseline period, the proportion of people who switched to an ADHD stimulant was 14% in people with a denied modafinil/armodafinil claim compared to 8% of people who ultimately received a paid claim for modafinil or armodafinil.
- Members with an evidence-supported diagnosis (such as OSA, narcolepsy, or depression) were more likely to have subsequent paid claims for a stimulant or other narcolepsy drugs (42%) compared to members without an evidence-supported diagnosis (26%). Of the 147 members with subsequent paid claims for modafinil and armodafinil, 92% had an evidence-based and funded diagnosis present in the medical claims (n=135). However, a significant proportion of people with an evidence-supported diagnosis in medical claims did not have subsequent paid claims for a stimulant (n=423). In people without an evidence-supported diagnosis, ADHD stimulants were the most common type of drug prescribed following a denied claim for modafinil or armodafinil.

Recommendations:

- Automatically approve requests of modafinil or armodafinil for members with narcolepsy when prescribed for doses at or below 200 mg of modafinil or 250 mg of armodafinil daily.
- Continue to require PA for other indications and for higher doses.
- Update PA criteria to allow members to use higher doses of modafinil if lower doses are only partially effective.

Background

Modafinil and armodafinil are stimulants that have evidence for use in a variety of conditions. They are approved by the Food and Drug Administration (FDA) for excessive sleepiness associated with narcolepsy, OSA, and shift-work disorder. Modafinil has been studied for a variety of off-label conditions and current PA criteria include coverage for fatigue related to depression, cancer, and multiple sclerosis. Modafinil and armodafinil have also been studied in fatigue related to other neurologic disorders (such as Parkinson's Disease, traumatic brain injury, post-polio syndrome), cognitive enhancement, drug-related fatigue, and ADHD. In 2021, the American Academy of Sleep Medicine updated guidelines related to hypersomnia disorders and provided recommendations for the following therapies (**Table 1**).[1] There are strong recommendations for modafinil, pitolisant, sodium oxybate, and solriamfetol in adults with narcolepsy and for modafinil in people with idiopathic hypersomnia.[1] There are conditional recommendations based on lower quality evidence for modafinil and armodafinil related to a variety of other fatigue-related conditions.[1] These stimulants are also recommended as adjunct treatments to positive airway pressure in OSA[2] and as an adjunct to antidepressants in people with treatment-resistant depression.[3]

Table 1. American Academy of Sleep Medicine Recommendations for Central Disorders of Hypersomnia[1]

Condition	Treatment	Strength of evidence
Primary hypersomnia		
Narcolepsy (adults)	Modafinil, pitolisant, sodium oxybate, solriamfetol	Strong
	Armodafinil, dextroamphetamine, methylphenidate	Conditional
Narcolepsy (pediatric)	Modafinil, sodium oxybate	Conditional
Idiopathic hypersomnia	Modafinil	Strong
	Clarithromycin, methylphenidate, pitolisant, sodium oxybate	Conditional
Hypersomnia due to other medical conditions		
Lewy body dementia	Armodafinil	Conditional
Parkinson's disease	Modafinil, sodium oxybate	Conditional
Traumatic brain injury	Modafinil, armodafinil	Conditional
Myotonic dystrophy	Modafinil	Conditional
Multiple sclerosis	Modafinil	Conditional

FDA-labeling for stimulants like modafinil includes warnings and precautions for serious skin reactions (e.g., Stevens' Johnson Syndrome), psychiatric symptoms (e.g., delusions, mania, aggression, suicidal ideation), and cardiovascular events (e.g., chest pain, palpitations, electrocardiogram changes, increased blood pressure).[4,8] Stimulants for ADHD include similar warnings and precautions related to cardiac and psychiatric adverse events.[5-7] All stimulants have risk for abuse, misuse, and addiction. The Drug Enforcement Agency (DEA) categorizes modafinil and armodafinil as schedule IV substances and stimulants for ADHD as schedule II substances.[4-8] In addition, stimulants for ADHD may be associated with serotonin syndrome, seizures, motor and verbal tics, and peripheral vasculopathy including Raynaud's phenomenon.[5-7]

In the Oregon Health Plan, PA is required before the Oregon Health Authority will pay for modafinil or armodafinil. Current PA criteria requires the following:

