# Clinical Policy: Nitisinone (Nityr, Orfadin)

Reference Number: ERX.SPA.264
Effective Date: 12.01.18
Last Review Date: 11.21
Line of Business: Commercial, Medicaid

Revision Log

**See Important Reminder at the end of this policy for important regulatory and legal information.**

**Description**
Nitisinone (Nityr®, Orfadin®) is a hydroxy-phenylpyruvate dioxygenase inhibitor.

**FDA Approved Indication(s)**
Nityr and Orfadin are 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.

**Policy/Criteria**
*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

*Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.*

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Nityr and Orfadin are **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Hereditary Tyrosinemia Type 1** (must meet all)**:**

1. Diagnosis of HT-1 as confirmed by one of the following (a or b):
   a. Genetic testing confirms a mutation of the *FAH* gene;
   b. Biochemical testing confirms elevated levels of succinylacetone in blood or urine;*
   **The lower limit of normal for succinylacetone is laboratory- and/or treatment center-specific; refer to laboratory- or clinic-specific reference ranges to determine elevated levels.*
2. Prescribed by or in consultation with an endocrinologist or a metabolic or genetic disease specialist;
3. Request is for use as an adjunct to dietary restriction of tyrosine and phenylalanine;
4. Dose does not exceed 2 mg/kg per day.

**Approval duration: 6 months**

**B. Other diagnoses/indications**

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

**II. Continued Therapy**

**A. Hereditary Tyrosinemia Type 1** (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Request is for use as an adjunct to dietary restriction of tyrosine and phenylalanine;
4. If request is for a dose increase, new dose does not exceed 2 mg/kg per day.

**Approval duration: 12 months**

**B. Other diagnoses/indications** (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.

**Approval duration: Duration of request or 6 months (whichever is less)**; or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

**III. Diagnoses/Indications for which coverage is NOT authorized:**

**A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*
FDA: Food and Drug Administration
HT-1: hereditary tyrosinemia type 1

*Appendix B: Therapeutic Alternatives*
Not applicable

*Appendix C: Contraindications/ Boxed Warnings*
None reported

**V. Dosage and Administration**

| Drug Name | Dosing Regimen | Maximum Dose |
|---|---|---|
| Nitisinone (Nityr) | 0.5 mg/kg PO BID | 2 mg/kg |
| Nitisinone (Orfadin) | 0.5 mg/kg PO BID | 2 mg/kg |

**VI. Product Availability**

| Drug Name | Product Availability |
|---|---|
| Nitisinone (Nityr) | Tablets: 2 mg, 5 mg, 10 mg |
| Nitisinone (Orfadin) | Capsules: 2 mg, 5 mg, 10 mg, 20 mg<br>Oral suspension: 4 mg/mL |

**VII. References**

1. Orfadin Prescribing Information. Waltham, MA: Sobi, Inc.; May 2019. Available at: http://www.orfadin.com/. Accessed August 16, 2021.
2. Nityr Prescribing Information. Centro Insema, Manno Switzerland: Rivopharm; June 2021. Available at: www.nityr.us. Accessed August 16, 2021.
3. Chinsky JM, Singh R, Ficicioglu C, et al. Diagnosis and treatment of tyrosinemia type I: a US and Canadian consensus group review and recommendations. Genetics in Medicine. Dec 2017;19(12).

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| Policy created | 08.28.18 | 11.18 |
| 4Q 2019 annual review: no significant changes; references reviewed and updated. | 08.15.19 | 11.19 |
| 4Q 2020 annual review: added requirement for adjunctive dietary restriction of tyrosine and phenylalanine, in line with the FDA-approved indication; references reviewed and updated. | 08.03.20 | 11.20 |
| 4Q 2021 annual review: added requirement for diagnosis confirmation by either genetic or biochemical testing; references reviewed and updated. | 08.17.21 | 11.21 |

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.