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: 11/06/2024

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 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of nitisinone products is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Hereditary Tyrosinemia Type 1.** Approve for 1 year if the patient meets ALL of 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 RECOMMENDED FOR APPROVAL

Coverage of nitisinone products is not recommended in the following situations:

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.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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.