

Cimzia® (Certolizumab Pegol)

Policy Number: CS2021D0083E
Effective Date: September 1, 2021

[Instructions for Use](#)

Table of Contents	Page
Application	1
Coverage Rationale	1
Applicable Codes	4
Background	14
Clinical Evidence	15
U.S. Food and Drug Administration	19
References	19
Policy History/Revision Information	20
Instructions for Use	22

Commercial Policy
<ul style="list-style-type: none"> Cimzia® (Certolizumab Pegol)

Application

This Medical Benefit Drug Policy only applies to the states of California, Nebraska, New York, Tennessee, Texas, and Wisconsin.

Refer to the guideline listed below for the following states:

State	Policy/Guideline
Indiana	Immunomodulators for Inflammatory Conditions (for Indiana Only)
Kentucky	Cimzia® (Certolizumab Pegol) (for Kentucky Only)

Coverage Rationale

This policy refers to Cimzia (certolizumab pegol) injection. Cimzia (certolizumab pegol) for self-administered subcutaneous injection is obtained under the pharmacy benefit.

Cimzia is proven and/or medically necessary for the treatment of:¹

- Crohn’s Disease (CD) when all of the following criteria are met:
 - For initial therapy, all of the following:
 - Diagnosis of moderately to severely active Crohn’s disease; and
 - One of the following:
 - History of failure to one of the following conventional therapies at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced:
 - Corticosteroids (e.g., prednisone, methylprednisolone, budesonide)
 - 6-mercaptopurine (Purinethol)
 - Azathioprine (Imuran)
 - Methotrexate (Rheumatrex, Trexall)
 - or
 - Patient is currently on Cimzia; or

- Patient has been previously treated with a biologic DMARD FDA-approved for the treatment of Crohn’s disease [e.g., Humira (adalimumab), Stelara (ustekinumab)]
 - and
 - Cimzia is initiated and titrated according to U.S. Food and Drug Administration labeled dosing for CD; and
 - Patient is not receiving Cimzia in combination with either of the following:
 - Biologic DMARD [e.g., Actemra (tocilizumab), Enbrel (etanercept), Rituxan (rituximab), Oencia (abatacept)]
 - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
 - and
 - Prescribed by or in consultation with a gastroenterologist; and
 - Initial authorization will be issued for 12 months
 - For continuation of therapy, all of the following:
 - Documentation of positive clinical response; and
 - Cimzia is initiated and titrated according to U.S. Food and Drug Administration labeled dosing for CD; and
 - Patient is not receiving Cimzia in combination with either of the following:
 - Biologic DMARD [e.g., Actemra (tocilizumab), Enbrel (etanercept), Rituxan (rituximab), Oencia (abatacept)]
 - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
 - and
 - Authorization will be issued for 12 months
- Rheumatoid Arthritis (RA) when all of the following criteria are met:
 - For initial therapy, all of the following:
 - Diagnosis of moderately to severely active rheumatoid arthritis; 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 DMARD FDA-approved for the treatment of rheumatoid arthritis [e.g., Humira (adalimumab), Simponi (golimumab)]; or
 - Patient is currently on Cimzia
 - and
 - Cimzia is initiated and titrated according to U.S. Food and Drug Administration labeled dosing for RA; and
 - Patient is not receiving Cimzia in combination with either of the following:
 - Biologic DMARD [e.g., Actemra (tocilizumab), Enbrel (etanercept), Rituxan (rituximab), Oencia (abatacept)]
 - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
 - and
 - Prescribed by or in consultation with a rheumatologist; and
 - Initial authorization will be issued for 12 months
 - For continuation of therapy, all of the following:
 - Documentation of positive clinical response; and
 - Cimzia is initiated and titrated according to U.S. Food and Drug Administration labeled dosing for RA; and
 - Patient is not receiving Cimzia in combination with either of the following:
 - Biologic DMARD [e.g., Actemra (tocilizumab), Enbrel (etanercept), Rituxan (rituximab), Oencia (abatacept)]
 - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
 - and
 - Authorization will be issued for 12 months
- Psoriatic Arthritis (PsA) when all of the following criteria are met:
 - For initial therapy, all of the following:
 - Diagnosis of active psoriatic arthritis; 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 DMARD FDA-approved for the treatment of psoriatic arthritis [e.g., Humira (adalimumab), Simponi (golimumab), Stelara (ustekinumab), Tremfya (guselkumab)]; or
 - Patient is currently on Cimzia

