UnitedHealthcare® Community Plan

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Medical Benefit Drug Policy

ACTEMRA® (TOCILIZUMAB) INJECTION FOR INTRAVENOUS INFUSION

Policy Number: CSLA2020D0043O **Effective Date**: **TBD**

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APPLICATION

This Medical Benefit Drug Policy only applies to state of Louisiana.

COVERAGE RATIONALE

Please refer to the Medical Benefit Drug Policy titled Oncology Medication Clinical Coverage for updated information based upon the National Comprehensive Cancer Network (NCCN) Drugs & Biologics Compendium® (NCCN Compendium®) for oncology indications.

This policy refers only to Actemra (tocilizumab) injection for intravenous infusion for the treatment of polyarticular juvenile idiopathic arthritis, rheumatoid arthritis, systemic juvenile idiopathic arthritis, and cytokine release syndrome. Actemra, for self-administered subcutaneous injection, is obtained under the pharmacy benefit and is indicated in the treatment of rheumatoid arthritis and giant cell arteritis.

Actemra is proven and medically necessary for the treatment of:

- **Polyarticular juvenile idiopathic arthritis when ALL of the following criteria are met**:[1]
  - For **initial therapy**, **all** of the following:
    - Diagnosis of polyarticular juvenile idiopathic arthritis (PJIA); **and**
    - Actemra is dosed according to U.S. Food and Drug Administration labeled dosing for polyarticular juvenile idiopathic arthritis up to a maximum of (or equivalent dose and interval schedule):
      - 10mg/kg every 4 weeks for patients weighing < 30kg
      - 8mg/kg every 4 weeks for patients weighing ≥ 30kg;

      and
    - Patient is not receiving Actemra in combination with either of the following:

- Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
- Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)][6]

and

- Initial authorization is for no more than 12 months

- For **continuation of therapy**, **all** of the following:
  - Patient has previously received Actemra injection for intravenous infusion; **and**
  - Documentation of positive clinical response to Actemra; **and**
  - Actemra is dosed according to U.S. Food and Drug Administration labeled dosing for polyarticular juvenile idiopathic arthritis up to a maximum of (or equivalent dose and interval schedule):
    - 10mg/kg every 4 weeks for patients weighing < 30kg
    - 8mg/kg every 4 weeks for patients weighing ≥ 30kg;

    and
  - Patient is not receiving Actemra in combination with either of the following:
    - Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
    - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]

    and
  - Authorization is for no more than 12 months

- **Rheumatoid arthritis when ALL of the following criteria are met**:[1]
  - For **initial therapy**, **all** of the following:
    - Diagnosis of moderately to severely active rheumatoid arthritis (RA); **and**
    - History of failure, contraindication, or intolerance to at least one non-biologic DMARD (e.g., methotrexate, leflunomide, sulfasalazine, hydroxychloroquine, minocycline, etc.);[1] **and**
    - Actemra is dosed according to U.S. Food and Drug Administration labeled dosing for rheumatoid arthritis up to a maximum of 800mg every 4 weeks (or equivalent dose and interval schedule); **and**
    - Patient is not receiving Actemra in combination with either of the following:[1]
      - Biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
      - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)][6]

      and
    - Initial authorization is for no more than 12 months

  - For **continuation of therapy**, **all** of the following:
    - Patient has previously received Actemra injection for intravenous infusion; **and**
    - Documentation of positive clinical response; **and**
    - Actemra is dosed according to U.S. Food and Drug Administration labeled dosing for rheumatoid arthritis up to a maximum of 800mg every 4 weeks (or equivalent dose and interval schedule); **and**
    - Patient is not receiving Actemra in combination with either of the following:[1]
      - Biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
      - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]

      and
    - Authorization is for no more than 12 months

- **Systemic juvenile idiopathic arthritis when ALL of the following criteria are met**:
  - For **initial therapy**, **all** of the following:
    - Diagnosis of systemic juvenile idiopathic arthritis (SJIA); **and**
    - Actemra is dosed according to U.S. Food and Drug Administration labeled dosing for systemic juvenile idiopathic arthritis up to a maximum of (or equivalent dose and interval schedule):
      - 12mg/kg every 2 weeks for patients weighing < 30kg
      - 8mg/kg every 2 weeks for patients weighing ≥ 30kg;

      and

- Patient is not receiving Actemra in combination with either of the following:[1]
  - Biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
  - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)][6]

  and
- Initial authorization is for no more than 12 months

- For **continuation of therapy**, **all** of the following:
  - Patient has previously received Actemra injection for intravenous infusion; **and**
  - Documentation of positive clinical response; **and**
  - Actemra is dosed according to U.S. Food and Drug Administration labeled dosing for systemic juvenile idiopathic arthritis up to a maximum of (or equivalent dose and interval schedule):
    - 12mg/kg every 2 weeks for patients weighing < 30kg
    - 8mg/kg every 2 weeks for patients weighing ≥ 30kg;

    and
  - Patient is not receiving Actemra in combination with either of the following:[1]
    - Biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
    - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]

    and
  - Authorization is for no more than 12 months

- **Cytokine release syndrome when ALL of the following criteria are met**:
- For **initial therapy**, **all** of the following:
  - Diagnosis of ~~chimeric antigen receptor (CAR) T cell-induced~~ cytokine release syndrome (CRS); **and**
  - **Patient has received treatment with one of the following:**
    - **Chimeric antigen receptor (CAR) T cell therapy [e.g., Kymriah (tisagenlecleucel), Yescarta (axicabtagene ciloleucel)]**
    - **Blincyto (blinatumomab)**

    and
  - Actemra is dosed according to FDA labeled dosing for CRS:
    - 12mg/kg for patients weighing < 30kg
    - 8mg/kg for patients weighing ≥ 30kg; up to a maximum of 800mg per infusion

    and
  - **Initial authorization is for no more than 4 doses** ~~Actemra is prescribed for a maximum of 4 doses~~

- For **continuation of therapy, all** of the following:
  - Documentation of positive clinical response; **and**
  - **Patient continues to experience signs and symptoms of CRS; and**
  - Actemra is dosed according to FDA labeled dosing for CRS:
    - 12mg/kg for patients weighing < 30kg
    - 8mg/kg for patients weighing ≥ 30kg; up to a maximum of 800mg per infusion

    and
  - **Authorization is for no more than 4 doses** ~~Actemra is prescribed for a maximum of 4 doses~~

Acute graft-versus-host disease (GVHD)
- For initial therapy, all of the following:
  - Diagnosis of steroid-refractory acute GVHD; and
  - One of the following:
    - Patient is receiving Actemra in combination with systemic corticosteroids
    - Patient is intolerant to systemic corticosteroid therapy

  and
- **Initial authorization is for no more than 4 doses**

- **For continuation of therapy, all of the following:**

- Documentation of positive clinical response; and
- Patient continues to experience acute GVHD; and
- One of the following:
  - Patient is receiving Actemra in combination with systemic corticosteroids
  - Patient is intolerant to systemic corticosteroid therapy

  and
- Authorization is for no more than 4 doses

Immune checkpoint inhibitor-related toxicities when ALL of the following criteria are met:[67]

- Patient has recently received checkpoint inhibitor therapy [e.g., Keytruda (Pembrolizumab), Opdivo (Nivolumab)];and
- Diagnosis of severe immunotherapy-related inflammatory arthritis; and
- No symptom improvement after 7 days of starting high-dose corticosteroids.; and
- History of failure, contraindication, or intolerance to infliximab (e.g., Inflectra, Remicade); and
- One of the following:
  - Patient is receiving Actemra in combination with systemic corticosteroids
  - Patient is intolerant to systemic corticosteroid therapy

  and
    - Authorization is for no more than 4 doses

APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Coverage Determination Guidelines may apply.

