Clinical Policy: Nitisinone (Nityr, Orfadin)

Reference Number: PA.CP.PHAR.132
Effective Date: 10/20 18
Last Review Date: 10/2024

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.

It is the policy of PA Health & Wellness® that nitisinone, Nityr, 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. Member is not using two different nitisinone products concurrently;
5. For requests for Nityr and Orfadin capsules, member must use generic nitisinone, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed 2 mg/kg per day.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

II. Continued Therapy

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

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA. PHARM.01) applies;
2. Member is responding positively to therapy;

3. Request is for use as an adjunct to dietary restriction of tyrosine and phenylalanine;
4. Member is not using two different nitisinone products concurrently;
5. For requests for Nityr and Orfadin capsules, member must use generic nitisinone, unless contraindicated or clinically significant adverse effects are experienced;
6. 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 PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA. PHARM.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

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 – PA.CP.PMN.53 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
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
nitisinone (Orfadin, Nityr)	0.5 mg/kg PO BID	2 mg/kg

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

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	Availability
Nitisinone (Nityr)	Tablets: 2 mg, 5 mg, 10 mg
Nitisinone (Orfadin)	Capsules: 2 mg, 5 mg, 10 mg, 20 mg Oral suspension: 4 mg/mL

VII. References

1. Orfadin Prescribing Information. Waltham, MA: Sobi, Inc.; November 2021. Available at: http://www.orfadin.com/. Accessed July 15, 2024.
2. Nityr Prescribing Information. Centro Insema, Manno Switzerland: Rivopharm; January 2024. Available at: www.nityr.us. Accessed August 8, 2024.
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).
4. Van Ginkel WG, Rodenburg IL, Harding CO, et al. Long-term outcomes and practical considerations in the pharmacological management of tyrosinemia type 1. Pediatr Drugs. 2019;21:413–26. https://doi.org/10.1007/s40272-019-00364-4.

Reviews, Revisions, and Approvals	Date
Policy created	10/2018
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/2019
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.	10/2020
4Q 2021 annual review: added requirement for diagnosis confirmation by either genetic or biochemical testing; references reviewed and updated.	10/2021
4Q 2022 annual review: no significant changes; references reviewed and updated.	10/2022
4Q 2023 annual review: no significant changes; added exclusion against concomitant use of multiple different nitisinone products; added generic redirection for 2 mg, 5 mg, 10 mg strengths (generic nitisinone 20 mg strength is either NF or same tier level as brand Orfadin 20 mg); references reviewed and updated.	10/2023
4Q 2024 annual review: Per SDC, for Orfadin revised generic redirection to apply generally to the capsule formulation (to now include the 20 mg strength); references reviewed and updated.	10/2024