



Drug Coverage Policy

Effective Date.....2/1/2025

Coverage Policy Number IP0146

Policy Title..... Nitisinone Products

Metabolic Disorders – Nitisinone Products

- Orfadin® (nitisinone capsules and suspension – Sobi, generic [capsules only])
- Nityr® (nitisinone tablets – Cycle)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

Nitisinone products are hydroxy-phenylpyruvate dioxygenase inhibitors indicated for the treatment of **hereditary tyrosinemia type 1** in combination with dietary restriction of tyrosine and phenylalanine in pediatric and adult patients.^{1,2}

Disease Overview

Hereditary tyrosinemia type 1 is a genetic disorder characterized by elevated blood levels of the amino acid tyrosine.^{3,4} It is caused by mutations in the *FAH* gene, which lead to a deficiency of the enzyme fumarylacetoacetate hydrolase that is required for the breakdown of tyrosine. Symptoms usually appear in the first few months after birth and include failure to thrive, diarrhea, vomiting, jaundice, cabbage-like odor, and increased tendency to bleed. Diagnosis is most often via newborn screening (i.e., elevated alpha-fetoprotein and succinyl acetone); however, carrier

genetic testing and prenatal diagnosis by detection of succinyl acetone in the amniotic fluid are also possible. Treatment should be initiated immediately upon diagnosis with a diet restricted in tyrosine and phenylalanine and with nitisinone, which blocks the second step in the tyrosine degradation pathway.

Medical Necessity Criteria

Nitisinone products are considered medically necessary when the following are met:

Hereditary Tyrosinemia Type 1. Individual meets **ALL** the following criteria:

- A. Documented diagnosis supported by ONE of the following:
 - i. Confirmed biallelic pathogenic variants in the *FAH* gene
 - ii. Individual has elevated urinary or plasma succinyl acetone levels
- B. Medication is prescribed in conjunction with a tyrosine- and phenylalanine-restricted diet
- C. Individual will not be taking the requested agent concurrently with another nitisinone product
- D. Medication is being prescribed by, or in consultation with, a metabolic disease specialist (or specialist who focuses on the treatment of metabolic diseases)
- E. Preferred product criteria are met for the products listed in the below table(s)

Employer Plans:

Product	Criteria
Orfadin (nitisinone) capsules and suspension	Documentation of failure, contraindication, or intolerance to Nityr (nitisinone) tablets [may require prior authorization]

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Reauthorization Criteria

Continuation of nitisinone products (nitisinone capsules, Nityr, Orfadin) are considered medically necessary for hereditary Tyrosinemia Type 1 when the above medical necessity criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration is up to 12 months.
 Reauthorization approval duration: up to 12 months.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven.

References

1. Orfadin® capsules and suspension [prescribing information]. Waltham, MA: Sobi; November 2021.
2. Nityr® tablets [prescribing information]. Cambridge, UK: Cycle; May 2024.
3. Tyrosinemia type 1. Genetic and Rare Diseases Information Center; National Institutes of Health, US Department of Health, and Human Services. Updated September 2024. Available at: <https://rarediseases.info.nih.gov/diseases/2658/tyrosinemia-type-1>. Accessed on October 31, 2024.
4. Tyrosinemia type 1. National Organization for Rare Disorders. Updated September 2019. Available at: <https://rarediseases.org/rare-diseases/tyrosinemia-type-1/>. Accessed on October 31, 2024.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	No criteria changes.	5/15/2024
Annual Revision	No criteria changes.	2/1/2025

The policy effective date is in force until updated or retired.

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