- and
- Cimzia is initiated and titrated according to U.S. Food and Drug Administration labeled dosing for PsA; and
- Patient is not receiving Cimzia in combination with either of the following:
 - Biologic DMARD [e.g., Actemra (tocilizumab), Enbrel (etanercept), Rituxan (rituximab), Orenzia (abatacept)]
 - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
 - Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]
- and
- Prescribed by or in consultation with one of the following:
 - Rheumatologist
 - Dermatologist
- and
- Initial authorization will be issued for 12 months
- For continuation of therapy, all of the following:
 - Documentation of positive clinical response; and
 - Cimzia is initiated and titrated according to U.S. Food and Drug Administration labeled dosing for PsA; and
 - Patient is not receiving Cimzia in combination with either of the following:
 - Biologic DMARD [e.g., Actemra (tocilizumab), Enbrel (etanercept), Rituxan (rituximab), Orenzia (abatacept)]
 - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
 - Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]
 - and
 - Authorization will be issued for 12 months
- Ankylosing Spondylitis (AS) and non-radiographic Axial Spondyloarthritis (nr-axSpA) when all of the following criteria are met:
 - For initial therapy, all of the following:
 - Diagnosis of active ankylosing spondylitis or non-radiographic axial spondyloarthritis; and
 - One of the following:
 - History of failure to two NSAIDs (e.g., ibuprofen, naproxen) at the maximally indicated doses, each used for at least 4 weeks, unless contraindicated or clinically significant adverse effects are experienced; or
 - Patient has been previously treated with a biologic DMARD FDA-approved for the treatment of ankylosing spondylitis [e.g., Humira (adalimumab), Simponi (golimumab)]; or
 - Patient is currently on Cimzia
 - and
 - Cimzia is initiated and titrated according to U.S. Food and Drug Administration labeled dosing for AS or nr-axSpA; and
 - and
 - Patient is not receiving Cimzia in combination with either of the following:
 - Biologic DMARD [e.g., Actemra (tocilizumab), Enbrel (etanercept), Rituxan (rituximab), Orenzia (abatacept)]
 - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
 - Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]
 - and
 - Prescribed by or in consultation with a rheumatologist; and
 - Initial authorization will be issued for 12 months
 - For continuation of therapy, all of the following:
 - Documentation of positive clinical response; and
 - Cimzia is initiated and titrated according to U.S. Food and Drug Administration labeled dosing for AS or nr-axSpA; and
 - and
 - Patient is not receiving Cimzia in combination with either of the following:
 - Biologic DMARD [e.g., Actemra (tocilizumab), Enbrel (etanercept), Rituxan (rituximab), Orenzia (abatacept)]
 - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
 - Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]
 - and
 - Authorization will be issued for 12 months

- Plaque Psoriasis (PS) when all of the following criteria are met:
 - For initial therapy, all of the following:
 - Diagnosis of moderate to severe plaque psoriasis; and
 - One of the following:
 - All of the following:
 - Greater than or equal to 3% body surface area involvement, palmoplantar, facial, genital involvement, or severe scalp psoriasis; and
 - History of failure to one of the following topical therapies, unless contraindicated or clinically significant adverse effects are experienced:
 - Corticosteroids (e.g., betamethasone, clobetasol, desonide)
 - Vitamin D analogs (e.g., calcitriol, calcipotriene)
 - Tazarotene
 - Calcineurin inhibitors (e.g., tacrolimus, pimecrolimus)
 - Anthralin
 - Coal tar
 - and
 - 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 is currently on Cimzia; or
 - Patient has been previously treated with a biologic DMARD FDA-approved for the treatment of plaque psoriasis [e.g., Humira (adalimumab), Skyrizi (risankizumab-rzaa), Stelara (ustekinumab), Tremfya (guselkumab)]
 - and
 - Cimzia is initiated and titrated according to U.S. Food and Drug Administration labeled dosing for PS; and
 - Patient is not receiving Cimzia in combination with either of the following:
 - Biologic DMARD [e.g., Actemra (tocilizumab), Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept)]
 - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
 - Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]
 - and
 - Prescribed by or in consultation with a dermatologist; and
 - Initial authorization will be issued for 12 months
- For continuation of therapy, all of the following:
 - Documentation of positive clinical response; and
 - Cimzia is initiated and titrated according to U.S. Food and Drug Administration labeled dosing for PS; and
 - Patient is not receiving Cimzia in combination with either of the following:
 - Biologic DMARD [e.g., Actemra (tocilizumab), Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept)]
 - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
 - Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]
 - and
 - Authorization will be issued for 12 months

