BlueCross BlueShield of Arizona
An Independent Licensee of the Blue Cross and Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 9/20/18
LAST REVIEW DATE: 9/20/18
LAST CRITERIA REVISION DATE:
ARCHIVE DATE:

DROXIA® (hydroxyurea) oral capsule

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.**

DROXIA® (hydroxyurea) oral capsule (cont.)

Criteria:

- **Criteria for initial therapy:** Droxia (hydroxyurea) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a Hematologist

  2. Individual is 18 years of age or older

  3. A confirmed diagnosis of **sickle cell anemia**, that
     - requires blood transfusions, and
     - with recurrent (having greater than or equal to 3 crises a year) moderate to severe painful crises

  4. Individual has failure, contraindication or intolerance to the following preferred step therapy agents:
     - Hydroxyurea (generic for Hydrea)

  5. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
     - Pregnancy test in a woman of reproductive potential
     - Complete blood count with differential
     - Reticulocyte count
     - Hemoglobin F level
     - Comprehensive metabolic panel
     - Uric acid level

  Initial approval duration: 12 months

- **Criteria for continuation of coverage (renewal request):** Droxia (hydroxyurea) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a Hematologist

  2. Individual's condition has responded while on therapy
     - Response is defined as **THREE** of the following:
       - Reduced number of painful crises by at least 30%
       - Reduced hospitalizations for painful crises by at least 50%
       - Reduced number of chest syndrome by at least 30%
       - Reduced number of transfusions by at least 30%
       - Increased time between painful crises by at least 50%
       - Increased fetal hemoglobin levels by at least 50%

  3. Individual has been adherent with the medication

  4. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use

DROXIA® (hydroxyurea) oral capsule (cont.)

- Contraindications as listed in the criteria for initial therapy section
- Significant adverse effect such as:
  - Cutaneous vasculitic ulcerations
  - Pancreatitis

5. There are no significant interacting drugs

Renewal duration: 12 months

Description:

Droxia (hydroxyurea) is indicated for the management of sickle cell anemia (SCA) to reduce the frequency of painful crises and to reduce the need for blood transfusions in patients with recurrent moderate to severe painful crises in adults.

The precise mechanism by which hydroxyurea produces cytotoxic and cytoreductive effects is not known. However, various studies support the hypothesis that hydroxyurea causes an immediate inhibition of DNA synthesis by acting as a ribonucleotide reductase inhibitor, without interfering with the synthesis of ribonucleic acid or of protein.

The mechanisms by which Droxia produces its beneficial effects in patients with SCA are uncertain. Known pharmacologic effects of Droxia that may contribute to its beneficial effects include increasing hemoglobin F (HgF) levels in red blood cells (RBCs), decreasing neutrophils, increasing the water content of RBCs, increasing deformability of sickled cells, and altering the adhesion of RBCs to endothelium. Hydroxyurea concentrates in leukocytes and erythrocytes.

Droxia dosage is increased until a maximum tolerated dosage (the highest dosage that does not produce toxic blood cell counts over 24 consecutive weeks) or a dose of 35 mg/kg/day is reached. If blood cell counts are considered toxic, hydroxyurea should be discontinued until hematologic recovery. Treatment may then be resumed after reducing the dosage with titration up or down until the patient is at a stable dosage that does not result in hematologic toxicity. Any dosage on which a patient develops hematologic toxicity twice, discontinue treatment. Discontinue for cutaneous vasculitic ulcerations; discontinue permanently for pancreatitis.

Definitions:

Moderate to severe symptoms: $\geq$ 3 painful episodes in a year

A painful crisis is defined in clinical studies as acute sickling-related pain that results in a visit to a medical facility, that lasts more than 4 hours, and that requires treatment with a parenteral narcotic or NSAID. Chest syndrome, priapism, and hepatic sequestration are also included in this definition.

DROXIA® (hydroxyurea) oral capsule (cont.)

Hematologic values for Droxia dosing:

	Acceptable ranges	Toxic
Neutrophils	≥ 2,500 cells/mm^3	< 2,000 cells/mm^3
Platelets	≥ 95,000/mm^3	< 80,000/mm^3
Hemoglobin	> 5.3 g/dL	< 4.5 g/dL
Reticulocytes	≥ 95,000/mm^3 if hemoglobin is < 9 g/dL	< 80,000/mm^3 if hemoglobin is < 9 g/dL

Resources:

Droxia. Package Insert. Revised by manufacturer 12/2017. Accessed 8/27/18.

National Heart, Lung, and Blood Institute (NHLBI). Evidence-based management of sickle cell disease: expert panel report, 2014. Bethesda, MD: National Institutes of Health; 2014. http://www.nhlbi.nih.gov/health-pro/guidelines/sickle-cell-disease-guidelines. Accessed 09-04-2018

UpToDate: Hydroxyurea use in sickle cell disease. Current through Aug 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/hydroxyurea-use-in-sickle-cell-disease?search=sickle%20cell%20anemia&source=search_result&selectedTitle=6~150&usage_type=default&display_rank=7

UpToDate: Clinical variability in sickle cell anemia. Current through Aug 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/clinical-variability-in-sickle-cell-anemia?search=sickle%20cell%20anemia&source=search_result&selectedTitle=4~150&usage_type=default&display_rank=4

UpToDate: Overview of the clinical manifestations of sickle cell disease. Current through Aug 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/overview-of-the-clinical-manifestations-of-sickle-cell-disease?search=sickle%20cell%20anemia&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1

UpToDate: Overview of the management and prognosis of sickle cell disease. Current through Aug 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/overview-of-the-management-and-prognosis-of-sickle-cell-disease?search=sickle%20cell%20anemia&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2

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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:

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

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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.