

# Orencia® (Abatacept) Injection for Intravenous Infusion

**Policy Number:** CS2024D0039AA  
**Effective Date:** November 1, 2024

[Instructions for Use](#)

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| Commercial Policy   |
|---|
| <ul style="list-style-type: none"> <li><a href="#">Orencia® (Abatacept) Injection for Intravenous Infusion</a></li> </ul> |

## Application

This Medical Benefit Drug Policy does not apply to the states listed below; refer to the state-specific policy/guideline, if noted:

| State          | Policy/Guideline   |
|----------------|--|
| Indiana        | Refer to the state’s Medicaid clinical policy  |
| Kansas         | Refer to the state’s Medicaid clinical policy  |
| Louisiana      | Refer to the state’s Medicaid clinical policy  |
| North Carolina | None   |
| Ohio           | <a href="#">Immunomodulatory Agents for Systemic Inflammatory Diseases (for Ohio Only)</a> |
| Pennsylvania   | Refer to the state’s Medicaid clinical policy  |
| Texas          | Refer to drug specific criteria found within the Texas Medicaid Provider Procedures Manual |
| Washington     | Refer to the state’s Medicaid clinical policy  |

## Coverage Rationale

This policy refers to Orencia (abatacept) injection for intravenous infusion. Orencia (abatacept) for self-administered subcutaneous injection is obtained under the pharmacy benefit.

**Orencia is proven and medically necessary for the treatment of:**

- **Polyarticular juvenile idiopathic arthritis when all of the following criteria are met:**<sup>2,5,15,20</sup>
  - For **initial therapy**, all of the following:
    - Diagnosis of moderately to severely active polyarticular juvenile idiopathic arthritis (PJIA); **and** Orencia is initiated and titrated according to U.S. Food and Drug Administration (FDA) labeled dosing for polyarticular juvenile idiopathic arthritis; **and**
    - Patient is not receiving Orencia in combination with either of the following:
      - Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), adalimumab, Cimzia (certolizumab), Simponi (golimumab)]
      - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib), Rinvoq (upadacitinib)]<sup>18</sup>



- and**
    - Prescribed by or in consultation with **one** of the following:
      - Rheumatologist
      - Dermatologist
    - and**
    - Initial authorization is for no more than 12 months
  - For **continuation of therapy**, **all** of the following:
    - Patient has previously received Orencia injection for intravenous infusion; **and**
    - Documentation of a positive clinical response; **and**
    - Orencia is dosed according to FDA labeled dosing for psoriatic arthritis; **and**
    - Patient is not receiving Orencia in combination with any of the following:
      - Biologic DMARD [e.g., Enbrel (etanercept), adalimumab, Cimzia (certolizumab), Simponi (golimumab)]
      - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib), Rinvoq (upadacitinib)]
      - Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]
    - and**
    - Authorization is for no more than 12 months
- **Chronic graft-versus-host disease (GVHD) when all of the following criteria are met:**
  - For **initial therapy**, **all** of the following:
    - Diagnosis of steroid-refractory chronic GVHD; **and**
    - **One** of the following:
      - Patient is receiving Orencia in combination with systemic corticosteroids
      - Patient is intolerant to systemic corticosteroid therapy
    - and**
    - Initial authorization is for no more than 12 months
  - For **continuation of therapy**, **all** of the following:
    - Documentation of positive clinical response; **and**
    - Patient continues to experience chronic GVHD; **and**
    - **One** of the following:
      - Patient is receiving Orencia in combination with systemic corticosteroids
      - Patient is intolerant to systemic corticosteroid therapy
      - Patient has been successfully tapered off of corticosteroid therapy
    - and**
    - Authorization is for no more than 12 months
- **Acute graft-versus-host disease (aGVHD) when all of the following criteria are met:**
  - Patient is at least 2 years old; **and**
  - One of the following:
    - Patient is undergoing hematopoietic stem cell transplantation (HSCT) from a matched donor
    - Patient is undergoing HSCT from a 1 allele-mismatched unrelated donor
  - and**
  - Patient is receiving Orencia in combination with a calcineurin inhibitor; **and**
  - Patient is receiving Orencia in combination with methotrexate
  - Authorization is for no more than 4 doses
- **Immune checkpoint inhibitor-related toxicities when all of the following criteria are met:**<sup>67</sup>
  - Patient has recently received checkpoint inhibitor therapy [e.g., Keytruda (Pembrolizumab), Opdivo (Nivolumab)]; **and**
  - Diagnosis of severe (G3) or life threatening (G4) immunotherapy-related myocarditis, pericarditis, arrhythmias; **or** impaired ventricular function, or conduction abnormalities; **and**
  - No improvement of toxicity within 24 hours of starting pulse-dose methylprednisolone; **and**
  - History of failure, contraindication, or intolerance to infliximab (e.g., Inflectra, Remicade); **and**
  - Authorization is for no more than 4 doses

**Orencia is unproven and not medically necessary for the treatment of:**

- Multiple sclerosis
- Systemic lupus erythematosus
- Uveitis associated with Behçet's disease

## Applicable Codes

The following list(s) of procedure 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 Guidelines may apply.

