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## Uridine Triacetate

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### Related Coverage Resources

#### 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.

### Overview

This policy supports medical necessity review for uridine triacetate (**Xuriden®**) oral granules.

### Medical Necessity Criteria

Uridine triacetate (Xuriden) oral granules are considered medically necessary when the following are met:

**Hereditary Orotic Aciduria (Orotic Aciduria Type 1).** Individual meets **ALL** of the following criteria:

- A. Diagnosis of Hereditary Orotic Aciduria confirmed by documentation of **ONE** of the following:
  - i. Molecular genetic testing confirming biallelic pathogenic variants in the *UMPS* gene
  - ii. Clinical diagnosis supported by **ALL** of the following:
    - a. Clinical manifestations consistent with orotic aciduria (for example, megaloblastic anemia, leukopenia, neutropenia, failure to thrive, intellectual disability)

- b. First-degree family relative (i.e., parent or sibling) with hereditary orotic aciduria
  - c. Urinary orotic acid level above the normal reference range for the reporting laboratory
- B. Medication is prescribed by, or in consultation with, a metabolic specialist, geneticist, or physician specializing in the condition being treated

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

## Reauthorization Criteria

Continuation of Uridine triacetate (Xuriden) oral granules are considered medically necessary for Hereditary Orotic Aciduria when the above medical necessity criteria are met AND there is documentation of beneficial response (for example, improved hematologic parameters, reduced urinary orotic acid and orotidine levels, improved growth).

## Authorization Duration

Initial approval duration: up to 12 months

Reauthorization approval duration: up to 12 months

## Conditions Not Covered

Any other use is considered experimental, investigational, or unproven (criteria will be updated as new published data are available).

## Background

### OVERVIEW

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

### Disease Overview

Hereditary orotic aciduria, also known as orotic aciduria type 1, is an extremely rare, autosomal recessive genetic disorder of pyrimidine metabolism.<sup>1-3</sup> 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, variants 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.

## References

1. Xuriden® oral granules [prescribing information]. Rockville, MD: Wellstat Therapeutics; August 2023.

2. Hereditary orotic aciduria. National Organization for Rare Disorders. Updated 2018. Available at: <https://rarediseases.org/rare-diseases/hereditary-orotic-aciduria/>. Accessed on August 6, 2024.
3. Orotic aciduria type 1. Genetic and Rare Diseases Information Center. Updated July 2024. Available at: <https://rarediseases.info.nih.gov/diseases/5429/hereditary-orotic-aciduria>. Accessed on August 6, 2024.

## Revision Details

Type of Revision	Summary of Changes	Date
Selected Revision	<b>Hereditary Orotic Aciduria (Orotic Aciduria Type 1).</b> <b>Updated from</b> “Hereditary Orotic Aciduria” <b>to</b> “Hereditary Orotic Aciduria (Orotic Aciduria Type 1)” <b>Added</b> “First-degree family relative (i.e., parent or sibling) with hereditary orotic aciduria”	12/15/2024

The policy effective date is in force until updated or retired.

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