Methotrexate Injectable Step Therapy Program Summary

This prior authorization applies to Commercial, SourceRx and Health Insurance Marketplace formularies.

OBJECTIVE

The intent of the methotrexate injectable step therapy (ST) program is to encourage the use of generic methotrexate injectable agents over brand Otrexup and Rasuvo. This program will accommodate the use of Otrexup and Rasuvo when there is a history of use of a generic methotrexate injectable; or if generic methotrexate injectable cannot be administered due to documented intolerance, FDA labeled contraindication, or hypersensitivity. The program allows continuation of therapy when there is documentation that the patient is receiving the requested agent. All strengths of the target agents are included in this program. Requests for brand agents will be reviewed when patient-specific documentation has been provided.

TARGET DRUGS

Otrexup™ (methotrexate auto-injector)
Rasuvo® (methotrexate auto-injector)

STEP THERAPY CRITERIA FOR APPROVAL

Brand methotrexate injectable will be approved when **ANY ONE** of the following is met:

1. The patient's medication history includes use of a generic methotrexate injectable in the past 365 days
   OR
2. There is documentation that the patient is currently using the requested agent
   OR
3. The prescriber states the patient is currently using the requested agent **AND** is at risk if therapy is changed
   OR
4. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to the available generic methotrexate injectable
   OR
5. The prescriber has documented that the patient has a physical or a mental disability limiting their ability to use the available generic methotrexate injectable agent

Length of Approval: 12 months

This pharmacy policy is not an authorization, certification, explanation of benefits or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All pharmacy policies are based on (i) information in FDA approved package inserts (and black box warning, alerts, or other information disseminated by the FDA as applicable); (ii) research of current medical and pharmacy literature; and/or (iii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and

treatment, including the type, quality, and levels of care and treatment.

The purpose of Blue Cross and Blue Shield of Alabama's pharmacy policies are to provide a guide to coverage. Pharmacy policies are not intended to dictate to physicians how to practice medicine. Physicians should exercise their medical judgment in providing the care they feel is most appropriate for their patients.

Neither this policy, nor the successful adjudication of a pharmacy claim, is guarantee of payment.

FDA APPROVED INDICATIONS AND DOSAGE[1,2]

Drug	Indication	Dosage and Administration	Limitation of Use
Otrexup™ (methotrexate auto-injector)	Management of patients with severe, active rheumatoid arthritis (RA) and polyarticular juvenile idiopathic arthritis (pJIA), who are intolerant of or had an inadequate response to first-line therapy Symptomatic control of severe, recalcitrant, disabling psoriasis in adults who are not adequately responsive to other forms of therapy	Starting doses: -RA: 7.5 mg once weekly -pJIA: 10 mg/m^2 once weekly -Psoriasis: 10-25 mg once weekly of an oral, intramuscular, subcutaneous, or intravenous formulation Adjust dose gradually to achieve optimal response	Not indicated for the treatment of neoplastic diseases
Rasuvo® (methotrexate auto-injector)	Management of patients with severe, active rheumatoid arthritis (RA) and polyarticular juvenile idiopathic arthritis (pJIA), who are intolerant of or had an inadequate response to first-line therapy Symptomatic control of severe, recalcitrant, disabling psoriasis in adults who are not adequately responsive to other forms of therapy	Starting doses: -RA: 7.5 mg once weekly -pJIA: 10 mg/m^2 once weekly -Psoriasis: 10-25 mg once weekly of an oral, intramuscular, subcutaneous, or intravenous formulation Adjust dose gradually to achieve optimal response	Not indicated for the treatment of neoplastic diseases

CLINICAL RATIONALE

Otrexup and Rasuvo are indicated for; the management of patients with severe, active rheumatoid arthritis (RA) and polyarticular juvenile idiopathic arthritis (pJIA) who are intolerant of or had an inadequate response to first-line therapy including full dose non-steroidal anti-inflammatory agents (NSAIDs); and the symptomatic control of severe, recalcitrant, disabling psoriasis in adults who are not adequately responsive to other forms of therapy. Otrexup and Rasuvo are only indicated for psoriasis when a diagnosis has been

established by a biopsy and/or dermatologic consultation as it is important to ensure that a psoriasis "flare" is not due to an undiagnosed concomitant disease affecting immune response. Otrexup and Rasuvo are not indicated for the treatment of neoplastic disease.[1,2]

Efficacy

The efficacy of Otrexup and Rasuvo for treatment in patients with rheumatoid arthritis was studied based on other formulations of methotrexate. In patients with rheumatoid arthritis, effects of methotrexate on articular swelling and tenderness can be seen as early as 3 to 6 weeks. Most studies of methotrexate in patients with rheumatoid arthritis are relatively short term (3 to 6 months). Limited data from long-term studies indicate that an initial clinical improvement is maintained for at least two years with continued therapy.[1,2]

The efficacy of Otrexup and Rasuvo for treatment in patients with polyarticular juvenile idiopathic arthritis was determined using other formulations of methotrexate. In a 6-month double-blind, placebo-controlled trial of 127 pediatric patients with pJIA (mean age, 10.1 years; age range, 2.5 to 18 years; mean duration of disease, 5.1 years) on background nonsteroidal anti-inflammatory drugs and/or prednisone, methotrexate given weekly at an oral dose of 10 mg/m^2 provided significant clinical improvement compared to placebo as measured by either the physician's global assessment, or by a patient composite (25% reduction in the articular-severity score plus improvement in parent and physician global assessments of disease activity). Over two-thirds of the patients in this trial had polyarticular-course JIA, and the numerically greatest response was seen in this subgroup treated with 10 mg/m^2/wk methotrexate. The overwhelming majority of the remaining patients had systemic-course JIA. All patients were unresponsive to NSAIDs; approximately one-third were using low dose corticosteroids. Weekly methotrexate at a dose of 5 mg/m^2 was not significantly more effective than placebo in this trial.[1,2]

Subcutaneous methotrexate has enhanced bioavailability vs. oral methotrexate. Subcutaneous methotrexate is an option in individuals with insufficient response to optimized oral methotrexate.[4-8]

Safety

Safety information is unchanged from other forms of methotrexate. Otrexup and Rasuvo are contraindicated in pregnancy, nursing mothers, alcoholism or liver disease, immunodeficiency syndromes, preexisting blood dyscrasias, and hypersensitivity to methotrexate.[1,2]

Otrexup and Rasuvo carry a black box warning for the following:[1,2]

- Serious toxic reactions and death have been reported with the use of methotrexate. Patients should be closely monitored for bone marrow, liver, lung, skin, and kidney toxicities.
- Methotrexate has been reported to cause fetal death and/or congenital anomalies and is contraindicated in pregnancy.
- Unexpectedly severe (sometimes fatal) bone marrow suppression, aplastic anemia, and gastrointestinal toxicity have been reported with concomitant administration of methotrexate (usually in high dosage) along with some nonsteroidal anti-inflammatory drugs.

- Hepatotoxicity, fibrosis, and cirrhosis may occur after prolonged use.
- Methotrexate may cause interstitial pneumonitis at any time during therapy and has been reported at low doses. Pulmonary symptoms (especially a dry, nonproductive cough) may require interruption of treatment and careful investigation.
- Diarrhea, ulcerative stomatitis, hemorrhagic enteritis, and death from intestinal perforation may occur.
- Severe, occasionally fatal, skin reactions have been reported.
- Potentially fatal opportunistic infections may occur.

REFERENCES

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2. Rasuvo prescribing information. Medac Pharma Inc. August 2015.
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