

## Clinical Policy: Nitisinone (Nityr, Orfadin)

Reference Number: CP.PHAR.132

Effective Date: 08.28.18

Last Review Date: 11.22

Line of Business: Commercial, HIM, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### Description

Nitisinone (Nityr<sup>®</sup>, Orfadin<sup>®</sup>) 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 health plans affiliated with Centene Corporation<sup>®</sup> 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 (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
  - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
  - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business:

- CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

## II. Continued Therapy

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

1. Member meets one of the following (a or b):
  - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
  - b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);
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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
  - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
  - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

## 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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

## CLINICAL POLICY

### Nitisinone

#### 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	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 August 27, 2022.
2. Nityr Prescribing Information. Centro Insema, Manno Switzerland: Rivopharm; June 2021. Available at: [www.nityr.us](http://www.nityr.us). Accessed August 27, 2022.
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; removed references to HIM non-formulary policy for Nityr; references reviewed and updated.	08.03.20	11.20
4Q 2021 annual review: added requirement for diagnosis confirmation by either genetic or biochemical testing; revised HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	08.17.21	11.21

**CLINICAL POLICY**  
Nitisinone

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2022 annual review: no significant changes; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	08.27.22	11.22

**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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

**CLINICAL POLICY****Nitisinone**

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

**Note:**

**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

©2018 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene<sup>®</sup> and Centene Corporation<sup>®</sup> are registered trademarks exclusively owned by Centene Corporation.