HCPCS Code	Description
J3262	Injection, tocilizumab, 1 mg

ICD-10 Diagnosis Code	Description
D89.810	Acute graft-versus-host disease
M05.00	Felty's syndrome, unspecified site
M05.011	Felty's syndrome, right shoulder
M05.012	Felty's syndrome, left shoulder
M05.019	Felty's syndrome, unspecified shoulder
M05.021	Felty's syndrome, right elbow
M05.022	Felty's syndrome, left elbow
M05.029	Felty's syndrome, unspecified elbow
M05.031	Felty's syndrome, right wrist
M05.032	Felty's syndrome, left wrist
M05.039	Felty's syndrome, unspecified wrist
M05.041	Felty's syndrome, right hand
M05.042	Felty's syndrome, left hand
M05.049	Felty's syndrome, unspecified hand
M05.051	Felty's syndrome, right hip
M05.052	Felty's syndrome, left hip
M05.059	Felty's syndrome, unspecified hip

ICD-10 Diagnosis Code	Description
M05.061	Felty's syndrome, right knee
M05.062	Felty's syndrome, left knee
M05.069	Felty's syndrome, unspecified knee
M05.071	Felty's syndrome, right ankle and foot
M05.072	Felty's syndrome, left ankle and foot
M05.079	Felty's syndrome, unspecified ankle and foot
M05.09	Felty's syndrome, multiple sites
M05.20	Rheumatoid vasculitis with rheumatoid arthritis of unspecified site
M05.211	Rheumatoid vasculitis with rheumatoid arthritis of right shoulder
M05.212	Rheumatoid vasculitis with rheumatoid arthritis of left shoulder
M05.219	Rheumatoid vasculitis with rheumatoid arthritis of unspecified shoulder
M05.221	Rheumatoid vasculitis with rheumatoid arthritis of right elbow
M05.222	Rheumatoid vasculitis with rheumatoid arthritis of left elbow
M05.229	Rheumatoid vasculitis with rheumatoid arthritis of unspecified elbow
M05.231	Rheumatoid vasculitis with rheumatoid arthritis of right wrist
M05.232	Rheumatoid vasculitis with rheumatoid arthritis of left wrist
M05.239	Rheumatoid vasculitis with rheumatoid arthritis of unspecified wrist
M05.241	Rheumatoid vasculitis with rheumatoid arthritis of right hand
M05.242	Rheumatoid vasculitis with rheumatoid arthritis of left hand
M05.249	Rheumatoid vasculitis with rheumatoid arthritis of unspecified hand
M05.251	Rheumatoid vasculitis with rheumatoid arthritis of right hip
M05.252	Rheumatoid vasculitis with rheumatoid arthritis of left hip
M05.259	Rheumatoid vasculitis with rheumatoid arthritis of unspecified hip
M05.261	Rheumatoid vasculitis with rheumatoid arthritis of right knee
M05.262	Rheumatoid vasculitis with rheumatoid arthritis of left knee
M05.269	Rheumatoid vasculitis with rheumatoid arthritis of unspecified knee
M05.271	Rheumatoid vasculitis with rheumatoid arthritis of right ankle and foot
M05.272	Rheumatoid vasculitis with rheumatoid arthritis of left ankle and foot
M05.279	Rheumatoid vasculitis with rheumatoid arthritis of unspecified ankle and foot
M05.29	Rheumatoid vasculitis with rheumatoid arthritis of multiple sites
M05.30	Rheumatoid heart disease with rheumatoid arthritis of unspecified site
M05.311	Rheumatoid heart disease with rheumatoid arthritis of right shoulder
M05.312	Rheumatoid heart disease with rheumatoid arthritis of left shoulder
M05.319	Rheumatoid heart disease with rheumatoid arthritis of unspecified shoulder
M05.321	Rheumatoid heart disease with rheumatoid arthritis of right elbow
M05.322	Rheumatoid heart disease with rheumatoid arthritis of left elbow
M05.329	Rheumatoid heart disease with rheumatoid arthritis of unspecified elbow
M05.331	Rheumatoid heart disease with rheumatoid arthritis of right wrist
M05.332	Rheumatoid heart disease with rheumatoid arthritis of left wrist
M05.339	Rheumatoid heart disease with rheumatoid arthritis of unspecified wrist
M05.341	Rheumatoid heart disease with rheumatoid arthritis of right hand

