Anti Narcolepsy Agents: Armodafinil/modafinil/Lumryz/Sunosi/Wakix/Xyrem/ Xywav

WA.PHAR.124 Effective Date: 6/1/2024

Note: *New-to-market drugs included in this class based on the Apple Health Preferred Drug List are non-preferred and subject to this prior authorization (PA) criteria. Non-preferred agents in this class require an inadequate response or documented intolerance due to severe adverse reaction or contraindication to at least TWO preferred agents. If there is only one preferred agent in the class documentation of inadequate response to ONE preferred agent is needed. If a drug within this policy receives a new indication approved by the Food and Drug Administration (FDA), medical necessity for the new indication will be determined on a case-by-case basis following FDA labeling.*

To see the list of the current publication of the Coordinated Care of Washington, Inc. Preferred Drug List (PDL), please visit: *https://www.coordinatedcarehealth.com/content/dam/centene/centene-pharmacy/pdl/FORMULARY-CoordinatedCare_Washington.pdf*

Medical necessity

Drug	Medical Necessity
Armodafinil (Nuvigil) Mixed oxybate salts (Xywav) Modafinil (Provigil) Pitolisant (Wakix) Sodium oxybate (Lumryz) Sodium oxybate (Xyrem) Solriamfetol (Sunosi)	**Anti-narcolepsy agents** may be considered medically necessary in patients who meet the criteria described in the clinical policy below. If all criteria are not met, the clinical reviewer may determine there is a medically necessary need and approve on a case-by-case basis. The clinical reviewer may choose to use the reauthorization criteria when a patient has been previously established on therapy and is new to Apple Health.

Clinical policy:

Clinical Criteria	
Idiopathic Hypersomnia Mixed oxybate salts (Xywav) Modafinil (Provigil)	Mixed oxybate salts (Xywav) or modafinil (Provigil) may be approved when all of the following criteria are met: 1. Patients 17 years of age or younger require a second opinion review with the agency-designated mental health specialist from the Second Opinion Network (SON) when one of the following is met: a. The patient is prescribed five or more mental health drugs; **OR** b. The patient is prescribed more than one drug in the same therapeutic class; **OR** 2. Patient is 18 years of age or older, **AND** 3. Prescribed by, or in consultation with a neurologist, psychiatrist, or sleep specialist; **AND**

	4. Diagnosis of idiopathic hypersomnia, confirmed with a sleep study and multiple sleep latency test (MSLT); **AND** 5. A quantitative assessment within the past 6 months is submitted (e.g. Epworth Sleepiness Scale, Maintenance of Wakefulness Test); **AND** 6. Provider attests cause of hypersomnia is not better explained by another medical disorder, use of substance, or medication; **AND** 7. If the request is for Xywav: History of failure, contraindication, or intolerance to ALL of the following: a. Modafinil for a minimum of 3 consecutive weeks; **AND** b. Amphetamine or methylphenidate-based stimulant for a minimum of 60 consecutive days For modafinil (Provigil): If ALL criteria are met, the request will be authorized for **12 months.** For mixed oxbate salts (Xywav): If ALL criteria are met, the request will be authorized for **6 months.**
	Criteria (Reauthorization) Mixed oxybate salts (Xywav) or modafinil (Provigil) may be approved when all of the following criteria are met: 1. A quantitative assessment within the past 6 months (e.g. Epworth Sleepiness Scale, Maintenance of Wakefulness Test) is submitted demonstrating disease stability or a positive clinical response; **AND** 2. Clinical documentation is submitted demonstrating improvement of patient's symptoms (e.g. improvement in ability to complete activity of daily living, improvement in ability to stay awake). If ALL criteria are met, the request will be authorized for **12 months.**
Narcolepsy with Excessive Daytime Sleepiness Armodafinil (Nuvigil) Mixed oxybate salts (Xywav) Modafinil (Provigil) Pitolisant (Wakix) Sodium oxybate (Lumryz) Sodium oxybate (Xyrem) Solriamfetol (Sunosi)	Armodafinil (Nuvigil), mixed oxybate salts (Xywav), modafinil (Provigil), pitolisant (Wakix), sodium oxybate (Lumryz), sodium oxybate (Xyrem), or solriamfetol (Sunosi) may be approved when all of the following criteria are met: 1. Patients 17 years of age or younger require a second opinion review with the agency-designated mental health specialist from the Second Opinion Network (SON) when one of the following is met: a. The patient is prescribed five or more mental health drugs; **OR** b. The patient is prescribed more than one drug in the same therapeutic class; **OR** 2. Patient is 18 years of age or older; **AND** 3. Prescribed by, or in consultation with a neurologist, psychiatrist, or sleep specialist; **AND**

