Orencia® (Abatacept) Injection for Intravenous Infusion

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Instructions for Use

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Related Commercial Policy

- Provider Administered Drugs – Site of Care

Community Plan Policy

- Orencia® (Abatacept) Injection for Intravenous Infusion

Coverage Rationale

See Benefit Considerations

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 for the treatment of polyarticular juvenile idiopathic arthritis when all of the following criteria are met:

- 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)]

    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 positive clinical response; and
  - Orencia is dosed according to 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)]

    and
  - Authorization is for no more than 12 months

Orencia is medically necessary for the treatment of polyarticular juvenile idiopathic arthritis when all of the following criteria are met:

- 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)]

    and
  - Prescribed by or in consultation with a rheumatologist; 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 positive clinical response; and
  - Orencia is dosed according to 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)]

    and
  - Authorization is for no more than 12 months

Orencia is proven for the treatment of rheumatoid arthritis when all of the following criteria are met:

- For initial therapy, all of the following:
  - Diagnosis of moderately to severely active rheumatoid arthritis (RA); and
  - Orencia is initiated and titrated according to FDA labeled dosing for rheumatoid arthritis; and
  - Patient is not receiving Orencia in combination with either 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)]

    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 positive clinical response; and
  - Orencia is dosed according to FDA labeled dosing for rheumatoid arthritis; and
  - Patient is not receiving Orencia in combination with either 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)]

    and
  - Authorization is for no more than 12 months

Orencia is medically necessary for the treatment of rheumatoid arthritis when all of the following criteria are met:

- For initial therapy, all of the following:
  - Diagnosis of moderately to severely active rheumatoid arthritis (RA); and
  - One of the following:
    - History of failure intolerance to a 3 month trial of one non-biologic disease modifying anti-rheumatic drug (DMARD) [e.g., methotrexate, leflunomide, sulfasalazine, hydroxychloroquine] at maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced; or
    - Patient has been previously treated with a biologic or targeted synthetic DMARD FDA-approved for the treatment of rheumatoid arthritis [e.g., Cimzia (certolizumab), adalimumab, Simponi (golimumab), Olumiant (baricitinib), Rinvoq (upadacitinib), Xeljanz (tofacitinib), Enbrel (etanercept)]; or
    - Patient is currently on Orencia

    and

- Orencia is initiated and titrated according to FDA labeled dosing for rheumatoid arthritis; and
- Patient is not receiving Orencia in combination with either 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)]

  and
- Prescribed by or in consultation with a rheumatologist; 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 positive clinical response; and
  - Orencia is dosed according to FDA labeled dosing for rheumatoid arthritis; and
  - Patient is not receiving Orencia in combination with either 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)]

    and
  - Authorization is for no more than 12 months

Orencia is proven for the treatment of psoriatic arthritis when all of the following criteria are met:

- For initial therapy, all of the following:
  - Diagnosis of active psoriatic arthritis (PsA); and
  - Orencia is initiated and titrated 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
  - 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

Orencia is medically necessary for the treatment of psoriatic arthritis when all of the following criteria are met:

- For initial therapy, all of the following:
  - Diagnosis of active psoriatic arthritis (PsA); and
  - One of the following
    - History of failure to a 3 month trial of methotrexate at the maximally indicated dose, unless contraindicated or clinically significant adverse effects are experienced; or
    - Patient has been previously treated with a biologic or targeted synthetic DMARD FDA-approved for the treatment of psoriatic arthritis [e.g., Cimzia (certolizumab), adalimumab, Simponi (golimumab), Stelara (ustekinumab), Tremfya (guselkumab), Xeljanz (tofacitinib), Otezla (apremilast), Enbrel (etanercept)]; or
    - Patient is currently on Orencia

    and
  - Orencia is initiated and titrated 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

- 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

Orencia is proven and/or medically necessary for the treatment of 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

Orencia is proven and/or medically necessary for the prophylaxis of 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; and
- Authorization is for no more than 4 doses

Orencia is proven and/or medically necessary for the treatment of 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 (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 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 the member specific benefit plan document 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

Diagnosis Code	Description
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
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

Diagnosis Code	Description
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
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

Diagnosis Code	Description
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
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

Diagnosis Code	Description
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
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

Diagnosis Code	Description
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
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

Diagnosis Code	Description
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
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

Diagnosis Code	Description
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
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

Diagnosis Code	Description
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
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.[6,7] This interaction provides a costimulatory signal necessary for full activation of T lymphocytes.[5]

Benefit Considerations

Some Certificates of Coverage allow coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare

diseases may occur when certain conditions are met. Refer to the Policy and Procedure addressing the treatment of serious rare diseases.

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.[22] 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 ≥ 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 ≥ 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.[26] 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.[17] 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.[27] 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_{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_{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.[19] 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).[31] 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).[32] 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 - Consider adding abatacept for the management of immunotherapy-related:
  - Severe (G3) or life-threatening (G4) myocarditis, pericarditis, arrhythmias, impaired ventricular function, or conduction abnormalities if no improvement within 24 hours of starting pulse-dose methylprednisolone

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.[23] 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.[8] 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).[9] 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.[13,14] 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 regard 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 of 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-α in the pathophysiology of PsA is underscored by the observation that there are elevated levels of TNF-α 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 myobacterial lung disease).[18] 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-erm (< 3 months) glucocorticoids is conditional recommended over initiation of a csDMARD with short-term glucocorticoids
  - Initiation of a csDMARD without longer term (≥ 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.[2]

- 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.[5]

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.[5]

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.[5]

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 self-inject 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.[5]

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Policy History/Revision Information

Date	Summary of Changes

05/01/2023	**Coverage Rationale**
	• Removed reference to medication brand name "Humira"
	• Revised list of examples of:
	  ○ Janus kinase inhibitors the patient must not be receiving in combination with Orencia; added "Rinvoq (upadacitinib)"
	  ○ Biologic or targeted synthetic DMARDs FDA-approved for the treatment of psoriatic/rheumatoid arthritis previously used to treat the patient; added "Enbrel (etanercept)"
	Supporting Information
	• Updated *Clinical Evidence* and *References* sections to reflect the most current information
	• Archived previous policy version 2022D0039R

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. 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.

This Medical Benefit Drug Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. 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.