ICD-10 Diagnosis Code	Description
M05.342	Rheumatoid heart disease with rheumatoid arthritis of left hand
M05.349	Rheumatoid heart disease with rheumatoid arthritis of unspecified hand
M05.351	Rheumatoid heart disease with rheumatoid arthritis of right hip
M05.352	Rheumatoid heart disease with rheumatoid arthritis of left hip
M05.359	Rheumatoid heart disease with rheumatoid arthritis of unspecified hip
M05.361	Rheumatoid heart disease with rheumatoid arthritis of right knee
M05.362	Rheumatoid heart disease with rheumatoid arthritis of left knee
M05.369	Rheumatoid heart disease with rheumatoid arthritis of unspecified knee
M05.371	Rheumatoid heart disease with rheumatoid arthritis of right ankle and foot
M05.372	Rheumatoid heart disease with rheumatoid arthritis of left ankle and foot
M05.379	Rheumatoid heart disease with rheumatoid arthritis of unspecified ankle and foot
M05.39	Rheumatoid heart disease with rheumatoid arthritis of multiple sites
M05.40	Rheumatoid myopathy with rheumatoid arthritis of unspecified site
M05.411	Rheumatoid myopathy with rheumatoid arthritis of right shoulder
M05.412	Rheumatoid myopathy with rheumatoid arthritis of left shoulder
M05.419	Rheumatoid myopathy with rheumatoid arthritis of unspecified shoulder
M05.421	Rheumatoid myopathy with rheumatoid arthritis of right elbow
M05.422	Rheumatoid myopathy with rheumatoid arthritis of left elbow
M05.429	Rheumatoid myopathy with rheumatoid arthritis of unspecified elbow
M05.431	Rheumatoid myopathy with rheumatoid arthritis of right wrist
M05.432	Rheumatoid myopathy with rheumatoid arthritis of left wrist
M05.439	Rheumatoid myopathy with rheumatoid arthritis of unspecified wrist
M05.441	Rheumatoid myopathy with rheumatoid arthritis of right hand
M05.442	Rheumatoid myopathy with rheumatoid arthritis of left hand
M05.449	Rheumatoid myopathy with rheumatoid arthritis of unspecified hand
M05.451	Rheumatoid myopathy with rheumatoid arthritis of right hip
M05.452	Rheumatoid myopathy with rheumatoid arthritis of left hip
M05.459	Rheumatoid myopathy with rheumatoid arthritis of unspecified hip
M05.461	Rheumatoid myopathy with rheumatoid arthritis of right knee
M05.462	Rheumatoid myopathy with rheumatoid arthritis of left knee
M05.469	Rheumatoid myopathy with rheumatoid arthritis of unspecified knee
M05.471	Rheumatoid myopathy with rheumatoid arthritis of right ankle and foot
M05.472	Rheumatoid myopathy with rheumatoid arthritis of left ankle and foot
M05.479	Rheumatoid myopathy with rheumatoid arthritis of unspecified ankle and foot
M05.49	Rheumatoid myopathy with rheumatoid arthritis of multiple sites
M05.50	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified site
M05.511	Rheumatoid polyneuropathy with rheumatoid arthritis of right shoulder
M05.512	Rheumatoid polyneuropathy with rheumatoid arthritis of left shoulder
M05.519	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified shoulder
M05.521	Rheumatoid polyneuropathy with rheumatoid arthritis of right elbow
M05.522	Rheumatoid polyneuropathy with rheumatoid arthritis of left elbow

ICD-10 Diagnosis Code	Description
M05.529	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified elbow
M05.531	Rheumatoid polyneuropathy with rheumatoid arthritis of right wrist
M05.532	Rheumatoid polyneuropathy with rheumatoid arthritis of left wrist
M05.539	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified wrist
M05.541	Rheumatoid polyneuropathy with rheumatoid arthritis of right hand
M05.542	Rheumatoid polyneuropathy with rheumatoid arthritis of left hand
M05.549	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified hand
M05.551	Rheumatoid polyneuropathy with rheumatoid arthritis of right hip
M05.552	Rheumatoid polyneuropathy with rheumatoid arthritis of left hip
M05.559	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified hip
M05.561	Rheumatoid polyneuropathy with rheumatoid arthritis of right knee
M05.562	Rheumatoid polyneuropathy with rheumatoid arthritis of left knee
M05.569	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified knee
M05.571	Rheumatoid polyneuropathy with rheumatoid arthritis of right ankle and foot
M05.572	Rheumatoid polyneuropathy with rheumatoid arthritis of left ankle and foot
M05.579	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified ankle and foot
M05.59	Rheumatoid polyneuropathy with rheumatoid arthritis of multiple sites
M05.60	Rheumatoid arthritis of unspecified site with involvement of other organs and systems
M05.611	Rheumatoid arthritis of right shoulder with involvement of other organs and systems
M05.612	Rheumatoid arthritis of left shoulder with involvement of other organs and systems
M05.619	Rheumatoid arthritis of unspecified shoulder with involvement of other organs and systems
M05.621	Rheumatoid arthritis of right elbow with involvement of other organs and systems
M05.622	Rheumatoid arthritis of left elbow with involvement of other organs and systems
M05.629	Rheumatoid arthritis of unspecified elbow with involvement of other organs and systems
M05.631	Rheumatoid arthritis of right wrist with involvement of other organs and systems
M05.632	Rheumatoid arthritis of left wrist with involvement of other organs and systems
M05.639	Rheumatoid arthritis of unspecified wrist with involvement of other organs and systems
M05.641	Rheumatoid arthritis of right hand with involvement of other organs and systems
M05.642	Rheumatoid arthritis of left hand with involvement of other organs and systems
M05.649	Rheumatoid arthritis of unspecified hand with involvement of other organs and systems
M05.651	Rheumatoid arthritis of right hip with involvement of other organs and systems
M05.652	Rheumatoid arthritis of left hip with involvement of other organs and systems
M05.659	Rheumatoid arthritis of unspecified hip with involvement of other organs and systems
M05.661	Rheumatoid arthritis of right knee with involvement of other organs and systems
M05.662	Rheumatoid arthritis of left knee with involvement of other organs and systems

ICD-10 Diagnosis Code	Description
M05.669	Rheumatoid arthritis of unspecified knee with involvement of other organs and systems
M05.671	Rheumatoid arthritis of right ankle and foot with involvement of other organs and systems
M05.672	Rheumatoid arthritis of left ankle and foot with involvement of other organs and systems
M05.679	Rheumatoid arthritis of unspecified ankle and foot with involvement of other organs and systems
M05.69	Rheumatoid arthritis of multiple sites with involvement of other organs and systems
M05.70	Rheumatoid arthritis with rheumatoid factor of unspecified site without organ or systems involvement
M05.711	Rheumatoid arthritis with rheumatoid factor of right shoulder without organ or systems involvement
M05.712	Rheumatoid arthritis with rheumatoid factor of left shoulder without organ or systems involvement
M05.719	Rheumatoid arthritis with rheumatoid factor of unspecified shoulder without organ or systems involvement
M05.721	Rheumatoid arthritis with rheumatoid factor of right elbow without organ or systems involvement
M05.722	Rheumatoid arthritis with rheumatoid factor of left elbow without organ or systems involvement
M05.729	Rheumatoid arthritis with rheumatoid factor of unspecified elbow without organ or systems involvement
M05.731	Rheumatoid arthritis with rheumatoid factor of right wrist without organ or systems involvement
M05.732	Rheumatoid arthritis with rheumatoid factor of left wrist without organ or systems involvement
M05.739	Rheumatoid arthritis with rheumatoid factor of unspecified wrist without organ or systems involvement
M05.741	Rheumatoid arthritis with rheumatoid factor of right hand without organ or systems involvement
M05.742	Rheumatoid arthritis with rheumatoid factor of left hand without organ or systems involvement
M05.749	Rheumatoid arthritis with rheumatoid factor of unspecified hand without organ or systems involvement
M05.751	Rheumatoid arthritis with rheumatoid factor of right hip without organ or systems involvement
M05.752	Rheumatoid arthritis with rheumatoid factor of left hip without organ or systems involvement
M05.759	Rheumatoid arthritis with rheumatoid factor of unspecified hip without organ or systems involvement
M05.761	Rheumatoid arthritis with rheumatoid factor of right knee without organ or systems involvement
M05.762	Rheumatoid arthritis with rheumatoid factor of left knee without organ or systems involvement