4. Diagnosis of narcolepsy with excessive somnolence, confirmed with a sleep study and multiple sleep latency test (MSLT); **AND**
5. A quantitative assessment within the past 6 months is submitted (e.g. Epworth Sleepiness Scale, Maintenance of Wakefulness Test); **AND**
6. If the request is for armodafinil, mixed oxybate salts, pitolisant, sodium oxybate, or solriamfetol: History of failure, contraindication, or intolerance to ALL of the following:
    a. For armodafinil (Nuvigil):
        i. Modafinil (Provigil) for a minimum of 60 consecutive days.
    b. For solriamfetol (Sunosi):
        i. Modafinil (Provigil) or armodafinil (Nuvigil) for a minimum of 60 consecutive days; **AND**
        ii. Amphetamine or methylphenidate-based stimulant for a minimum of 60 consecutive days.
    c. For pitolisant (Wakix), generic sodium oxbate, and Xyrem:
        i. Modafinil or armodafinil for a minimum of 60 consecutive days; **AND**
        ii. Amphetamine or methylphenidate-based stimulant for a minimum of 60 consecutive days; **AND**
        iii. Solriamfetol (Sunosi) for a minimum of 30 consecutive days.
    d. For Xywav and Lumryz:
        i. Modafinil or armodafinil for a minimum of 60 consecutive days; **AND**
        ii. Amphetamine or methylphenidate-based stimulant for a minimum of 60 consecutive days; **AND**
        iii. Solriamfetol (Sunosi) for a minimum of 30 consecutive days; **AND**
        iv. Generic sodium oxybate or Xyrem for a minimum of 8 consecutive weeks

For armodafinil (Nuvigil), modafinil (Provigil), and solriamfetol (Sunosi): If ALL criteria are met, the request will be authorized for **12 months.**

For pitolisant (Wakix), mixed oxybate salts (Xywav), sodium oxybate (Lumryz), and sodium oxybate Xyrem)**:** If ALL criteria are met, the request will be authorized for **6 months.**

Criteria (Reauthorization)

Armodafinil (Nuvigil), mixed oxybate salts (Xywav), modafinil (Provigil), pitolisant (Wakix), sodium oxybate (Lumryz), sodium oxybate (Xyrem), or solriamfetol (Sunosi) may be approved when all of the following criteria are met:

	1. A quantitative assessment within the past 6 months (e.g. Epworth Sleepiness Scale, Maintenance of Wakefulness Test) is submitted demonstrating disease stability or a positive clinical response. If ALL criteria are met, the request will be authorized for **12 months.**
Narcolepsy with Cataplexy Mixed oxybate salts (Xywav) Pitolisant (Wakix) Sodium oxybate (Lumryz) Sodium oxybate (Xyrem)	Mixed oxybate salts (Xywav), pitolisant (Wakix), sodium oxybate (Lumryz), or sodium oxybate (Xyrem) may be approved when all of the following criteria are met: 1. Patients 17 years of age or younger require a second opinion review with the agency-designated mental health specialist from the Second Opinion Network (SON) when one of the following is met: a. The patient is prescribed five or more mental health drugs; **OR** b. The patient is prescribed more than one drug in the same therapeutic class; **OR** 2. Patient is 18 years of age or older; **AND** 3. Prescribed by, or in consultation with a neurologist, psychiatrist, or sleep specialist; **AND** 4. Diagnosis of narcolepsy with cataplexy, confirmed with a sleep study and multiple sleep latency test (MSLT); **AND** 5. A quantitative assessment within the past 6 months is submitted (e.g. Epworth Sleepiness Scale, Maintenance of Wakefulness Test); **AND** 6. Clinical documentation supports presence of cataplexy (e.g. documented episodes of sudden loss of muscle tone) and impairment/limitation of activities of daily living (e.g. unable to attend school, unable to attend work, unable to drive); **AND** 7. If the request is for Xywav or Lumryz: History of failure, contraindication, or intolerance to ALL of the following: a. For Xywav and Lumryz: i. Pitolisant (Wakix) for a minimum of 8 consecutive weeks; **AND** ii. Generic sodium oxybate or Xyrem for a minimum of 4 consecutive weeks If ALL criteria are met, the request will be authorized for **6 months.**
	Criteria (Reauthorization) Mixed oxybate salts (Xywav), pitolisant (Wakix), sodium oxybate (Lumryz), or sodium oxybate (Xyrem) may be approved when all of the following criteria are met: 1. A quantitative assessment within the past 6 months (e.g. Epworth Sleepiness Scale, Maintenance of Wakefulness Test) is submitted demonstrating disease stability or a positive clinical response; **AND**

