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

PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
ORIGINAL EFFECTIVE DATE:	**7/20/17**
LAST REVIEW DATE:	**8/02/18**
LAST CRITERIA REVISION DATE:	**8/02/18**
ARCHIVE DATE:	

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 (cont.)

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. Individual is 2.5 years of age or older

2. A confirmed diagnosis of **ONE** of the following:
   - Acute lymphoblastic leukemia (ALL) as a component of a combination chemotherapy maintenance regimen
   - 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)

3. Individual has failed, or is intolerant to, or has a contraindication such that the individual is unable to use **ALL** of the following preferred step therapy agents:
   - Oral methotrexate tabs
   - Methotrexate injection

4. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
   - A negative pregnancy test in an individual of child bearing potential
   - Complete blood count
   - Comprehensive metabolic panel to assess liver and kidney function

5. There are **NO** contraindications:
   - Contraindication include:
     - Individual who is pregnant
     - Severe hypersensitivity to methotrexate

6. Will not be used with live virus vaccines

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

8. Will not be used with other methotrexate formulations

9. Will not be used with probenecid

10. Woman patient of child bearing potential should use effective contraception during and for 6 months after therapy

11. Woman patient who is breast feeding an infant or child should stop breast feeding during therapy

12. Male patient with a female partner of reproductive potential should use effective contraception during and for 3 months after therapy

XATMEP™ (methotrexate) oral solution (cont.)

Initial approval duration: 12 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's condition responded while on therapy [this can be modified or changed
   - Response is defined as **TWO** of the following:
     - Achieved or maintains a 30% improvement in ACR Core Data Set and is without fevers
     - Reduced number of joints with active arthritis over baseline
     - Reduced number of joints with limited range of motion over baseline
     - Reduced pain
     - Reduced number of acute flares
2. Individual has been adherent with the medication
3. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
   - Contraindications as listed in the criteria for initial therapy section
   - Significant adverse effect such as:
     - Bone marrow suppression
     - Kidney toxicity
     - Liver toxicity
     - Pulmonary toxicity
     - Gastrointestinal perforation, ulceration, or bleeding
     - Infection from bacteria, fungal, or viral pathogens
     - Dermatologic toxicity such as toxic epidermal necrolysis, Stevens-Johnson syndrome, exfoliative dermatitis, skin necrosis, erythema multiforme
     - Development of secondary malignancy such as lymphoproliferative disease
4. There are no significant interacting drugs

Renewal duration: 12 months

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.

XATMEP™ (methotrexate) oral solution (cont.)

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.

American College of Rheumatology 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. Package Insert. Revised by manufacturer 04/2017. Accessed 05-29-2017.

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.

Xatmep (methotrexate) oral solution product information accessed 07-15-18 at DailyMed: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=aec9984e-34c5-481b-b6bf-9bb5caf1daf8

Pincus T. The American College of Rheumatology (ACR) Core Data Set and derivative "patient only" indicies to assess rheumatoid arthritis. Clin Exp Rheumatol 2005; 23 (Suppl 39): S109-S113

UpToDate: Polyarticular juvenile idiopathic arthritis: Treatment. Current through Jun 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/polyarticular-juvenile-idiopathic-arthritis-treatment?search=polyarticular%20juvenile%20idiopathic%20arthritis&source=search_result&selectedTitle=2~31&usage_type=default&display_rank=2

UpToDate: Polyarticular juvenile idiopathic arthritis: Clinical manifestations, diagnosis, and complications. Current through Jun 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/polyarticular-juvenile-idiopathic-arthritis-clinical-manifestations-diagnosis-and-complications?search=polyarticular%20juvenile%20idiopathic%20arthritis&source=search_result&selectedTitle=1~31&usage_type=default&display_rank=1

UpToDate: Classification of juvenile arthritis. Current through Jun 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/classification-of-juvenile-arthritis?search=polyarticular%20juvenile%20idiopathic%20arthritis&source=search_result&selectedTitle=3~31&usage_type=default&display_rank=3

BlueCross BlueShield of Arizona

An Independent Licensee of the Blue Cross and Blue Shield Association

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

BlueCross BlueShield of Arizona

An Independent Licensee of the Blue Cross and Blue Shield Association

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.