Applicable Codes

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

CPT Code	Description
96372	Therapeutic, prophylactic or diagnostic injection (specify substance or drug); subcutaneous or intramuscular
96401	Chemotherapy administration, subcutaneous or intramuscular; non-hormonal anti-neoplastic

CPT® is a registered trademark of the American Medical Association

HCPCS Code	Description
J0717	Injection, certolizumab pegol, 1 mg (code may be used when drug administered under the direct supervision of a physician, not for use when drug is self-administered)

Diagnosis Code	Description
K31.6	Fistula of stomach and duodenum
K50.00	Crohn's disease of small intestine without complications
K50.011	Crohn's disease of small intestine with rectal bleeding
K50.012	Crohn's disease of small intestine with intestinal obstruction
K50.013	Crohn's disease of small intestine with fistula
K50.014	Crohn's disease of small intestine with abscess
K50.018	Crohn's disease of small intestine with other complication
K50.019	Crohn's disease of small intestine with unspecified complications
K50.10	Crohn's disease of large intestine without complications
K50.111	Crohn's disease of large intestine with rectal bleeding
K50.112	Crohn's disease of large intestine with intestinal obstruction
K50.113	Crohn's disease of large intestine with fistula
K50.114	Crohn's disease of large intestine with abscess
K50.118	Crohn's disease of large intestine with other complication
K50.119	Crohn's disease of large intestine with unspecified complications
K50.80	Crohn's disease of both small and large intestine without complications
K50.811	Crohn's disease of both small and large intestine with rectal bleeding
K50.812	Crohn's disease of both small and large intestine with intestinal obstruction
K50.813	Crohn's disease of both small and large intestine with fistula
K50.814	Crohn's disease of both small and large intestine with abscess
K50.818	Crohn's disease of both small and large intestine with other complication
K50.819	Crohn's disease of both small and large intestine with unspecified complications
K50.90	Crohn's disease, unspecified, without complications
K50.911	Crohn's disease, unspecified, with rectal bleeding
K50.912	Crohn's disease, unspecified, with intestinal obstruction
K50.913	Crohn's disease, unspecified, with fistula
K50.914	Crohn's disease, unspecified, with abscess
K50.918	Crohn's disease, unspecified, with other complication
K50.919	Crohn's disease, unspecified, with unspecified complications
K60.3	Anal fistula
K60.4	Rectal fistula
K60.5	Anorectal fistula
K63.2	Fistula of intestine
L40.0	Psoriasis vulgaris
L40.50	Arthropathic psoriasis, unspecified
L40.51	Distal interphalangeal psoriatic arthropathy
L40.52	Psoriatic arthritis mutilans
L40.53	Psoriatic spondylitis

Diagnosis Code	Description
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
M05.10	Rheumatoid lung disease with rheumatoid arthritis of unspecified site
M05.111	Rheumatoid lung disease with rheumatoid arthritis of right shoulder
M05.112	Rheumatoid lung disease with rheumatoid arthritis of left shoulder
M05.119	Rheumatoid lung disease with rheumatoid arthritis of unspecified shoulder
M05.121	Rheumatoid lung disease with rheumatoid arthritis of right elbow
M05.122	Rheumatoid lung disease with rheumatoid arthritis of left elbow
M05.129	Rheumatoid lung disease with rheumatoid arthritis of unspecified elbow
M05.131	Rheumatoid lung disease with rheumatoid arthritis of right wrist
M05.132	Rheumatoid lung disease with rheumatoid arthritis of left wrist
M05.139	Rheumatoid lung disease with rheumatoid arthritis of unspecified wrist
M04.141	Rheumatoid lung disease with rheumatoid arthritis of right hand
M05.142	Rheumatoid lung disease with rheumatoid arthritis of left hand
M05.149	Rheumatoid lung disease with rheumatoid arthritis of unspecified hand
M05.151	Rheumatoid lung disease with rheumatoid arthritis of right hip
M05.152	Rheumatoid lung disease with rheumatoid arthritis of left hip
M05.159	Rheumatoid lung disease with rheumatoid arthritis of unspecified hip
M05.161	Rheumatoid lung disease with rheumatoid arthritis of right knee