	2. Clinical documentation is submitted showing a reduction in cataplexy events. If ALL criteria are met, the request will be authorized for **12 months.**
Obstructive Sleep Apnea with Excessive Daytime Sleepiness Armodafinil (Nuvigil) Modafinil (Provigil) Solriamfetol (Sunosi)	Armodafinil (Nuvigil), modafinil (Provigil) or solriamfetol (Sunosi) may be approved when all of the following criteria are met: 1. Patients 17 years of age or younger require a second opinion review with the agency-designated mental health specialist from the Second Opinion Network (SON) when one of the following is met: a. The patient is prescribed five or more mental health drugs; **OR** b. The patient is prescribed more than one drug in the same therapeutic class; **OR** 2. Patient is 18 years of age or older; **AND** 3. Prescribed by, or in consultation with a neurologist, psychiatrist, or sleep specialist; **AND** 4. Diagnosis of obstructive sleep apnea with residual excessive somnolence, confirmed with a sleep study; **AND** 5. A quantitative assessment within the past 6 months is submitted (e.g. Epworth Sleepiness Scale, Maintenance of Wakefulness Test); **AND** 6. Clinical documentation is submitted demonstrating ONE of the following: a. Client has achieved normalized breathing, as evident by compliance data showing apnea-hypopnea index less than 5 incidents per hour, and oxygenation with continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BIPAP)therapy; **AND** i. Documentation within the past 6 months demonstrating client is adherent to CPAP or BIPAP therapy. Client is determined to be adherent when CPAP or BIPAP is used for 70% of nights for a minimum of 4 hours per night; **OR** b. Documentation within the past 6 months demonstrating that client is adherent to mandibular advancement device; **AND** 7. If the request is for armodafinil or solriamfetol: History of failure, contraindication, or intolerance to ALL of the following: a. For Armodafinil (Nuvigil): Modafinil (Provigil) for a minimum of 60 consecutive days. b. For Solriamfetol (Sunosi): Modafinil (Provigil) or armodafinil (Nuvigil) for a minimum of 60 consecutive days. If ALL criteria are met, the request will be authorized for **6 months.**
	Criteria (Reauthorization)

	Armodafinil (Nuvigil), modafinil (Provigil) or solriamfetol (Sunosi) may be approved when all of the following criteria are met: 1. A quantitative assessment within the past 6 months (e.g. Epworth Sleepiness Scale, Maintenance of Wakefulness Test) is submitted demonstrating disease stability or a positive clinical response. 2. Documentation demonstrating ONE of the following: a. Documentation within the past 6 months demonstrating client continues to be adherent to CPAP or BIPAP therapy. Client is determined to be adherent when CPAP or BIPAP is used for 70% of nights for a minimum of 4 hours per night; **OR** b. Documentation within the past 6 months demonstrating client continues to be adherent to mandibular advancement device. If ALL criteria are met, the request will be authorized for **6 months.**
Shift Work Sleep Disorder Armodafinil (Nuvigil) Modafinil (Provigil)	Armodafinil (Nuvigil) or modafinil (Provigil) may be approved when all of the following criteria are met: 1. Patients 17 years of age or younger require a second opinion review with the agency-designated mental health specialist from the Second Opinion Network (SON) when one of the following is met: a. The patient is prescribed five or more mental health drugs; **OR** b. The patient is prescribed more than one drug in the same therapeutic class; **OR** 2. Patient is 18 years of age or older; **AND** 3. Diagnosis of shift work sleep disorder; **AND** 4. Clinical documentation demonstrates concomitant use of nonpharmacologic interventions (i.e. counseling, sleep hygiene); **AND** 5. If the request is for armodafinil: History of failure, contraindication, or intolerance to ALL of the following: a. Modafinil for a minimum of 60 consecutive days. If ALL criteria are met, the request will be authorized for **3 months.**
	Criteria (Reauthorization)
	Armodafinil (Nuvigil) or modafinil (Provigil) may be approved when all of the following criteria are met: 1. Documentation is submitted demonstrating patient still requires treatment and there is a positive clinical response [e.g. improvement of symptoms which include improvement in their ability to complete activities of daily living or stay awake]. If ALL criteria are met, the request will be authorized for **6 months.**

Dosage and quantity limits

Drug	Indication	Approved Dose	Dosage Form and Quantity Limit
Armodafinil (Nuvigil)	Narcolepsy with excessive daytime sleepiness	Adults: -Up to 250 mg once daily	Adults: • 50 mg tablets: 2 tablets per day • 150 mg tablets: 1 tablet per day • 200 mg tablets: 1 tablet per day • 250 mg tablets: 1 tablet per day
Armodafinil (Nuvigil)	Obstructive sleep apnea with excessive daytime sleepiness	Adults: -Up to 250 mg once daily	Adults: • 50 mg tablets: 2 tablets per day • 150 mg tablets: 1 tablet per day • 200 mg tablets: 1 tablet per day • 250 mg tablets: 1 tablet per day
Armodafinil (Nuvigil)	Shift work sleep disorder	Adults: -150 mg once daily	Adults: • 150 mg tablets: 1 tablet per day
Mixed oxybate salts (Xywav)	Idiopathic hypersomnia	Adults: -Once nightly dosing: Up to 6 grams per night -Twice nightly dosing: Up to 9 grams per night in two divided doses	500 mg per 1 mL, 180 mL bottle: Quantity is limited based on the following daily doses. • Up to 3 grams per night: 1 bottle per 30 days • Greater than (>) 3 to 6 grams per night: 2 bottles per 30 days • Greater than (>) 6 to 9 grams per night: 3 bottles per 30 days
Mixed oxybate salts (Xywav)	Narcolepsy with cataplexy	Pediatrics: -7 years or older and less than 20 kg: No specific recommendations -7 years or older and 20 to less than 30 kg: Up to 6 grams per night in two divided doses -7 years or older and 30 to less than 45 kg: Up to 7.5 grams per night in two divided doses -7 years or older and 45 kg or greater: Up to 9 grams per night in 2 divided doses Adults: -Up to 9 grams per night in two divided doses	500 mg per 1 mL, 180 mL bottle: Quantity is limited based on the following daily doses. • Up to 3 grams per night: 1 bottle per 30 days • Greater than (>) 3 to 6 grams per night: 2 bottles per 30 days • Greater than (>) 6 to 9 grams per night: 3 bottles per 30 days
Mixed oxybate salts (Xywav)	Narcolepsy with excessive daytime sleepiness	Pediatrics: -7 years or older and less than 20 kg: No specific recommendations	500 mg per 1 mL, 180 mL bottle: Quantity is limited based on the following daily doses. • Up to 3 grams per night: 1 bottle per 30 days