- Diagnosis of a funded and evidence-supported condition (including narcolepsy, OSA, cancer, depression, or multiple sclerosis)
- Prescription by, or in consultation with, a relevant specialist for the condition
- Documentation of recent fatigue severity score
- When applicable, documentation of pregnancy risk assessment
- When applicable, use of first-line treatment for OSA

Approvals are limited to the FDA-recommended maintenance doses (200 mg daily for modafinil and 250 mg daily for armodafinil). In clinical trials, modafinil was studied for narcolepsy at doses of 100-600 mg daily, and up to 400 mg has been evaluated for other off-label conditions.[1,9] In clinical trials for narcolepsy, higher doses of modafinil were not associated with improved efficacy.[4] The most common adverse events occurring in more than 5% of patients included headache, nausea, nervousness, rhinitis, diarrhea, back pain, anxiety, insomnia, dizziness, and dyspepsia.[4] Headache and anxiety occurred more commonly with higher doses.[4] Modafinil and armodafinil are rarely covered for shift work disorder and primary hypersomnia because these conditions are currently unfunded. However, other stimulants that are approved by the FDA for ADHD may have fewer utilization controls. For the FFS population, preferred stimulants for ADHD do not require PA if they are prescribed within FDA-approved doses and age limits. For members enrolled in a coordinated care organization (CCO), most simulants for ADHD are covered by the CCO. The purpose of this drug evaluation is to evaluate whether members are prescribed an alternative stimulant after receiving a denied claim for modafinil or armodafinil.

Methods:
The index event (IE) was defined as the first denied FFS pharmacy claim for modafinil or armodafinil during the claims evaluation window. If members had a paid and denied claim on the same day, the claim was classified as paid.

Time periods for review:

- The claims evaluation window was from 10/1/2023 to 09/30/2024
- The baseline period was defined as the 6 months before the IE (inclusive of the IE)
- The follow-up period was defined as the 6 months following the IE (exclusive of the IE)

Inclusion criteria:

- At least one denied FFS pharmacy claim for modafinil or armodafinil (defined based on HICL Sequence Numbers [HSNs]: 010865 and 034868) during the claim evaluation window. Denied claims were included if they were associated with an error code indicating PA was required or quantity limit was exceeded but were not associated with claims indicating errors in billing (**Appendix 1; Table A1**).

Exclusion criteria:

- Patients with non-Medicaid primary insurance coverage or third-party liability (TPL) effective during the baseline or follow-up period.
- Less than 75% of days Medicaid eligibility in the baseline or follow-up period.
- Claims for benefit plans indicating Medicare or limited drug benefit during the baseline or follow-up period. Claims data for these members may be incomplete.

Category	Benefit Package	Description
Medicare Part D coverage	BMM	Qualified Medicare Beneficiary + Oregon Health Plan with Limited Drug
	BMD	Oregon Health Plan with Limited Drug
	MED	Qualified Medicare Beneficiary
Limited or no Medicaid drug benefit	MND	Transplant package
	CWM	Citizenship Waived Emergency Medical
	SMF	Special Low-Income Medicare Beneficiary Only
	SMB	Special Low-Income Medicare Beneficiary Only

Population descriptors and definitions:

- CCO enrollment, age, sex at birth, and race were evaluated at the time of the IE.
- Patients were categorized as new starts if they had no paid claims for the IE drug in the baseline period.
- Stimulants for ADHD and other drugs for narcolepsy were defined based on HSNs in **Appendix 1, Table A2**.
- Sleep disorder diagnoses were evaluated during the baseline period (see **Appendix 1, Table A3**) and categorized as funded, unfunded, and evidence-supported.
- Denial reason codes were classified according to the error code on the claim. A single denied claim can be associated with multiple error codes.
- Denied PA requests were evaluated for key terms to determine the probable reason for the denial. The following terms were used to identify denial reasons:

Key Term	Probable Denial Reason
“Fatigue severity” or “Epworth”	- Inadequate documentation of baseline fatigue severity or improvement in symptoms
“Specialist”	- No documentation the drug was prescribed by or in consultation with a relevant specialist
“Funded” or “OHP-funded”	- No documentation the drug was prescribed for a funded condition
“Pregnancy” or “pregnant” or “teratogenic”	- No documentation of pregnancy risk assessment
“First-line” or “first line”	- No documentation for use or adherence to first-line treatment for OSA (e.g., CPAP or similar device)
“Dose” or “200mg” or “200 mg”	- Daily dose prescribed above recommended maintenance dose
“Covered indication”	- No documentation of an evidence-supported indication