| HCPCS Code | Description                 |
|------------|-----------------------------|
| J0129      | Injection, abatacept, 10 mg |

| Diagnosis Code | Description  |
|----------------|--|
| D89.811        | Chronic graft-versus-host disease  |
| D89.812        | Acute on chronic graft versus host disease: (acute exacerbation of a chronic GVHD status, or acute manifestation of a preexisting GVHD associated condition) |
| L40.50         | Arthropathic psoriasis, unspecified  |
| L40.51         | Distal interphalangeal psoriatic arthropathy   |
| L40.52         | Psoriatic arthritis mutilans   |
| L40.53         | Psoriatic spondylitis  |
| L40.54         | Psoriatic juvenile arthropathy   |
| L40.59         | Other psoriatic arthropathy  |
| 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  |
| 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  |

| Diagnosis Code | Description  |
|----------------|--|
| 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                 |
| 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                   |

| Diagnosis Code | Description   |
|----------------|---|
| 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                     |
| 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   |

| Diagnosis Code | Description  |
|----------------|--|
| 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                           |
| 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            |
| M05.769        | Rheumatoid arthritis with rheumatoid factor of unspecified knee without organ or systems involvement     |

| Diagnosis Code | Description  |
|----------------|--|
| 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             |
| M05.7A         | Rheumatoid arthritis with rheumatoid factor of other specified site 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  |
| M05.8A         | Other rheumatoid arthritis with rheumatoid factor of other specified site                                      |
| 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  |
| 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  |



| Diagnosis Code | Description  |
|----------------|--|
| 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             |
| M06.0A         | Rheumatoid arthritis without rheumatoid factor, other specified site       |
| M06.1          | Adult-onset Still's disease  |
| 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                           |
| 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                       |
| M06.8A         | Other specified rheumatoid arthritis, other specified site                 |
| M06.9          | Rheumatoid arthritis, unspecified  |
| M08.00         | Unspecified juvenile rheumatoid arthritis of unspecified site              |
| M08.0A         | Unspecified juvenile rheumatoid arthritis, other specified 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            |

| Diagnosis Code | Description   |
|----------------|---|
| 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                 |
| 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             |
| M08.2A         | Juvenile rheumatoid arthritis with systemic onset, other specified site       |

| Diagnosis Code | Description   |
|----------------|---|
| 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     |
| M08.9A         | Juvenile arthritis, unspecified, other specified site |
| 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     |

| Diagnosis Code | Description  |
|----------------|--|
| 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              |

## Background

Orencia is a fully human, soluble, fusion protein, selective co-stimulation modulator which inhibits T lymphocyte activation by binding to CD80 and CD86, thereby blocking interaction with CD28.<sup>6,7</sup> This interaction provides a costimulatory signal necessary for full activation of T lymphocytes.<sup>5</sup>

## Clinical Evidence

### Proven

#### *Psoriatic Arthritis*

A randomized, placebo-controlled Phase 3 trial assessed the efficacy and safety of abatacept in adult patients (> 18 years old) with psoriatic arthritis.<sup>22</sup> Patients were randomly assigned in a double-blind manner to receive either subcutaneous abatacept 125mg weekly or placebo for 24 weeks. Patients who had not achieved  $\geq 20\%$  improvement in swollen and tender joint counts from baseline to week 16 were switched to open-label abatacept weekly for 28 weeks. At the end of the open-label period, patients had the option of entering a 1-year, long-term extension. Primary efficacy endpoint was the proportion of patients with ACR20 responses at week 24. Abatacept significantly increased ACR20 response versus placebo at week 24 (39.4% vs 22.3%;  $p < 0.001$ ). Although abatacept numerically increased Health Assessment Questionnaire–Disability Index response rates (reduction from baseline  $\geq 0.35$ ) at week 24, this was not statistically significant (31.0% vs 23.7%;  $p = 0.097$ ). The benefits of abatacept were seen in ACR20 responses regardless of TNF inhibitor exposure and in other musculoskeletal manifestations, but significance could not be attributed due to ranking below Health Assessment Questionnaire–Disability Index response in hierarchical testing. The benefit on psoriasis lesions was modest. Efficacy was maintained or improved up to week 52. Abatacept was well tolerated with no new safety signals. The authors concluded that abatacept treatment of PsA in achieved its primary end point, ACR20 response, showed beneficial trends overall in musculoskeletal manifestations and was well tolerated. There was only a modest impact on psoriasis lesions.

#### *Rheumatoid Arthritis*

In a Phase 3b double-blind, double-dummy, 6 month study, Genovese et al, compared the efficacy and safety of subcutaneous (SC) and intravenous (IV) abatacept.<sup>26</sup> Patients with rheumatoid arthritis (RA) and with inadequate response to methotrexate (MTX), were randomized to receive either 125mg SC abatacept on days 1 and 8 and weekly thereafter (plus an IV loading dose 10mg/kg on day 1) or IV abatacept 10mg/kg on days 1, 15, and 29 and every 4 weeks thereafter. The primary end point for determining the noninferiority of SC abatacept to IV abatacept was the proportion of patients in each group meeting the American College of Rheumatology 20% improvement criteria (achieving an ACR20 response) at month 6. Of 1,457 patients, 693 of 736 (94.2%) treated with SC abatacept and 676 of 721 (93.8%) treated with IV abatacept completed 6 months. At month 6, 76.0% (95% confidence interval 72.9, 79.2) of SC abatacept–treated patients versus 75.8% (95% confidence interval 72.6, 79.0) of IV abatacept–treated patients achieved an ACR20 response (estimated difference between groups 0.3% [95% confidence interval – 4.2, 4.8]), confirming noninferiority of SC abatacept to IV abatacept. Onset and magnitude of ACR responses and disease activity and physical function improvements were comparable between the SC and IV abatacept–treated groups. The proportions of adverse events (AEs) and serious AEs over 6 months were 67.0% and 4.2%, respectively, in the SC abatacept–treated group and 65.2% and 4.9%, respectively, in the IV abatacept–treated group, with comparable frequencies of serious infections, malignancies, and autoimmune events between groups. SC injection site reactions (mostly mild) occurred in 19 SC abatacept (IV placebo)–treated patients (2.6%) and 18 IV abatacept (SC placebo)–treated patients (2.5%). Abatacept-induced antibodies occurred in 1.1% of SC abatacept–treated patients and 2.3% of IV abatacept–treated patients. No major differences in ACR responses were observed between intravenous and subcutaneous treatment groups in

subgroups based on weight categories (less than 60 kg, 60 to 100 kg, and more than 100 kg). The authors concluded that SC abatacept provides efficacy and safety comparable with that of IV abatacept.

