nitisinone (Nityr™; Orfadin®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO140

Description

Nitisinone (Nityr; Orfadin) competitively inhibits 4-hydroxyphenyl-pyruvate dioxygenase (4HPPD), an enzyme present early in the tyrosine degradation pathway, thereby preventing the accumulation of toxic metabolites.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity Limits

Product Name	Dosage Form	Indication	Quantity Limit
nitisinone (nitisinone)	2 mg capsule	Hereditary tyrosinemia type 1	2 mg/kg/day
	5 mg capsule		
	10 mg capsule		
nitisinone (Nityr)	2 mg tablet		
	5 mg tablet		
	10 mg tablet		
nitisinone (Orfadin)	2 mg capsule		
	5 mg capsule		
	10 mg capsule		
	20 mg capsule		
	4 mg/mL suspension		

Initial Evaluation

I. Nitisinone (Nityr; Orfadin) may be considered medically necessary when the following criteria below are met:
   A. Medication is prescribed by, or in consultation with, a provider who specializes in the treatment of genetic or metabolic disorders; **AND**
   B. A diagnosis of **hereditary tyrosinemia type 1 (HT-1)** when the following are met:
      1. Elevated succinylacetone (SA); **AND**
      2. Documentation of baseline plasma tyrosine level; **AND**
      3. Treatment will be used in conjunction with a diet restricted in tyrosine and phenylalanine

II. Nitisinone (Nityr; Orfadin) is considered <u>investigational</u> when used for all other conditions, including but not limited to:
   A. Alkaptonuria

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
II. Member is not established on therapy through the use of samples, manufacturer coupons, or otherwise. Initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member has exhibited improvement or stability of disease symptoms (e.g. biochemical and/or clinical response).

Supporting Evidence

I. In patients with HT-1, tyrosine metabolism is interrupted due to a lack of the enzyme (fumarylacetoacetate hydrolase) needed in the last step of tyrosine degradation. Toxic metabolites of tyrosine, succinylacetoacetate (SAA) and succinylacetone (SA), accumulate and cause liver and kidney toxicity. Nitisinone (Nityr; Orfadin) competitively inhibits 4-hydroxyphenyl-pyruvate dioxygenase (4HPPD), an enzyme present early in the tyrosine degradation pathway, thereby preventing the build-up of the toxic metabolites SAA and SA.
II. Nitisinone (Nityr; Orfadin) must be used in conjunction with a diet restricted in tyrosine and phenylalanine to prevent further increased tyrosine levels. Dose is titrated as needed based on biochemical and/or clinical response. If the biochemical response is satisfactory, the dosage should be adjusted only according to body weight gain. Dose should not be adjusted according to tyrosine concentration.
III. Nitisinone (Nityr; Orfadin) should be started as early as possible (i.e. immediately after diagnosis of HT1 by blood or urine measurement of SA).
IV. If the biochemical parameters (except plasma SA) have not normalized within one month of starting therapy, the dose should be increased to 1.5 mg/kg/day. The dose of nitisinone should be adjusted to completely suppress excretion of SA; however, it may take as long as three months for complete suppression of SA to occur. A dose of 2 mg/kg/day may be needed, especially in infants; although, this dose should be considered maximal. Monitoring of the nitisinone blood levels is recommended for dose adjustment and also to check adherence.

Investigational or Not Medically Necessary Uses

I. Nitisinone (Nityr; Orfadin) has not been sufficiently evaluated in the following settings. Limited evidence is available; however, safety and efficacy have not been established for:
    A. Alkaptonuria

References

1. Orfadin [Prescribing Information]. Waltham, MA: Sobi, Inc; May 2019.
2. Nityr [Prescribing Information]. Cambridge, United Kingdom: Cycle Pharmaceuticals Ltd.; November 2018.
3. UpToDate, Inc. Disorders of tyrosine metabolism. UpToDate [database online]. Waltham, MA. Last updated August 08, 2019 Available at: http://www.uptodate.com/home/index.html.

Policy Implementation/Update:

Date Created	December 2019
Date Effective	December 2019
Last Updated	December 2019
Last Reviewed	12/2019

Action and Summary of Changes	Date