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5.70.037

Section:	Prescription Drugs	Effective Date:	July 1, 2026
Subsection:	Analgesics and Anesthetics	Original Policy Date:	January 9, 2015
Subject:	Methotrexate Injections	Page:	1 of 6

Last Review Date: June 11, 2026

Methotrexate Injections

Description

Otrexup, Rasuvo, RediTrex (methotrexate)

Background

Otrexup, Rasuvo, and RediTrex are types of medication that mimics folate, a natural human vitamin, to interfere with the growth of quickly dividing cells in the body. By lowering the ability of these cells to replicate, the immune system is unable to respond as quickly or effectively. This process decreases symptoms of diseases where the immune system of a person attacks itself (autoimmune), such as rheumatoid arthritis and psoriasis. Otrexup and Rasuvo are injected underneath the skin via an auto-injector device. RediTrex is available as a single-dose pre-filled syringe. Other forms of methotrexate include oral tablets and solutions for injection. Otrexup, Rasuvo, and RediTrex are only for once a week use and is not to be used daily (1-3).

Regulatory Status

FDA-approved indications: Otrexup, Rasuvo, and RediTrex are folate analog metabolic inhibitors indicated for: (1-3)

Rheumatoid Arthritis (RA) including Polyarticular Juvenile Idiopathic Arthritis (pJIA) – Otrexup, Rasuvo, and RediTrex are indicated in the management of patients with severe, active rheumatoid arthritis (RA) or children with active polyarticular juvenile idiopathic arthritis (pJIA), who are not intolerant of or had an inadequate response to first-line therapy.

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Psoriasis – Otrexup, Rasuvo, and RediTrex are indicated in adults for the symptomatic control of severe, recalcitrant, disabling psoriasis that is not adequately responsive to other forms of therapy.

Limitations of Use – Otrexup, Rasuvo, and RediTrex are not indicated for the treatment of neoplastic diseases (1-3).

Otrexup, Rasuvo, and RediTrex carry boxed warnings regarding severe toxic reactions, including embryo-fetal toxicity. Otrexup, Rasuvo, and RediTrex should only be prescribed by physicians with experience with antimetabolites therapy. Because of the potential for possibly fatal and toxic reactions, Otrexup, Rasuvo, and Reditrex should only be used in patients with severe and disabling RA or psoriasis that is not responsive to other therapies. Close monitoring for acute and/or chronic bone marrow, liver, lung, skin, and kidney toxicities is required (1-3).

Because methotrexate has been reported to cause fetal death and/or congenital anomalies, Otrexup, Rasuvo, and RediTrex are contraindicated in pregnant women. Use in women of reproductive potential without a reliable form of birth control is not recommended (1-3).

Prolonged use of methotrexate can cause hepatic fibrosis and cirrhosis. Liver enzyme elevations are commonly seen but are not always indicative of hepatic disease; therefore, periodic liver biopsies are recommended for those under long term methotrexate treatment (1-3).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Otrexup, Rasuvo, and RediTrex may be considered **medically necessary** if the conditions indicated below are met.

Otrexup, Rasuvo, and RediTrex may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnoses

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Patient must have **ONE** of the following:

Age 2 years of age or older

1. Active Polyarticular Juvenile Idiopathic Arthritis (pJIA)
 - a. An inadequate response, intolerance, or contraindication to NSAIDs, and oral methotrexate

Age 18 years of age or older

1. Severely Active Rheumatoid Arthritis (RA)
 - a. An inadequate response, intolerance, or contraindication to NSAIDs, and oral methotrexate

OR

2. Active Psoriasis (PsO)
 - a. An inadequate response, intolerance, or contraindication to NSAIDs, topical corticosteroids and oral methotrexate

AND ALL of the following:

1. Must have documented reason for requiring special injection device such as: lack of dexterity, visual acuity issues
2. **NOT** being used in combination with another form or brand of methotrexate
3. Prescriber agrees to comply with regular monitoring of blood counts, renal function, and hepatic function testing
4. Females of reproductive potential **only**:
 - a. Must have a negative pregnancy test prior to initiating therapy
 - b. **Otrexup** and **Reditrex**: patient will be advised to use effective contraception during treatment and for 6 months after the final dose
 - c. **Rasuvo**: patient will be advised to use effective contraception during treatment and for at least one ovulatory cycle after the final dose
5. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment and for at least 3 months after the final dose

Prior – Approval *Renewal* Requirements

Diagnoses

Patient must have **ONE** of the following:

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Age 2 years of age or older

1. Polyarticular Juvenile Idiopathic Arthritis (JIA)

Age 18 years of age or older

1. Rheumatoid Arthritis (RA)
2. Psoriasis (PsO)

AND ALL of the following:

1. Condition has improved or stabilized
2. **NOT** being used in combination with another form or brand of methotrexate
3. Prescriber agrees to comply with regular monitoring of blood counts, renal function, and hepatic function testing
4. Females of reproductive potential **only**:
 - a. **Otrexup** and **Reditrex**: patient will be advised to use effective contraception during treatment and for 6 months after the final dose
 - b. **Rasuvo**: patient will be advised to use effective contraception during treatment and for at least one ovulatory cycle after the final dose
5. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment and for at least 3 months after the final dose

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

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Otrexup, Rasuvo, and RediTrex are folate analog metabolic inhibitors indicated for the treatment of Polyarticular Juvenile Idiopathic Arthritis (pJIA), moderately to severely Active Rheumatoid arthritis (RA), and active psoriasis (PsO), who have failed other first-line therapies. Otrexup, Rasuvo, and RediTrex carry boxed warnings regarding severe toxic reactions, including embryo-fetal toxicity. Close monitoring for acute and/or chronic bone marrow, liver, lung, skin, and kidney toxicities is required (1-3).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of methotrexate injections while maintaining optimal therapeutic outcomes.

References

1. Otrexup [package insert]. Ewing, NJ: Antares Pharma, Inc; December 2019.
2. Rasuvo [package insert]. Chicago, IL: Medexus Pharma Inc; December 2024.
3. RediTrex [package insert]. Nashville, TN: Cumberland Pharmaceuticals Inc.; March 2023.

Policy History

Date	Action
December 2014	Addition to PA
March 2015	Annual editorial review and reference update
March 2016	Annual editorial review Policy number changed from 5.02.37 to 5.70.37
March 2017	Annual editorial review and reference update
March 2018	Annual editorial review and reference update. Addition of “no combination with other methotrexate products” in renewal criteria
March 2019	Annual review and reference update
February 2020	Addition of RediTrex
March 2020	Annual review
March 2021	Annual editorial review and reference update. Addition of pregnancy testing/effective contraception requirement as well as blood count, renal function, and hepatic monitoring requirement per SME
June 2022	Annual review and reference update
June 2023	Annual review. Changed policy number to 5.70.037
December 2023	Annual review
June 2024	Annual review
December 2024	Annual review and reference update
June 2025	Annual review
June 2026	Annual review and reference update

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Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 11, 2026 and is effective on July 1, 2026.