Clinical Policy: Methotrexate (Otrexup, Rasuvo, Xatmep)

Reference Number: PA.CP.PHAR.134
Effective Date: 10.17.18 Revision Log
Last Review Date: 10.17.18

Description
Methotrexate injection (Otrexup™, Rasuvo®) and oral solution (Xatmep®) are folate analog metabolic inhibitors.

FDA Approved Indication(s)
Otrexup and Rasuvo are indicated for:

- Management of selected adults with severe, active rheumatoid arthritis (RA), or children 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)
- In adults for the symptomatic control of severe, recalcitrant, disabling psoriasis (PsO) that is not adequately responsive to other forms of therapy, but only when the diagnosis has been established, as by biopsy and/or after dermatologic consultation

Limitation(s) of use: Otrexup and Rasuvo are not indicated for the treatment of neoplastic diseases.

Xatmep is indicated for:

- Treatment of pediatric patients with acute lymphoblastic leukemia (ALL) as a component of a combination chemotherapy maintenance regimen
- Management of pediatric patients with active polyarticular juvenile idiopathic arthritis (pJIA) who are intolerant of or had an inadequate response to first-line therapy

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with PA Health & Wellness® that Otrexup, Rasuvo, and Xatmep are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Polyarticular Juvenile Idiopathic Arthritis (must meet all)**:**

1. Diagnosis of PJIA;
2. Prescribed by or in consultation with a rheumatologist;
3. Member meets one of the following (a or b):
   a. For Otrexup or Rasuvo: age ≥ 2 years;
   b. For Xatmep: age ≤ 18 years;
4. For Otrexup or Rasuvo: failure of generic methotrexate injection, unless contraindicated or clinically significant adverse effects are experienced;
5. For Xatmep: documentation supports inability to swallow pills;
6. Prescribed dose does not exceed the following:

a. Otresup or Ravuso: 20 mg/m^2 per week;
b. Xatmep: 30 mg/m^2 per week.

Approval duration: 6 months

B. Rheumatoid Arthritis or Psoriasis (must meet all)**:**
1. Request is for Otrexup or Rasuvo;
2. Diagnosis of RA or PsO;
3. For RA: prescribed by or in consultation with a rheumatologist;
4. For PsO: by or in consultation with a rheumatologist or a dermatologist;
5. Age ≥ 2 years;
6. Failure of generic methotrexate injection, unless contraindicated or clinically significant adverse effects are experienced;
7. Prescribed dose does not exceed the following:
   a. RA: 20 mg per week;
   b. Psoriasis: 30 mg per week.

Approval duration: 6 months

C. Acute Lymphoblastic Leukemia (must meet all):
1. Request is for Xatmep;
2. Diagnosis of ALL;
3. Prescribed by by or in consultation with an oncologist or hematologist;
4. Age ≤ 18 years;
5. Medical justification as to why member cannot use methotrexate tablets;
6. Dose does not exceed 30 mg/m^2 per week.

Approval duration: 6 months

D. Other diagnoses/indications
1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
   b. Documentation supports that member is currently receiving Xatmep for ALL and has received this medication for at least 30 days
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed the following:
   a. Otrexup or Ravuso:
      i. RA, pJIA: 20 mg/m^2 per week;
      ii. Psoriasis: 30 mg per week;
   b. Xatmep: 30 mg/m^2 per week.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – PA.CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation Key

ALL: acute lymphoblastic leukemia
FDA: Food and Drug Administration
PJIA: polyarticular juvenile idiopathic arthritis
PsO: psoriasis
RA: rheumatoid arthritis

Appendix B: Therapeutic Alternatives

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
methotrexate injection	**RA** 7.5 mg SC once weekly **PJIA** 10 mg/m^2 SC once weekly **PsO** 10-25 mg SC once weekly	RA, pJIA: 20 mg/week; PsO: 30 mg/week
methotrexate tablets	**ALL, PJIA** 10 – 30 mg/m^2 once weekly	30 mg/m^2/week

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: General Information

- Otrexup and Rasuvo are not indicated for the treatment of neoplastic diseases.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Methotrexate injection (Otrexup, Rasuvo)	RA	7.5 mg SC once weekly	20 mg/week
	PJIA	10 mg/m^2 SC once weekly	20 mg/week
	PsO	10-25 mg SC once weekly	30 mg/week
Methotrexate oral solution (Xatmep)	ALL	20 mg/m^2 PO once weekly	20 mg/m^2/week
	PJIA	10 mg/m^2 PO once weekly	30 mg/m^2/week

VI. Product Availability

Drug	Availability
Methotrexate injection (Otrexup)	Auto-injector: 10 mg/0.4 mL, 12.5 mg/0.4 mL, 15 mg/0.4 mL, 17.5 mg/0.4 mL, 20 mg/0.4 mL, 22.5 mg/0.4 mL, 25 mg/0.4 mL
Methotrexate injection (Rasuvo)	Auto-injector: 7.5 mg/0.15 mL, 10 mg/0.2 mL, 12.5 mg/0.25 mL, 15 mg/0.3 mL, 17.5 mg/0.35 mL, 20 mg/0.4 mL, 22.5 mg/0.45 mL, 25 mg/0.5 mL, 30 mg per 0.6 mL
Methotrexate oral solution (Xatmep)	2.5 mg/mL in a 120 mL bottle

VII. References

1. Otrexup Prescribing Information. Ewing, NJ : Antares Pharma, Inc. Februray 2018. Available at: www.otrexup.com. Accessed July 18, 2018.
2. Rasuvo Prescribing Information. Chicago, IL : Medac Pharma, Inc. March 2018. Availale at: http://cdn.rasuvo.com/assets/pdf/Prescribing-Information-current.pdf. Accessed July 18, 2018.
3. Xatmep Prescribing Information. Greenwood Village, CO: Silvergate Pharmaceuticals, Inc.; April 2017. Available at: http://silvergatepharma.com/wp-content/uploads/2017/04/PI-4-26-17.pdf. Accessed July 18, 2018.
4. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: http://www.clinicalpharmacology-ip.com/. Accessed July 18, 2018.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	10/18	