A post-hoc subgroup analysis was conducted for people without claims for an ADHD stimulant in the baseline period. Members were categorized into the following groups:

- People who had subsequent paid claims for modafinil/armodafinil in the follow-up period (e.g., before any paid claims for an ADHD stimulant or in absence of an ADHD stimulant).
- Everyone else (including people without subsequent paid claims for modafinil/armodafinil and people with paid claims for an ADHD stimulant before the first paid claim for modafinil/armodafinil in the follow-up period).

Outcomes:

- Subsequent paid FFS or CCO claims in the follow-up period for stimulants (e.g., modafinil, armodafinil, or stimulants for ADHD) or other agents for narcolepsy (e.g., pitolisant, sodium oxybate, or solriamfetol).

Results:

This drug evaluation identified 1295 members with denied claims for modafinil or armodafinil over a 1-year period from 10/1/2023 to 09/30/2024. After exclusion of people with potentially incomplete claims data, 1080 people were included in the analysis (**Table 1**). The majority of participants identified as female (64%) and white (63%). Modafinil was prescribed in 84% of members (**Table 2**), and about 22% of members were prescribed more than one tablet per day which may be indicative of twice daily dosing or dosing above the FDA-recommended maintenance doses. The most common diagnoses identified in medical claims during the 6-month baseline period included depression (39%), OSA (29.3%), and narcolepsy (13.5%; **Table 3**). About 67% of members had a diagnosis that was both funded and evidence supported, 4% had an evidence-supported and unfunded diagnosis, and 29% of members did not have an evidence-supported diagnosis for modafinil or armodafinil identified in the 6-month baseline period.

Table 1. Included members

Exclusion Criteria	Denied IE #	Denied IE %
Members with FFS denied claims for modafinil or armodafinil	1,295	
After exclusion of members with Medicare, TPL, or limited drug benefit	1,151	88.9%
After exclusion of members with <75% eligibility in the baseline or follow-up period	1,080	83.4%
Total members included in the analysis	1,080	83.4%

Table 2. Baseline Demographics

	Denied IE	
	1,080	%
Age		
<18 years	0	0.0%
>=18 years	1,080	100.0%
Sex		
Male	392	36.3%
Female	688	63.7%
CCO enrollment at the time of the IE		
FFS	24	2.2%
CCO	1,056	97.8%
Race		
White	685	63.4%
Unknown	267	24.7%
Native American/Alaskan Native	54	5.0%
Other	74	6.9%
IE Drug		
Modafinil	908	84.1%
Armodafinil	172	15.9%
Daily Quantity (tablets per day)		
<1	49	4.5%
1	796	73.7%
>1 to 2	214	19.8%
>2	21	1.9%

Table 3. Diagnoses and claims in the baseline period

	Denied IE	
	1,080	%
Funded and evidence supported diagnoses	**725**	**67.1%**
Fatigue related to depression	423	39.2%
Obstructive sleep apnea	316	29.3%
Narcolepsy with or without cataplexy	146	13.5%
Fatigue related to multiple sclerosis	68	6.3%
Fatigue related to cancer	27	2.5%
Evidence-supported and unfunded diagnoses	**41**	**3.8%**
Idiopathic (primary) hypersomnia	28	2.6%
Shift work disorder	14	1.3%
No evidence supported diagnoses	**314**	**29.1%**
Other and chronic fatigue	65	6.0%
ADHD	65	6.0%
Other hypersomnia	24	2.2%
Insomnia	21	1.9%
Other and unspecified sleep disorders	12	1.1%
Other sleep apnea	12	1.1%
Other circadian rhythm sleep disorders	2	0.2%
Parasomnia	1	0.1%
Sleep-related movement disorders	1	0.1%

Of members with an initial denied claim for modafinil or armodafinil, most members (63%) did not have subsequent paid claims for any type of stimulant or narcolepsy drug (**Table 4**). PA was not submitted for 39% of members, and PA was denied for 23% of members. An evaluation of PA denial letters indicate that most PA requests had more than one reason for denial. The most common reasons for denial included inadequate documentation for fatigue severity (75%), no documentation of consultation with a relevant specialist (54%), and prescription for an unfunded diagnosis (49%; **Table 6**). Even for members with a funded and evidence-supported diagnosis present in the medical claims, about 40% of denied PA letters referenced unfunded conditions indicating that the diagnosis submitted on the PA request and in chart notes is often different than diagnoses present in medical claims.