		-7 years or older and 20 to less than 30 kg: Up to 6 grams per night in two divided doses -7 years or older and 30 to less than 45 kg: Up to 7.5 grams per night in two divided doses -7 years or older and 45 kg or greater: Up to 9 grams per night in 2 divided doses Adults: -Up to 9 grams per night	• Greater than (>) 3 to 6 grams per night: 2 bottles per 30 days • Greater than (>) 6 to 9 grams per night: 3 bottles per 30 days
Modafinil (Provigil)	Narcolepsy with excessive daytime sleepiness	Adults: -Up to 400 mg per day	• 100 mg tablets: 1 tablet per day • 200 mg tablets: 2 tablets per day
Modafinil (Provigil)	Obstructive sleep apnea with excessive daytime sleepiness	Adults: -Up to 400 mg per day	• 100 mg tablets: 1 tablet per day • 200 mg tablets: 2 tablets per day
Modafinil (Provigil)	Shift work sleep disorder	Adults: -Up to 200 mg per day	• 200 mg tablets: 1 tablet per day
Pitolisant (Wakix)	Narcolepsy with cataplexy	Adults: -Up to 35.6 mg per day	• 4.45 mg tablets: 14 tablets per 7 days • 17.8 mg tablets: 2 tablets per day
Pitolisant (Wakix)	Narcolepsy with excessive daytime sleepiness	Adults: -Up to 35.6 mg per day	• 4.45 mg tablets: 14 tablets per 7 days • 17.8 mg tablets: 2 tablets per day
Sodium oxybate (Lumryz)	Narcolepsy with cataplexy	Adults: -Up to 9 grams per night	• 4.5 gram packets: 30 packets per 30 days • 6 gram packets: 30 packets per 30 days • 7.5 gram packets: 30 packets per 30 days • 9 gm packets: 30 packets per 30 days
Sodium oxybate (Lumryz)	Narcolepsy with excessive daytime sleepiness	Adults: -Up to 9 grams per night	• 4.5 gram packets: 30 packets per 30 days • 6 gram packets: 30 packets per 30 days • 7.5 gram packets: 30 packets per 30 days • 9 gm packets: 30 packets per 30 days
Sodium oxybate (Xyrem)	Narcolepsy with cataplexy	Pediatrics: -7 years or older and less than 20 kg: No specific recommendations -7 years or older and 20 to less than 30 kg: Up to 6 grams per night in two divided doses -7 years or older and 30 to less than 45 kg: Up to 7.5 grams per night in two divided doses -7 years or older and 45 kg or greater: Up to 9 grams per night in 2 divided doses	500 mg per 1 mL, 180 mL bottle: • Up to 3 grams per night: 1 bottle per 30 days • Greater than (>) 3 to 6 grams per night: 2 bottles per 30 days • Greater than (>) 6 to 9 grams per night: 3 bottles per 30 days

		Adults: -Up to 9 grams per night in 2 divided doses	
Sodium oxybate (Xyrem)	Narcolepsy with excessive daytime sleepiness	Pediatrics: -7 years or older and less than 20 kg: No specific recommendations -7 years or older and 20 to less than 30 kg: Up to 6 grams per night in two divided doses -7 years or older and 30 to less than 45 kg: Up to 7.5 grams per night in two divided doses -7 years or older and 45 kg or greater: Up to 9 grams per night in 2 divided doses Adults: -Up to 9 grams per night in 2 divided doses	500 mg per 1 mL, 180 mL bottle: • Up to 3 grams per night: 1 bottle per 30 days • Greater than (>) 3 to 6 grams per night: 2 bottles per 30 days • Greater than (>) 6 to 9 grams per night: 3 bottles per 30 days
Solriamfetol (Sunosi)	Narcolepsy with excessive daytime sleepiness	Adults: -Up to 150 mg per day	• 75 mg tablets: 1 tablet per day • 150 mg tablets: 1 tablet per day
Solriamfetol (Sunosi)	Obstructive sleep apnea with excessive daytime sleepiness	Adults: -Up to 150 mg per day	• 75 mg tablets: 1 tablet per day • 150 mg tablets: 1 tablet per day

