Protocol for Nitisinone Products

Approved January 2022

Background:
Tyrosinemia type 1 is a rare autosomal recessive genetic metabolic disorder characterized by lack of the enzyme fumarylacetoacetate hydrolase (FAH), which is needed for the final break down of the amino acid tyrosine. Failure to properly break down tyrosine leads to abnormal accumulation of tyrosine and its metabolites in the liver, potentially resulting in severe liver disease. Tyrosine may also accumulate in the kidneys and central nervous system.

Nityr and Orfadin are hydroxyphenyl-pyruvate dioxygenase inhibitors 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.

Criteria for approval:

Patient meets ALL the following:

1. Patient has a diagnosis of Hereditary Tyrosinemia (HT-1) confirmed by one of the following:
   a. Genetic testing confirmed a mutation of the FAH gene; OR
   b. The patient has elevated serum levels of alpha-fetoprotein (AFP) and succinylacetone; OR
   c. The patient was diagnosed with HT-1 by the presence of succinylacetone in the urine or plasma
2. Medication is prescribed in conjunction with a tyrosine and phenylalanine restriction diet
3. Patient will not take Nityr and Orfadin concurrently
4. Medication is prescribed by or in consultation with a provider who has expertise in this disease
5. Medication is prescribed in accordance with Food and Drug Administration (FDA) established indication and dosing regimens or in accordance with medically appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs (Lexicomp), national guidelines, or other peer reviewed evidence
6. Weight will be monitored for drugs that have weight-based dosing
7. Patient's platelet and white blood cell counts will be monitored during therapy

Initial Approval Duration: 3 months

Continuation of therapy:

1. Documentation that patient has disease stabilization or improvement from baseline
2. Patient is tolerating treatment
3. Medication is prescribed in accordance with Food and Drug Administration (FDA) established indication and dosing regimens or in accordance with medically appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs (Lexicomp), national guidelines, or other peer reviewed evidence

Renewal Approval Duration: 6 months

References:

1. Nityr (nitisinone) [package insert]. Cycle Pharmaceutical Ltd., Cambridge, UK; November 2018.
2. Orfadin (nitisinone) [package insert]. Apoteket Produktion & Laboratorier AB, Sweden; May 2019.
3. Clinical Pharmacology® Gold Standard Series [Internet database]. Tampa FL. Elsevier 2019. Updated periodically
4. National Organization for Rare Disorders. Tyrosinemia type I. NORD Compendium of Rare Diseases and Disorders. [New Rochelle, NY] https://rarediseases.org/rare-diseases/tyrosinemia-type-1/ Accessed November 29, 2021
5. Chinsky JM et al. Diagnosis and treatment of tyrosinemia type I: a US and Canadian consensus group review and recommendations. Genetics in Medicine volume 19, page1380 (2017)