Only 37% of people had a subsequent paid claim for a stimulant or other drug for narcolepsy (**Table 4**). The most common stimulants prescribed in the 6 months following a denied claim for modafinil or armodafinil were mixed amphetamine salts (17%), modafinil or armodafinil (14%), methylphenidate (9%), and lisdexamfetamine (3%). Utilization of both modafinil or armodafinil and ADHD stimulants increased from the 6-month baseline period to the 6-month follow-up period (**Table 5**). In the baseline period, 19% of members had paid claims for an ADHD stimulant compared to 26% of members in the 6-month follow-up period. ADHD stimulants were more frequently prescribed than modafinil or armodafinil (**Table 4**).

Table 4. Subsequent paid claims for stimulants or other narcolepsy drugs

	Denied IE	
	1,080	%
Subsequent paid claims in the follow-up period	398	36.9%
Modafinil or armodafinil	147	13.6%
Pitolisant, sodium oxybate, or solriamfetol	17	1.6%
ADHD stimulant	282	26.1%
Dextroamphetamine/amphetamine	184	17.0%
Methylphenidate	100	9.3%
Lisdexamphetamine	30	2.8%
Dexmethylphenidate	6	0.6%
No subsequent paid claims in the follow-up period	682	63.1%
PA never submitted	419	38.8%
PA submitted	263	24.4%
Denied	251	23.2%
Approved	12	1.1%

Table 5. Stimulant prescribing before and after a denied claim for modafinil/armodafinil

			Denied IE	
	1,080	%	1,080	%
	Baseline period		Follow-up period	
Paid FFS or CCO claims (not including the IE)				
Modafinil or armodafinil	101	9.4%	147	13.6%
ADHD stimulant	202	18.7%	282	26.1%
Pitolisant, sodium oxybate, or solriamfetol	14	1.3%	17	1.6%

Table 6. Denial reasons for prior authorization

	Evidence-supported & funded diagnosis		Evidence-supported & unfunded diagnosis		No evidence-supported diagnosis		Total	
	174	%	8	%	69	%	251	%
Denial related to inadequate documentation for:								
Fatigue severity score	135	77.6%	5	62.5%	49	71.0%	189	75%
Specialist involvement	86	49.4%	3	37.5%	47	68.1%	136	54%
Funded condition	70	40.2%	7	87.5%	46	66.7%	123	49%
Pregnancy risk assessment	52	29.9%	1	12.5%	16	23.2%	69	27%
First-line treatments for OSA	31	17.8%	1	12.5%	5	7.2%	37	15%
Appropriate dose	22	12.6%	2	25.0%	5	7.2%	32	13%
Evidence-supported indication	17	9.8%	1	12.5%	14	20.3%	29	12%
None of the above	2	1.1%	0	0.0%	1	1.4%	3	1%

The proportion of members with subsequent paid claims for stimulants or other drugs for narcolepsy was generally consistent across demographic groups (e.g., sex and race). Members with an evidence-supported diagnosis were more likely to have subsequent paid claims for a stimulant or other narcolepsy drug (42%) compared to members without an evidence-supported diagnosis (26%; **Table 7**). Of the 147 members with subsequent paid claims for modafinil and armodafinil, 92% had an evidence-based and funded diagnosis present in the medical claims (n=135). About 70% of people with claims for an ADHD stimulant had an evidence-supported diagnosis for modafinil or armodafinil. In members without an evidence-supported diagnosis, most (74%, n=233) did not have a subsequent claim for a stimulant. In people with subsequent claims but without an evidence-supported diagnosis, ADHD stimulants were the most common type of drug prescribed.

