UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2026 P 2412-2
Program	Prior Authorization/Medical Necessity
Medication	Nitisinone Products: Harliku™ (nitisinone) tablets, nitisinone (generic Orfadin) capsules, Nityr® (nitisinone)* tablets, Orfadin® (nitisinone) capsules and oral suspension
P&T Approval Date	2/2026, 4/2026
Effective Date	5/1/2026

1. Background:

Nitisinone is a hydroxyphenyl-pyruvate dioxygenase inhibitor. Nitisinone (generic Orfadin®), Nityr® (nitisinone), and Orfadin® (nitisinone) 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.[2-3] Harliku™ (nitisinone) is indicated for the reduction of urine homogentisic acid (HGA) in adult patients with alkaptonuria (AKU).[1] Treatment of AKU with nitisinone in combination with a regular diet has demonstrated an improvement in HGA levels. The pivotal studies for Orfadin were used as the basis for the FDA approval of Harliku.[5-6] There were no additional clinical trials evaluating the efficacy and safety of Harliku. Orfadin also holds European Medicines Agency (EMA)-approval for AKU.[4]

2. Coverage Criteria[a]:

A. Alkaptonuria

1. **Initial Authorization**

a. **Harliku** or **Orfadin** will be approved based on **all** of the following criteria:

(1) Diagnosis of alkaptonuria

-AND-

(2) Patient is ≥ 18 years old

-AND-

(3) Submission of medical records (e.g., chart notes, laboratory values) confirming **one** of the following:

(a) Urinary homogentisic acid (HGA) excretion > 0.4g/24 hours
(b) Biallelic mutation in homogentisate 1,2-dioxygenase (*HGD*) gene confirmed by genetic testing

-AND-

(4) The requested drug will not be used in combination with another nitisinone product

-AND-

(5) Prescribed by or in consultation with a metabolic disease specialist or rheumatologist

Authorization will be issued for 12 months.

Educational Statement: Nitisinone is a hydroxyphenyl-pyruvate dioxygenase inhibitor. Nitisinone (generic Orfadin), Nityr (nitisinone), and Orfadin (nitisinone) 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.[2-3] Harliku (nitisinone) is indicated for the reduction of urine homogentisic acid (HGA) in adult patients with alkaptonuria (AKU).[1] Treatment of AKU with nitisinone in combination with a regular diet has demonstrated an improvement in HGA levels. The pivotal studies for Orfadin were used as the basis for the FDA approval of Harliku.[5-6] There were no additional clinical trials evaluating the efficacy and safety of Harliku. Orfadin also holds European Medicines Agency (EMA)-approval for AKU.[4]

2. **Reauthorization**

a. **Harliku** or **Orfadin** will be approved based on the following criteria:

(1) Documentation of positive clinical response [e.g., reduced urinary homogentisic acid (HGA) levels, improvement in joint symptoms] while on therapy

-AND-

(2) The requested drug will not be used in combination with another nitisinone product

-AND-

(3) Prescribed by or in consultation with a metabolic disease specialist or rheumatologist

Authorization will be issued for 12 months.

Educational Statement: Nitisinone is a hydroxyphenyl-pyruvate dioxygenase inhibitor. Nitisinone (generic Orfadin), Nityr (nitisinone), and Orfadin (nitisinone) 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.[2-3] Harliku (nitisinone) is indicated for the reduction of urine homogentisic acid (HGA) in adult patients with alkaptonuria (AKU).[1] Treatment of AKU with nitisinone in combination with a regular diet has demonstrated an improvement in HGA levels. The pivotal studies for Orfadin were used as the basis for the FDA approval of Harliku.[5-6] There were no additional clinical trials evaluating the efficacy and safety of Harliku. Orfadin also holds European Medicines Agency (EMA)-approval for AKU.[4]

B. Hereditary Tyrosinemia Type 1

1. **Initial Authorization**

   a. **Nityr*** or **Orfadin** will be approved based on the following criteria:

      (1) Diagnosis of hereditary tyrosinemia type 1

      -AND-

      (2) Submission of medical records (e.g., chart notes, laboratory values) confirming **one** of the following:

         (a) Elevated levels of succinylacetone (SA) in serum or urine
         (b) Biallelic mutation in fumarylacetoacetate hydrolase (*FAH*) gene confirmed by genetic testing

      -AND-

      (3) Prescribed in conjunction with a tyrosine- and phenylalanine- restricted diet

      -AND-

      (4) The requested drug will not be used in combination with another nitisinone product

      -AND-

      (5) Prescribed by or in consultation with a metabolic disease specialist

   Authorization will be issued for 12 months.

2. **Reauthorization**

   a. **Nityr*** or **Orfadin** will be approved based on the following criteria:

      (1) Documentation of positive clinical response (e.g., decrease in urinary/plasma succinylacetone and alpha-1-microglobulin levels) while on therapy

      -AND-

      (2) The requested drug will not be used in combination with another nitisinone product

      -AND-

      (3) Prescribed by or in consultation with a metabolic disease specialist

   Authorization will be issued for 12 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

*Nityr is typically excluded from coverage. Tried/failed criteria may be in place. Please refer to plan specifics to determine exclusion status.

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may be in place.

4. References:

1. Harliku [package insert]. Cambridge, United Kingdom: Cycle Pharmaceuticals Ltd.; June 2025.
2. Nityr [package insert]. Cambridge, United Kingdom: Cycle Pharmaceuticals Ltd.; May 2024.
3. Orfadin [prescribing information]. Waltham, MA: Sobi, Inc.; November 2021.
4. European Medicines Agency (EMA). Orfadin Product Information. Last updated April 7, 2025. Orfadin | European Medicines Agency (EMA). Accessed January 22, 2026.
5. Davison AS, Norman BP. Alkaptonuria - Past, present and future. Adv Clin Chem. 2023;114:47-81.
6. Ranganath LR, Milan AM, Hughes AT, et al. Suitability of nitisinone in alkaptonuria 1 (SONIA 1): an international, multicentre, randomised, open-label, no-treatment controlled, parallel-group, dose-response study to investigate the effect of once daily nitisinone on 24-h urinary homogentisic acid excretion in patients with alkaptonuria after 4 weeks of treatment. *Ann Rheum Dis*. 2016;75(2):362-367.
7. Ranganath LR, Psarelli EE, Arnoux JB, et al. Efficacy and safety of once-daily nitisinone for patients with alkaptonuria (SONIA 2): an international, multicentre, open-label, randomised controlled trial. *Lancet Diabetes Endocrinol*. 2020;8(9):762-772.
8. Lindstedt S, Holme E, Lock EA, Hjalmarson O, Strandvik B. Treatment of hereditary tyrosinaemia type I by inhibition of 4-hydroxyphenylpyruvate dioxygenase. *Lancet*. 1992;340(8823):813-817.
9. Guffon N, Bröijersén A, Palmgren I, Rudebeck M, Olsson B. Open-Label Single-Sequence Crossover Study Evaluating Pharmacokinetics, Efficacy, and Safety of Once-Daily Dosing of Nitisinone in Patients with Hereditary Tyrosinemia Type 1. *JIMD Rep*. 2018;38:81-88.

Program	Prior Authorization/Medical Necessity – Nitisinone Products: Harliku tablets, nitisinone capsules, Nityr tablets, Orfadin capsules and oral suspension
Change Control	
2/2026	New program
4/2026	Added educational note to AKU reauthorization section.