Original Effective Date: 02/01/2020
Current Effective Date: 06/27/2024
Last P&T Approval/Version: 04/24/2024
Next Review Due By: 04/2025
Policy Number: C17997-A

Wakix (pitolisant)

PRODUCTS AFFECTED

Wakix (pitolisant)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Excessive daytime sleepiness (EDS) or cataplexy with narcolepsy

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. EXCESSIVE DAYTIME SLEEPINESS WITH NARCOLEPSY:
   1. Documented diagnosis of narcolepsy confirmed by polysomnography and multiple sleep latency test (MSLT) [DOCUMENTATION REQUIRED]
      AND

2. Documented treatment failure, serious side effects or FDA labeled contraindication to BOTH of the following for at least 90 days: (i) ONE formulary central nervous system (CNS) stimulant (e.g., methylphenidate, dexmethylphenidate, dextroamphetamine); AND (ii) ONE wakefulness promoting agent (i.e., modafinil, armodafinil)
   MOLINA REVIEWER NOTE: For Nevada Marketplace, please see Appendix.
   AND
3. Documentation of prescriber baseline disease activity evaluation and goals for treatment to be used to evaluate efficacy of therapy at renewal (e.g., symptoms of excessive daytime sleepiness, OR Epworth Sleepiness Scale (ESS), Clinical Global Impression of Change or Maintenance of Wakefulness Test (MWT))
   AND
4. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Wakix (pitolisant) include: Known hypersensitivity to pitolisant or any component of the formulation, Severe hepatic impairment (Child-Pugh C), avoid use with drugs that increase the QT interval and in patients with risk factors for prolonged QT interval, avoid use with centrally acting H1 receptor antagonists]

B. CATAPLEXY WITH NARCOLEPSY:
1. Documented diagnosis of narcolepsy confirmed by polysomnography and multiple sleep latency test (MSLT) [DOCUMENTATION REQUIRED]
   AND
2. Documentation member experiences episodes of cataplexy
   AND
3. Documented treatment failure, serious side effects, or FDA labeled contraindication to ONE of the following: a tricyclic antidepressant (TCA) [e.g., amitriptyline, desipramine, imipramine], a selective serotonin reuptake inhibitor (SSRI) [e.g., fluoxetine, sertraline, paroxetine], or venlafaxine.
   MOLINA REVIEWER NOTE: For Nevada Marketplace, please see Appendix.
   AND
4. Documentation of prescriber baseline disease activity evaluation and goals for treatment to be used to evaluate efficacy of therapy at renewal (e.g., frequency or severity of cataplexy events/attacks, symptoms of excessive daytime sleepiness, OR Epworth Sleepiness Scale (ESS), Clinical Global Impression of Change or Maintenance of Wakefulness Test (MWT))
   AND
5. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Wakix (pitolisant) include: Known hypersensitivity to pitolisant or any component of the formulation, Severe hepatic impairment (Child-Pugh C), avoid use with drugs that increase the QT interval and in patients with risk factors for prolonged QT interval, avoid use with centrally acting H1 receptor antagonists]

CONTINUATION OF THERAPY:

A. EXCESSIVE DAYTIME SLEEPINESS OR CATAPLEXY WITH NARCOLEPSY:
1. Adherence to therapy at least 85% of the time as verified by Prescriber and member's medication fill history (review Rx history for compliance)
   AND
2. Documentation of positive response to therapy as noted by prescriber's assessment (e.g., decrease or reduction in the frequency or severity of cataplexy events/attacks, decrease or reduction in symptoms of excessive daytime sleepiness, OR improvement in the Epworth Sleepiness Scale (ESS), Clinical Global Impression of Change or Maintenance of Wakefulness Test (MWT))
   AND
3. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

DURATION OF APPROVAL:
Initial authorization: 6 months, Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a neurologist or sleep disorder specialist [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
18 years of age and older

QUANTITY:
Week 1: Initiate with a dosage of 8.9 mg (two 4.45 mg tablets) once daily
Week 2: Increase dosage to 17.8 mg (one 17.8 mg tablet) once daily
Week 3: May increase to the maximum recommended dosage of 35.6 mg (two 17.8 mg tablets) once daily
Maximum of 35.6 mg daily using the least number of tablets as possible while allowing titration schedules.

