PRIOR AUTHORIZATION POLICY

POLICY: Metabolic Disorders – Xuriden Prior Authorization Policy
- Xuriden® (uridine triacetate oral granules – Wellstat Therapeutics)

REVIEW DATE: 08/16/2023

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Xuriden, a pyrimidine analog for uridine replacement, is indicated for the treatment of **hereditary orotic aciduria** in adults and pediatric patients.[1]

Disease Overview

Hereditary orotic aciduria, also known as orotic aciduria type 1, is an extremely rare, autosomal recessive genetic disorder of pyrimidine metabolism.[1-3] It is estimated to affect less than 1:1,000,000 live births. Only about 20 cases have been reported in the medical literature. In hereditary orotic aciduria, a mutation in the *UMPS* gene leads to defective uridine 5'monophosphate synthase. Deficiency in this enzyme prevents the last two steps in pyrimidine biosynthesis, leading to inadequate levels of uridine monophosphate and excess levels of orotic acid (a uridine precursor). Because the condition is so rare, hereditary orotic aciduria is not fully understood. Affected infants may develop megaloblastic anemia, developmental delays, or failure to thrive. Orotic acid crystals in the urine can lead to urinary obstruction. Xuriden replaces uridine in the circulation, and as a result of feedback inhibition, overproduction of orotic acid is reduced. Diagnosis is made by detailed patient and family history as well as thorough clinical evaluation and examination of urine. Most individuals have their diagnosis confirmed through molecular genetic testing; however, this is only available at specialized laboratories.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Xuriden. Because of the specialized skills required for evaluation and diagnosis of patients treated with Xuriden, approval requires the requested medication to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Xuriden® (uridine triacetate oral granules – Wellstat Therapeutics) is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indication

1. **Hereditary Orotic Aciduria (Orotic Aciduria Type 1).** Approve for 1 year if the patient meets the following (A and B):
   - **A)** Patient has hereditary orotic aciduria confirmed by at least one of the following (i or ii):
     - **i.** Molecular genetic testing confirming biallelic pathogenic mutations in the *UMPS* gene; OR
     - **ii.** Clinical diagnosis supported by all of the following (a, b, and c):
       - **a)** At least one clinical manifestation consistent with orotic aciduria type 1; AND
         Note: Examples of clinical manifestations include megaloblastic anemia, immunodeficiency, developmental delays, and failure to thrive.
       - **b)** First-degree family relative (i.e., parent or sibling) with hereditary orotic aciduria; AND
       - **c)** Urinary orotic acid level above the normal reference range for the reporting laboratory; AND
   - **B)** Xuriden is prescribed by, or in consultation with, a metabolic specialist, geneticist, or physician specializing in the condition being treated.

CONDITIONS NOT COVERED

Xuriden® (uridine triacetate oral granules – Wellstat Therapeutics) is(are) considered experimental, investigational, or unproven for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

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

REFERENCES

1. Xuriden® oral granules [prescribing information]. Rockville, MD: Wellstat Therapeutics; December 2019.
2. Hereditary orotic aciduria. National Organization for Rare Disorders. Updated 2018. Available at: https://rarediseases.org/rare-diseases/hereditary-orotic-aciduria/. Accessed on August 1, 2023.
3. Orotic aciduria type 1. Genetic and Rare Diseases Information Center. Updated November 8, 2021. Available at: https://rarediseases.info.nih.gov/diseases/5429/hereditary-orotic-aciduria. Accessed on August 1, 2023.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Hereditary Orotic Aciduria (Orotic Aciduria Type 1):** In the criterion regarding molecular genetic testing, it was clarified that "biallelic mutations" are needed to confirm the diagnosis; previously, this was listed as "mutation". In the criterion regarding a clinical diagnosis, it was added that a patient must have at least one clinical manifestation consistent with orotic aciduria type 1. A Note was added with examples of clinical manifestations.	08/03/2022
Annual Revision	No criteria changes.	08/16/2023