BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
ORIGINAL EFFECTIVE DATE:	**7/20/2017**
LAST REVIEW DATE:	**5/19/2022**
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XATMEP™ (methotrexate) oral solution

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.**

XATMEP™ (methotrexate) oral solution

Criteria:

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

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist or Rheumatologist depending upon indication or use

  2. Individual is 2.5 years of age or older up to 18 years of age

  3. A confirmed diagnosis of **ONE** of the following:
     a. Acute lymphoblastic leukemia (ALL) as a component of a combination chemotherapy maintenance regimen **OR** other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

     b. Active polyarticular juvenile idiopathic arthritis (pJIA) in an individual who is intolerant or had an inadequate response to first-line therapy including full dose non-steroidal anti-inflammatory drugs (NSAID)

  4. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
     a. A negative pregnancy test in an individual of child bearing potential

  5. Individual has failure, contraindication per FDA label or intolerance to **ALL** the following agents:
     a. Oral methotrexate tabs
     b. Methotrexate injection

  6. There are **NO** FDA-label contraindications, such as:
     a. Individual who is pregnant

  7. Will not be used with live virus vaccines

  8. Will not be used in an individual with chronic liver disease

  9. Will not be used with other methotrexate formulations

  Initial approval duration: 6 months

- **Continuation of coverage (renewal request):** Xatmep (methotrexate) oral solution is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist or Rheumatologist depending upon indication or use

XATMEP™ (methotrexate) oral solution

2. Individual's condition responded while on therapy
    a. Response is defined as **ONE** of the following:
        i. For acute lymphoblastic leukemia:
            1. No evidence of disease progression
        ii. For polyarticular juvenile idiopathic arthritis: **TWO** of the following:
            1. Achieved and maintains a 30% improvement in ACR Core Data Set and is without fevers
            2. Reduced number of joints with active arthritis over baseline
            3. Reduced number of joints with limited range of motion over baseline
            4. Reduced pain
            5. Reduced number of acute flares

3. Individual has been adherent with the medication

4. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use
    a. Contraindications as listed in the criteria for initial therapy section
    b. Significant adverse effect such as:
        i. Bone marrow suppression
        ii. Dermatologic toxicity such as toxic epidermal necrolysis, Stevens-Johnson syndrome, exfoliative dermatitis, skin necrosis, erythema multiforme
        iii. Development of secondary malignancy such as lymphoproliferative disease
        iv. Gastrointestinal perforation, ulceration, or bleeding
        v. Infection from bacteria, fungal, or viral pathogens
        vi. Kidney toxicity
        vii. Liver toxicity
        viii. Pulmonary toxicity

5. Will not be used in an individual with chronic liver disease

6. Will not be used with other methotrexate formulations

7. There are no significant interacting drugs

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**

XATMEP™ (methotrexate) oral solution

Description:

Xatmep (methotrexate) oral solution is indicated for the treatment of pediatric patients with acute lymphoblastic leukemia (ALL) as part of a multi-phase, combination chemotherapy maintenance regimen; it is also indicated in the management of pediatric patients with active polyarticular juvenile idiopathic arthritis (pJIA) who have had an insufficient therapeutic response to, or are intolerant of, an adequate trial of first-line therapy including full dose non-steroidal anti-inflammatory agents (NSAIDs).

Methotrexate, a folate analog, inhibits the enzyme dihydrofolic acid reductase. Dihydrofolate must be reduced to tetrahydrofolate by this enzyme before they can be utilized as carriers of one-carbon groups in the synthesis of purine nucleotides and thymidylate. Methotrexate interferes with DNA synthesis, repair, and cellular replication. Actively proliferating tissues such as malignant cells, bone marrow, fetal cells, buccal and intestinal mucosa, and cells of the urinary bladder are in general more sensitive to this effect of methotrexate. The mechanism of action for methotrexate in pJIA is unknown; it may affect immune function.

Definitions:

American College of Rheumatology (ACR) Core Data Set

1. Swollen joint count
2. Tender joint count
3. Physician global assessment
4. Acute phase reactant – ESR or CRP
5. Physical function
6. Pain
7. Patient global assessment
8. Radiograph, if study includes more than 1 year

Resources:

Xatmep (methotrexate) oral solution product information, revised by Azurity Pharmaceuticals, Inc. 09-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 08, 2022.

Weiss PF. Polyarticular juvenile idiopathic arthritis: Treatment. In: UpToDate, Klein-Gitelman M, TePas E (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated January 19, 2022. Accessed May 08, 2022.

Horton TM, Steuber CP. Overview of the treatment of acute lymphoblastic leukemia/lymphoma in children and adolescents. In: UpToDate, Park JR, Rosmarin AG (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated May 04, 2020. Accessed May 08, 2022.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Acute Lymphoblastic Leukemia Version 1.2022 – Updated April 04, 2022. Available at https://www.nccn.org. Accessed May 08, 2022.

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Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.