Effective Date **4/1/2024**
Next Review Date **4/1/2025**
Coverage Policy Number **IP0411**

Methotrexate for Injection

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for the following non-covered methotrexate for injection products:

- **Otrexup®** (methotrexate subcutaneous injection autoinjector)
- **Rasuvo®** (methotrexate subcutaneous injection autoinjector)
- **RediTrex®** (methotrexate subcutaneous injection prefilled syringe)

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Coverage criteria are listed for products **in below table:**

Employer Plans:

Product	Criteria
Otrexup	**Otrexup** is considered medically necessary when there is documentation of failure, contraindication, or intolerance to generic methotrexate injection

Product	Criteria
(methotrexate subcutaneous injection autoinjector)	
Rasuvo (methotrexate subcutaneous injection autoinjector)	**Rasuvo** is considered medically necessary when there is documentation of failure, contraindication, or intolerance to **ALL** of the following: 1. generic methotrexate injection 2. Otrexup (methotrexate subcutaneous injection autoinjector) 3. RediTrex (methotrexate subcutaneous injection prefilled syringe)
RediTrex (methotrexate subcutaneous injection prefilled syringe)	**RediTrex** is considered medically necessary when there is documentation of failure, contraindication, or intolerance to generic methotrexate injection

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of methotrexate for injection products are considered medically necessary when the above medical necessity criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration: up to 12 months.
Reauthorization approval duration: up to 12 months.

Background

OVERVIEW
Methotrexate has been widely studied and is commonly used for treatment of **inflammatory conditions**, including rheumatoid arthritis, juvenile idiopathic arthritis, and plaque psoriasis.[1]

All of the injectable methotrexate products require proper patient training in sterile injection technique and require a patient to have the manual dexterity to self-inject.[5] For inflammatory conditions, the dose of methotrexate is initiated low and adjusted gradually to achieve optimal response and/or tolerability, generally to a maximum of 25 to 30 mg/week.[1,6-8] Flexibility to decrease or increase methotrexate dosing, including in 2.5-mg increments, may be needed in clinical practice. Generic injectable methotrexate is available as a 25 mg/mL injection solution (single-dose and multi-dose vials) and provides flexibility in dose adjustments.[5] Otrexup, Rasuvo, and RediTrex are available as preservative-free, single-dose injections for subcutaneous use.[6-8] A formulation other than Otrexup, Rasuvo, or RediTrex should be used for patients who require a route of administration other than subcutaneous, for doses that are not available in the respective product, and for dose adjustments in < 2.5 mg increments.

References

1. Methotrexate injection [prescribing information]. Durham, NC: Accord; June 2021.
2. Braun J, Kästner P, Flaxenberg P, et al. Comparison of the clinical efficacy and safety of subcutaneous versus oral methotrexate in patients with active rheumatoid arthritis: results of a six-month, multicenter, randomized, double-blind, controlled, phase IV trial. *Arthritis Rheum.* 2008;58(1):73-81.

3. Wegrzyn J, Adeleine P, Miossec P. Better efficacy of methotrexate given by intramuscular injection than orally in patients with rheumatoid arthritis. *Ann Rheum Dis*. 2004;63(10):1232-1234.
4. Abolmaali SS, Tamaddon AM, Dinarvand R. A review of therapeutic challenges and achievements of methotrexate delivery systems for treatment of cancer and rheumatoid arthritis. *Cancer Chemother Pharmacol*. 2013;71(5):1115-1130.
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2023. Available at: http://www.clinicalpharmacology-ip.com/Default.aspx. Accessed on November 28, 2023. Search term: methotrexate.
6. Otrexup® subcutaneous injection [prescribing information]. Ewing, NJ: Antares; November 2022.
7. Rasuvo® subcutaneous injection [prescribing information]. Chicago, IL: Medac; September 2023.
8. RediTrex® subcutaneous injection [prescribing information]. Nashville, TN: Cumberland; November 2019.