ICD-10 Diagnosis Code	Description
M05.769	Rheumatoid arthritis with rheumatoid factor of unspecified knee without organ or systems involvement
M05.771	Rheumatoid arthritis with rheumatoid factor of right ankle and foot without organ or systems involvement
M05.772	Rheumatoid arthritis with rheumatoid factor of left ankle and foot without organ or systems involvement
M05.779	Rheumatoid arthritis with rheumatoid factor of unspecified ankle and foot without organ or systems involvement
M05.79	Rheumatoid arthritis with rheumatoid factor of multiple sites without organ or systems involvement
M05.80	Other rheumatoid arthritis with rheumatoid factor of unspecified site
M05.811	Other rheumatoid arthritis with rheumatoid factor of right shoulder
M05.812	Other rheumatoid arthritis with rheumatoid factor of left shoulder
M05.819	Other rheumatoid arthritis with rheumatoid factor of unspecified shoulder
M05.821	Other rheumatoid arthritis with rheumatoid factor of right elbow
M05.822	Other rheumatoid arthritis with rheumatoid factor of left elbow
M05.829	Other rheumatoid arthritis with rheumatoid factor of unspecified elbow
M05.831	Other rheumatoid arthritis with rheumatoid factor of right wrist
M05.832	Other rheumatoid arthritis with rheumatoid factor of left wrist
M05.839	Other rheumatoid arthritis with rheumatoid factor of unspecified wrist
M05.841	Other rheumatoid arthritis with rheumatoid factor of right hand
M05.842	Other rheumatoid arthritis with rheumatoid factor of left hand
M05.849	Other rheumatoid arthritis with rheumatoid factor of unspecified hand
M05.851	Other rheumatoid arthritis with rheumatoid factor of right hip
M05.852	Other rheumatoid arthritis with rheumatoid factor of left hip
M05.859	Other rheumatoid arthritis with rheumatoid factor of unspecified hip
M05.861	Other rheumatoid arthritis with rheumatoid factor of right knee
M05.862	Other rheumatoid arthritis with rheumatoid factor of left knee
M05.869	Other rheumatoid arthritis with rheumatoid factor of unspecified knee
M05.871	Other rheumatoid arthritis with rheumatoid factor of right ankle and foot
M05.872	Other rheumatoid arthritis with rheumatoid factor of left ankle and foot
M05.879	Other rheumatoid arthritis with rheumatoid factor of unspecified ankle and foot
M05.89	Other rheumatoid arthritis with rheumatoid factor of multiple sites
M05.9	Rheumatoid arthritis with rheumatoid factor, unspecified
M06.00	Rheumatoid arthritis without rheumatoid factor, unspecified site
M06.011	Rheumatoid arthritis without rheumatoid factor, right shoulder
M06.012	Rheumatoid arthritis without rheumatoid factor, left shoulder
M06.019	Rheumatoid arthritis without rheumatoid factor, unspecified shoulder
M06.021	Rheumatoid arthritis without rheumatoid factor, right elbow
M06.022	Rheumatoid arthritis without rheumatoid factor, left elbow
M06.029	Rheumatoid arthritis without rheumatoid factor, unspecified elbow
M06.031	Rheumatoid arthritis without rheumatoid factor, right wrist

ICD-10 Diagnosis Code	Description
M06.032	Rheumatoid arthritis without rheumatoid factor, left wrist
M06.039	Rheumatoid arthritis without rheumatoid factor, unspecified wrist
M06.041	Rheumatoid arthritis without rheumatoid factor, right hand
M06.042	Rheumatoid arthritis without rheumatoid factor, left hand
M06.049	Rheumatoid arthritis without rheumatoid factor, unspecified hand
M06.051	Rheumatoid arthritis without rheumatoid factor, right hip
M06.052	Rheumatoid arthritis without rheumatoid factor, left hip
M06.059	Rheumatoid arthritis without rheumatoid factor, unspecified hip
M06.061	Rheumatoid arthritis without rheumatoid factor, right knee
M06.062	Rheumatoid arthritis without rheumatoid factor, left knee
M06.069	Rheumatoid arthritis without rheumatoid factor, unspecified knee
M06.071	Rheumatoid arthritis without rheumatoid factor, right ankle and foot
M06.072	Rheumatoid arthritis without rheumatoid factor, left ankle and foot
M06.079	Rheumatoid arthritis without rheumatoid factor, unspecified ankle and foot
M06.08	Rheumatoid arthritis without rheumatoid factor, vertebrae
M06.09	Rheumatoid arthritis without rheumatoid factor, multiple sites
M06.1	Adult-onset Still's disease
M06.20	Rheumatoid bursitis, unspecified site
M06.211	Rheumatoid bursitis, right shoulder
M06.212	Rheumatoid bursitis, left shoulder
M06.219	Rheumatoid bursitis, unspecified shoulder
M06.221	Rheumatoid bursitis, right elbow
M06.222	Rheumatoid bursitis, left elbow
M06.229	Rheumatoid bursitis, unspecified elbow
M06.231	Rheumatoid bursitis, right wrist
M06.232	Rheumatoid bursitis, left wrist
M06.239	Rheumatoid bursitis, unspecified wrist
M06.241	Rheumatoid bursitis, right hand
M06.242	Rheumatoid bursitis, left hand
M06.249	Rheumatoid bursitis, unspecified hand
M06.251	Rheumatoid bursitis, right hip
M06.252	Rheumatoid bursitis, left hip
M06.259	Rheumatoid bursitis, unspecified hip
M06.261	Rheumatoid bursitis, right knee
M06.262	Rheumatoid bursitis, left knee
M06.269	Rheumatoid bursitis, unspecified knee
M06.271	Rheumatoid bursitis, right ankle and foot
M06.272	Rheumatoid bursitis, left ankle and foot
M06.279	Rheumatoid bursitis, unspecified ankle and foot
M06.28	Rheumatoid bursitis, vertebrae
M06.29	Rheumatoid bursitis, multiple sites