A randomized, multicenter, active controlled Phase 3b trial, the Assessing Very Early Rheumatoid arthritis Treatment (AVERT) trial (n = 351) of 24 months, with a 12-month, double-blind treatment period, evaluated clinical remission with subcutaneous abatacept plus methotrexate (MTX) and abatacept monotherapy in patients with early rheumatoid arthritis (RA), and maintenance of remission following the rapid withdrawal of all RA treatment.<sup>17</sup> During the 12 month treatment period, patients were randomized (1:1:1) to receive abatacept plus MTX (n = 119), abatacept monotherapy (n = 116), or MTX monotherapy (n = 116), stratified by corticosteroid use at baseline. Patients with a Disease Activity Score (DAS) 28 (CRP) < 3.2 at month 12 could enter the 12-month withdrawal period where abatacept was immediately stopped and MTX and steroids tapered over 1 month. Patients with DAS28 ≥ 3.2 discontinued the study. After month 15, patients in the withdrawal period who experienced a flare could re-start open label SC abatacept 125mg plus MTX. Co-primary endpoints were the proportion of randomized and treated patients in DAS-defined remission (CRP < 2.6) at month 12 and months 12 and 18 for abatacept plus MTX versus MTX. For the abatacept plus MTX versus MTX, DAS28 (CRP) < 2.6 was achieved in 60.9% versus 45.2% (p = 0.010) at 12 months, and following treatment withdrawal, in 14.8% versus 7.8% (p = 0.045) at both 12 and 18 months. DAS28 (CRP) < 2.6 was achieved for abatacept monotherapy in 42.5% (month 12) and 12.45% (both months 12 and 18). Both abatacept arms had a safety profile comparable to MTX alone. The authors concluded that abatacept plus MTX demonstrated efficacy compared with MTX alone in early RA, with a comparable safety profile to MTX. Abatacept achieved some sustained remission following withdrawal of all RA therapy in the respective groups.

### ***Polyarticular Juvenile Idiopathic Arthritis***

Brunner et al investigated the pharmacokinetics, effectiveness, and safety of subcutaneous (SC) abatacept in patients with polyarticular juvenile idiopathic arthritis (PJIA) over 24 months.<sup>27</sup> This Phase 3, open-label, international, multicenter, single-arm study enrolled patients in two cohorts: cohort 1, ages 6 to 17 years and cohort 2, ages 2 to 5 years, each in whom treatment with ≥ 1 DMARD was unsuccessful. Patients received weight-tiered SC abatacept weekly: 10 to < 25 kg (50 mg), 25 to < 50 kg (87.5 mg), ≥ 50 kg (125 mg). Patients who had met the JIA–American College of Rheumatology 30% improvement criteria (achieved a JIA-ACR 30 response) at month 4 were given the option to continue SC abatacept to month 24. The primary end point was the abatacept steady-state serum trough concentration ( $C_{\text{minss}}$ ) in cohort 1 at month 4. Other outcome measures included JIA-ACR 30, 50, 70, 90, 100, and inactive disease status, the median Juvenile Arthritis Disease Activity Score in 71 joints using the C-reactive protein level (JADAS-71–CRP) over time, safety, and immunogenicity. The median abatacept  $C_{\text{minss}}$  at month 4 and at month 24 was above the target therapeutic exposure (10 µg/ml) in both cohorts. The percentage of patients who had achieved JIA-ACR 30, 50, 70, 90, or 100 responses or had inactive disease responses at month 4 (intent-to-treat population) was 83.2%, 72.8%, 52.6%, 28.3%, 14.5%, and 30.1%, respectively, in cohort 1 (n = 173) and 89.1%, 84.8%, 73.9%, 58.7%, 41.3%, and 50.0%, respectively, in cohort 2 (n = 46); the responses were maintained to month 24. Improvements were sustained to month 24, at which time 27 of 173 patients (cohort 1) and 11 of 22 patients (cohort 2) had achieved JADAS-71–CRP remission. No unexpected adverse events were reported; 4 of 172 patients (2.3%) in cohort 1 and 4 of 46 (8.7%) in cohort 2 developed anti-abatacept antibodies, with no clinical effects. The JIA ACR 30, 50, 70 responses assessed at 4 months in the 2- to 17-year-old patients were consistent with the results from the intravenous study, JIA-1.