Table 7. Subsequent claims by subgroup for members with a denied IE

					Type of Subsequent Paid Claims*					
	No subsequent paid claim		Subsequent paid claim for any drug		Modafinil or armodafinil		ADHD stimulant		Pitolisant, sodium oxybate, or solriamfetol	
	682	63%	398	37%	147	%	282	%	17	%
CCO enrollment at the time of the IE										
FFS	18	75.0%	6	25%	1	0.7%	6	2.1%	0	0.0%
CCO	664	62.9%	392	37%	146	99.3%	276	97.9%	1	5.9%
IE Drug										
Modafinil	593	65.3%	315	35%	112	76.2%	224	79.4%	13	76.5%
Armodafinil	89	51.7%	83	48%	35	23.8%	58	20.6%	4	23.5%

Diagnoses in the baseline period										
Funded and evidence supported	423	58.3%	***302***	***42%***	135	91.8%	197	69.9%	15	88.2%
Unfunded and evidence-supported	26	63.4%	***15***	***37%***	1	0.7%	14	5.0%	1	5.9%
Not evidence-supported	233	74.2%	***81***	***26%***	11	7.5%	71	25.2%	1	5.9%
Paid claims in the baseline period										
Modafinil or armodafinil	19	18.8%	82	81%	72	49.0%	29	10.3%	8	47.1%
ADHD stimulant	34	16.8%	168	83%	27	18.4%	163	57.8%	8	47.1%
Pitolisant, sodium oxybate, or solriamfetol	1	7.1%	13	93%	7	4.8%	7	2.5%	12	70.6%

*Members may be categorized in more than one group if they had claims for more than one drug in the 6 months following the IE. For members with more than one type of paid claim in the follow-up period, this analysis did not evaluate if drugs were prescribed concurrently or sequentially.

Similar trends were observed in a subgroup of members who did not have claims for an ADHD stimulant in the baseline period (**Table 8**). Like the broader population, most members in this subgroup did not have subsequent paid claims for any type of stimulant (n=651; 75%). ADHD stimulants were prescribed for 9 members (8%) who had subsequent paid claims for modafinil or armodafinil. By comparison, in people with only denied claims for modafinil or armodafinil (n=775), use of ADHD stimulants was slightly more frequent (n=104; 14%).

Table 8. Subsequent stimulant use for members without an ADHD stimulant in the baseline period

	Subsequent paid claims for modafinil/armodafinil*		**No subsequent paid claims for modafinil/armodafinil**		**Total**	
	116	%	755	%	871	%
Subsequent ADHD stimulant in the follow-up period	9	7.8%	104	13.8%	113	13.0%
No subsequent ADHD stimulant in the follow-up period	107	92.2%	651	86.2%	758	87.0%

*Includes people with modafinil/armodafinil paid claims in the follow-up period before any ADHD stimulant **OR** those with modafinil/armodafinil paid claims in the follow-up period and no ADHD stimulant in the follow-up period

Discussion and Limitations:

The results of this analysis indicate that most people with a denied claim for modafinil or armodafinil do not have subsequent paid claims for a comparable medication. However, this analysis is based on claims data which has several inherent limitations.

First, we did not attempt to evaluate the proportion of people who may be paying cash for their prescriptions. Both modafinil and armodafinil are available as generic medications and are relatively inexpensive. Additionally, because most members are enrolled in a CCO, claims data on how many members may have received subsequent denied claims or had PA requests for an ADHD stimulant is lacking. ADHD stimulants are categorized as physical health drugs and are paid for by the CCOs. Policies for stimulants may vary between CCOs.

The proportion of people prescribed both modafinil or armodafinil and ADHD stimulants increased in the 6 months following a denied claim. In general, use of stimulants for ADHD has increased over time in the Oregon Medicaid population as a result of both increased prescribing and a larger Medicaid population. This analysis did not control for general trends over time. Notably, switching to an ADHD stimulant was slightly more common in people with only denied claims for modafinil or armodafinil (14%) compared to people with subsequent paid claims for modafinil or armodafinil (8%).

