Clinical Policy Title:	pitolisant
Policy Number:	RxA.783
Drug(s) Applied:	Wakix®
Original Policy Date:	01/17/2023
Last Review Date:	01/17/2023
Line of Business Policy Applies to:	All lines of business

Background

Wakix® is a histamine-3 (H3) receptor antagonist/inverse agonist indicated for the treatment of excessive daytime sleepiness (EDS) or cataplexy in adult patients with narcolepsy

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
pitolisant (Wakix®)	Narcolepsy (excessive daytime sleepiness/cataplexy)	The recommended dosage range is 17.8 mg to 35.6 mg daily. Titrate dosage as follows: • Week 1: Initiate with 8.9 mg once daily • Week 2: Increase dosage to 17.8 mg once daily • Week 3: May increase to the maximum recommended dosage of 35.6 mg once daily.	35.6 mg once daily
		Hepatic impairment: Moderate hepatic impairment: Initial dosage is 8.9 mg once daily. Titrate to a maximum dosage of 17.8 mg once daily after 14 days	17.8 mg once daily
		Renal impairment: Moderate and severe impairment: Initial dosage is 8.9 mg once daily. Titrate to maximum dosage of 17.8 mg once daily after 7 days	17.8 mg once daily
		End–stage renal disease (ESRD):	

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
		Not recommended Poor Metabolizers of CYP2D6: Initiate Wakix® at 8.9 mg once daily and titrate to a maximum dose of 17.8 mg once daily after 7 days	17.8 mg once daily

Dosage Forms

- Tablets: 4.45 mg, 17.8 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Narcolepsy with Cataplexy (must meet all):

1. Prescribed for the treatment of cataplexy in narcolepsy;
2. Prescribed by or in consultation with a neurologist or sleep medicine specialist;
3. Age ≥ 18 years;
4. Diagnosis has been confirmed through any of one of the following (a or b):
   a. Sleep lab evaluation [e.g., polysomnography and/or multiple sleep latency test (MSLT)];
   b. Lumbar puncture shows cerebrospinal fluid (CSF) hypocretin-1 level ≤ 110 pg/mL;
5. Dose does not exceed 35.6 mg per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

B. Narcolepsy with Excessive Daytime Sleepiness (must meet all):

1. Diagnosis of narcolepsy with EDS;
2. Prescribed by or in consultation with a neurologist or sleep medicine specialist;
3. Age ≥ 18 years;
4. Diagnosis has been confirmed through sleep lab evaluation [e.g., polysomnography and/or multiple sleep latency test (MSLT)];
5. Trial and failure of a 1-month trial of one of the following generic central nervous system stimulants, unless clinically significant adverse effects are experienced or all are contraindicated: amphetamine, dextroamphetamine, or methylphenidate;
   *Prior authorization may be required for CNS stimulants
6. Trial and failure of a 1-month trial of armodafinil (Nuvigil®) or modafinil (Provigil®), unless clinically significant side effects are experienced or both are contraindicated;
   *Prior authorization may be required for armodafinil/modafinil

7. Dose does not exceed 35.6 mg per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy as evidenced by, but not limited to, improvement in any of the following parameters (a or b):
   a. Reduction in frequency of cataplexy attacks;
   b. Reported daytime improvements in wakefulness;
3. If request is for a dose increase, new dose does not exceed 35.6 mg per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
CNS: central nervous system
EDS: excessive daytime sleepiness
FDA: Food and Drug Administration
IR: immediate-release
MSLT: multiple sleep latency test
PSG: polysomnography
SOREMP: sleep-onset rapid eye movement period
ESRD: End−stage renal disease

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Cataplexy		
venlafaxine (Effexor®)*	37.5 to 75 mg twice daily (immediate release), or 37.5 to 150 mg once daily (extended release)	150 mg/day
Excessive Daytime Sleepiness		
amphetamine/ dextroamphetamine (Adderall®)	5 to 60 mg orally once daily in divided doses	60 mg/day
dextroamphetamine (Dexedrine® Spansule®, ProCentra®)		
amphetamine (Evekeo®)		

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
methylphenidate (Ritalin® [LA, SR], Metadate® ER, Methylin®,)	Dosing varies; 10 to 60 mg orally divided 2 to 3 times daily 30 to 45 min before meals	60 mg/day
armodafinil (Nuvigil®)	150 mg to 250 mg orally once daily in the morning	250 mg/day
modafinil (Provigil®)	200 mg orally once daily in the morning	400 mg/day
Sunosi®	Initiate at 75 mg orally once a day; dose may be doubled at intervals of at least 3 days	150 mg/day

Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only
*Off-label

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):*
  - Known hypersensitivity to pitolisant or any component of the formulation;
  - Severe hepatic impairment;

  *Contraindications listed reflect direct statements made in the manufacturer's package insert; for additional uses, warnings, and precautions, please refer to clinical guidelines.

- Boxed Warning(s):
  - None reported

APPENDIX D: General Information

- Increases in QT interval. Avoid use with drugs that also increase the QT interval and in patients with risk factors for prolonged QT interval. Monitor patients with hepatic or renal impairment for increased QTc

References

1. Wakix® Prescribing Information. Plymouth Meeting, PA: Harmony Biosciences, LLC; March 2021. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=8daa5562-824e-476c-9652-26ceef3d4b0e&type=display. Accessed December 20, 2022.
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3. Epstein LJ, Kristo D, Strollo PJ Jr, et al. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med. 2009; 15;5(3):263-76. Available at: https://pubmed.ncbi.nlm.nih.gov/19960649/. Accessed December 20, 2022.
4. Bassetti CL, Kallweit U, Vignatelli, et al. European guideline and expert statements on the management of narcolepsy in adults and children. J Sleep Res. 2021;00:e13387. DOI: 10.1111/jsr.13387. Available at: https://pubmed.ncbi.nlm.nih.gov/34173288/. Accessed December 20, 2022.
5. Clinical Pharmacology. Tampa, FL: Gold Standard, Inc; 2022. Available at: http://www.clinicalpharmacology-ip.com/. Accessed December 20, 2022.
6. Lexi-Drugs. Lexicomp. Wolters Kluwer. Hudson, Oh. Available at https://online.lexi.com. Accessed December 20,

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Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	12/20/2022	01/17/2023