The long-term extension (LTE) phase of a pivotal phase III study examining the efficacy and safety of abatacept in patients with juvenile idiopathic arthritis (JIA) reported the efficacy and safety outcomes of treatment (up to 10mg/kg every 4 weeks), with or without non-biologic DMARDs, for up to 7 years of follow-up.<sup>19</sup> One hundred fifty-three of 190 patients (80.5%) entered the LTE phase, with only 69 patients (36.3%) completing the study. The overall incidence rate (events per 100 patient-years) of adverse events decreased from 433.61 events during the short-term phase compared to 132.39 events during the LTE phase. Serious adverse events (6.82 vs. 5.60), malignancies (1.12 vs. 0), and autoimmune events (2.26 vs. 1.18) also were reduced. Serious infections were slightly increased (1.13 vs. 1.72). American College of Rheumatology (ACR) Pediatric 30 (Pedi 30), Pedi 70, responses, and clinically inactive disease status were maintained throughout the extension phase in those patients continuing to receive therapy. Improvements in the Child Health Questionnaire summary scores were also maintained over the course of the study. The authors concluded that long-term abatacept therapy, for up to 7 years, was associated with consistent safety, efficacy, and quality of life benefits in patients with JIA.

### ***Prophylaxis of Acute Graft Versus Host Disease***

In a multicenter, two cohort clinical study (GVHD-1), abatacept, in combination with a calcineurin inhibitor (CNI) and methotrexate (MTX), was evaluated in patients age 6 years and older who underwent hematopoietic stem cell transplantation (HSCT) from a matched or 1 allele-mismatched unrelated donor (URD).<sup>31</sup> The two cohorts included an open-label, single-arm study for 43 patients who underwent a 7 of 8 Human Leukocyte Antigen (HLA)-matched HSCT (7 of 8 cohort) and a randomized (1:1), double-blind, placebo-controlled study of patients who underwent an 8 of 8 HLA-

matched HSCT who received Orencia or placebo in combination with a CNI and MTX (8 of 8 cohort). In both the 7/8 and 8/8 cohorts, abatacept was administered at a dose of 10 mg/kg (1,000 mg maximum dose) as an intravenous infusion over 60 minutes, beginning on the day before transplantation (Day -1), followed by administration on Days 5, 14, and 28 after transplantation. Efficacy was established based on overall survival (OS) and grade II-IV aGVHD free survival (GFS) results assessed at Day 180 post-transplantation. Abatacept plus CNI and MTX did not significantly improve grade III-IV GFS versus placebo plus CNI and MTX at Day 180 post-transplantation. In the 8/8 cohort, the efficacy of abatacept plus CNI and MTX at Day 180 post-transplantation for grade III-IV GFS rate and hazard ratio, grade II-IV GFS rate and hazard ratio, and OS rate and hazard ratio were 87% and 0.55, 50% and 0.54, and 97% and 0.33, respectively. In the placebo plus CNI and MTX, the efficacy results at Day 180 post-transplantation for grade III-IV GFS rate, grade II-IV GFS rate, and OS rate were 75%, 32%, and 84%, respectively. In an exploratory analysis of the 7/8 cohort of abatacept-treated patients (n = 43), the rates of grade III-IV GVHD-free survival, grade II-IV GVHD-free survival, and overall survival at Day 180 post-transplantation were 95%, 53%, and 98%, respectively.

The GVHD-2 study was a clinical study that used data from the Center for International Blood and Marrow Transplant Research (CIBMTR).<sup>32</sup> The study analyzed outcomes of abatacept in combination with a CNI and MTX, versus a CNI and MTX alone, for the prophylaxis of aGVHD, in patients 6 years of age or older who underwent HSCT from a 1 allele-mismatched URD between 2011 and 2018. The abatacept plus CNI and MTX-treated group (n = 54) included 42 patients from GVHD-1, in addition to 12 patients treated with abatacept outside of GVHD-1. The comparator group (n = 162) was randomly selected in a 3:1 ratio to the abatacept-treated group from the CIBMTR registry from patients who had not received abatacept during the study period. Analyses used propensity score matching and inverse probability of treatment weighting to help address the impact of selection bias. Efficacy was based on OS at Day 180 post-HSCT. The OS rate at Day 180 in the abatacept plus CNI and MTX group was 98% and the OS rate at Day 180 in the CNI and MTX group was 75%.

### ***NCCN Recommended Uses***

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

- Chronic graft-versus-host disease (GVHD) as additional therapy in conjunction with systemic corticosteroids following no response (steroid-refractory disease) to first-line therapy options
- Immune checkpoint inhibitor-related toxicities – Used as additional immunosuppression for the management of immunotherapy-related:
  - Myocarditis as a single agent if no improvement within 24-48 hours of starting high-dose methylprednisolone
  - Concomitant myositis and myocarditis in combination with ruxolitinib

### ***Unproven Multiple Sclerosis***

Khoury et al conducted ACCLAIM (A Cooperative Clinical Study of Abatacept in Multiple Sclerosis), a Phase II, randomized, double-blind, placebo-controlled, multi-center trial.<sup>23</sup> In the trial, 65 of 123 planned participants with relapsing-remitting multiple sclerosis (RRMS) were randomized to monthly intravenous infusions of abatacept or placebo for 24 weeks and then switched to the other treatment at 28 weeks. The primary endpoint was the mean number of new gadolinium-enhancing (Gd+) lesions obtained on magnetic resonance imaging (MRI) scans performed every 4 weeks. There was not a statistically significant difference observed between the abatacept and placebo groups for in mean number of new Gd+ MRI lesions. Additionally, no statistically significant differences were found in other MRI and clinical parameters of RRMS disease activity. The authors conclude that the ACCLAIM study did not demonstrate efficacy of abatacept in reducing the number of new Gd+ MRI lesions, or clinical measures of disease activity in RRMS.

