STEP THERAPY POLICY

POLICY: Methotrexate Injection Step Therapy Policy

- Methotrexate sodium (solution for injection - various manufacturers)
- Otrexup® (methotrexate subcutaneous injection autoinjector– Antares)
- Rasuvo® (methotrexate subcutaneous injection autoinjector – Medac)
- RediTrex® (methotrexate subcutaneous injection prefilled syringe – Cumberland)

REVIEW DATE: 12/06/2023

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.

CIGNA NATIONAL FORMULARY COVERAGE:

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.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.
Note: Unless administered by a healthcare provider, all of the injectable methotrexate products, including Rasuvo, Otrexup, and RediTrex, require proper patient training in sterile injection technique and require a patient or caregiver to have the manual dexterity to inject.

Methotrexate Injection product(s) is(are) covered as medically necessary when the following step therapy criteria is(are) met. Any other exception is considered not medically necessary.

Step 1: Generic methotrexate injection (single- or multi-dose vials)

Step 2: Otrexup, Rasuvo, RediTrex

CRITERIA

1. If the patient has tried ONE Step 1 Product, approve a Step 2 Product.

2. If, according to the prescriber, the patient and/or caregiver is/are unable to administer generic methotrexate injection (single-dose or multi-dose vial NOT including Otrexup, Rasuvo, or RediTrex), approve a Step 2 Product.

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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	12/21/2022
Annual Revision	No criteria changes.	12/06/2023