ICD-10 Diagnosis Code	Description
M06.30	Rheumatoid nodule, unspecified site
M06.311	Rheumatoid nodule, right shoulder
M06.312	Rheumatoid nodule, left shoulder
M06.319	Rheumatoid nodule, unspecified shoulder
M06.321	Rheumatoid nodule, right elbow
M06.322	Rheumatoid nodule, left elbow
M06.329	Rheumatoid nodule, unspecified elbow
M06.331	Rheumatoid nodule, right wrist
M06.332	Rheumatoid nodule, left wrist
M06.339	Rheumatoid nodule, unspecified wrist
M06.341	Rheumatoid nodule, right hand
M06.342	Rheumatoid nodule, left hand
M06.349	Rheumatoid nodule, unspecified hand
M06.351	Rheumatoid nodule, right hip
M06.352	Rheumatoid nodule, left hip
M06.359	Rheumatoid nodule, unspecified hip
M06.361	Rheumatoid nodule, right knee
M06.362	Rheumatoid nodule, left knee
M06.369	Rheumatoid nodule, unspecified knee
M06.371	Rheumatoid nodule, right ankle and foot
M06.372	Rheumatoid nodule, left ankle and foot
M06.379	Rheumatoid nodule, unspecified ankle and foot
M06.38	Rheumatoid nodule, vertebrae
M06.39	Rheumatoid nodule, multiple sites
M06.80	Other specified rheumatoid arthritis, unspecified site
M06.811	Other specified rheumatoid arthritis, right shoulder
M06.812	Other specified rheumatoid arthritis, left shoulder
M06.819	Other specified rheumatoid arthritis, unspecified shoulder
M06.821	Other specified rheumatoid arthritis, right elbow
M06.822	Other specified rheumatoid arthritis, left elbow
M06.829	Other specified rheumatoid arthritis, unspecified elbow
M06.831	Other specified rheumatoid arthritis, right wrist
M06.832	Other specified rheumatoid arthritis, left wrist
M06.839	Other specified rheumatoid arthritis, unspecified wrist
M06.841	Other specified rheumatoid arthritis, right hand
M06.842	Other specified rheumatoid arthritis, left hand
M06.849	Other specified rheumatoid arthritis, unspecified hand
M06.851	Other specified rheumatoid arthritis, right hip
M06.852	Other specified rheumatoid arthritis, left hip
M06.859	Other specified rheumatoid arthritis, unspecified hip
M06.861	Other specified rheumatoid arthritis, right knee

ICD-10 Diagnosis Code	Description
M06.862	Other specified rheumatoid arthritis, left knee
M06.869	Other specified rheumatoid arthritis, unspecified knee
M06.871	Other specified rheumatoid arthritis, right ankle and foot
M06.872	Other specified rheumatoid arthritis, left ankle and foot
M06.879	Other specified rheumatoid arthritis, unspecified ankle and foot
M06.88	Other specified rheumatoid arthritis, vertebrae
M06.89	Other specified rheumatoid arthritis, multiple sites
M06.9	Rheumatoid arthritis, unspecified
M08.00	Unspecified juvenile rheumatoid arthritis of unspecified site
M08.011	Unspecified juvenile rheumatoid arthritis, right shoulder
M08.012	Unspecified juvenile rheumatoid arthritis, left shoulder
M08.019	Unspecified juvenile rheumatoid arthritis, unspecified shoulder
M08.021	Unspecified juvenile rheumatoid arthritis, right elbow
M08.022	Unspecified juvenile rheumatoid arthritis, left elbow
M08.029	Unspecified juvenile rheumatoid arthritis, unspecified elbow
M08.031	Unspecified juvenile rheumatoid arthritis, right wrist
M08.032	Unspecified juvenile rheumatoid arthritis, left wrist
M08.039	Unspecified juvenile rheumatoid arthritis, unspecified wrist
M08.041	Unspecified juvenile rheumatoid arthritis, right hand
M08.042	Unspecified juvenile rheumatoid arthritis, left hand
M08.049	Unspecified juvenile rheumatoid arthritis, unspecified hand
M08.051	Unspecified juvenile rheumatoid arthritis, right hip
M08.052	Unspecified juvenile rheumatoid arthritis, left hip
M08.059	Unspecified juvenile rheumatoid arthritis, unspecified hip
M08.061	Unspecified juvenile rheumatoid arthritis, right knee
M08.062	Unspecified juvenile rheumatoid arthritis, left knee
M08.069	Unspecified juvenile rheumatoid arthritis, unspecified knee
M08.071	Unspecified juvenile rheumatoid arthritis, right ankle and foot
M08.072	Unspecified juvenile rheumatoid arthritis, left ankle and foot
M08.079	Unspecified juvenile rheumatoid arthritis, unspecified ankle and foot
M08.08	Unspecified juvenile rheumatoid arthritis, vertebrae
M08.09	Unspecified juvenile rheumatoid arthritis, multiple sites
M08.20	Juvenile rheumatoid arthritis with systemic onset, unspecified site
M08.211	Juvenile rheumatoid arthritis with systemic onset, right shoulder
M08.212	Juvenile rheumatoid arthritis with systemic onset, left shoulder
M08.219	Juvenile rheumatoid arthritis with systemic onset, unspecified shoulder
M08.221	Juvenile rheumatoid arthritis with systemic onset, right elbow
M08.222	Juvenile rheumatoid arthritis with systemic onset, left elbow
M08.229	Juvenile rheumatoid arthritis with systemic onset, unspecified elbow
M08.231	Juvenile rheumatoid arthritis with systemic onset, right wrist
M08.232	Juvenile rheumatoid arthritis with systemic onset, left wrist

ICD-10 Diagnosis Code	Description
M08.239	Juvenile rheumatoid arthritis with systemic onset, unspecified wrist
M08.241	Juvenile rheumatoid arthritis with systemic onset, right hand
M08.242	Juvenile rheumatoid arthritis with systemic onset, left hand
M08.249	Juvenile rheumatoid arthritis with systemic onset, unspecified hand
M08.251	Juvenile rheumatoid arthritis with systemic onset, right hip
M08.252	Juvenile rheumatoid arthritis with systemic onset, left hip
M08.259	Juvenile rheumatoid arthritis with systemic onset, unspecified hip
M08.261	Juvenile rheumatoid arthritis with systemic onset, right knee
M08.262	Juvenile rheumatoid arthritis with systemic onset, left knee
M08.269	Juvenile rheumatoid arthritis with systemic onset, unspecified knee
M08.271	Juvenile rheumatoid arthritis with systemic onset, right ankle and foot
M08.272	Juvenile rheumatoid arthritis with systemic onset, left ankle and foot
M08.279	Juvenile rheumatoid arthritis with systemic onset, unspecified ankle and foot
M08.28	Juvenile rheumatoid arthritis with systemic onset, vertebrae
M08.29	Juvenile rheumatoid arthritis with systemic onset, multiple sites
M08.3	Juvenile rheumatoid polyarthritis (seronegative)
M08.80	Other juvenile arthritis, unspecified site
M08.811	Other juvenile arthritis, right shoulder
M08.812	Other juvenile arthritis, left shoulder
M08.819	Other juvenile arthritis, unspecified shoulder
M08.821	Other juvenile arthritis, right elbow
M08.822	Other juvenile arthritis, left elbow
M08.829	Other juvenile arthritis, unspecified elbow
M08.831	Other juvenile arthritis, right wrist
M08.832	Other juvenile arthritis, left wrist
M08.839	Other juvenile arthritis, unspecified wrist
M08.841	Other juvenile arthritis, right hand
M08.842	Other juvenile arthritis, left hand
M08.849	Other juvenile arthritis, unspecified hand
M08.851	Other juvenile arthritis, right hip
M08.852	Other juvenile arthritis, left hip
M08.859	Other juvenile arthritis, unspecified hip
M08.861	Other juvenile arthritis, right knee
M08.862	Other juvenile arthritis, left knee
M08.869	Other juvenile arthritis, unspecified knee
M08.871	Other juvenile arthritis, right ankle and foot
M08.872	Other juvenile arthritis, left ankle and foot
M08.879	Other juvenile arthritis, unspecified ankle and foot
M08.88	Other juvenile arthritis, vertebrae
M08.89	Other juvenile arthritis, multiple sites
M08.90	Juvenile arthritis, unspecified, unspecified site