A randomized, double-blind, placebo-controlled Phase II study of 128 patients was initiated to evaluate the use of abatacept in patients with relapsing-remitting multiple sclerosis.<sup>8</sup> The primary objective was to demonstrate the relative safety and preliminary clinical efficacy of 2 different doses of abatacept (10 mg/kg and 2 mg/kg) compared with placebo in subjects with relapsing-remitting MS by showing a reduction in the cumulative number of new or recurrent gadolinium-enhancing lesions on T1-weighted (Gd-T1) magnetic resonance imaging (MRI) over Day 85 through Day 225. However, the study terminated early because the Drug Safety Monitoring Board (DSMB) responsible for reviewing blinded safety data from the study expressed concerns that one of the treatment groups (subsequently found to be the 2 mg/kg abatacept group) had more subjects exhibiting an increase in Gd-enhancing T1-weighted MRI lesions and at least 1 multiple sclerosis exacerbation.

### ***Systemic Lupus Erythematosus***

A Phase II multi-center, randomized, double-blind, placebo-controlled study was conducted to evaluate the efficacy and safety of abatacept (n = 121) versus placebo (n = 59) for patients with systemic lupus erythematosus (SLE).<sup>9</sup> The abatacept group received the study drug (weight-tiered dosing) administered intravenously on Day 1, 15, 29, and every 28

days thereafter. Planned treatment duration for the double-blind period was 12 months. Prednisone or prednisone equivalent oral tablets was given on a defined tapering schedule at the time of randomization along with the study medication or placebo. The study failed to meet the primary efficacy endpoint, which was to assess the proportion of subjects who experienced a new SLE flare, based on adjudication of all BILAG 'A' or 'B' events, following resolution of the entry flare and/or the start of prednisone or prednisone equivalent taper schedule across the 12-month double-blind treatment period.

## ***Uveitis Associated With Behçet's Disease***

Blockade of antigen non-specific co-stimulatory signals is theorized to be effective for Behçet's disease.<sup>13,14</sup> However, there is currently insufficient clinical evidence of the safety and efficacy of abatacept in published peer-reviewed medical literature for this condition.

## **Professional Societies**

### ***Psoriatic Arthritis***

In 2018, the American College of Rheumatology and the National Psoriasis Foundation published treatment guideline for the treatment of psoriatic arthritis. In regards to psoriatic arthritis (PsA) and abatacept, the guidelines state:

- Recommendations for treatment of patients with active psoriatic arthritis despite treatment with an oral small molecule (OSM):
  - Switch to a TNFi biologic over abatacept:
    - Conditional recommendation based on low-quality evidence; may consider abatacept if the patient has contraindications to TNFi biologics, including congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease
  - Switch to an IL-17i biologic over abatacept:
    - Conditional recommendation based on low-quality evidence; may consider abatacept in patients with recurrent or serious infections
  - Switch to an IL-12/23i biologic over abatacept:
    - Conditional recommendation based on low-quality evidence; may consider abatacept in patients with recurrent or serious infections
- Recommendations for treatment of patients with active psoriatic arthritis despite treatment with a TNFi biologic, as monotherapy or in combination with MTX:
  - Switch to a different TNFi biologic over switching to abatacept:
    - Conditional recommendation based on low-quality evidence; may consider abatacept if the patient had a primary TNFi biologic efficacy failure or TNFi biologic-associated serious adverse effect
  - Switch to an IL-17i biologic over abatacept:
    - Conditional recommendation based on low-quality evidence; may consider abatacept if the patient prefers IV dosing or in patients with recurrent or serious infections
  - Switch to an IL-12/23i biologic over abatacept:
    - Conditional recommendation based on low-quality evidence; may consider abatacept if the patient prefers IV dosing or in patients with recurrent or serious infections

The American Academy of Dermatology (AAD) defines psoriatic arthritis (PsA) as mild, moderate, or severe. Where mild disease responds to NSAIDs, moderate disease requires DMARDs or TNF blockers. Appropriate treatment of severe PsA requires DMARDs plus TNF blockers or other biologic therapies. If PsA is diagnosed, treatment should be initiated to alleviate signs and symptoms of PsA, inhibit structural damage, and maximize quality of life (QOL). According to the 2019 AAD Practice Guidelines for the management of psoriatic arthritis, the potential importance of TNF- $\alpha$  in the pathophysiology of PsA is underscored by the observation that there are elevated levels of TNF- $\alpha$  in the synovium, joint fluid, and skin of patients with PsA. The guidelines support the use of infliximab for PsA based on evidence ranked as consistent, good quality, and patient oriented. (Strength of Recommendation: A).

### ***Rheumatoid Arthritis***

The 2021 American College of Rheumatology (ACR) RA updated treatment guideline addresses the use of DMARDs, including conventional synthetic DMARDs, biologic DMARDs, and targeted synthetic DMARDs, glucocorticoids, and the use of DMARDs in certain high-risk populations (i.e., those with liver disease, heart failure, lymphoproliferative disorders, previous serious infections, and nontuberculosis mycobacterial lung disease).<sup>18</sup> 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.

