



PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 5/19/16
LAST REVIEW DATE: 5/17/18
LAST CRITERIA REVISION DATE: 5/17/18
ARCHIVE DATE:

XURIDEN™ (uridine triacetate) oral granules

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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XURIDEN™ (uridine triacetate) oral granules (cont.)

Criteria:

- **Criteria for Initial therapy:** Xuriden (uridine triacetate) is considered *medically necessary* and will be approved when **ALL** of the following criteria are met:

1. Provider is a specialist in inborn errors of metabolism or metabolic diseases
2. Individual is 2 months of age or older
3. A confirmed diagnosis of hereditary orotic aciduria with all of the following features:
 - Megaloblastic anemia unresponsive to iron, folic acid, or vitamin B12
 - Excessive urinary excretion of orotic acid
4. **ALL** of the following baseline tests have been completed before initiation of treatment:
 - Complete blood count with differential
 - Urinalysis for orotic acid and orotidine levels

Initial approval duration: 120 packs per month for 12 months

- **Criteria for continuation of coverage (renewal request):** Xuriden (uridine triacetate) is considered *medically necessary* with documentation of **ALL** of the following:

1. Individual continues to be seen by a specialist in inborn errors of metabolism or metabolic diseases
2. Individual's condition responded while on therapy
 - Response is defined as any of the following:
 - Achieved and maintains stable CBC
 - Reduced urine orotic acid levels
 - Reduced urine orotidine levels
3. Individual has been adherent with the medication

Renewal duration: 120 packs per month for 12 months

Description:

Xuriden (uridine triacetate) is a pyrimidine analog indicated for uridine replacement therapy for the treatment of hereditary orotic aciduria (HOA). Uridine triacetate is an acetylated form of uridine. Following oral administration, uridine triacetate is deacetylated by nonspecific esterases to uridine. The safety and effectiveness of Xuriden (uridine triacetate) was evaluated in a six-week, open-label trial in four patients with HOA. There has also been a retrospective review of the clinical course of 18 patients with HOA treated with uridine triacetate. The estimated birth prevalence is < 1:1,000,000, the disorder has been identified in less than 20 patients worldwide, with only four known patients in the United States. Uridine triacetate is also available as Vistogard® 10 gram granule packet that

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is indicated for the emergency treatment of fluorouracil or capecitabine overdose or overexposure. Xuriden™ is available as 2 gram granule packets.

HOA is a rare congenital autosomal recessive metabolic disorder in infants and children caused by a deficiency in uridine 5'-monophosphate (UMP) synthase. Deficiency of UMP synthase results in the inability to normally synthesize uridine nucleotides (a necessary component of ribonucleic acid) and causes developmental delays, failure to gain weight / failure to thrive, hematologic abnormalities (such as megaloblastic anemia with anisocytosis, poikilocytosis, and moderate hypochromia, and leukopenia), and excessive urinary excretion of orotic acid crystals, which can lead to urinary obstruction. The anemia does not respond to iron, folic acid or vitamin B12.

Other treatments for HOA include therapy with uridine supplements. Xuriden (uridine triacetate) delivers 4-7 times more uridine than oral administration of uridine itself.

The urea cycle is the body's primary system for removing waste nitrogen produced by the metabolism of protein and other nitrogen-containing molecules. Several enzymes, each encoded by a different gene, are involved in the urea cycle; mutations in any of the urea cycle genes may cause a urea cycle defect.

Orotic acid may be elevated in patients with urea cycle disorders and other causes of elevated ammonia. Elevated levels of urine orotic acid are seen in ornithine transcarbamylase (OTC) deficiency, citrullinemia type I, argininosuccinate lyase deficiency, arginase deficiency, lysinuric protein intolerance, and hyperornithinemia-hyperammonemia-homocitrullinemia. Elevated levels of urine orotic acid can also be due to purine nucleoside phosphorylase deficiency, Rett syndrome, Reye syndrome, Lesch-Nyhan syndrome, certain cases of pervasive developmental delay, and drugs such as allopurinol and 6-azauridine. Pregnant women may have higher than normal orotic acid excretion; and orotic aciduria has also been reported in traumatized individuals as a marker of catabolism.

Definitions:

Other causes of Urinary Orotic Acid Excretion:

Urea cycle disorders

Ornithine transcarbamylase (OTC) deficiency

Citrullinemia

Argininosuccinic aciduria

Arginase deficiency

Pyrimidine and pyrimidine metabolism disorders

Uridine monophosphate synthase deficiency (UMPS, hereditary orotic aciduria)

UMPS, type I

UMPS, type II

Hereditary orotic aciduria without megaloblastic anemia (OAWA)

Purine nucleoside phosphorylase (PNP) deficiency

Drugs (via inhibition of orotidine-5'-monophosphate decarboxylase)

Allopurinol

6-azauridine

Severe Traumatic injuries

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Motor vehicle accidents, accidental falls, and/or crush injuries
Multiple bone fractures, head injuries, and/or extensive soft-tissue damage
Gunshot wounds to the abdomen, chest and face
Sepsis and severe abdominal trauma - abdominal compartment syndrome
Non-accidental trauma, child abuse and/or penetrating injuries
Other disorders/syndromes
Lysinuric protein intolerance
Hyperornithinemia, hyperammonemia, and homocitrullinuria (HHH) syndrome
Rett syndrome
Reye syndrome
Lesch-Nyhan syndrome
Pervasive developmental delay (PPD)

Resources:

Xuriden product information accessed 04-30-18 at DailyMed:

<https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=40606ca9-4f14-45b7-8632-fc2d17d11a2e>

Xuriden. Package Insert. Revised by manufacturer 2/2017. Accessed 03-14-2017.

Xuriden. Package Insert. Revised by manufacturer 9/2015. Accessed 04-21-2016.

Tim-Aroon T, Anderson IM, Shein S, and Bedoyan JK: A Novel Description of Increased Urinary Orotic Acid Excretion in Pediatric Trauma. J Endocrinol Metab. 2014; 4(1-2):32-35.

Anonymous: In Brief: Uridine Triacetate (Xuriden) for Hereditary Orotic Aciduria (online only). The Medical Letter on Drugs and Therapeutics. March 28, 2016 Issue 1491



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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com. Call 866-325-1794 to check the status of a request. All requested data must be provided. Incomplete forms or forms without the chart notes will be returned. Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.

REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:
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Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity:	Refills:
		Duration of Therapy/Use:

Check if requesting **brand** only Check if requesting **generic**

Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

Standard Urgent. Sign here: _____ Exigent (requires prescriber to include a written statement)

Clinical Information

1. What is the diagnosis? Please specify below.
ICD-10 Code: _____ **Diagnosis Description:** _____

2. Yes No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. Yes No **There is absence of ALL contraindications.**

4. What medication(s) has the individual tried and failed for this diagnosis? Please specify below.
 Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. Are there any supporting labs or test results? Please specify below.

Date	Test	Value

Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: _____ Date: _____

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.