Background:

Obstructive sleeping apnea (OSA) is a common sleep-related breathing disorder defined as having five or more apnea or hypopnea even per hour of sleep. Patients with OSA often experience excessive daytime sleepiness which significantly limits their ability to maintain wakefulness and alertness during day. The American Academy of Sleep Medicine (AASM) guidelines strongly recommend positive airway pressure (PAP) to treat OSA with excessive sleepiness. Oral appliances and surgical intervention are alternative options. For patients who still experience excessive daytime sleepiness despite adequate OSA treatment, AASM recommends trial of wakefulness-promoting agents. Medications approved to treat excessive somnolence in the setting of OSA include modafinil, armodafinil, and solriamfetol. Solfiamfetol has not been compared to any other treatment option (e.g, modafinil, armodafinil); therefore, the comparative safety and efficacy is unknown. Notably, other stimulants (e.g. methylphenidate and amphetamines) have not been studied in this disease state.

"Narcolepsy is a neurological disorder that affects the brain's ability to control sleep. People with narcolepsy experience excessive daytime sleepiness throughout the day which affects activities of daily living. Some people also experience cataplexy, a sudden loss of muscle tone which leads to weakness and loss of voluntary muscle control."[8] For adults, the AASM guidelines strongly recommend the use of modafinil, pitolisant, sodium oxybate and solriamfetol and conditionally recommends the use of armodafinil and dextroamphetamine for the treatment of narcolepsy in patients without cataplexy. For patients experiencing narcolepsy with cataplexy, the AASM guidelines strongly recommend the use of pitolisant and sodium oxybate and conditionally recommends dextroamphetamine. For pediatrics, the AASM conditionally recommends modafinil and sodium oxybate for the treatment of narcolepsy without cataplexy. For pediatrics with narcolepsy and cataplexy, sodium oxybate is conditionally recommended.

"Shift work sleep disorders are caused by shift work, defined as non-standard work schedules, including permanent or intermittent night work, early morning work, and rotating schedules."[7] These work schedules may cause difficulties with sleep which impact wakefulness and ability to perform activities of daily living. The AASM guidelines recommend non-pharmacologic and pharmacologic interventions for the treatment of shift work sleep disorders. Non-pharmacologic interventions include planned napping and timed light exposure to improve alertness with night shift work. Pharmacologic therapies include modafinil, caffeine, and stimulants with modafinil and caffeine having established safety in situations where therapy is needed. Stimulants were shown to have less evidence and chronic use may lead to abuse potential. Modafinil and armodafinil and the only products supported in compendia.

"Idiopathic hypersomnia is a neurological sleep disorder that causes excessive daytime sleepiness, difficulty waking from nighttime sleep and naps, and may cause affected individuals to fall asleep unintentionally."[3] This impacts the ability to complete activities of daily living. The exact cause of idiopathic hypersomnia is unknown and extended sleep does not improve wakefulness. For adults, the AASM guideline strongly recommends the use of modafinil and conditionally recommends the use of clarithromycin, methylphenidate, pitolisant and sodium oxybate for the treatment of idiopathic hypersomnia. No treatment recommendations are currently provided for the treatment of idiopathic hypersomnia in pediatric patients.

The safety and efficacy of armodafinil (Nuvigil) was established for obstructive sleep apnea (OSA), narcolepsy and shift work disorder in two, one, and one double-blind, placebo-controlled clinical trials, respectively. For OSA, participants were required to be compliant with CPAP, using it for 4 or more hours per night for 70% or more of nights. In the first trial (n=395) and second trial (n=264), the armodafinil groups showed a significant improvement in both the Maintenance of Wakefulness Test (MWT) and Clinical Global Impression of Change (CGI-C). The change in MWT from baseline (shown as change/baseline) was 1.7/21.5, 2.2/23.3, and -1.7/23.2 for study 1 for the armodafinil 150 mg group, armodafinil 250 mg group, and placebo group, respectively. The change in MWT from baseline in trial 2 was 2.3/23.7 and -1.3/23.3 for the armodafinil 150 mg and placebo groups, respectively. For the CGI-C endpoint, 71%, 74% and 37% of patients in trial 1 had an improvement in CGI-C at final visit for the armodafinil 150 mg, armodafinil 250 mg, and placebo groups, respectively. In trial 2, 71% and 53% of patients had an improvement in CGI-C at final visit for the armodafinil 150 mg and placebo groups, respectively. In the one trial evaluating armodafinil for narcolepsy with excessive sleepiness (n=196), MWT and CGI-C were significantly improved in the armodafinil group vs placebo. The change in MWT from baseline (shown as change/baseline) was 1.3/12.1, 2.6/9.5, and -1.9/12.5 for the armodafinil 150 mg, armodafinil 250 mg and placebo groups, respectively. For the CGI-C endpoint, 69%, 73% and 33% of patients had an improvement in the CGI-C at final visit for the armodafinil 150 mg, armodafinil 250 mg, and placebo groups, respectively. In the one trial evaluating armodafinil for shift work disorder (n=254), the Multiple Sleep Latency Test (MSLT) and CGI-C were significantly improved in the armodafinil group vs placebo. The change in MSLT (shown as change/baseline) was 3.1/2.3 and 0.4/2.4 for the armodafinil 150 mg group and placebo group, respectively. 79% in the armodafinil and 59% in the placebo group experienced an improvement in the CGI-C. The adverse effects profile >2% for armodafinil include headache, nausea, dizziness, insomnia, anxiety, diarrhea, dry mouth, depression, dyspepsia, fatigue, palpitations, rash, and upper abdominal pain. In addition, serious dermatologic reactions have been reported in association with use of armodafinil or modafinil. This includes Stevens-Johnson Syndrome and toxic epidermal necrosis which have been reported with an incidence of 0.8% in pediatric patients in clinical trials. These reports have continued worldwide post-marketing.

