MEDICAL MUTUAL®

Drug Policy

Policy:	Orfadin (nitisinone) and Nityr (nitisinone)	**Annual Review Date:** **10/17/2024** **Last Revised Date:** **10/17/2024**

OVERVIEW

Orfadin and Nityr are both indicated for the treatment of hereditary tyrosinemia type 1 (HT-1) in combination with dietary restriction of tyrosine and phenylalanine. HT-1 is the most severe disorder of tyrosine metabolism. Fumarylacetoacetate (FAA) causes damage as it accumulates in the liver and kidney. FAA also causes oxidative damage to cells. To diagnose a patient with HT-1 the metabolites of FAA, succinylacetoacetate (SAA) and succinylacetone (SA), can be measured. Nitisinone is the primary treatment for HT-1 as it limits formation of the toxic compounds such as FAA and its metabolite SA.

POLICY STATEMENT

This policy involves the use of Orfadin (brand and generic) and Nityr. Prior authorization is recommended for pharmacy benefit coverage of Orfadin (brand and generic) and Nityr. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Orfadin and Nityr as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Orfadin and Nityr be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Orfadin, generic nitisinone, or Nityr is recommended in those who meet the following criteria:

1. Initial, Hereditary Tyrosinemia Type 1

Patient must meet the following criteria (A, B, C, D, E and F)

A) Nitisinone is prescribed by or in consultation with a physician who specializes in treatment of inherited metabolic disorder/genetic diseases; AND
B) Laboratory baseline succinylacetone (SA) level are provided and elevated prior to treatment*; AND
C) The patient is following a diet consisting of tyrosine and phenylalanine restriction; AND

D) Baseline hepatic imaging and baseline labs have been obtained and reviewed such as: liver evaluation (PT, PTT , ALT/AST), renal function (BUN, creatine, etc), plasma amino acids, and a complete blood count (CBC); AND
E) Baseline ophthalmologic examination including slit-lamp examination has been completed prior to treatment; AND
F) If the request is for brand Orfadin or Nityr, the patient has a documented intolerance to or has failed at least a three-month trial of generic nitisinone.

2. Continuation, Hereditary Tyrosinemia Type 1
Patient must meet the following criteria (A, B, C, D and E)

A) The provider has been monitoring for plasma amino acids, blood or urinary SA, liver function, serum AFP increases, and CBC; AND
B) The provider is regularly monitoring for ophthalmologic changes including eye pain, or signs of inflammation such as redness, swelling, or burning of the eyes and conducted slit-lamp reexamination if tyrosine levels are > 500 micromol/L.
C) The provider states the patient is having a beneficial response to therapy based on assessment*; AND
D) The patient continues to follow a diet consisting of tyrosine and phenylalanine restriction; AND
E) If the request is for brand Orfadin, the patient has a documented intolerance to or has failed at least a three-month trial of generic nitisinone.

***Documentation Required:** When documentation is required, the prescriber must provide written documentation supporting the trials of these other agents, noted in the criteria as *. Documentation should include chart notes, prescription claims records, and/or prescription receipts.

Initial Approval/ Extended Approval.
A) *Initial and Extended Approval:* 6 months (180 days)

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Orfadin and Nitry has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Orfadin [package insert]. Sobi, Inc. Waltham, MA. Updated May 22, 2019 .
2. Nityr [packaged insert]. Cycle Pharmaceuticals Ltd. Cambridge, UK. September 9, 2020 .
3. Grompe M. Disorders of tyrosine metabolism. UptoDate. August 08, 2018.
4. Chinsky, JM et al. Diagnosis and treatment of tyrosinemia type I: a US and Canadian consensus group review and recommendations. Genet Med. 2017 Dec; 19(12). doi: [10.1038/gim.2017.101]
5. Nitisinone. In: DRUGDEX [online database]. Truven Health Analytics; Greenwood Village, CO. Last updated 23 September 2019. Accessed on 13 October 2019.