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| **Clinical Policy Title:** | nitisinone |
| **Policy Number:** | RxA.238 |
| **Drug(s) Applied:** | Nityr®, Orfadin® |
| **Original Policy Date:** | 02/07/2020 |
| **Last Review Date:** | 06/10/2021 |
| **Line of Business Policy Applies to:** | All lines of business |

## Background

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

## Dosing Information

| Drug Name | Indication | Dosing Regimen | Maximum Dose |
|---|---|---|---|
| nitisinone (Nityr®) | HT-1 | 0.5 mg/kg PO BID<br><br>The total dose may be given once daily (e.g., 1 to 2 mg/kg once daily) to patients with undetectable serum and urine succinylacetone concentrations after a minimum of 4 weeks on a stable nitisinone dosage. | 2 mg/kg |
| nitisinone (Orfadin®) | | | |

## Dosage Forms

- nitisinone (Nityr®): 2 mg, 5 mg, 10 mg tablets
- nitisinone (Orfadin®):
  - Capsules: 2 mg, 5 mg, 10 mg, 20mg
  - Oral suspension: 4 mg/mL

## Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

**I. Initial Approval Criteria**

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

1. Member has a clinical diagnosis of HT-1 confirmed by biochemical testing (e.g., detection of succinylacetone in the urine or blood), enzyme assay, or genetic testing;
2. Prescribed by or in consultation with an endocrinologist or a metabolic or genetic disease specialist;
3. Dose does not exceed 2 mg/kg per day.

**Approval Duration**
**Commercial:** 12 months
**Medicaid:** 12 months

**II. Continued Therapy Approval**

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

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 2 mg/kg per day.

**Approval Duration**
**Commercial:** 12 months
**Medicaid:** 12 months

**III. Appendices**

**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**

- Contraindication(s):
  - None reported

- Boxed Warning(s):
  - None reported

**APPENDIX D: General Information**

- Elevated plasma tyrosine Levels, ocular symptoms, developmental delay, and hyperkeratotic plaques: Inadequate restriction of tyrosine and phenylalanine intake can lead to elevations in plasma tyrosine, which at levels above 500 micromol/L can result in symptoms, intellectual disability, and developmental delay or painful hyperkeratotic plaques on the soles and palms; do not adjust nitisinone dosage in order to lower the plasma tyrosine concentration. Obtain slit-lamp examination prior to treatment, regularly during treatment; re-examine patients if symptoms develop or tyrosine levels are 500 micromol/L or greater. Assess plasma tyrosine levels in patients with an abrupt change in neurologic status.
- Leukopenia and severe thrombocytopenia: Monitor platelet and white blood cell counts.
- Risk of adverse reactions due to glycerol content of Orfadin® oral suspension: Doses of 20 mL of Orfadin® oral suspension may cause headache, upset stomach, and diarrhea due to the glycerol content. Consider switching patients to Orfadin® capsules.

**References**

1. Orfadin Prescribing Information. Waltham, MA: Sobi, Inc.; May 2019. Available at: http://www.orfadin.com/. Accessed February 24, 2021.
2. Nityr Prescribing Information. Centro Insema, Manno Switzerland: Rivopharm; October 2020. Available at: www.nityr.us. Accessed February 24, 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. 2017. Dec; 19(12). Accessed February 24, 2021.

| Review/Revision History | Review/Revision Date | P&T Approval Date |
|---|---|---|
| Policy established. | 01/2020 | 02/07/2020 |
| Policy was reviewed:<br>1. Clinical Policy Title was updated.<br>2. Drug(s) Applied was updated.<br>3. Line of Business Policy Applies to was update to all lines of business.<br>4. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..."<br>5. Dosing Information was updated to include “The total dose may be given once daily (e.g., 1 to 2 mg/kg once daily) to patients with undetectable serum and urine succinylacetone concentrations after a minimum of 4 weeks on a stable nitisinone dosage.”<br>6. References were updated. | 07/30/2020 | 09/14/2020 |
| Policy was reviewed:<br>1. Updated initial criteria for approval and duration of approval.<br>2. Continued Therapy criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance..."<br>3. Appendix D was added.<br>4. References were reviewed and updated. | 02/24/2021 | 06/10/2021 |