Diagnoses were only evaluated in the 6 months before the first denied claim for modafinil or armodafinil which may not accurately categorize members who have a chronic condition like OSA or narcolepsy. About 67% (n=725) of people had a funded and evidence-supported diagnosis in their medical claims. However, even in members with an evidence-supported indication in medical claims, 40% of denied PAs referenced unfunded indications and 10% referenced indications that are not currently covered under the OHP policy. Many diagnoses and medications can contribute to fatigue or excessive sleepiness, and not all of these diagnoses were included in this analysis. Based on low quality evidence, guidelines from the American Academy of Sleep Medicine include conditional recommendations for modafinil in fatigue related to Lewy body dementia, Parkinson's disease, traumatic brain injury, and myotonic dystrophy, and conditional recommendations for armodafinil in Lewy body dementia and traumatic brain injury. A more comprehensive review of both unfunded and off-label indications is currently planned for a future Pharmacy & Therapeutics meeting.

In practice, modafinil is often prescribed twice daily because patients report limited duration of effect which does not last the entire day. About 22% of members with denied claims were prescribed more than one tablet per day and 17% of denied PA requests appear to be for doses higher than recommended in the FDA-labeling. There is limited evidence to support improved efficacy of modafinil above 200 mg daily, but also very limited evidence to show that higher doses of modafinil are less safe than other stimulants or other drugs for narcolepsy. All stimulants have similar warnings and precautions for cardiovascular adverse effects, psychiatric adverse events, and abuse or misuse.

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Appendix 1: Drug Coding

Table A1. Error Codes associated with denied claims

Error Code	Error Status Description	
3002	NDC REQUIRES PA	**Include**
4167	DRUG QUANTITY PER DAY LIMIT EXCEEDED	**Include**
3000	UNITS EXCEED AUTHORIZED UNITS ON PA MASTER FILE	**Include**
3024	DRUG OPTIMAL DOSAGE EXCEEDED	**Include**
5001	EXACT DUPLICATE	Exclude
4002	Non-Covered Drug	Exclude
2508	RECIPIENT COVERED BY PRIVATE INSURANCE (PHARMACY)	Exclude
4890	Non covered drug class	Exclude
2002	RECIPIENT NOT ELIGIBLE FOR HEADER DATE OF SERVICE	Exclude
513	RECIPIENT NAME AND NUMBER DISAGREE	Exclude
4025	AGE IS NOT ALLOWED FOR NDC	Exclude
238	RECIPIENT NAME IS MISSING	Exclude
4891	Not covered drug class	Exclude
2017	RECIPIENT SERVICES COVERED BY HMO PLAN	Exclude
503	DATE DISPENSED AFTER BILLING DATE	Exclude
628	Other Coverage Reject Code Required for OCC 3	Exclude
209	DISPENSE AS WRITTEN CODE 02 NOT ALLOWED.	Exclude
221	DAYS SUPPLY MISSING	Exclude
268	BILLED AMOUNT MISSING	Exclude
270	HEADER TOTAL BILLED AMOUNT INVALID	Exclude
2507	RECIPIENT HAS MORE THAN ONE INSURANCE CARRIER	Exclude

Table A2. Codes for stimulants and related drugs for narcolepsy

HSN	Generic Name	Category
002064	amphetamine sulfate	ADHD drug
043652	amphetamine	ADHD drug
013449	dextroamphetamine/amphetamine	ADHD drug
022987	dexmethylphenidate HCl	ADHD drug
002065	dextroamphetamine sulfate	ADHD drug
047926	dextroamphetamine	ADHD drug
034486	lisdexamfetamine dimesylate	ADHD drug
002067	methamphetamine HCl	ADHD drug
033556	methylphenidate	ADHD drug

001682	methylphenidate HCl	ADHD drug
047187	serdexmethylphen/dexmethylphen	ADHD drug
010865	modafinil	IE drug
034868	armodafinil	IE drug
012346	sodium oxybate	Other narcolepsy drug
046743	sodium,calcum,mag,pot oxybate	Other narcolepsy drug
045666	solriamfetol	Other narcolepsy drug
045575	pitolisant	Other narcolepsy drug

Table A3. Sleep Disorder Diagnoses

ICD-10 codes	Description	Category
G4733	Obstructive Sleep apnea	Funded and evidence-supported
G474x	Narcolepsy and cataplexy	
F32x-F33x	Depression (fatigue)	
G35x	Multiple sclerosis (fatigue)	
R530, C00x-C96x	Cancer (fatigue)	
G4711-G4712	Idiopathic (primary) hypersomnia	Unfunded and evidence-supported
G4726	Shift work disorder	
G4720-G4725, G4727-G4729	Other circadian rhythm sleep disorders	Not evidence supported
G4730-G4732, G4734-G4739	Other sleep apnea	
G4710, G4713-G4719	Other hypersomnia	
G470x	Insomnia	
G475x	Parasomnia	
G476x	Sleep-related movement disorders	
G478x-G479x	Other and unspecified sleep disorders	
R538x, G9332, G9339	Other and chronic fatigue	
F90x	ADHD	

