BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
ORIGINAL EFFECTIVE DATE:	**5/19/2016**
LAST REVIEW DATE:	**5/19/2022**
LAST CRITERIA REVISION DATE:	**5/20/2021**
ARCHIVE DATE:	

XURIDEN™ (uridine triacetate)

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.

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.**

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 5/19/2016
LAST REVIEW DATE: 5/19/2022
LAST CRITERIA REVISION DATE: 5/20/2021
ARCHIVE DATE:

XURIDEN™ (uridine triacetate)

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 physician specializing in the patient's diagnosis or is in consultation with a Geneticist, Endocrinologist, Pediatrician, Hematologist, or Specialist in Metabolic Disorders

  2. Individual is 2 months of age or older

  3. A confirmed diagnosis of hereditary orotic aciduria with **ALL** of the following features:
     a. Megaloblastic anemia unresponsive to iron, folic acid, or vitamin B12
     b. Excessive urinary excretion of orotic acid

  4. **ALL** of the following baseline tests have been completed before initiation of treatment:
     a. Complete blood count with differential
     b. Urinalysis for orotic acid and orotidine levels

  Initial approval duration: 6 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 physician specializing in the patient's diagnosis or is in consultation with a Geneticist, Endocrinologist, Pediatrician, Hematologist, or Specialist in Metabolic Disorders

  2. Individual's condition responded while on therapy
     a. Response is defined as any of the following:
        i. Achieved and maintains stable Complete Blood Count
        ii. Reduced urine orotic acid levels
        iii. Reduced urine orotidine levels

  3. Individual has been adherent with the medication

  Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

  1. **Off-Label Use of Non-Cancer Medications**

  2. **Off-Label Use of Cancer Medications**

XURIDEN™ (uridine triacetate)

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 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

XURIDEN™ (uridine triacetate)

- 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
  - 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 (uridine triacetate) granules product information, revised by Wellstat Therapeutics Corporation 12-2019. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 08, 2022.

Vistogard (uridine triacetate) granules product information, revised by Wellstat Therapeutics Corporation 02-2017. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 08, 2022.

Sutton VR. Inborn errors of metabolism: Epidemiology, pathogenesis, and clinical features. In: UpToDate, Patterson MC, TePas E (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated February 01, 2022. Accessed May 09, 2022.