## Recommendations for DMARD-Naïve Patients

- A treat-to-target approach is strongly recommended over usual care for patients who have not been previously treated with bDMARDs or tsDMARDs regardless of disease activity level
- A minimal initial treatment goal of low disease activity is conditionally recommended over a goal of remission
- Moderate-to-high disease activity
  - Methotrexate is strongly recommended over hydroxychloroquine or sulfasalazine
  - Methotrexate is conditionally recommended over leflunomide
  - Methotrexate monotherapy is strongly recommended over bDMARD or tsDMARD monotherapy
  - Methotrexate monotherapy is conditionally recommended over dual or triple csDMARD therapy
  - Methotrexate monotherapy is conditionally recommended over methotrexate plus a tumor necrosis factor (TNF) inhibitor
  - Initiation of a csDMARD without short-term (< 3 months) glucocorticoids is conditionally recommended over initiation of a csDMARD with short-term glucocorticoids
  - Initiation of a csDMARD without longer term ( $\geq$  3 months) glucocorticoids is strongly recommended over initiation of a csDMARD with longer-term glucocorticoids
- Low disease activity
  - Hydroxychloroquine is conditionally recommended over other csDMARDs, sulfasalazine is conditionally recommended over methotrexate, and methotrexate is conditionally recommended over leflunomide

## Recommendations for DMARD-Experienced Patients

- A treat-to-target approach is conditionally recommended over usual care for patients who have had an inadequate response to bDMARDs or tsDMARDs.
- Methotrexate monotherapy is conditionally recommended over the combination of methotrexate plus a bDMARD or tsDMARD.
- Oral methotrexate is conditionally recommended over subcutaneous methotrexate for patients initiating methotrexate.
- Initiation/titration of methotrexate to a weekly dose of at least 15 mg within 4 to 6 weeks is conditionally recommended over initiation/titration to a weekly dose of less than 15 mg.
- A split dose of oral methotrexate over 24 hours or weekly subcutaneous injections, and/or an increased dose of folic/folinic acid, is conditionally recommended over switching to alternative DMARD(s) for patients not tolerating oral weekly methotrexate.
- Switching to subcutaneous methotrexate is conditionally recommended over the addition of/switching to alternative DMARD(s) for patients taking oral methotrexate who are not at target.

## Recommendations for Treatment Modification

- Addition of a bDMARD or tsDMARD is conditionally recommended over triple therapy (i.e., addition of sulfasalazine and hydroxychloroquine) for patients taking maximally tolerated doses of methotrexate who are not at target.
- Switching to a bDMARD or tsDMARD of a different class is conditionally recommended over switching to a bDMARD or tsDMARD belonging to the same class for patients taking a bDMARD or tsDMARD who are not at target.
- Addition of/switching to DMARDs is conditionally recommended over continuation of glucocorticoids for patients taking glucocorticoids to remain at target.
- Addition of/switching to DMARDs (with or without intraarticular [IA] glucocorticoids) is conditionally recommended over the use of IA glucocorticoids alone for patients taking DMARDs who are not at target.
- Continuation of all DMARDs at their current dose is conditionally recommended over a dose reduction of a DMARD, dose reduction is conditionally recommended over gradual discontinuation of a DMARD, and gradual discontinuation is conditionally recommended over abrupt discontinuation of a DMARD for patients who are at target for at least 6 months.
- Gradual discontinuation of sulfasalazine is conditionally recommended over gradual discontinuation of hydroxychloroquine for patients taking triple therapy who wish to discontinue a DMARD.
- Gradual discontinuation of methotrexate is conditionally recommended over gradual discontinuation of the bDMARD or tsDMARD for patients taking methotrexate plus a bDMARD or tsDMARD who wish to discontinue a DMARD.

## Recommendations for Specific Patient Populations

- Subcutaneous nodules



- Methotrexate is conditionally recommended over alternative DMARDs for patients with subcutaneous nodules who have moderate-to-high disease activity Switching to a non-methotrexate DMARD is conditionally recommended over continuation of methotrexate for patients taking methotrexate with progressive subcutaneous nodules
- Pulmonary disease
  - Methotrexate is conditionally recommended over alternative DMARDs for the treatment of inflammatory arthritis for patients with clinically diagnosed mild and stable airway or parenchymal lung disease, or incidental disease detected on imaging, who have moderate-to-high disease activity
- Lymphoproliferative Disorder
  - Rituximab is conditionally recommended over other DMARDs for patients who have a previous lymphoproliferative disorder for which rituximab is an approved treatment and who have moderate-to-high disease activity
- Heart Failure
  - Addition of a non-TNF inhibitor bDMARD or tsDMARD is conditionally recommended over addition of a TNF inhibitor for patients with New York Heart Association (NYHA) class III or IV heart failure and an inadequate response to csDMARDs
  - Switching to a non-TNF inhibitor bDMARD or tsDMARD is conditionally recommended over continuation of a TNF inhibitor for patients taking a TNF inhibitor who develop heart failure
- Hepatitis B
  - Prophylactic antiviral therapy is strongly recommended over frequent monitoring of viral load and liver enzymes alone for patients initiating rituximab who are hepatitis B core antibody positive (regardless of hepatitis B surface antigen status)
  - Prophylactic antiviral therapy is strongly recommended over frequent monitoring alone for patients initiating any bDMARD or tsDMARD who are hepatitis B core antibody positive and hepatitis B surface antigen positive
  - Frequent monitoring alone of viral load and liver enzymes is conditionally recommended over prophylactic antiviral therapy for patients initiating a bDMARD other than rituximab or a tsDMARD who are hepatitis B core antibody positive and hepatitis B surface antigen negative
- Nonalcoholic fatty liver disease (NAFLD)
  - Methotrexate is conditionally recommended over alternative DMARDs for DMARD-naive patients with NAFLD, normal liver enzymes and liver function tests, and no evidence of advanced liver fibrosis who have moderate-to-high disease activity
  - Persistent hypogammaglobulinemia without infection
  - In the setting of persistent hypogammaglobulinemia without infection, continuation of rituximab therapy for patients at target is conditionally recommended over switching to a different bDMARD or tsDMARD
- Serious Infections
  - Addition of csDMARDs is conditionally recommended over addition of a bDMARD or tsDMARD for patients with a serious infection within the previous 12 months who have moderate-to-high disease activity despite csDMARD monotherapy
  - Addition of/switching to DMARDs is conditionally recommended over initiation/dose escalation of glucocorticoids for patients with a serious infection within the previous 12 months who have moderate-to-high disease activity
- Lung Disease
  - Use of the lowest possible dose of glucocorticoids (discontinuation if possible) is conditionally recommended over continuation of glucocorticoids without dose modification for patients with NTM lung disease This recommendation is based on studies suggesting an increased risk of NTM lung disease in patients receiving either inhaled or oral glucocorticoids (54,55)
  - Addition of csDMARDs is conditionally recommended over addition of a bDMARD or tsDMARD for patients with NTM lung disease who have moderate-to-high disease activity despite csDMARD monotherapy This recommendation is based on the lower expected risk of NTM lung disease associated with csDMARDs compared to bDMARDs and tsDMARDs (56)
  - Abatacept is conditionally recommended over other bDMARDs and tsDMARDs for patients with NTM lung disease who have moderate-to high disease activity despite csDMARDs

