BlueCross BlueShield of Louisiana

An independent licensee of the Blue Cross and Blue Shield Association.

tetrabenazine (Xenazine®)

Policy # 00304
Original Effective Date: 08/17/2011
Current Effective Date: 08/20/2014

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 the use of tetrabenazine (Xenazine®)‡ † for the treatment of chorea associated with Huntington's disease to be **eligible for coverage**.

Patient Selection Criteria
Coverage eligibility for the use of tetrabenazine (Xenazine) will be considered when the following criterion is met:

- Patient has documented chorea associated with Huntington's disease.

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 tetrabenazine (Xenazine) when the patient selection criterion is not met to be **investigational.***

Background/Overview

Xenazine reversibly depletes monoamines (such as dopamine, serotonin, norepinephrine, and histamine) from nerve terminals and is indicated for the treatment of chorea associated with Huntington's disease. Xenazine, and its major circulating metabolites (α-dihydrotetrabenazine [HTBZ] and β-HTBZ), reversibly inhibits vesicular monoamine transporter type 2 (VMAT2), resulting in decreased uptake of monoamines into synaptic vesicles and depletion of monoamine stores. Xenazine is supplied as 12.5mg and 25mg tablets. Individualization of dose with careful weekly titration is required. See package insert for dosing details.

Neuroleptic malignant syndrome (NMS), akathisia, agitation, parkinsonism, dysphagia, and QT prolongation–related arrhythmias have been reported with use of Xenazine. Xenazine should not be used in combination with drugs known to prolong QTc (which in certain circumstances can lead to torsades de pointes and/or sudden death), in patients with congenital long QT syndrome, or in patients with a history of cardiac arrhythmias. A potentially irreversible syndrome of involuntary, dyskinetic movements called tardive dyskinesia (TD) may develop in patients treated with neuroleptic drugs. If signs and symptoms of TD appear in a patient treated with Xenazine, drug discontinuation should be considered. Adverse reactions associated with Xenazine, such as QTc prolongation, NMS, and extrapyramidal disorders, may be exaggerated by concomitant use of dopamine antagonists.

tetrabenazine (Xenazine®)

Policy # 00304
Original Effective Date: 08/17/2011
Current Effective Date: 08/20/2014

Huntington's Disease
Huntington's Disease (HD) is a devastating neurodegenerative disease that causes progressive movement disorders, cognitive dysfunction and behavioral changes and is ultimately a fatal condition. Chorea is the most common symptom, affecting approximately 90% of HD patients, and is characterized by excessive, involuntary and repetitive movements, which are the most visible and dangerous manifestations of HD and interfere with patients' abilities to perform activities of daily living, including dressing, bathing and caring for themselves. It is estimated that approximately 30,000 people are affected in the U.S.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Xenazine was approved on August 15, 2008 for the treatment of chorea associated with HD. Xenazine has been designated as an "orphan drug" by the FDA. There is a boxed warning indicating the risk of depression as well as suicidal thoughts and behavior in patients with HD and the use of Xenazine (see package insert).

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. FDA 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.

Study 1 was a randomized, double-blind, placebo-controlled multi-center trial conducted in ambulatory patients with a diagnosis of HD that examined the efficacy of Xenazine as a treatment for the chorea of HD. The diagnosis of HD was based on family history, neurological exam, and genetic testing. Treatment duration was 12 weeks, including a 7-week dose titration period and a 5-week maintenance period followed by a 1-week washout. The dose of Xenazine was started at 12.5mg/day and titrated upward at weekly intervals in 12.5mg increments until satisfactory control of chorea was achieved, until intolerable side effects occurred, or until a maximal dose of 100mg per day was reached.

The primary efficacy endpoint was the Total Chorea Score, an item of the Unified Huntington's Disease Rating Scale (UHDRS). On this scale, chorea is rated from 0 to 4 (with 0 representing no chorea) for 7 different parts of the body. The total score ranges from 0 to 28.

Total Chorea Scores for subjects in the drug group declined by an estimated 5.0 units during maintenance therapy (average of Week 9 and Week 12 scores versus baseline), compared to an estimated 1.5 units in the placebo group. The treatment effect of 3.5 units was highly statistically significant. At the Week 13 follow-up in Study 1 (1 week after discontinuation of the study medication), the Total Chorea Scores of subjects receiving Xenazine returned to baseline.

Study 2 was performed in patients who had been treated with open-label Xenazine for at least 2 months (mean duration of treatment was 2 years). They were randomized to continuation of tetrabenazine at the same dose (n=12) or to placebo (n=6) for 3 days, at which time their chorea scores were compared.

tetrabenazine (Xenazine®)

Policy # 00304
Original Effective Date: 08/17/2011
Current Effective Date: 08/20/2014

Although the comparison did not reach statistical significance (p=0.1), the estimate of the treatment effect was similar to that seen in Study 1 (about 3.5 units).

References

1. Xenazine® tablets [package insert]. Deerfield, IL: Ovation Pharmaceuticals, Inc.; Revised May 2011.
2. Express Scripts. Proactive Prior Authorization Policy. Tetrabenazine tablets (Xenazine®). June 23, 2010.
3. Kenney C, Jankovic J. Tetrabenazine in the treatment of hyperkinetic movement disorders. *Expert Rev Neurotherapeutics.* 2006;6:7-17.
4. Tetrabenazine. In DRUGDEX® System. Thomson Reuters (Healthcare) Inc. Available at: http://www.thomsonhc.com.
5. Kenney C, Hunter C, Jankovic J. Long-term tolerability of tetrabenazine in the treatment of hyperkinetic movement disorders. *Mov Disord.* 2007;22:193-197.
6. Paleacu D, Giladi N, Moore O, et al. Tetrabenazine treatment in movement disorders. *Clin Neuropharmacol.* 2004;27:230-233.

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2013 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. *Applicable FARS/DFARS apply.*

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J3490, J8499
ICD-9 Diagnosis	333.4
ICD-9 Procedure	No codes

Policy History

Original Effective Date: 08/17/2011
Current Effective Date: 08/20/2014
08/04/2011 Medical Policy Committee review
08/17/2011 Medical Policy Implementation Committee approval. New policy.
08/02/2012 Medical Policy Committee review
08/15/2012 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

tetrabenazine (Xenazine®)

Policy # 00304
Original Effective Date: 08/17/2011
Current Effective Date: 08/20/2014

02/19/2013	Coding updated
08/01/2013	Medical Policy Committee review
08/21/2013	Medical Policy Implementation Committee approval. Reworded the patient selection criteria, however there is no coverage change. Rearranged the background section. Made a few wording changes to the rationale/source section.
08/07/2014	Medical Policy Committee review
08/20/2014	Medical Policy Implementation Committee approval. No change to coverage.

Next Scheduled Review Date: 08/2015

*****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:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. 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.

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.