

## Clinical Policy: Methotrexate (Otrexup, Rasuvo, Xatmep, Reditrex)

Reference Number: CP.PHAR.134

Effective Date: 12.01.18

Last Review Date: 11.19

Line of Business: Commercial, HIM, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### Description

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

### FDA Approved Indication(s)

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

Xatmep is indicated for:

- Treatment of pediatric patients with acute lymphoblastic leukemia (ALL) as part of a multi-phase, combination chemotherapy maintenance regimen
- 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 NSAIDs

### 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 Centene Corporation® that Otrexup, Rasuvo, Xatmep, and Reditrex 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, Rasuvo, or Reditrex: age  $\geq$  2 years;

- b. For Xatmep: age  $\leq$  18 years;
- 4. For Otrexup, Rasuvo, or Reditrex: failure of generic methotrexate injection, unless contraindicated or clinically significant adverse effects are experienced;
- 5. For Xatmep: documentation supports inability to swallow pills;
- 6. Dose does not exceed the following (a or b):
  - a. Otrexup, Ravuso, or Reditrex: 20 mg per week;
  - b. Xatmep: 30 mg/m<sup>2</sup> per week.

**Medicaid/HIM** – 6 months

**Commercial** – 6 months or to the member’s renewal date, whichever is longer

**B. Rheumatoid Arthritis or Psoriasis (must meet all):**

- 1. Diagnosis of RA or PsO;
- 2. Request is for Otrexup, Rasuvo, or Reditrex;
- 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  $\geq$  2 years;
- 6. Failure of generic methotrexate injection, unless contraindicated or clinically significant adverse effects are experienced;
- 7. Dose does not exceed the following (a or b):
  - a. RA: 20 mg per week;
  - b. Psoriasis: 30 mg per week.

**Medicaid/HIM** – 6 months

**Commercial** – 6 months or to the member’s renewal date, whichever is longer

**C. Acute Lymphoblastic Leukemia (must meet all):**

- 1. Diagnosis of ALL;
- 2. Request is for Xatmep;
- 3. Prescribed by by or in consultation with an oncologist or hematologist;
- 4. Age  $<$  18 years;
- 5. Documentation supports inability to swallow pills;
- 6. Request meets one of the following (a or b):\*
  - a. Dose does not exceed 30 mg/m<sup>2</sup> per week;
  - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

*\*Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration:**

**Medicaid/HIM** – 6 months

**Commercial** – Length of Benefit

**D. Other diagnoses/indications**

- 1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid and HIM-Medical Benefit.

## 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 Centene benefit or member has previously met initial approval criteria;
  - 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 or b):
  - a. Otrexup, Ravuso, or Reditrex:
    - i. RA, pJIA: 20 mg per week;
    - ii. Psoriasis: 30 mg per week;
  - b. Xatmep:
    - i. pJIA: 30 mg/m<sup>2</sup> per week;
    - ii. ALL: Request meets one of the following (1 or 2):\*
      1. Dose does not exceed 20 mg/m<sup>2</sup> per week;
      2. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

\*Prescribed regimen must be FDA-approved or recommended by NCCN.

### Approval duration:

**Medicaid/HIM** – 12 months

**Commercial** – Otrexup, Rasuvo, and Reditrex: 6 months or to the member's renewal date, whichever is longer;

Xatmep: Length of Benefit

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

**Approval duration: Duration of request or 12 months (whichever is less);** or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

## 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 – CP.CPA.09 for commercial, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

## IV. Appendices/General Information

### Appendix A: Abbreviation Key

ALL: acute lymphoblastic leukemia

FDA: Food and Drug Administration

NSAID: non-steroidal anti-inflammatory drug

PJIA: polyarticular juvenile idiopathic arthritis

PsO: psoriasis

RA: rheumatoid arthritis

*Appendix B: Therapeutic Alternatives*

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

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

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s):
  - Otrexup, Rasuvo, Reditrex: pregnancy; nursing mothers; alcoholism or liver disease; immunodeficiency syndromes; pre-existing blood dyscrasias; hypersensitivity
  - Xatmep: pregnancy; severe hypersensitivity to methotrexate
- Boxed warning(s):
  - Otrexup, Rasuvo, Reditrex: fetal death and/or congenital anomalies; reduced elimination when impaired renal function; bone marrow suppression, aplastic anemia, gastrointestinal toxicity; hepatotoxicity, fibrosis and cirrhosis; methotrexate-induced lung disease; diarrhea and ulcerative stomatitis; malignant lymphomas; tumor lysis syndrome; severe, occasionally fatal, skin reactions; opportunistic infections; soft tissue necrosis and osteonecrosis when used with radiotherapy
  - Xatmep: bone marrow suppression; serious infections; renal toxicity; gastrointestinal toxicity; hepatic toxicity; pulmonary toxicity; hypersensitivity and dermatologic reactions; embryo-fetal toxicity, including fetal death

*Appendix D: General Information*

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

**V. Dosage and Administration**

Drug Name	Indication	Dosing Regimen	Maximum Dose
Methotrexate injection (Otrexup, Rasuvo, Reditrex)	RA	7.5 mg SC once weekly	20 mg/week
	PJIA	10 mg/m <sup>2</sup> SC once weekly	20 mg/week
	PsO	10-25 mg SC once weekly	30 mg/week
Methotrexate oral solution (Xatmep)	ALL	20 mg/m <sup>2</sup> PO once weekly	20 mg/m <sup>2</sup> /week
	PJIA	10 mg/m <sup>2</sup> PO once weekly	30 mg/m <sup>2</sup> /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 injection (Reditrex)	Single-dose pre-filled injection: 7.5 mg, 10 mg, 12.5 mg, 15 mg, 17.5 mg, 20 mg, 22.5 mg, 25 mg
Methotrexate oral solution (Xatmep)	2.5 mg/mL in a 60 mL or 120 mL bottle

**VII. References**

- Otrexup Prescribing Information. Ewing, NJ: Antares Pharma, Inc. March 2018. Available at: [www.otrexup.com](http://www.otrexup.com). Accessed August 22, 2019.
- Rasuvo Prescribing Information. Chicago, IL: Medac Pharma, Inc. March 2018. Available at: <http://cdn.rasuvo.com/assets/pdf/Prescribing-Information-current.pdf>. Accessed August 22, 2019.
- Xatmep Prescribing Information. Greenwood Village, CO: Silvergate Pharmaceuticals, Inc.; December 2018. Available at: [www.xatmep.com](http://www.xatmep.com). Accessed August 22, 2019.
- Reditrex Prescribing Information. Nashville, TN: Cumberland Pharmaceuticals, Inc.; November 2019. Available at: [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2019/210737s000lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/210737s000lbl.pdf). Accessed December 27, 2019.
- Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: <http://www.clinicalpharmacology-ip.com/>. Accessed August 22, 2019.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created: adapted from CP.CPA.193 added Medicaid and HIM Medical added; added Xatmep to policy; added specialist requirement; added age limits; references reviewed and updated.	07.31.18	11.18
No significant changes; revised off-label use policy references to relevant lines of business.	06.24.19	
4Q 2019 annual review: no significant changes; added HIM NF language for Xatmep; references reviewed and updated.	08.22.19	11.19
RT4: added Reditrex to policy; revised HIM-medical benefit to HIM line of business.	03.17.20	

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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