### ***Juvenile Idiopathic Arthritis***

The 2019 American College of Rheumatology (ACR) and Arthritis Foundation guideline for the treatment of juvenile idiopathic arthritis include abatacept.<sup>2</sup>

- 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.

Orencia is indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis. Orencia may be used as monotherapy or concomitantly with DMARDs other than tumor necrosis factor (TNF) antagonists.<sup>5</sup>

Orencia is also indicated for reducing signs and symptoms in pediatric patients 2 years of age and older with moderately to severely active polyarticular juvenile idiopathic arthritis. Orencia may be used as monotherapy or concomitantly with methotrexate. Orencia is also indicated for the treatment of adult patients with active psoriatic arthritis.<sup>5</sup>

The labeling for Orencia states that it should not be administered concomitantly with TNF antagonists or with other biologic RA therapy, such as Kineret (anakinra), an interleukin-1 receptor antagonist. In controlled clinical trials in patients with adult RA, patients receiving concomitant Orencia and TNF antagonist therapy experienced more infections (63%) and serious infections (4.4%) compared to patients treated with only TNF antagonists (43% and 0.8%, respectively). These trials failed to demonstrate superiority of results with concomitant administration of Orencia and TNF antagonists. Therefore, clinical evidence does not support concurrent therapy with Orencia and TNF antagonists.<sup>5</sup>

Orencia prefilled syringes and Orencia ClickJect autoinjectors are intended for use under the guidance of a physician or healthcare practitioner. After proper training in subcutaneous injection technique, a patient or caregiver may inject with Orencia if a physician/healthcare practitioner determines that it is appropriate. Patients and caregivers should be instructed to follow the directions provided in the Instructions for Use section of the prescribing information for additional details on medication administration.<sup>5</sup>

## References

1. Saag KG, Teng GG, Patkar NM, et al. American College of Rheumatology 2008 Recommendations for the Use of Nonbiologic and Biologic Disease-Modifying Antirheumatic Drugs in Rheumatoid Arthritis. *Arthritis Care & Research. Arthritis Rheum.* 2008;59(6):762-84.
2. Ringold S, Angeles-Han ST, Beukelman T, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Treatment of Juvenile Idiopathic Arthritis: Therapeutic Approaches for Non-Systemic Polyarthritis, Sacroiliitis, and Enthesitis. *Arthritis Care Res (Hoboken).* 2019 Jun;71(6):717-734.
3. Rheumatoid Arthritis. Centers for Disease Control and Prevention Information Page.
4. Voll RE, Kalden JR. Do We Need New Treatment That Goes Beyond Tumor Necrosis Factor Blockers for Rheumatoid Arthritis? *Ann N Y Acad Sci.* 2005;1051:799-810.
5. Orencia [prescribing information]. Princeton, NJ: Bristol-Myers Squibb Company; October 2023.
6. Pollard L, Choy E. Rheumatoid Arthritis: Non-Tumor Necrosis Factor Targets. *Curr Opin Rheumatol.* 2005;17(3):242-46.
7. Ruderman EM, Pope RM. The Evolving Clinical Profile of Abatacept (CTLA4Ig): A Novel Co-Stimulatory Modulator for the Treatment of Rheumatoid Arthritis. *Arthritis Res Ther.* 2005;7 Suppl 2:S21-S25.

