LOUISIANA BLUE

methotrexate oral solution (Xatmep™, Jylamvo®)

Policy # 00602
Original Effective Date: 01/17/2018
Current Effective Date: 02/10/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider Xatmep™‡ (methotrexate oral solution) and Jylamvo®‡ (methotrexate oral solution) to be **eligible for coverage**** when the patient selection criteria are met.

Xatmep (methotrexate oral solution)

Patient Selection Criteria
Coverage eligibility for Xatmep (methotrexate oral solution) will be considered when the following criteria are met:

- Patient is LESS than 18 years of age; AND
- Patient is UNable to receive other forms of oral methotrexate; AND
- Patient is NOT currently taking other medications in a tablet and/or capsule form; AND
- Patient has a diagnosis of:
    - Acute lymphoblastic leukemia (with Xatmep being used as a component of a combination chemotherapy maintenance regimen); OR
    - Active polyarticular juvenile idiopathic arthritis AND the patient had an intolerance or inadequate response to first-line therapy (for example non-steroidal anti-inflammatory drugs [NSAIDs] and/or prednisone).

*(Note: the criterion requiring the patient to be unable to receive other forms of oral methotrexate as well as the criterion requiring that patients are not currently taking other medications in a tablet and/or capsule form are additional Company requirements for coverage eligibility and will be denied as not medically necessary** if not met).*

methotrexate oral solution (Xatmep™, Jylamvo®)

Policy # 00602
Original Effective Date: 01/17/2028
Current Effective Date: 02/10/2025

Jylamvo (methotrexate oral solution)

Patient Selection Criteria
Coverage eligibility for Jylamvo (methotrexate oral solution) will be considered when the following criteria are met:

- Patient is 18 years of age or older; AND
- Patient is UNable to receive other forms of oral methotrexate; AND
- Patient is NOT currently taking other medications in a tablet and/or capsule form; AND
- Patient has a diagnosis of:
    - Acute lymphoblastic leukemia (with Jylamvo being used as a component of a combination chemotherapy maintenance regimen); OR
    - Relapsed or refractory non-Hodgkin lymphoma (with Jylamvo being used as a component of a metronomic combination regimen); OR
    - Mycosis fungoides; OR
    - Rheumatoid arthritis; OR
    - Severe psoriasis.

*(Note: the criterion requiring the patient to be unable to receive other forms of oral methotrexate as well as the criterion requiring that patients are not currently taking other medications in a tablet and/or capsule form are additional Company requirements for coverage eligibility and will be denied as not medically necessary** if not met).*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of Xatmep (methotrexate oral solution) and Jylamvo (methotrexate oral solution) when the patient is able to receive other forms of oral methotrexate OR when the patient is currently taking other medications in tablet and/or capsule form to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of Xatmep (methotrexate oral solution) for any indication other than those that are FDA approved OR for members 18 years of age or older to be **investigational.***

Based on review of available data, the Company considers the use of Jylamvo (methotrexate oral solution) for any indication other than those that are FDA approved to be **investigational.***

methotrexate oral solution (Xatmep™, Jylamvo®)

Policy # 00602
Original Effective Date: 01/17/2028
Current Effective Date: 02/10/2025

Background/Overview

Xatmep is methotrexate oral solution supplied as 2.5 mg/mL. Xatmep is indicated for the treatment of pediatric patients with acute lymphoblastic leukemia as a component of a combination chemotherapy maintenance regimen as well as for the management of pediatric patients with active polyarticular juvenile idiopathic arthritis who are intolerant of or had an inadequate response to first-line therapy. The recommended dosage for use in acute lymphoblastic leukemia is 20 mg/m^2 one time weekly and the recommended starting dosage for polyarticular juvenile idiopathic arthritis is 10 mg/ m^2 one time weekly.

Jylamvo is methotrexate oral solution supplied as 2 mg/mL. Jylamvo is indicated for the treatment of adults with acute lymphoblastic leukemia (ALL) as part of a combination chemotherapy maintenance regimen, the treatment of adults with mycosis fungoides, the treatment of adults with relapsed or refractory non-Hodgkin lymphoma as part of a metronomic combination regimen, the treatment of adults with rheumatoid arthritis, and for the treatment of adults with severe psoriasis. The recommended dose for use in ALL is 20 mg/m^2. For use in mycosis fungoides, the recommended dose is 25 to 75 mg orally once weekly, while the dose for use in mycosis fungoides is 10 mg/m^2 orally twice weekly as part of combination chemotherapy. In relapsed or refractory non-Hodgkin lymphoma, the recommended dose is 2.5 mg orally two to four times per week. The recommended starting dose in rheumatoid arthritis is 7.5 mg orally once weekly that can be adjusted to achieve and optimal response, while the recommended dose in psoriasis is 10 to 25 mg orally once weekly until an adequate response is achieved.

Juvenile Idiopathic Arthritis

Juvenile idiopathic arthritis includes the inflammation of joints and presence of arthritis in children. Juvenile idiopathic arthritis typically occurs in a symmetrical manner with knees, wrists, and ankles most frequently affected. However certain subgroups of children do have predominantly asymmetrical involvement. Typically, first line treatments such as non-steroidal anti-inflammatory drugs and/or prednisone are used. If those are failed, then DMARDs (disease modifying anti-rheumatic drugs) can be used to treat this condition. An example of a DMARD would include methotrexate.

Rheumatoid Arthritis

Rheumatoid arthritis is a chronic (long-term) disease that causes inflammation of the joints and surrounding tissues. It can also affect other organs. It is considered an autoimmune disease. In an autoimmune disease, the immune system confuses healthy tissue for foreign substances. Typically, first line treatments such as traditional DMARDs are used to treat this condition. An example of a traditional DMARD would include methotrexate.

