Pharmacy Policy Bulletin

Title: Hereditary Tyrosinemia Agents

Policy #: Rx.01.250

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

The intent of this policy is to communicate the medical necessity criteria for **Nitisinone (Nityr®, Orfadin®)** as provided under the member's prescription drug benefit.

Description:

Tyrosine is an aromatic amino acid important in the synthesis of thyroid hormones, catecholamines, and melanin. Impaired catabolism of tyrosine is a feature of several acquired and genetic disorders that may result in elevated plasma tyrosine concentrations. Tyrosinemia is a genetic disorder characterized by disruptions in the break down of the amino acid tyrosine, a building block of most proteins. If untreated, tyrosine and its byproducts build up in tissues and organs. Hereditary tyrosinemia type 1 (HT1; MIM# 276700), also known as hepatorenal tyrosinemia, is the most severe disorder of tyrosine metabolism.

Nitisinone (Nityr®, Orfadin®) is a competitive inhibitor of 4-hydroxyphenyl-pyruvate dioxygenase, an enzyme upstream of fumarylacetoacetate hydrolase (FAH) in the tyrosine catabolic pathway. By inhibiting the normal catabolism of tyrosine in patients with HT-1, nitisinone prevents the accumulation of the catabolic intermediates maleylacetoacetate and fumarylacetoacetate. In patients with HT-1, these catabolic intermediates are converted to the toxic metabolites succinylacetone and succinylacetoacetate, which are responsible for the observed liver and kidney toxicity. Succinylacetone can also inhibit the porphyrin synthesis pathway leading to the accumulation of 5-aminolevulinate, a neurotoxin responsible for the porphyric crises characteristic of HT-1.

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:

INITIAL CRITERIA Nitisinone (Nityr®, Orfadin®) is approved when all of the following are met:

1. Diagnosis of hereditary tyrosinemia type 1; and
2. Will be used in combination with dietary restriction of tyrosine and phenylalanine

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Nitisinone (Nityr®, Orfadin®) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Black Box Warning as shown in the drug Prescribing Information:

N/A

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

Nityr® (nitisinone) [package insert] Cambridge, UK: Cycle Pharmaceuticals Ltd. October 2021. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209449s000lbl.pdf. Accessed October 04, 2022.

Orfadin® (nitsinone) [package insert] Stockholm, Sweden: Swedish Orphan Biovitrum. November 2021. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/206356s000lbl.pdf. Accessed October 04, 2022.

Tyrosinemia: MedlinePlus Genetics. Medlineplus.gov. Available from: https://medlineplus.gov/genetics/condition/tyrosinemia/. Accessed October 04, 2022.

Grompe M. Disorders of tyrosine metabolism. UpToDate. November 2020. Available at: https://www.uptodate.com/contents/disorders-of-tyrosine metabolism?search=orfadin&source=search_result&selectedTitle=2~3&usage_type=default&display_rank=1. Accessed October 04, 2022.

Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name	Generic Name
Nityr®, Orfadin®	Nitisinone

Cross References:

Rx.01.33 Off Label Use

Policy Version Number:	2.00
P&T Approval Date:	September 15, 2022
Policy Effective Date:	January 01, 2023
Next Required Review Date:	September 15, 2023