ICD-10 Diagnosis Code	Description
M08.911	Juvenile arthritis, unspecified, right shoulder
M08.912	Juvenile arthritis, unspecified, left shoulder
M08.919	Juvenile arthritis, unspecified, unspecified shoulder
M08.921	Juvenile arthritis, unspecified, right elbow
M08.922	Juvenile arthritis, unspecified, left elbow
M08.929	Juvenile arthritis, unspecified, unspecified elbow
M08.931	Juvenile arthritis, unspecified, right wrist
M08.932	Juvenile arthritis, unspecified, left wrist
M08.939	Juvenile arthritis, unspecified, unspecified wrist
M08.941	Juvenile arthritis, unspecified, right hand
M08.942	Juvenile arthritis, unspecified, left hand
M08.949	Juvenile arthritis, unspecified, unspecified hand
M08.951	Juvenile arthritis, unspecified, right hip
M08.952	Juvenile arthritis, unspecified, left hip
M08.959	Juvenile arthritis, unspecified, unspecified hip
M08.961	Juvenile arthritis, unspecified, right knee
M08.962	Juvenile arthritis, unspecified, left knee
M08.969	Juvenile arthritis, unspecified, unspecified knee
M08.971	Juvenile arthritis, unspecified, right ankle and foot
M08.972	Juvenile arthritis, unspecified, left ankle and foot
M08.979	Juvenile arthritis, unspecified, unspecified ankle and foot
M08.98	Juvenile arthritis, unspecified, vertebrae
M08.99	Juvenile arthritis, unspecified, multiple sites
T45.1X5A	Adverse effect of antineoplastic and immunosuppressive drugs, initial encounter
T45.1X5D	Adverse effect of antineoplastic and immunosuppressive drugs, subsequent encounter
T45.1X5S	Adverse effect of antineoplastic and immunosuppressive drugs, sequela
T86.5	Complications of stem cell transplant
T80.89XA	Other complications following infusion, transfusion and therapeutic injection, initial encounter
T80.89XD	Other complications following infusion, transfusion and therapeutic injection, subsequent encounter
T80.89XS	Other complications following infusion, transfusion and therapeutic injection, sequela
T80.90XA	Unspecified complication following infusion and therapeutic injection, initial encounter
T80.90XD	Unspecified complication following infusion and therapeutic injection, subsequent encounter
T80.90XS	Unspecified complication following infusion and therapeutic injection, sequela
T81.89XA	Other complications of procedures, not elsewhere classified, initial encounter
T81.89XD	Other complications of procedures, not elsewhere classified, subsequent encounter
T81.89XS	Other complications of procedures, not elsewhere classified, sequela

ICD-10 Diagnosis Code	Description
T81.9XXA	Unspecified complication of procedure, initial encounter
T81.9XXD	Unspecified complication of procedure, subsequent encounter
T81.9XXS	Unspecified complication of procedure, sequela

BACKGROUND

Actemra (tocilizumab) is a recombinant humanized anti-human interleukin 6 (IL-6) receptor monoclonal antibody. It binds specifically to both soluble and membrane-bound IL-6 receptors, and has been shown to inhibit IL-6-mediated signaling through these receptors. IL-6 is a pro-inflammatory cytokine and has been shown to be involved in diverse physiological processes such as T-cell activation, induction of immunoglobulin secretion, initiation of hepatic acute phase protein synthesis, and stimulation of hematopoietic precursor cell proliferation and differentiation. IL-6 is also produced by synovial and endothelial cells leading to local production of IL-6 in joints affected by inflammatory processes such as rheumatoid arthritis.[1]

CLINICAL EVIDENCE

Rheumatoid Arthritis

Huizinga et al, published the analysis for the 2-year and 3-year results of the double-blind, placebo-controlled, parallel-group ACT-RAY trial that assessed the efficacy and safety of tocilizumab (TCZ) plus methotrexate/placebo (MTX/PBO) and the course of disease activity in patients who discontinued TCZ due to sustained remission. [8] During the first 24 weeks, all patients (N=556) were randomized either to continue oral MTX with the addition of open-label TCZ 8 mg/kg intravenously every 4 weeks (add-on strategy) or switch to TCZ alone with PBO (switch strategy). Between weeks 24 and 52, treatment with TCZ plus blinded MTX/PBO continued unchanged; however, if Disease Activity Score in 28 joints based on erythrocyte sedimentation rate (DAS28-ESR) was >3.2 at week 24, an open-label conventional synthetic disease-modifying antirheumatic drug (csDMARD) (sulfasalazine, leflunomide, hydroxychloroquine or azathioprine; choice and dose at investigator's discretion) was added. If DAS28-ESR was >3.2 at week 36 with an added csDMARD, the patient was moved to the maintenance arm (TCZ+blinded MTX/PBO + open-label csDMARD) for the remainder of the study, with the option to receive an additional open-label csDMARD per the investigator's discretion. Between weeks 52 and 104, open-label treatment was adapted based on response every 12 weeks, and patients continued the study in one of four treat-to-target strategies. The primary endpoint has previously been published. [9] Secondary endpoints included rate and time to TCZ-free and drug-free remission, time to flare after TCZ-free remission, and time to restart of treatment after TCZ-free remission. Radiographic endpoints included progression of joint destruction based on the Genant-modified Sharp Score (GSS) at weeks 24, 52, and 104 among others. Of the randomized patients, 76% (472) completed year 2, where 50.4% discontinued TCZ by week 104, with no significant difference between treatment groups [129 (53.1%) add-on vs. 109 (47.6%) switch patients; p = 0.170)]. Twenty-eight (11.8%) of 238 patients achieved total drug-free remission due to sustained achievement of DAS28-ESR <2.6. A significantly higher proportion of patients in the add-on arm achieved drug-free remission compared with patients in the switch arm [21/243 (8.6%) vs 7/229 (3.1%); p=0.010]. A total of 200 patients subsequently flared following TCZ-free remission, with 82.5% (95% CI 75.4% to 88.5%) and 88.5% (95% CI 81.5% to 93.7%) of patients in the add-on and switch arms, respectively, experiencing flare within 52 weeks after achieving TCZ-free remission. At week 104, the majority of patients demonstrated minimal progression of radiographic structural damage. The adjusted mean change in total GSS was 0.35 for add-on and 0.95 for switch (p=0.034). The overall safety profile was similar for both treatment groups. The frequencies of adverse events (AE), serious AE (SAE), and discontinuations due to AEs were similar between the two treatment groups. The investigators concluded that treat-to-target strategies could be successful with TCZ to achieve a sustained free remission after discontinuation. TCZ free remission was maintained on average of three months prior to flaring, which then was controlled with resumption of TCZ.

