LOUISIANA BLUE

nitisinone (Orfadin®, Nityr™, generics)

Policy # 00586
Original Effective Date: 01/01/2018
Current Effective Date: 12/09/2024

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 nitisinone (Orfadin®, Nityr™, generics)‡ for the treatment of hereditary tyrosinemia, type 1 (HT-1) to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for nitisinone (Orfadin, Nityr, generics) will be considered when the following criteria are met:

- Patient has a diagnosis of hereditary tyrosinemia, type 1 (HT-1); AND
- Requested drug will be used in combination with dietary restriction of tyrosine and phenylalanine; AND
- If the request is for brand Orfadin, there is clinical evidence or patient history that suggests the use of Nityr AND generic nitisinone will be ineffective or cause an adverse reaction to the patient.
  *(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 brand nitisinone (Orfadin) when there is an absence of clinical evidence or patient history that suggests the use of nitisinone (Nityr) AND generic nitisinone (Orfadin) will be ineffective or cause an adverse reaction to the patient to be **not medically necessary.****

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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 nitisinone (Orfadin, Nityr, generics) without dietary restriction of tyrosine and phenylalanine or for any diagnosis other than HT-1 to be **investigational.***

Background/Overview

Nitisinone is the drug of choice for the treatment of hereditary tyrosinemia type 1 (HT-1), a disease caused by deficiency of the last enzyme in the pathway of tyrosine metabolism (fumaryloacetoacetate hydrolase). Nitisinone inhibits one of the first enzymes in this tyrosine degradation pathway (4-hydroxyphenyl-pyruvate dioxygenase) to limit the formation and accumulation of the toxic metabolites. It is available in two bioequivalent brands, Orfadin (capsules and suspension) and Nityr (tablets). Additionally, Orfadin capsules are available as generics. Orfadin products require refrigeration prior to opening and the capsules must be dosed at least one hour before or two hours after a meal. The Orfadin suspension and Nityr tablets do not have a food requirement. Nityr does not require refrigeration. Both the Orfadin capsules and Nityr tablets may be dissolved in water or applesauce for easier administration. Both products should be dosed twice daily in patients under five years of age and may be administered once daily in patients five years of age and older who have undetectable serum and urine succinylacetone concentrations after a minimum of 4 weeks on a stable dosage of nitisinone.

HT-1 is a rare, autosomal recessive disease with a prevalence of 1:12,000 to 1:100,000 individuals of northern European descent. The deficiency in the enzyme fumaryloacetoacetate hydrolase and resulting accumulation of toxic metabolites manifests as severe progressive liver disease and renal tubular dysfunction. If untreated, patients have a significantly shortened lifespan often dying of acute liver failure before the second year of life. HT-1 is diagnosed based on the measurement of one of the toxic metabolites, succinylacetone (SA) in either the blood or urine. This test can be performed immediately after birth and is part of routine newborn screening in most states (including Louisiana).

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Nitisinone (Orfadin, Nityr) is indicated for the treatment of patients with hereditary tyrosinemia type 1 (HT-1) in combination with dietary restriction of tyrosine and phenylalanine.

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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, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Both Orfadin and Nityr were approved based on an open-label, uncontrolled study of 207 patients with HT-1. All patients were treated with nitisinone in addition to dietary restriction of tyramine and phenylalanine. To assess efficacy, 2 and 4 year survival probabilities were compared to historical controls treated with dietary restriction alone. Patients presenting with HT-1 younger than 2 months of age who were treated with nitisinone and dietary restriction had both 2 and 4 year survival probabilities of 88%. In comparison, historical control patients presenting with HT-1 younger than 2 months of age and treated with dietary restriction alone had both 2 and 4 year survival probabilities of 29%. Patients presenting with HT-1 between ages 2 and 4 months and treated with nitisinone and dietary restriction had both 2 and 4 year survival probabilities of 94%. Historical controls in this group had 2 and 4 year survival probabilities of 74% and 60%, respectively.

This study also evaluated effects on urine and plasma succinylacetone, porphyrin metabolism, and urinary alpha-1-microglobulin and found statistically significant improvements in nitisinone-treated patients compared to pre-treatment baseline.

References

1. Orfadin [package insert]. Apotek. Waltham, MA. Feb 2017.
2. Nityr [package insert]. Rivopharm SA. Manno, Switzerland. September 2020.

Policy History

Original Effective Date: 01/01/2018
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10/05/2017	Medical Policy Committee review
10/18/2017	Medical Policy Implementation Committee approval. New policy.
10/04/2018	Medical Policy Committee review
10/17/2018	Medical Policy Implementation Committee approval. No change to coverage.
11/07/2019	Medical Policy Committee review
11/13/2019	Medical Policy Implementation Committee approval. Added new generic to policy.
11/05/2020	Medical Policy Committee review
11/11/2020	Medical Policy Implementation Committee approval. Updated Nityr dosing information.

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11/04/2021	Medical Policy Committee review
11/10/2021	Medical Policy Implementation Committee approval. No change to coverage.
11/03/2022	Medical Policy Committee review
11/09/2022	Medical Policy Implementation Committee approval. No change to coverage.
11/02/2023	Medical Policy Committee review
11/08/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
11/07/2024	Medical Policy Committee review
11/13/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 11/2025

*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 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.

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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: 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.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

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