CareSource Rxinnovations

# PHARMACY POLICY STATEMENT
## Indiana Medicaid

| DRUG NAME | Nitisinone (Orfadin and Nityr) |
|---|---|
| BENEFIT TYPE | Pharmacy |
| STATUS | Prior Authorization Required |

Nitisinone, approved by the FDA in 2002, is a hydroxy-phenylpyruvate dioxygenase inhibitor indicated for the treatment of adult and pediatric patients with hereditary tyrosinemia type 1 (HT-1) in combination with dietary restriction of tyrosine and phenylalanine. It is supplied as generic nitisinone capsules, brand name Orfadin capsules or oral suspension, and brand name Nityr tablets. Nitisinone in combination with prescribed diet leads to far greater survival and clinical outcomes compared to untreated HT-1 patients. Strict adherence to therapy is crucial.

HT-1 is a genetic metabolic disorder that usually presents before 6 months of age. Fumarylacetoacetate hydrolase (FAH) is the deficient enzyme responsible for HT-1. It is the terminal step in the tyrosine catabolic pathway. Mutations in the *FAH* gene lead to HT-1.

Nitisinone inhibits an enzyme in the normal catabolic pathway of tyrosine to prevent accumulation of catabolic intermediates that convert to the toxic metabolites succinylacetone (SA) and succinylacetoacetate (SAA) responsible for the liver and kidney symptoms of HT-1. Neurologic porphyric-like crises may also occur. SA is the primary marker used to screen for HT-1.

Nitisinone will be considered for coverage when the following criteria are met:

## Hereditary Tyrosinemia Type 1 (HT-1)

For **initial** authorization:

1. Medication must be prescribed by or in consultation with an endocrinologist, geneticist, dietician, hepatologist, or nephrologist; AND
2. Member has a diagnosis of hereditary tyrosinemia type 1 (HT-1) confirmed by at least one of the following:
   a) Biochemical testing (i.e., presence of succinylacetone in the urine or blood)
   b) Genetic test results showing pathogenic mutation of the *FAH* gene; AND
3. Member has a baseline succinylacetone level documented in chart notes; AND
4. Member is using medication in combination with dietary restriction of tyrosine and phenylalanine (commonly found in high-protein food); AND
5. Chart notes must document that the member has had or will have a slit-lamp ophthalmic exam completed prior to initiating treatment; AND
6. If the request is for brand name Orfadin capsules or suspension or Nityr tablets, clinical justification must be provided why generic nitisinone capsules cannot be used.
7. **Dosage allowed/Quantity limit:** Max total daily dosage of 2 mg/kg (orally), based on evaluation of biochemical and/or clinical response. See prescribing info for details.

***If all the above requirements are met, the medication will be approved for 12 months.***

For **reauthorization**:
1. Member must continue dietary restriction of tyrosine and phenylalanine; AND
2. Chart notes must show a reduced succinylacetone (SA) level compared to baseline.

***If all the above requirements are met, the medication will be approved for an additional 12 months.***

## CareSource considers nitisinone not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

| DATE | ACTION/DESCRIPTION |
|---|---|
| **04/30/2020** | New policy for Orfadin created. |
| **11/01/2022** | Transferred to new template. Renamed policy to generic name and added Nityr brand name. Amended dosing section. Added specialist requirement. Split diagnostic confirmation into 2 parts and added name of mutated gene. Changed wording of slit-lamp exam requirement. Updated references. Added criterion requiring generic caps. |
| **10/11/2024** | Annual review; no updates to clinical criteria. |

References:


1. Orfadin [prescribing information]. Sobi, Inc; 2021.
2. Nityr [prescribing information]. Cycle Pharmaceuticals Ltd; 2024.
3. Jack RM, Scott CR. Validation of a therapeutic range for nitisinone in patients treated for tyrosinemia type 1 based on reduction of succinylacetone excretion. JIMD reports. 2019;46(1)75-78.
4. Chinsky JM, Singh R, Ficicioglu C, et al. Diagnosis and treatment of tyrosinemia type I: a US and Canadian consensus group review and recommendations. *Genet Med*. 2017;19(12):. doi:10.1038/gim.2017.101.
5. Sniderman King L, Trahms C, Scott CR. Tyrosinemia Type I. 2006 Jul 24 [Updated 2017 May 25]. In: Adam MP, Everman DB, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1515/


Effective date: 06/30/2025
Revised date: 10/11/2024