8. A Phase II Randomized, Double-Blind, Placebo controlled Study to Evaluate the Preliminary Efficacy, Pharmacokinetics, and Immunogenicity of BMS-188667 Administered to Subjects with Relapsing-Remitting Multiple Sclerosis. Clinical Study Report IM101200. Reported July 23, 2004.
9. Merrill JT, Burgos-Vargas R, Westhovens R, et al. The Efficacy and Safety of Abatacept in Patients with Non-Life-Threatening Manifestations of Systemic Lupus Erythematosus: Results of a Twelve-Month, Multicenter, Exploratory, Phase IIb, Randomized, Double-Blind, Placebo-Controlled Trial. *Arthritis Rheum*. 2010 Oct;62(10):3077-87.
10. Simpson D. New Developments in the Prophylaxis and Treatment of Graft Versus Host Disease. *Expert Opin Pharmacother*. 2001;2(7):1109-1117.
11. Open Clinical Trial. Study NCT01012492. Safety and Tolerability Trial of Abatacept-based Immunosuppression for Prevention of Acute Graft Versus Host Disease (aGVHD) During Transplant.
12. Mease P, Genovese MC, Gladstein G, et al. Abatacept in the Treatment of Patients with Psoriatic Arthritis: Results of a Double-Blind, Randomized, Placebo-Controlled Phase II Trial. *Arthritis Rheum*. 2011 Apr;63(4):939-48.
13. Lim L, Suhler EB, Smith JR. Biologic Therapies for Inflammatory Eye Disease. *Clinical and Experimental Ophthalmology*. 2006;34(4):365-374.
14. Ritchlin C. Newer Therapeutic Approaches: Spondyloarthritis and Uveitis. *Rheum Dis Clin N Am*. 2006;32(1):75-90.
15. MCG™ Care Guidelines, Ambulatory Care, 24<sup>th</sup> Edition. Abatacept.
16. Singh JA, Furst DE, Bharat A, et al. 2012 Update of the 2008 American College of Rheumatology Recommendations for the Use of Disease-Modifying Antirheumatic Drugs and Biologic Agents in the Treatment of Rheumatoid Arthritis. *Arthritis Care & Research*. 2012 May;64(5):625-639.
17. Emery P, Burmester GR, Bykerk VP, et al. Evaluating drug-free remission with abatacept in early rheumatoid arthritis: results from the phase 3b, multicentre, randomised, active-controlled AVERT study of 24 months, with a 12-month, double-blind treatment period. *Ann Rheum Dis*. 2015 Jan;74(1):19-26.
18. Xeljanz [prescribing information]. New York, NY: Pfizer Labs; January 2022.
19. Lovell DJ, Ruperto N, Mouy R, et al. Long-term safety, efficacy, and quality of life in patients with juvenile idiopathic arthritis treated with intravenous abatacept for up to seven years. *Arthritis Rheumatol*. 2015 Oct;67(10):2759-70.
20. Ringold S, Weiss PF, Beukelman T, et al. 2013 update of the 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: recommendations for the medical therapy of children with systemic juvenile idiopathic arthritis and tuberculosis screening among children receiving biologic medications. *Arthritis Rheum*. 2013 Oct;65(10):2499-512.
21. Singh JA, Saag KG, Bridges SL, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Care & Research*. *Arthritis Rheum*. 2016;68(1):1-26.
22. Mease PJ, Gottlieb AB, van der Heijde D, et al. Efficacy and safety of abatacept, a T-cell modulator, in a randomised, double-blind, placebo-controlled, phase III study in psoriatic arthritis. *Ann Rheum Dis*. 2017 May 4.
23. Khoury SJ, Rochon J, Ding L, Byron M, Ryker K, Tosta P, Gao W, Freedman MS, Arnold DL, Sayre PH, Smilek DE; ACCLAIM Study Group. ACCLAIM: A randomized trial of abatacept (CTLA4-Ig) for relapsing-remitting multiple sclerosis. *Mult Scler*. 2017 Apr;23(5):686-695.
24. Singh JA, Guyatt G, Ogdie A, et al. Special Article: 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. *Arthritis Care Res (Hoboken)*. 2019 Jan;71(1):2-29.
25. Menter A, Korman NJ, Elmets CA, Feldman SR, Gelfand JM, Gordon KB, Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 6. Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol*. 2011 Jul;65(1):137-74.
26. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol*. 2019 Apr;80(4):1029-1072.
27. Genovese MC, Covarrubias A, Leon G, et al. Subcutaneous abatacept versus intravenous abatacept: a phase IIIb noninferiority study in patients with an inadequate response to methotrexate. *Arthritis Rheum*. 2011 Oct;63(10):2854-64.
28. Brunner HI, Tzaribachev N, Vega-Cornejo G, et al. Subcutaneous Abatacept in Patients With Polyarticular-Course Juvenile Idiopathic Arthritis: Results From a Phase III Open-Label Study. *Arthritis Rheumatol*. 2018 Jul;70(7):1144-1154.
29. Nahas MR, Soiffer RJ, Kim HT, et al. Phase 1 clinical trial evaluating abatacept in patients with steroid-refractory chronic graft-versus-host disease. *Blood*. 2018 Jun 21;131(25):2836-2845.

30. NCCN Drugs & Biologics Compendium® (NCCN Compendium®). Available at [www.nccn.org](http://www.nccn.org). Accessed on February 7, 2024.
31. Kean, L, et. al. Abatacept combined with a calcineurin inhibitor and methotrexate for graft versus host disease prophylaxis: a randomized controlled trial. Available at [clinicaltrials.gov](https://clinicaltrials.gov) (NCT01743131). Accessed on February 14, 2022.
32. Bristol-Myers Squivv Company. Abatacept. Primary Clinical Study Report for Study IM101311: Abatacept Combined with a Calcineurin Inhibitor and Methotrexate for Graft Versus Host Disease Prophylaxis.
33. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Care Res. 2021 Jul;73(7):924-939.

## Policy History/Revision Information

| Date       | Summary of Changes  |
|------------|---|
| 11/01/2024 | <p><b>Application Ohio</b></p> <ul style="list-style-type: none"> <li>• Updated reference link to reflect current title for state-specific policy version</li> </ul> <p><b>Supporting Information</b></p> <ul style="list-style-type: none"> <li>• Archived previous policy version CS2024D0039Z</li> </ul> |

## 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 InterQual® criteria, 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.