oxybate Products (Xyrem®, Xywav™)

Policy # 00532
Original Effective Date: 01/01/2017
Current Effective Date: 09/13/2021

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider oxybate products (Xyrem®, Xywav™)‡ for the treatment of cataplexy in narcolepsy or excessive daytime sleepiness in narcolepsy to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for oxybate products (Xyrem, Xywav) will be considered when the following criteria are met:

- Patient has a diagnosis of Narcolepsy type 1 (narcolepsy with cataplexy) with presence of daily periods of irrepressible need to sleep or daytime lapses into sleep occurring for at least 3 months that is confirmed by diagnostic testing consistent with BCBSLA medical policies; OR
  *(Note: The 3 month timeframe is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Patient has a diagnosis of Narcolepsy type 2 (narcolepsy without cataplexy) with the presence of daily periods of irrepressible need to sleep or daytime lapses into sleep occurring for at least 3 months that is confirmed by diagnostic testing consistent with BCBSLA medical policies; AND
  - Patient has tried and failed (inadequate response or intolerance) at least ONE of the following generic medications unless there is clinical evidence or patient history that suggests the use of the generic alternatives will be ineffective or cause an adverse reaction to the patient: modafinil, armodafinil, methylphenidate, dextroamphetamine, or amphetamine/dextroamphetamine salt

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*(Note: The 3 month timeframe and the requirement for prior use of at least one generic alternative therapy are additional Company requirements for coverage eligibility and will be denied as not medically necessary** if not met)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of oxybate (Xyrem, Xywav) WITHOUT a trial and failure of at least one generic drug for Narcolepsy Type 2 to be **not medically necessary.****

Based on review of available data, the Company considers the use of oxybate (Xyrem, Xywav) WITHOUT the presence of daily periods of irrepressible need to sleep or daytime lapses into sleep occurring for at least 3 months for Narcolepsy Type 1 or Narcolepsy Type 2 to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of oxybate (Xyrem, Xywav) for any indication other than the FDA approved indications to be **investigational.***

Background/Overview

Xyrem and Xywav are gamma hydroxybutyrate (GHB) salts approved for the treatment of cataplexy in narcolepsy and excessive daytime sleepiness in narcolepsy. Both products have the same concentration of oxybate with Xyrem including only sodium cations and Xywav including a mix of calcium, magnesium, potassium, and sodium cations. According to the manufacturer, Xywav has 92% less sodium, which may be important for patients sensitive to salt intake (e.g., those with heart failure, hypertension, or renal impairment). The mechanism of action of these products in narcolepsy is unknown. It is hypothesized that the therapeutic effects are mediated through $GABA_B$ actions at noradrenergic and dopaminergic neurons and also at thalamocortical neurons. Guidelines from the American Academy of Sleep Medicine have not yet been updated to include Xywav, but list Xyrem as an effective treatment of cataplexy, daytime sleepiness, and disrupted sleep due to narcolepsy.

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The guidelines also list modafinil type products as effective for the treatment of daytime sleepiness due to narcolepsy. Amphetamine, dextroamphetamine, their combo, and methylphenidate are considered effective for the treatment of daytime sleepiness as well. For narcolepsy type 2, the generically available alternatives are a more economical option.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Xyrem was approved in 2002 for the treatment of cataplexy in narcolepsy and excessive daytime sleepiness in narcolepsy. Xywav was approved in 2020 for the treatment of cataplexy or excessive daytime sleepiness in patients 7 years of age and older with narcolepsy.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The intent of this policy is to ensure that Xyrem and Xywav are being used according to the FDA approved package insert indication as well as to ensure that more economical, yet equally efficacious alternatives are being used where applicable.

References

1. Xyrem [package insert]. Jazz Pharmaceuticals, Inc. Palo Alto, CA. Updated September 2020.
2. Morgenthaler TI, Kapur VK,.Brown TM, et al. Practice Parameters for the Treatment of Narcolepsy and other Hypersomnias of Central Origin: An American Academy of Sleep Medicine Report. Available at: http://www.aasmnet.org/Resources/PracticeParameters/PP_Narcolepsy.pdf. Accessed on November 13, 2015.
3. Wise MS, Arand DL, Auger R, et al. Treatment of narcolepsy and other hypersomnias of central origin: An American Academy of Sleep Medicine Review. Available at:

http://www.aasmnet.org/Resources/PracticeParameters/Review_Narcolepsy.pdf. Accessed on November 13, 2015.
4. Xywav [package insert]. Jazz Pharmaceuticals, Inc. Palo Alto, CA. Updated October 2020.
5. Xyrem/Xywav Prior Authorization Policy. Express Scripts. Updated June 2021.

Policy History

Original Effective Date: 01/01/2017
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09/08/2016	Medical Policy Committee review
09/21/2016	Medical Policy Implementation Committee approval. New policy.
09/07/2017	Medical Policy Committee review
09/20/2017	Medical Policy Implementation Committee approval. No change to coverage.
09/06/2018	Medical Policy Committee review
09/19/2018	Medical Policy Implementation Committee approval. No change to coverage.
09/05/2019	Medical Policy Committee review
09/11/2019	Medical Policy Implementation Committee approval. No change to coverage.
09/03/2020	Medical Policy Committee review
09/09/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/04/2021	Medical Policy Committee review
02/10/2021	Medical Policy Implementation Committee approval. Added new product, Xywav, to policy with relevant background information.
08/05/2021	Medical Policy Committee review
08/11/2021	Medical Policy Implementation Committee approval. Changed criterion requiring trial and failure of two generics to only require trial and failure of one generic. Also updated Xywav criteria to remove step through Xyrem.

Next Scheduled Review Date: 08/2022

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

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A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

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NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.