Appendix 2: Proposed Prior Authorization Criteria

Sleep-Wake Medications

Goal(s):

- To promote safe use of drugs for obstructive sleep apnea and narcolepsy.
- Limit use to diagnoses where there is sufficient evidence of benefit and uses that are funded by OHP. Excessive daytime sleepiness related to shift-work is not funded by OHP. Accommodate individual review for individuals under the EPSDT program.

- Limit use to safe doses.

Length of Authorization:
- Initial approval of 90 days if criteria met; approval of up to 12 months with documented benefit

Requires PA:
- Modafinil or armodafinil without previous claims evidence of narcolepsy
- Solriamfetol
- Pitolisant

Covered Alternatives:
- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Table 1. Funded and Evidence-Supported Indications.

Indication	Modafinil (Provigil™)	Armodafinil (Nuvigil™)	Solriamfetol (Sunosi™)	Pitolisant (Wakix™)
• Excessive daytime sleepiness in narcolepsy	X	X	X	X
• Residual excessive daytime sleepiness in obstructive sleep apnea patients treated with CPAP	X	X	X	Not FDA approved; insufficient evidence
• Depression augmentation (unipolar or bipolar I or II acute or maintenance phase) • Cancer-related fatigue • Multiple sclerosis-related fatigue	X	Not FDA approved; insufficient evidence		
• Drug-related fatigue • Excessive daytime sleepiness or fatigue related to other neurological disorders (e.g. Parkinson's Disease, traumatic brain injury, post-polio syndrome) • ADHD • Cognition enhancement for any condition	Not FDA approved; insufficient evidence			

Table 2. Maximum Recommended Dose (consistent evidence of benefit with lower doses).

Generic Name	Minimum Age	Maximum FDA-Approved Daily Dose
Armodafinil	18 years	250 mg
Modafinil	18 years	200 mg
Solriamfetol	18 years	150 mg

Pitolisant	6 years	17.8 mg (poor CYP2D6 metabolizers)

Table 3. Recommended safety assessments

Modafinil or Armodafinil	Solriamfetol	Pitolisant
For people of childbearing potential, documentation that the provider and patient have discussed the teratogenic risks of the drug if the patient were to become pregnant.	Renal assessment. Dose adjustment is recommended for moderate impairment (EGFR <60 mL/min) and use in end stage renal disease is not recommended.	Renal assessment. Dose adjustment is recommended for moderate renal (EGFR <60 mL/min) and use in end stage renal disease is not recommended.
	Recent cardiovascular risk assessment (including blood pressure) within the past 3 months. Use of solriamfetol is not recommended in patients with uncontrolled hypertension or serious heart problems.	

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code.	
2. Is this a funded diagnosis? Non-funded diagnoses: • Shift work disorder (ICD10 G4720-4729; G4750-4769; G478) • Unspecified hypersomnia (ICD10 G4710)	**Yes:** Go to #4	**No:** If not eligible for EPSDT review: Pass to RPh. Deny; not funded by the OHP If eligible for EPSDT review: Go to #3