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Histamine H3-Receptor Antagonist/Inverse Agonists

FDA-APPROVED USES:
Indicated for the treatment of excessive daytime sleepiness (EDS) or cataplexy in adult patients with narcolepsy

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
Reserved for State specific information. *Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.*

State Specific Information
State Marketplace
Nevada (Source: Nevada Legislature)
"Chapter 689A of Nevada Revised Statutes (NRS) is hereby amended by adding thereto a new section to read as follows:

1. A policy of health insurance which provides coverage for prescription drugs must not require an insured to submit to a step therapy protocol before covering a drug approved by the Food and Drug Administration that is prescribed to treat a psychiatric condition of the insured, if:
    a. The drug has been approved by the Food and Drug Administration with indications for the psychiatric condition of the insured or the use of the drug to treat that psychiatric condition is otherwise supported by medical or scientific evidence;
    b. The drug is prescribed by:
        i. A psychiatrist
        ii. A physician assistant under the supervision of a psychiatrist;

iii. An advanced practice registered nurse who has the psychiatric training and experience prescribed by the State Board of Nursing pursuant to NRS 632.120; or
iv. A primary care provider that is providing care to an insured in consultation with a practitioner listed in subparagraph (1), (2) or (3), if the closest practitioner listed in subparagraph (1), (2) or (3) who participates in the network plan of the insurer is located 60 miles or more from the residence of the insured; and

c. The practitioner listed in paragraph (b) who prescribed the drug knows, based on the medical history of the insured, or reasonably expects each alternative drug that is required to be used earlier in the step therapy protocol to be ineffective at treating the psychiatric condition…

3. As used in this section:
   c. *'Step therapy protocol' means a procedure that requires an insured to use a prescription drug or sequence of prescription drugs other than a drug that a practitioner recommends for treatment of a psychiatric condition of the insured before his or her policy of health insurance provides coverage for the recommended drug*."

Molina Reviewer Note: Medical necessity review for a psychiatric condition cannot require trial of other medications first. This is applicable to formulary medications that require prior authorization and non-formulary medications and is not limited to only medications designated 'ST'. If the requested drug is a brand name and the generic is on formulary, request can be reviewed for specific medical reason generic cannot be used.

ICSD-3 diagnostic criteria
The American Academy of Sleep Medicine (AASM) International Classification of Sleep Disorders – Third Edition (ICSD-3) contains diagnostic criteria for sleep disorders, including narcolepsy.

Narcolepsy type 1
- Excessive daytime sleepiness daily for ≥3 months*
- One or both of the following:
  - Cataplexy and mean sleep latency ≤8 minutes and ≥2 SOREMPs on MSLT; SOREMP (≤15 min after sleep onset) on preceding nocturnal PSG may replace one of the SOREMPs on MSLT†
  - Low or absent CSF hypocretin-1 levels‡

Narcolepsy type 2
- Excessive daytime sleepiness and MSLT findings as above, but without cataplexy§
- CSF hypocretin-1 levels are unknown or are above the threshold for narcolepsy type 1§
- The hypersomnolence and/or MSLT findings are not better explained by other causes, such as insufficient sleep, OSA, delayed sleep phase disorder, or the effect of medications or substances or their withdrawal

Notes:
*In young children, narcolepsy may sometimes present as excessively long night sleep or as resumption of previously discontinued daytime napping.
†If narcolepsy type 1 is strongly suspected clinically, but MSLT criteria are not met, consider repeating the MSLT.
‡Low or absent CSF hypocretin-1 levels = CSF hypocretin-1 concentration measured by immunoreactivity is either ≤110 pg/mL or <1/3 of mean values in healthy subjects using the same assay.
§If cataplexy develops later or low or absent CSF hypocretin-1 levels are discovered, reclassify as narcolepsy type 1.
CSF, cerebrospinal fluid; ICSD, International Classification of Sleep Disorders; MSLT, multiple sleep latency test; PSG, polysomnography; SOREMP, sleep-onset REM period.

