Zurampic®, Duzallo® (lesinurad Products)

Policy # 00546
Original Effective Date: 02/15/2017
Current Effective Date: 01/17/2018

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.

Zurampic®±

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 Zurampic (lesinurad) for the treatment of hyperuricemia associated with gout to be **eligible for coverage** when the patient selection criteria are met.

Patient Selection Criteria
Coverage eligibility for Zurampic (lesinurad) will be considered when all of the following criteria are met:

- Patient has hyperuricemia associated with gout; AND
- Patient is unable to achieve target serum uric acid levels while on a xanthine oxidase inhibitor [such as generic allopurinol or Uloric®± (febuxostat)]; AND
- Patient is unable to achieve target serum uric acid levels after the addition of generic probenecid to a xanthine oxidase inhibitor [such as generic allopurinol or Uloric (febuxostat)]; AND
  *(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Patient will use Zurampic (lesinurad) in combination with a xanthine oxidase inhibitor (e.g. not as monotherapy). Examples of xanthine oxidase inhibitors include generic allopurinol or Uloric (febuxostat).

When Services Are Considered Not Medically Necessary
Based on review of available data, the Company considers the use of Zurampic (lesinurad) when there is NO attempt to add generic probenecid to a xanthine oxidase inhibitor [such as generic allopurinol or Uloric (febuxostat)] prior to requesting Zurampic (lesinurad) OR when the patient is able to achieve target serum uric acid levels after the addition of generic probenecid to a xanthine oxidase inhibitor [such as generic allopurinol or Uloric (febuxostat)] 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.

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Based on review of available data, the Company considers the use of Zurampic (lesinurad) when the patient selection criteria are not met to be **investigational*** (with the exception of those denoted above as **not medically necessary**).**

Duzallo®±

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 Duzallo (allopurinol/lesinurad) for the treatment of hyperuricemia associated with gout to be **eligible for coverage** when the patient selection criteria are met.

Patient Selection Criteria:
Coverage eligibility for Duzallo (allopurinol/lesinurad) will be considered when all of the following criteria are met:

- The patient has hyperuricemia associated with gout; AND
- Patient was unable to achieve target serum uric acid levels on allopurinol alone; AND
- Patient was unable to achieve target serum uric acid levels on allopurinol PLUS probenecid (unless patient has nephrolithiasis, cystinuria, or is currently taking penicillamine).
  *(Note: This specific patient criterion is an additional Company requirement 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 Duzallo (allopurinol/lesinurad) when there is NO attempt to add generic probenecid to allopurinol prior to requesting Duzallo (allopurinol/lesinurad) OR when the patient is able to achieve target serum uric acid levels after the addition of generic probenecid to allopurinol 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 Duzallo (allopurinol/lesinurad) when the patient selection criteria are not met to be **investigational*** (with the exception of those denoted above as **not medically necessary**).**

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Background/Overview

Lesinurad is a URAT1 (uric acid transport 1) inhibitor indicated in combination with a xanthine oxidase inhibitor for the treatment of hyperuricemia associated with gout in patients who have not achieved target serum uric acid levels with a xanthine oxidase inhibitor alone. Lesinurad is not recommended for the treatment of asymptomatic hyperuricemia and it should not be used as monotherapy. Failure to take lesinurad with a xanthine oxidase inhibitor may increase the risk of renal adverse reactions. Lesinurad should not be initiated if the patient's creatinine clearance is below 45 mL/min and should be stopped if the creatinine clearance consistently falls below 45 mL/min. Lesinurad is available alone as Zurampic tablets and in combination with allopurinol as Duzallo. Zurampic tablets contain 200 mg of lesinurad with the recommended dosing to begin at 200 mg once daily (in combination with a xanthine oxidase inhibitor such as allopurinol or Uloric). The maximum daily dose of Zurampic is 200 mg once daily. Duzallo tablets contain 200 mg of lesinurad formulated with either 200 mg or 300 mg of allopurinol. The recommended dose of Duzallo is one tablet once daily with food and water.

In the setting of gout, xanthine oxidase inhibitors (e.g. allopurinol, Uloric) are the recommended approach for first line therapy in the treatment of gout. If the desired serum uric acid level has not been met with an appropriate dose of a xanthine oxidase inhibitor, then a uricosuric agent, such as probenecid, should be added to the xanthine oxidase inhibitor. Lesinurad is also a uricosuric agent and acts as an alternative agent to probenecid.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Zurampic was approved by the FDA in December of 2015 for use in combination with a xanthine oxidase inhibitor for the treatment of hyperuricemia associated with gout in patients who have not achieved target serum uric acid levels with a xanthine oxidase inhibitor alone.

Duzallo was approved by the FDA in August 2017 for the treatment of hyperuricemia associated with gout in patients who have not achieved target serum uric acid levels with a medically appropriate daily dose of allopurinol alone.

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.

The efficacy of lesinurad plus a xanthine oxidase inhibitor was established in three phase III, randomized double blind studies in patients with hyperuricemia and gout. All studies lasted 12 months and subjects received prophylaxis for gout flares with colchicine or non-steroidal anti-inflammatory drugs for the first 5 months of treatment. It should be noted that there was not a significant difference in the number of gout

flares requiring treatment (month 6 thru month 12) with lesinurad plus a xanthine oxidase inhibitor versus placebo in any of the studies. In the first two studies, lesinurad plus allopurinol increased the proportion of patients who achieved a serum uric acid level of <6 mg/dL at month 6 by about 2-fold vs. allopurinol alone (54% vs. 28% in the first study and 55% vs. 23% in the second study). In the third study, there was no significant difference at month 6 between Zurampic plus Uloric vs. febuxostat alone in the proportion of patients with a serum uric acid level < 5mg/dL.

There have been no phase 3 clinical trials specifically with Duzallo, but bioequivalence of Duzallo to co-administered lesinurad and allopurinol has been demonstrated.

Based on the clinical data associated with this drug and the existing products on the market, lesinurad plus a xanthine oxidase inhibitor or Duzallo are alternatives for those that are unable to reach a target serum uric acid level after trying a combination of a xanthine oxidase inhibitor plus probenecid.

References

1. Zurampic [package insert]. AstraZeneca. Wilmington, Delaware. Updated January 2016.
2. Zurampic Drug Evaluation. Express Scripts. Updated February 2016.
3. Duzallo [package insert]. Ironwood Pharmaceuticals. Cambridge, MA. Updated November 2017.

Policy History

Original Effective Date: 02/15/2017
Current Effective Date: 01/17/2018

02/02/2017	Medical Policy Committee review
02/15/2017	Medical Policy Implementation Committee approval. New policy.
01/04/2018	Medical Policy Committee review
01/17/2018	Medical Policy Implementation Committee approval. Policy title changed and added a new lesinurad-containing product, Duzallo

Next Scheduled Review Date: 01/2019

*****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. 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.

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**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.

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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.