The safety and efficacy of modafinil (Provigil) was established for narcolepsy, obstructive sleep apnea, and shift work disorder in two, two, and one placebo-controlled trials, respectively. Off-label compendia support was established from a review by the Sleep Deprivation and Stimulant Task Force of the American Academia of Sleep Medicine. For narcolepsy with excessive daytime sleepiness (EDS), two 9-week, placebo controlled trials (n=558), the primary outcomes of sleep latency (assessed by MWT) and change in overall diseases status (assessed by change in CGI-C) were significantly improved compared to placebo. Change in MWT (shown as change/baseline) for trial 1 was 2.3/5.8, 2.3/6.6 and -0.7/5.8 for modafinil 200mg, modafinil 400 mg, and placebo, respectively. For trial 2 change in MWT (shown as change/baseline) was 2.2/6.1, 2.0/5.9, and -0.7/6.0 for modafinil 200 mg, 400 mg, and placebo, respectively. For the CGI-C endpoint in trial 1, 64%, 72%, and 37% of patients had an improvement in the CGI-C at final visit for modafinil 200 mg, 400 mg, and placebo, respectively. For trial 2, 58%, 60%, and 38% of patients in the modafinil 200 mg, 400 mg, and placebo achieved an improvement in CGI-C, respectively. For OSA, the first trial (n=327) was 12 weeks and the primary outcomes included sleep latency (assessed by MWT) and change in overall disease status (assessed by CGI-C). The change in MWT (shown as change/baseline) was 1.6/13.1, 1.5/13.6, and -1.1/13.8 for modafinil 200 mg, modafinil 400 mg, and placebo, respectively. The percent of patients who had improvement in CGI-C at final visit was 61%, 68%, and 37% for modafinil 200 mg, modafinil 400 mg, and placebo, respectively. The second trial (n=157) was 4 -weeks and the primary outcome was change in Epworth Sleepiness Scale (ESS) from baseline. There was significant difference in ESS at week 4 with a reduction of (shown as change/baseline) of 4.6/14.2 and 2.0/14.4 for modafinil 400 mg and placebo, respectively. For shift work disorder one trial (n=209) showed significant differences in sleep latency (assessed by MSLT during a simulated night shift) and change in overall disease status (assessed by CGI-C). The change in MSLT (shown as change/baseline) was 1.7/2.1 and 0.3/2.0 for modafinil 200 mg and placebo, respectively. The percent of patients who showed improvement in the CGI-C was 74% and 36% for modafinil 200 mg and placebo, respectively. For sleep deprivation, 9 of 10 clinical studies, at the time of review, found that reaction time or response time was found to be significantly improved during sleep-deprivation periods from 36 to 88 hours after receiving modafinil. In addition, 5 of 5 studies showed significant increases in the MSLT and MWT sleep-latency tests when compared to placebo. Common adverse effects ≥2% include headache, nausea, nervousness, rhinitis, back pain, diarrhea, anxiety, dizziness, dyspepsia, insomnia, anorexia, dry mouth, pharyngitis, chest pain, hypertension, abnormal liver function, constipation, depression, palpitation, paresthesia, somnolence, tachychardia, and vasodilation. In addition, serious dermatologic reactions including Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis have been reported with an incidence of 0.8% in pediatric patients in clinical trials. These reports have continued worldwide post-marketing.

The safety and efficacy of solriamfetol (Sunosi) was established in two randomized phase 3, double-blind, placebo-controlled clinical trials. The first trial (n=239) demonstrated that solriamfetol 150 mg daily significantly improved ability to stay awake during the Maintenance of Wakefulness Test (MWT) after 12 weeks in the setting of narcolepsy. In the setting of OSA (n=476), all doses of solriamfetol (37.5mg, 75mg, and 150mg) similarly improved WMT after 12 weeks. For both trials, the effect was observed after one week. Common adverse effects (≥2%) include decreased appetite, insomnia, anxiety, irritability, headache, heart palpitations, nausea, abdominal pain, dry mouth, dizziness, and constipation. Certain adverse effects, including headache, nausea, decreased appetite, and anxiety, occurred more frequently at higher doses. Eleven participants (3%) discontinued Sunosi during the clinical trial compared to <1% for placebo. Discontinuation reasons included anxiety, heart palpitations, and restlessness. Notably, blood pressure should also be monitored while taking Sunosi.