NCCN Recommended Uses

According to the NCCN Drugs & Biologics Compendium, NCCN recommends (2A) tocilizumab for the treatment of:

- Acute lymphoblastic leukemia
  - Consider as supportive care for patients who develop refractory cytokine release syndrome (CRS) related to blinatumomab therapy.

- Castleman's disease
  - Subsequent therapy as a single agent for multicentric Castleman's Disease (CD) that has progressed following treatment of relapsed/refractory or progressive disease
  - Second-line therapy as a single agent for relapsed or refractory unicentric CD for patients who are human immunodeficiency virus-negative and human herpesvirus-8-negative
- Acute graft-versus-host disease (GVHD) - as additional therapy in conjunction with systemic corticosteroids following no response (steroid-refractory disease) to first-line therapy options.
  - Therapy for steroid-refractory acute GVHD is often used in conjunction with the original immunosuppressive agent
- Immune checkpoint inhibitor-related toxicities - Consider adding tocilizumab for the management of immunotherapy-related:
  - Severe immunotherapy-related inflammatory arthritis if symptoms do not improve within 2 weeks of starting high-dose corticosteroids
- CAR T-Cell-Related Toxicities
  - Prolonged (>3 days) G1 cytokine release syndrome (CRS) in patients with significant symptoms and/or comorbidities
    - Assess need for subsequent dosing after each dose (no more than 3 doses in 24 hours up to a maximum of 4 doses)
  - G2-4 cytokine release syndrome (CRS)
    - Assess need for subsequent dosing after each dose (no more than 3 doses in 24 hours up to a maximum of 4 doses)
  - G1-4 neurotoxicity as additional single-dose therapy if concurrent CRS
    - Repeat dosing as needed (no more than 3 doses in 24 hours up to a maximum of 4 doses) if not responsive to IV fluids or increasing supplemental oxygen

Professional Societies

American College of Rheumatology (ACR)

Rheumatoid Arthritis

The 2015 American College of Rheumatology (ACR) RA treatment guideline addresses the use of DMARDS, biologics, tofacitinib, and glucocorticoids in early (<6 months) and established (≥ 6 months) RA and the use of various treatment approaches in frequently encountered clinical scenarios, including treat-to-target, switching between therapies, tapering of therapy, the use of biologics and DMARDs in high-risk RA patients, vaccination in patients with RA receiving DMARDs or biologics, TB screening with biologics or tofacitinib, and laboratory monitoring with DMARDs.[10] The guideline recommendations apply to common clinical situations, since the panel considered issues common to most patients, not exceptions. Recommendations are classified as either strong or conditional. A strong recommendation means that the panel was confident that the desirable effects of following the recommendation outweigh the undesirable effects (or vice versa), so the course of action would apply to most patients, and only a small proportion would not want to follow the recommendation. A conditional recommendation means that the desirable effects of following the recommendation probably outweigh the undesirable effects, so the course of action would apply to the majority of patients, but some may not want to follow the recommendation. As a result, conditional recommendations are preference sensitive and warrant a shared decision-making approach.

Supplementary Appendix 5, of the 2015 ACR RA guideline, summarizes recommendations for patients with early RA, established RA, and high-risk comorbidities:[10]

Recommendations for Early RA Patients

- The panel strongly recommends using a treat-to-target strategy rather than a non-targeted approach, regardless of disease activity level. The ideal target should be low disease activity or remission, as determined by the clinician and the patient. In some cases, another target may be chosen because risk tolerance by patients or comorbidities may mitigate the usual choices.
- For DMARD-naïve patients with early, symptomatic RA, the panel strongly recommends DMARD monotherapy over double or triple DMARD therapy in patients with low disease activity and conditionally recommends DMARD monotherapy over double or triple DMARD therapy in patients with moderate or high disease activity. Methotrexate should be the preferred initial therapy for most patients with early RA with active disease.

- For patients with moderate or high disease activity despite DMARD therapy (with or without glucocorticoids), the panel strongly recommends treatment with a combination of DMARDs *or* a TNFi *or* a non-TNF biologic, with or without methotrexate (MTX) in no particular order of preference, rather than continuing DMARD monotherapy alone. Biologic therapy should be used in combination with MTX over biologic monotherapy, when possible, due to superior efficacy.
- For patients with moderate or high disease activity despite any of the above DMARD or biologic therapies, the panel conditionally recommends adding low-dose glucocorticoids (defined as ≤10 mg/day of prednisone or equivalent). Low-dose glucocorticoids may also be used in patients who need a bridge until realizing the benefits of DMARD therapy. The risk/benefit ratio of glucocorticoid therapy is favorable as long as the dose is low and the duration of therapy is short.
- For patients experiencing a flare of RA, the panel conditionally recommends adding short-term glucocorticoids (< 3 months of treatment) at the lowest possible dose for the shortest possible duration, to provide a favorable benefit-risk ratio for the patient.

Recommendations for Established RA Patients

- The panel strongly recommends using a treat-to-target strategy rather than a non-targeted approach, regardless of disease activity level. The ideal target should be low disease activity or remission, as determined by the clinician and the patient. In some cases, however, another target may be chosen because tolerance by patients or comorbidities may mitigate the usual choices.
- For DMARD-naïve patients with low disease activity, the panel strongly recommends using DMARD monotherapy over a TNFi. For DMARD-naïve patients with moderate or high disease activity, the panel conditionally recommends DMARD monotherapy over double or triple DMARD therapy and DMARD monotherapy over tofacitinib. In general, MTX should be the preferred initial therapy for most patients with established RA with active disease.
- For patients with moderate or high disease activity despite DMARD monotherapy including methotrexate, the panel strongly recommends using combination DMARDs or adding a TNFi or a non-TNF biologic or tofacitinib (all choices with or without methotrexate) in no particular order of preference, rather than continuing DMARD monotherapy alone. Biologic therapy should be used in combination with MTX over biologic monotherapy, when possible, due to its superior efficacy.

