

## PRIOR AUTHORIZATION POLICY

- POLICY:** Metabolic Disorders – Nitisinone Products
- Orfadin (nitisinone capsules and suspension – Sobi, Inc., generic [capsules only])
  - Nityr (nitisinone tablets – Cycle Pharmaceuticals)

**REVIEW DATE:** 11/04/2020

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### OVERVIEW

Nitisinone products are hydroxy-phenylpyruvate dioxygenase inhibitors indicated for the treatment of adult and pediatric patients with **hereditary tyrosinemia type 1** in combination with dietary restriction of tyrosine and phenylalanine.<sup>1-2</sup>

### Disease Overview

Hereditary tyrosinemia type 1 is a genetic disorder characterized by elevated blood levels of the amino acid tyrosine.<sup>3-4</sup> 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 is also possible. Treatment should be 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 Indications

- 1. Hereditary Tyrosinemia Type 1.** Approve for 1 year if the patient meets the following criteria (A, B, C, and D):
  - A)** According to the prescriber, diagnosis is supported by one of the following (i or ii):
    - i.** Genetic testing confirmed a mutation of the *FAH* gene; OR
    - ii.** Patient has elevated serum levels of alpha-fetoprotein (AFP) and succinylacetone; 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.

Note: Examples of nitisinone products include Orfadin, generic nitisinone capsules, and Nityr. Concurrent use of these agents is not allowed; AND

- 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 [prescribing information]. Waltham, MA: Sobi, Inc.; May 2019.
2. Nityr [prescribing information]. Cambridge, UK: Cycle Pharmaceuticals; September 2020.
3. Genetic and Rare Diseases Information Center; National Institutes of Health, US Department of Health and Human Services [Web site]. Tyrosinemia type 1. Updated on: December 21, 2017. Accessed on October 2, 2019. Available at: <https://rarediseases.info.nih.gov/diseases/2658/tyrosinemia-type-1>.
4. National Organization for Rare Disorders. Tyrosinemia type 1. Accessed on October 2, 2019. Available at: <https://rarediseases.org/rare-diseases/tyrosinemia-type-1/>.