The safety and efficacy of pitolisant (Wakix) was established in two randomized, double-blind, placebo-controlled studies, NCT01067222 and NCT01638403. In NCT01067222 (n=95), pitolisant demonstrated a significant improvement in Epworth sleepiness scale (ESS) score (-3.1; 95% CI [-5.73, -0.46]) compared to placebo after an 8 week treatment period. In NCT01067222, pitolisant was also compared to modafinil and pitolisant failed to demonstrate non-inferiority. In NCT01638403 (n=166), pitolisant demonstrated a significant improvement in ESS compared to placebo (-2.2; 95%CI [-4.17, -0.22]) after 8 weeks of treatment. Cataplexy reduction was evaluated in NCT01800045 (n=106) and pitolisant demonstrated a significant reduction in the weekly cataplexy rate (75%) when compared to the placebo group (38%), with a rate ratio of 0.51 (0.44-0.60, p<0.0001). Common adverse effects ≥2% include headache, insomnia, nausea, upper respiratory tract infection, musculoskeletal pain, anxiety, increased heart rate, hallucinations, irritability, abdominal pain, sleep disturbance, decreased appetite, cataplexy, dry mouth, and rash. Pitolisant is contraindicated in patients with severe hepatic impairment due to its metabolism by the liver. Pitolisant also causes QT prolongation and should be avoided.

The safety and efficacy of Lumryz for narcolepsy with cataplexy or excessive daytime sleepiness was established in a single double-blind, randomized, placebo-controlled trial (n=212). The primary endpoints include the Maintenance of Wakefulness Test (MWT), Clinical Global Impression-Improvement (CGI-I), and mean change in weekly cataplexy attacks. The mean MWT at baseline was 5 minutes and 4.7 minutes and the mean number of cataplexy attacks per week at baseline was 18.9 and 19.8 for the Lumryz and placebo groups, respectively. The change in MWT for the 6 g, 7.5 g and 9 g Lumryz dose was 8.1 vs 3.1, 9.6 vs 3.3, and 10.8 vs 4.7 minutes for Lumryz vs placebo, respectively. The proportion of patients with a “very much improved” or “much improved” CGI-I for the 6 g, 7.5 g and 9 g Lumryz dose was 40 vs 6, 64 vs 22 and 73 vs 32 for Lumryz vs placebo, respectively. The change in mean cataplexy attacks for the 6 g, 7.5 g and 9 g Lumryz dose was -7.4 vs -2.6, -10.0 vs -3.7, and -11.5 vs -4.9 for Lumryz vs placebo, respectively. Adverse reactions ≥2% include vomiting, nausea, weight decrease, decreased appetite, dizziness, somnolence, headache, enuresis, anxiety, and somnambulism. Due to its risks of central nervous system depression and potential for abuse and misuse, Lumryz is only available through a restricted distribution program, Lumryz REMS.

The safety and efficacy of Xyrem for the treatment of narcolepsy with cataplexy was established in two randomized, double-blind, placebo-controlled trials. The primary endpoint was the frequency of cataplexy attacks. In the first trial (n=136), the baseline number of cataplexy attacks per week was reduced from a median 20.5, 23.0 and 23.5 at baseline by -4, -10, and -16 attacks per week after 4 weeks for the placebo, Xyrem 6 g, and Xyrem 9 g groups, respectively. In trial 2 (n=55), a randomized-withdrawal study, the baseline number of cataplexy attacks per 2 weeks was 4.0 and 1.9 for placebo and Xyrem, respectively. After 2 weeks, median change of cataplexy attacks per 2 weeks was 21 and 0 for the placebo and Xyrem groups, respectively. The safety and efficacy of Xyrem for the treatment of narcolepsy with excessive daytime sleepiness was established in two randomized, double-blind, placebo-controlled trials. In trial 1 (n=228), the primary endpoint were the Epworth Sleepiness Scale (ESS) and the Clinical Global Impression of Change (CGI-C). The baseline ESS was 17.5, 19.0, and 19.0 for placebo, Xyrem 6 g per night, and Xyrem 9 g per night groups, respectively. After 8 weeks the change in ESS was -0.5, -2.0, and -5.0 for the placebo, Xyrem 6 g per night, and Xyrem 9 g per night groups, respectively. The proportion of study participants having "very much improved" or "much improved" from baseline on the CGI-C was 22%, 52%, and 64% for placebo, Xyrem 6 g per night, and Xyrem 9 g per night, respectively. In trial 2 (n=222), the primary endpoint was the Maintenance of Wakefulness Test (MWT) at 8 weeks. The baseline MWT scores was 9.7, 11.3, and 10.4 at baseline for the placebo, Xyrem, and Xyrem plus modafinil groups. The mean change in MWT from baseline was -2.7, 0.6, and 2.7 minutes for the placebo, Xyrem, and Xyrem plus modafinil groups. The safety and efficacy of Xyrem for the treatment of narcolepsy with excessive daytime sleepiness and cataplexy in pediatric patients was established in a single double-blind, placebo-controlled trial (n=106). The primary endpoint was change in frequency of cataplexy attacks, the CGI-C for cataplexy severity, and the change in ESS score for excessive daytime sleepiness. The baseline median number of cataplexy attacks per week was 4.7 and 3.5 and the baseline ESS scores was 11 and 8 for placebo and Xyrem groups, respectively. After 2 weeks of treatment the median change in cataplexy attacks per week from baseline was 12.7 and 0.3, the median change in ESS was 3 and 0, and the proportion of study participants who were "much worse" or "very much worse" for cataplexy severity was 66% and 17% for placebo and Xyrem, respectively. Adverse reactions ≥2% include nausea, vomiting, diarrhea, upper abdominal pain, dry mouth, feeling drunk, peripheral edema, cataplexy, muscle spasms, pain in extremities, dizziness, somnolence, tremor, paresthesia, sleep paralysis, disorientation, sleepwalking, anxiety, enuresis, and hyperhidrosis. Due to its risks of central nervous system depression and potential for abuse and misuse, Xyrem is only available through a restricted distribution program, Xyrem REMS.