Plaque Psoriasis
Psoriasis is a common skin condition that is caused by an increase in production of skin cells. It is characterized by frequent episodes of redness, itching and thick, dry silvery scales on the skin. It is most commonly seen on the trunk, elbows, knees, scalp, skin folds and fingernails. This condition can appear suddenly or gradually and may affect people of any age; it most commonly begins between the ages of 15 and 35. Psoriasis is not contagious. It is an inherited disorder related to an inflammatory response in which the immune system produces too much TNF-alpha. It may be severe in immunosuppressed people or those who have other autoimmune disorders such as rheumatoid arthritis. Typical treatments for severe cases of plaque psoriasis include ultraviolet therapy or systemic therapies such as methotrexate or cyclosporine.

Acute Leukemia
Acute leukemia is the most common form of cancer in children, with acute lymphoblastic leukemia being five times more common than acute myeloid leukemia. Treatment regimens vary for this condition based on prognostic indicators at presentation. If methotrexate is used, it is used in a combination therapy regimen.

Non-Hodgkin Lymphoma
Non-Hodgkin lymphomas (NHL) are a group of hematologic malignancies that are variously derived from B cell progenitors, T cell progenitors, mature B cells, mature T cells, or less commonly, natural killer cells. Treatment for NHL depends on several factors, including type, extent of disease, and other patient factors.

Mycosis Fungoides
Mycosis fungoides is a type of non-Hodgkin lymphoma that primarily affects the skin, but can also include involvement of the lymph nodes, blood, and visceral organs. Common features of this condition include skin lesions that may present as patches, plaques, and/or tumors with itching being one of the most common symptoms. The cause of mycosis fungoides is unknown, but T cell receptor/T cell activation, altered JAK-STAT signaling, RNA splicing abnormalities, and epigenetic alterations are commonly known to be involved. Treatment options vary from topical agents including corticosteroids, retinoids, and phototherapy to systemic therapies such as methotrexate, brentuximab vedotin, and bexarotene depending on disease severity.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Xatmep is indicated for the treatment of pediatric patients with acute lymphoblastic leukemia as a component of a combination chemotherapy maintenance regimen as well as for the management of pediatric patients with active polyarticular juvenile idiopathic arthritis who are intolerant of or had an inadequate response to first-line therapy.

methotrexate oral solution (Xatmep™, Jylamvo®)

Policy # 00602
Original Effective Date: 01/17/2028
Current Effective Date: 02/10/2025

Jylamvo is indicated for the treatment of adults with acute lymphoblastic leukemia (ALL) as part of a combination chemotherapy maintenance regimen, the treatment of adults with mycosis fungoides, the treatment of adults with relapsed or refractory non-Hodgkin lymphoma as part of a metronomic combination regimen, the treatment of adults with rheumatoid arthritis, and for the treatment of adults with severe psoriasis.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

Xatmep and Jylamvo were approved by the FDA based on studies of other dosage forms of methotrexate in the approved conditions. The intent of this policy is to ensure FDA approved label usage as well as dosage form use requirements. The patient selection criteria presented in this policy takes into consideration whether or not the patient can tolerate other forms of oral methotrexate. Based on a review of the data, if the above mentioned criteria are not met, there is no advantage to the use of Xatmep or Jylamvo over other forms of oral methotrexate.

References

1. Xatmep [package insert]. Silvergate Pharmaceuticals, Inc. Greenwood Village, Colorado.
2. Overview of the treatment of acute lymphoblastic leukemia in children and adolescents. UpToDate. Updated through November 2017.
3. Jylamvo [package insert]. Lukare Medical, LLC. Scotch Plains, New Jersey. Updated November 2022.
4. Clinical manifestations, pathologic features, and diagnosis of mycosis fungoides. UpToDate. Updated through November 2024.
5. Treatment of early stage (IA to IIA) mycosis fungoides. UpToDate. Updated through November 2024.
6. Clinical presentation and initial evaluation of non-Hodgkin lymphoma. Updated through November 2024.

Policy History

Original Effective Date: 01/17/2018
Current Effective Date: 02/10/2025
01/04/2018 Medical Policy Committee review
01/17/2018 Medical Policy Implementation Committee approval. New policy.
01/10/2019 Medical Policy Committee review
01/23/2019 Medical Policy Implementation Committee approval. No change to coverage.

methotrexate oral solution (Xatmep™, Jylamvo®)

Policy # 00602
Original Effective Date: 01/17/2028
Current Effective Date: 02/10/2025

01/03/2020	Medical Policy Committee review
01/08/2020	Medical Policy Implementation Committee approval. No change to coverage.
01/07/2021	Medical Policy Committee review
01/13/2021	Medical Policy Implementation Committee approval. No change to coverage.
01/06/2022	Medical Policy Committee review
01/12/2022	Medical Policy Implementation Committee approval. No change to coverage.
01/05/2023	Medical Policy Committee review
01/11/2023	Medical Policy Implementation Committee approval. No change to coverage.
01/04/2024	Medical Policy Committee review
01/10/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/02/2025	Medical Policy Committee review
01/08/2025	Medical Policy Implementation Committee approval. Added new drug, Jylamvo, to policy with criteria. Title changed from "Xatmep (methotrexate oral solution)" to "methotrexate oral solution (Xatmep, Jylamvo)". Updated relevant sections.

Next Scheduled Review Date: 01/2026

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and

C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.