

Clinical Policy Title: Methotrexate (Otrexup®, Rasuvo®, Xatmep®)

Policy Number: RxA.304

Drug(s) Applied: Methotrexate (Otrexup®, Rasuvo®, Xatmep®)

Last Review Date: 1/2020

Line of Business: Commercial, Medicaid, HIM-Medical Benefit

Background

Methotrexate injection (Otrexup™, Rasuvo®) and oral solution (Xatmep®) are folate analog metabolic inhibitors. 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 part of a multiphase, 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

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

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 60 mL or 120 mL bottle

This clinical policy has been developed to authorize, modify, or determine coverage for individuals with similar conditions. Specific care and treatment may vary depending on individual need and benefits covered by the plan. This policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. This document may contain prescription brand name drugs that are trademarks of pharmaceutical manufacturers that are not affiliated with RxAdvance.

Clinical Policy

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

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 \geq 2 years;
 - b. For Xatmep: age \leq 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. Dose does not exceed the following (a or b):
 - a. Otrexup or Rasuvo: 20 mg per week;
 - b. Xatmep: 30 mg/m² per week.

Approval duration:

Medicaid – 6 months

HIM – 6 months for Otrexup and Rasuvo

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 or Rasuvo;
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 of age or older;
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.

Approval duration:

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 less than 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/m² 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 – 6 months

Commercial – Length of 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 RxAdvance 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 or Rasuvo:
 - i. RA, pJIA: 20 mg per week; ii. Psoriasis: 30 mg per week;
 - b. Xatmep:
 - i. pJIA: 30 mg/m² per week;
 - ii. ALL: Request meets one of the following (1 or 2):*
 1. Dose does not exceed 20 mg/m² 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 – 12 months

HIM – 12 months for Otrexup and Rasuvo

Commercial – Otrexup and Rasuvo: 6 months or to the member's renewal date, whichever is longer; Xatmep: Length of Benefit

III. Appendices

Appendix A: Abbreviation Key

ALL: acute lymphoblastic leukemia

FDA: Food and Drug Administration

NSAID: non-steroidal anti-inflammatory

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>RA 7.5 mg SC once weekly</p> <p>PJIA mg/m² SC once weekly</p> <p>PsO 10-25 mg SC once weekly</p>	<p>RA, pJIA: 20 mg/week;</p> <p>PsO: 30 mg/week</p>
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: Contraindications/Boxed Warnings

- Contraindication(s):
 - Otrexup, Rasuvo: 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: 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 and Rasuvo are not indicated for the treatment of neoplastic diseases.

References

1. Otrexup Prescribing Information. Ewing, NJ: Antares Pharma, Inc. March 2018. Available at: www.otrexup.com. Accessed August 22, 2019.
2. 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.
3. Xatmep Prescribing Information. Greenwood Village, CO: Silvergate Pharmaceuticals, Inc.; December 2018. Available at: www.xatmep.com. Accessed August 22, 2019.
4. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: <http://www.clinicalpharmacology-ip.com/>. Accessed August 22, 2019.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020