Approval Criteria		
3. Is there documentation that the condition is of sufficient severity that it impacts the patient's health (quality of life, function, growth, development, ability to participate in school, perform activities of daily living, etc) despite lifestyle modifications (e.g., strategic bright light receipt or avoidance, sleep hygiene, dietary changes, etc)?	**Yes:** Document symptom severity. Go to #4 Evidence supports modafinil and armodafinil in moderate-severe shift work disorder (e.g., sleep latency ≤ 6 minutes) and risks likely outweigh benefits in patients with mild symptoms.	**No:** Pass to RPh. Deny; medical necessity
4. Is the requested medication for an FDA-approved age (Table 2) and evidence-supported indication (Table 1)?	**Yes:** Go to #5	**No:** Pass to RPh. Deny; medical appropriateness. Providers for patients 7 to 17 years of age may also submit a request for sodium oxybate as it is FDA-approved for narcolepsy in this age group.
5. Is the request for continuation of therapy at maintenance dosage previously approved by the FFS program?	**Yes:** Go to **Renewal Criteria**	**No:** Go to #6
6. Is the drug prescribed by or in consultation with an appropriate specialist for the condition (e.g., sleep specialist, neurologist, or pulmonologist)?	**Yes:** Go to #7	**No:** Pass to RPh. Deny; medical appropriateness
7. Will prescriber consider a preferred alternative?	**Yes:** Inform prescriber of preferred alternatives (e.g., preferred methylphenidate)	**No:** Go to #8
8. Is the prescribed daily dose higher than recommended in Table 2?	**Yes:** Go to #9	**No:** Go to #11
9. Is the request for modafinil 200 mg twice daily (total daily dose of 400 mg) with documentation of inadequate symptom improvement with lower doses?	**Yes:** Go to #11	**No:** Go to #10

Approval Criteria		
10. Is the request for pitolisant in a patient with documentation of all the following: • CYP2D6 testing which indicates the patient is not a poor metabolizer • Chart notes or provider attestation indicating lack of hepatic or renal impairment	**Yes:** Go to #11 Max dose for pitolisant is 35.6 mg daily.	**No:** Pass to RPh. Deny; medical appropriateness.
11. Is there baseline documentation of fatigue severity using a validated measure (e.g., Epworth score, Brief Fatigue Inventory, or other validated measure)?	**Yes:** Go to #12 Document baseline scale and score	**No:** Pass to RPh. Deny; medical appropriateness
12. Is there documentation or provider attestation of recent safety assessments for the requested drug (Table 3)?	**Yes:** Go to #13	**No:** Pass to RPh. Deny; medical appropriateness
13. Is the request for treatment of narcolepsy or fatigue secondary to major depression (MDD), MS, or cancer? Note: Methylphenidate is recommended first-line for cancer.	**Yes:** Approve for 90 days and inform prescriber further approval will require documented evidence of clinical benefit.	**No:** Go to #14
14. Is the request for treatment of obstructive sleep apnea (OSA) (without narcolepsy)?	**Yes:** Go to #15	**No:** Go to #16
15. Is the patient compliant with recommended first-line treatments (e.g., CPAP or other primary therapy)?	**Yes:** Approve for 90 days and inform prescriber further approval will require documented evidence of clinical benefit.	**No:** Pass to RPh; Deny; medical appropriateness
16. All other diagnoses must be evaluated as to the OHP-funding level and evidence for clinical benefit. • Evidence supporting treatment for excessive daytime sleepiness (EDS) or fatigue as a result of other conditions is currently insufficient and should be denied for “medical appropriateness”. • Evidence to support cognition enhancement is insufficient and should be denied for “medical appropriateness”. If new evidence is provided by the prescriber, please forward request to Oregon DMAP for consideration and potential modification of current PA criteria.		

Renewal Criteria		
1. Is the request for solriamfetol?	**Yes:** Go to #2	**No:** Go to #3
2. Is there documentation of a recent blood pressure evaluation (within the last 3 months)?	**Yes:** Go to #3	**No:** Pass to RPh. Deny; medical appropriateness
3. Is the request for treatment of obstructive sleep apnea?	**Yes:** Go to #4	**No:** Go to #5
4. Is the patient adherent to primary OSA treatment (e.g.,CPAP) based on chart notes?	**Yes:** Go to #5	**No:** Pass to RPh. Deny; medical appropriateness
5. Is there documentation of clinical benefit and tolerability from baseline? The same clinical measure used to diagnose excessive daytime sleepiness (EDS), fatigue secondary to MS and/or cancer, major depressive disorder (MDD) is recommended to document clinical benefit. For Epworth Sleepiness Scale, and improvement of at least 3 points is considered clinically significant.	**Yes:** Approve for up to 12 months	**No:** Pass to RPh. Deny; medical appropriateness

P&T Review: *8/25; 4/23; 10/20 (DE); 2/20; 7/19; 03/16; 09/15*
Implementation: *9/15/25; 5/1/23; 11/1/20; 3/1/2020; 8/19/19; 8/16, 1/1/16*