DSM-5 diagnostic criteria
The American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) contains diagnostic criteria for sleep-wake disorders, including narcolepsy, designed for use by mental health and medical clinicians.
- Recurrent periods of an irrepressible need to sleep, lapsing into sleep, or napping occurring within the same day. These must have been occurring ≥3 times per week over the past 3 months
- The presence of at least one of the following:
  1. Episodes of cataplexy, defined as either (a) or (b), occurring at least a few times per month:

a. In individuals with long-standing disease, brief (seconds to minutes) episodes of sudden bilateral loss of muscle tone with maintained consciousness that are precipitated by laughter or joking
b. In children or in individuals within 6 months of onset, spontaneous grimaces or jaw-opening episodes with tongue thrusting or a global hypotonia, without any obvious emotional triggers

2. Hypocretin deficiency, as measured using CSF hypocretin-1 immunoreactivity values (≤1/3 of values obtained in healthy subjects tested using the same assay, or ≤110 pg/mL). Low CSF levels of hypocretin-1 must not be observed in the context of acute brain injury, inflammation, or infection
3. Nocturnal sleep PSG showing REM sleep latency ≤15 minutes, or an MSLT showing a mean sleep latency ≤8 minutes and ≥2 SOREMPs

Notes: DSM, Diagnostic and Statistical Manual of Mental Disorders.

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Wakix is a histamine-3 (H3) receptor antagonist/inverse agonist indicated for the treatment of adults who experience excessive daytime sleepiness (EDS) with narcolepsy. Wakix is contraindicated in patients with severe hepatic impairment and can cause QT interval prolongation and should be avoided in patients who have risk factors for prolonged QT interval, or who take medications that also increase the QT interval. Hormonal contraceptives have shown a decrease in efficacy when used with Wakix. Patients using hormonal contraception are advised to use an alternative, non- hormonal contraceptive when taking during the same period as Wakix as well as for 21 days following discontinuation of therapy. Wakix use with centrally acting histamine-1 receptor antagonists is not recommended as Wakix increases the levels of histamine in the brain and the effect of Wakix may be reduced by H1 receptor antagonists that cross the blood-brain barrier (e.g., diphenhydramine, TCA's, Mirtazapine etc.) Other drug interactions of note: using Wakix with strong CYP2D6 inhibitors or strong CYP3A4 inducers could impact the exposure of pitolisant and therefore may require a dosage adjustment in the Wakix. Concomitant administration of Wakix with strong CYP2D6 inhibitors increases pitolisant exposure by 2.2-fold, therefore recommendation is to reduce the dose of Wakix by half. Concomitant use of Wakix with strong CYP3A4 inducers decreases exposure of pitolisant by 50%, therefore assess for loss of efficacy after initiation of a strong CYP3A4 inducer. For patients stable on Wakix 8.9 mg or 17.8 mg once daily, increase the dose of Wakix to reach double the original daily dose (i.e., 17.8 mg or 35.6 mg, respectively) over 7 days. If concomitant dosing of a strong CYP3A4 inducer is discontinued, decrease Wakix dosage by half.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Wakix (pitolisant) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to Wakix (pitolisant) include: Known hypersensitivity to pitolisant or any component of the formulation, Severe hepatic impairment (Child-Pugh C), avoid use with drugs that increase the QT interval and in patients with risk factors for prolonged QT interval, avoid use with centrally acting H1 receptor antagonists.

OTHER SPECIAL CONSIDERATIONS:

None

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Wakix TABS 4.45MG
Wakix TABS 17.8MG

REFERENCES

1. Wakix (pitolisant) [prescribing information]. Plymouth Meeting, PA: Harmony Biosciences, LLC; December 2022.
2. Dauvilliers Y, et al. Pitolisant versus placebo or modafinil in patients with narcolepsy: a double- blind, randomized trial. Lancet Neurol. 2013; 12: 1068–75
3. Morgenthaler, T, Kapur Vishesh et al. Practice Parameters for the Treatment of Narcolepsy and other Hypersomnias of Central Origin. SLEEP. 2007; Vol 30, No. 12: 1705–10
4. Ruoff, C., & Rye, D. (2016). The ICSD-3 and DSM-5 guidelines for diagnosing narcolepsy: clinical relevance and practicality. Current Medical Research And Opinion, 32(10), 1611- 1622. doi: 10.1080/03007995.2016.1208643
5. Scammell TE. The Neurobiology, diagnosis, and treatment of Narcolepsy. AnnNeurol2003; 53:154.

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION-Notable Revisions: Required Medical Information	Q2 2024
REVISION-Notable Revisions: Diagnosis Required Medical Information Continuation of Therapy Prescriber Requirements FDA-Approved Uses Appendix Contraindications/Exclusions/Discontinuation Other Special Considerations Available Dosage Forms References	Q2 2023
REVISION-Notable Revisions: Required Medical Information Continuation of Therapy Prescriber Requirements	Q2 2022
Q2 2022 Established tracking in new format	Historical changes on file