Drug and Biologic Coverage Policy

Effective Date **8/1/2023**
Next Review Date… **8/1/2024**
Coverage Policy Number **IP0146**

Nitisinone

Table of Contents

Related Coverage Resources

Pharmacogenetic Testing

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. 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

This policy supports medical necessity review for the following nitisinone products.

- **Nitisinone** capsules
- **Nityr**® (nitisinone) tablets
- **Orfadin**® (nitisinone) capsules and suspension

Additional criteria that support the review for medical necessity exceptions of non-covered products are located in the Non-Covered Product Table by the respective plan type and drug list where applicable.

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

Medical Necessity Criteria

Nitisinone products (nitisinone capsules, Nityr, Orfadin) are considered medically necessary when the following are met:

Hereditary Tyrosinemia Type 1. Individual meets **ALL** of 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 succinylacetone levels
B. The 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 in the treatment of metabolic diseases)
E. Non-Covered Product Criteria is met, refer to below table

Employer Group Non-Preferred Products and Preferred Covered Alternatives by Drug List:

Non-Covered 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.

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.

Background

OVERVIEW
Nitisinone products are hydroxy-phenylpyruvate dioxygenase inhibitors indicated for the treatment of adults and pediatric patients with **hereditary tyrosinemia type 1** in combination with dietary restriction of tyrosine and phenylalanine.[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 succinylacetone); however, carrier genetic testing and prenatal diagnosis by detection of succinylacetone 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.

References

1. Orfadin® capsules and suspension [prescribing information]. Waltham, MA: Sobi; November 2021.
2. Nityr® tablets [prescribing information]. Cambridge, UK: Cycle; July 2022.
3. Tyrosinemia type 1. Genetic and Rare Diseases Information Center; National Institutes of Health, US Department of Health and Human Services. Updated November 8, 2021. Available at: https://rarediseases.info.nih.gov/diseases/2658 /tyrosinemia-type-1. Accessed on November 7, 2022.
4. Tyrosinemia type 1. National Organization for Rare Disorders. Updated 2019. Available at: https://rarediseases.org/rare-diseases/tyrosinemia-type-1/. Accessed on November 7, 2022.