PRIOR AUTHORIZATION POLICY

POLICY: Metabolic Disorders – Nitisinone Products Prior Authorization Policy
- Orfadin® (nitisinone capsules and suspension – Sobi, generic [capsules only])
- Nityr® (nitisinone tablets – Cycle)

REVIEW DATE: 11/15/2023

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.

CIGNA NATIONAL FORMULARY COVERAGE:

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 patients and adults.[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.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of nitisinone products. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with nitisinone products as well as the monitoring required for adverse events and long-term efficacy, approval requires the agent to be prescribed by or in consultation with a physician who specializes in the condition being treated.

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

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indication

1. **Hereditary Tyrosinemia Type 1.** Approve for 1 year if the patient meets the following (A, B, C, and D):
   - **A)** According to the prescriber, diagnosis is supported by one of the following (i or ii):
     - **i.** Genetic testing confirms biallelic pathogenic/likely pathogenic variants in the FAH gene; OR
     - **ii.** Patient has elevated levels of succinylacetone in the serum or urine; AND
   - **B)** The medication is prescribed in conjunction with a tyrosine- and phenylalanine-restricted diet; AND
   - **C)** Patient will not be taking the requested agent concurrently with another nitisinone product; AND
     Note: Examples of nitisinone products include Orfadin, generic nitisinone capsules, and Nityr. Concurrent use of these agents is not allowed.
   - **D)** The medication is prescribed by or in consultation with a metabolic disease specialist (or specialist who focuses in the treatment of metabolic diseases).

CONDITIONS NOT COVERED

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

is(are) considered experimental, investigational or unproven for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Concomitant Therapy with Nitisinone Products.** Note: For example, concomitant use of Orfadin, generic nitisinone capsules, and/or Nityr. There are no data available to support concomitant use.

REFERENCES

1. Orfadin® capsules and suspension [prescribing information]. Waltham, MA: Sobi; November 2021.
2. Nityr® tablets [prescribing information]. Cambridge, UK: Cycle; June 2021.
3. Tyrosinemia type 1. Genetic and Rare Diseases Information Center; National Institutes of Health, US Department of Health and Human Services. Updated February 2023. Available at: https://rarediseases.info.nih.gov/diseases/2658/tyrosinemia-type-1. Accessed on November 9, 2023.
4. Tyrosinemia type 1. National Organization for Rare Disorders. Updated September 2019. Available at: https://rarediseases.org/rare-diseases/tyrosinemia-type-1/. Accessed on November 9, 2023.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	11/09/2022
Selected Revision	**Hereditary Tyrosinemia Type 1:** Revised the criteria for diagnosis to require genetic testing confirmation of biallelic pathogenic/likely pathogenic variants in the FAH gene or patient has elevated succinylacetone levels in serum or urine. Previously, diagnosis could be supported by genetic testing confirmation of a mutation of the FAH gene or patient has elevated serum levels of alpha-fetoprotein (AFP) and succinylacetone.	05/24/2023
Annual Revision	No criteria changes.	11/15/2023