For all scenarios for established RA below, treatment may be with or without MTX:

- For moderate or high disease activity despite TNFi therapy in patients currently not on a DMARD, the panel strongly recommends that one or two DMARDs be added to TNFi therapy rather than continuing TNFi therapy alone.
- If disease activity is moderate or high despite single TNFi biologic therapy, the panel conditionally recommends using a non-TNF biologic.
- If disease activity is moderate or high despite non-TNF biologic therapy, the panel conditionally recommends using another non-TNF biologic. However, if a patient has failed multiple non-TNF biologics and they are TNFi-naïve with moderate or high disease activity, the panel conditionally recommends treatment with a TNFi.
- For patients with moderate or high disease activity despite prior treatment with at least one TNFi and at least one non-TNF-biologic (sequentially, not combined), the panel conditionally recommends first treating with another non-TNF biologic. However, when a non-TNF biologic is not an option (e.g., patient declines non-TNF biologic therapy due to inefficacy or side effects), the panel conditionally recommends treatment with tofacitinib.
- If disease activity is moderate or high despite the use of multiple (2+) TNFi therapies (in sequence, not concurrently), the panel conditionally recommends non-TNF biologic therapy and then conditionally treating with tofacitinib when a non-TNF biologic is not an option.
- If disease activity is moderate or high despite any of the above DMARD or biologic therapies, the panel conditionally recommends adding low-dose glucocorticoids.
- If patients with established RA experience an RA flare while on DMARD, TNFi, or non-TNF biologic therapy, the panel conditionally recommends adding short-term glucocorticoids (< 3 months of treatment) at the lowest possible dose and for shortest possible duration to provide the best benefit-risk ratio for the patient.
- In patients with established RA and low disease activity but not remission, the panel strongly recommends continuing DMARD therapy, TNFi, non-TNF biologic or tofacitinib rather than discontinuing respective medication.
- In patients with established RA currently in remission, the panel conditionally recommends tapering DMARD therapy, TNFi, non-TNF biologic, or tofacitinib.

- The panel strongly recommends not discontinuing all therapies in patients with established RA in disease remission.

Recommendations for RA Patients with High-Risk Comorbidities

- Congestive Heart Failure:
  - In patients with established RA with moderate or high disease activity and New York Heart Association (NYHA) class III or IV congestive heart failure (CHF), the panel conditionally recommends using combination DMARD therapy, a non-TNF biologic, or tofacitinib rather than a TNFi.
  - If patients in this population are treated with a TNFi and their CHF worsens while on the TNFi, the panel conditionally recommends switching to combination DMARD therapy, a non-TNF biologic, or tofacitinib rather than a different TNFi.
- Hepatitis B:
  - In patients with established RA with moderate or high disease activity and evidence of active hepatitis B infection (hepatitis surface antigen positive > 6 months), who are receiving or have received effective antiviral treatment, the panel strongly recommends treating them the same as patients without this condition.
  - For a patient with natural immunity from prior exposure to hepatitis B (i.e., HB core antibody and HBS antibody positive and normal liver function tests), the panel recommends the same therapies as those without such findings as long as the patient's viral load is monitored.
  - For patients with chronic hepatitis B who are untreated, referral for antiviral therapy is appropriate prior to immunosuppressive therapy.
- Hepatitis C:
  - In patients with established RA with moderate or high disease activity and evidence of chronic hepatitis C virus (HCV) infection, who are receiving or have received effective antiviral treatment, the panel conditionally recommends treating them the same as the patients without this condition.
  - The panel recommends that rheumatologists work with gastroenterologists and/or hepatologists who would monitor patients and reassess the appropriateness of antiviral therapy. This is important considering the recent availability of highly effective therapy for HCV, which may lead to a greater number of HCV patients being treated successfully.
  - If the same patient is not requiring or receiving antiviral treatment for their hepatitis C, the panel conditionally recommends using DMARD therapy rather than TNFi.
- Malignancy:
  - Previous Melanoma and Non-Melanoma Skin Cancer:
    - In patients with established RA and moderate or high disease activity and a history of previously treated or untreated skin cancer (melanoma or non-melanoma), the panel conditionally recommends the use of DMARD therapy over biologics or tofacitinib.
  - Previous Lymphoproliferative Disorders:
    - In patients with established RA with moderate or high disease activity and a history of a previously treated lymphoproliferative disorder, the panel strongly recommends using rituximab rather than a TNFi and conditionally recommends using combination DMARD therapy, abatacept or tocilizumab rather than TNFi.
  - Previous Solid Organ Cancer:
    - In patients with established RA with moderate or high disease activity and previously treated solid organ cancer, the panel conditionally recommends that they be treated for RA just as one would treat an RA patient without a history of solid organ cancer.
- Serious Infections:
  - In patients with established RA with moderate or high disease activity and previous serious infection(s), the panel conditionally recommends using combination DMARD therapy or abatacept rather than TNFi.

Juvenile Idiopathic Arthritis

The 2019 American College of Rheumatology (ACR) and Arthritis Foundation guideline for the treatment of juvenile idiopathic arthritis includes the use of tocilizumab..[7]

- General medication recommendations for children and adolescents with JIA and polyarthritis:
  - Biologic DMARDS:

        - In children and adolescents with JIA and polyarthritis initiating treatment with a biologic (etanercept, adalimumab, golimumab, abatacept, or tocilizumab) combination therapy with a DMARD is conditionally recommended over biologic monotherapy
- General guidelines for the initial and subsequent treatment of children and adolescents with JIA and polyarthritis
    - Subsequent therapy: Moderate/high disease activity (cJADAS-10 >2.5)
        - If patient is receiving DMARD monotherapy: Adding a biologic to original DMARD is conditionally recommended over changing to a second DMARD. Adding a biologic is conditionally recommended over changing to triple DMARD therapy.
        - If patient is receiving first TNFi (± DMARD): Switching to a non-TNFi biologic (tocilizumab or abatacept) is conditionally recommended over switching to a second TNFi. A second TNFi may be appropriate for patients with good initial response to their first TNFi (i.e., secondary failure).
        - If patient is receiving second biologic: Using TNFi, abatacept, or tocilizumab (depending on prior biologics received) is conditionally recommended over rituximab.

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Actemra is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more disease-modifying anti-rheumatic drugs (DMARDs). For this indication, Actemra may be used alone or in combination with methotrexate or other DMARDs.[1]

Actemra is also indicated for the treatment of active polyarticular juvenile idiopathic arthritis and active systemic juvenile idiopathic arthritis in patients 2 years of age and older. For these indications, Actemra may be used alone or in combination with methotrexate.[1]

Actemra is also indicated for the treatment of chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome in adults and pediatric patients 2 years of age and older. Actemra may be used alone or in combination with corticosteroids.[1]

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Medicare does not have a National Coverage Determination (NCD) for Actemra® (tocilizumab) . Local Coverage Determinations (LCDs) do not exist at this time.

In general, Medicare covers outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. Refer to the Medicare Benefit Policy Manual, Chapter 15, §50 - Drugs and Biologicals.

(Accessed February 4, 2020)

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POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
TBD	Added NCCN recommended uses. Added acute GVHD and immunotherapy-related cardiotoxicity.

INSTRUCTIONS FOR USE

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.