The safety and efficacy of Xywav for the treatment of narcolepsy with cataplexy and excessive daytime sleepiness was established in a single double-blind, placebo-controlled, randomized-withdrawal study (n=201). The study had 2 parts consisting of a 12-week open-label treatment and titration period, followed by a 2-week stable dose period, and lastly a 2-week double-blind randomized-withdrawal period. The primary endpoint was the change in frequency of cataplexy attacks from the 2 weeks of the stable-dose period to the 2 weeks of the double-blind randomized withdrawal period. The baseline mean number of cataplexy attacks was 7.2 and 8.9 with changes of 11.5 and 0.1 for placebo and Xywav, respectively. The baseline median number of cataplexy attacks was 1.0 and 1.1 with changes of 2.4 and 0.0 for placebo and Xywav, respectively. The baseline mean ESS score was 12.6 and 13.6 with changes of 3.0 and 0.0 for placebo and Xywav, respectively. The baseline median ESS score was 13.0 and 14.0 with changes of 2.0 and 0.0 for placebo and Xywav, respectively. The safety and efficacy of Xywav for the treatment of narcolepsy with cataplexy and excessive daytime sleepiness in a pediatric population was established based on the clinical trial with Xyrem, summarized above. The safety and efficacy of Xywav for the treatment of idiopathic hypersomnia was established in a double-blind, placebo-controlled, randomized-withdrawal study (n=154). The primary endpoint was the change in ESS score, as a measure of reduction in excessive daytime sleepiness from the end of the stable dose period to the end of the double-blind randomized withdrawal period. The median ESS score was 5.0 and 6.5 at baseline and 14.0 and 7.0 at the end of the double-blind randomized withdrawal period for placebo and Xywav, respectively.

RCW 69.50.402 establishes regulation that includes when "it is unlawful to prescribe any amphetamine, including its salts, optical isomers, and salts of optical isomers classified as a schedule II controlled substance and any nonnarcotic stimulant classified as a schedule II controlled substance and designated as a nonnarcotic stimulant by the commission."[24]

RCW 74.09.490 establishes regulation that includes when "a second opinion review is required for children prescribed psychotropic medications."[25]

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History

Approved Date	Effective Date	Version	Action and Summary of Changes
3/14/2024	6/1/2024	61.40.00-3	Updated column header from "Compendia supported dosing" to "Approved Dose" on the Dosing and quantity limits table.
12/13/2023	6/1/2024	61.40.00-3	Policy Update – Approved by DUR Board on 12/13/2023 -Updating language for medical necessity -Updating policy to include clinical criteria for sodium oxybate (Xyrem and Lumryz) and mixed oxybate salts (Xywav). -Added coverage criteria for idiopathic hypersomnia
8/16/2023	2/1/2024	61.40.00-2	Policy Update - Approved by DUR Board on 8/16/2023 -Updating policy to new HCA clinical policy format. -Updating policy to include clinical criteria for pitolisant and solriamfetol. -Removed sleep deprivation from policy as it was determined not to be medically necessary.
8/18/2021	2/1/2022	61.40.00.AA-1	Approved by DUR Board on 8/18/2021. Policy was updated 9/3/2021 to include bilevel positive airway pressure and mandibular advancement devices as options demonstrating treatment for obstructive sleep apnea. Clinical policy and dosage and quantity limits updated to include shift work sleep disorder and sleep deprivation as compendia-supported indications.