Diagnosis Code	Description
M05.162	Rheumatoid lung disease with rheumatoid arthritis of left knee
M05.169	Rheumatoid lung disease with rheumatoid arthritis of unspecified knee
M05.171	Rheumatoid lung disease with rheumatoid arthritis of right ankle and foot
M05.172	Rheumatoid lung disease with rheumatoid arthritis of left ankle and foot
M05.179	Rheumatoid lung disease with rheumatoid arthritis of unspecified ankle and foot
M05.19	Rheumatoid lung disease with rheumatoid arthritis of 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

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

Diagnosis Code	Description
M05.539	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified wrist
M05.541	Rheumatoid polyneuropathy with rheumatoid arthritis of right hand
M05.542	Rheumatoid polyneuropathy with rheumatoid arthritis of left hand
M05.549	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified hand
M05.551	Rheumatoid polyneuropathy with rheumatoid arthritis of right hip
M05.552	Rheumatoid polyneuropathy with rheumatoid arthritis of left hip
M05.559	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified hip
M05.561	Rheumatoid polyneuropathy with rheumatoid arthritis of right knee
M05.562	Rheumatoid polyneuropathy with rheumatoid arthritis of left knee
M05.569	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified knee
M05.571	Rheumatoid polyneuropathy with rheumatoid arthritis of right ankle and foot
M05.572	Rheumatoid polyneuropathy with rheumatoid arthritis of left ankle and foot
M05.579	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified ankle and foot
M05.59	Rheumatoid polyneuropathy with rheumatoid arthritis of multiple sites
M05.60	Rheumatoid arthritis of unspecified site with involvement of other organs and systems
M05.611	Rheumatoid arthritis of right shoulder with involvement of other organs and systems
M05.612	Rheumatoid arthritis of left shoulder with involvement of other organs and systems
M05.619	Rheumatoid arthritis of unspecified shoulder with involvement of other organs and systems
M05.621	Rheumatoid arthritis of right elbow with involvement of other organs and systems
M05.622	Rheumatoid arthritis of left elbow with involvement of other organs and systems
M05.629	Rheumatoid arthritis of unspecified elbow with involvement of other organs and systems
M05.631	Rheumatoid arthritis of right wrist with involvement of other organs and systems
M05.632	Rheumatoid arthritis of left wrist with involvement of other organs and systems
M05.639	Rheumatoid arthritis of unspecified wrist with involvement of other organs and systems
M05.641	Rheumatoid arthritis of right hand with involvement of other organs and systems
M05.642	Rheumatoid arthritis of left hand with involvement of other organs and systems
M05.649	Rheumatoid arthritis of unspecified hand with involvement of other organs and systems
M05.651	Rheumatoid arthritis of right hip with involvement of other organs and systems
M05.652	Rheumatoid arthritis of left hip with involvement of other organs and systems
M05.659	Rheumatoid arthritis of unspecified hip with involvement of other organs and systems
M05.661	Rheumatoid arthritis of right knee with involvement of other organs and systems
M05.662	Rheumatoid arthritis of left knee with involvement of other organs and systems
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
M05.7A	Rheumatoid arthritis with rheumatoid factor of other specified site without organ or systems involvement
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

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

Diagnosis Code	Description
M05.871	Other rheumatoid arthritis with rheumatoid factor of right ankle and foot
M05.872	Other rheumatoid arthritis with rheumatoid factor of left ankle and foot
M05.879	Other rheumatoid arthritis with rheumatoid factor of unspecified ankle and foot
M05.89	Other rheumatoid arthritis with rheumatoid factor of multiple sites
M05.9	Rheumatoid arthritis with rheumatoid factor, unspecified
M06.0A	Rheumatoid arthritis without rheumatoid factor, other specified site
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
M06.1	Adult-onset Still's disease
M06.20	Rheumatoid bursitis, unspecified site
M06.211	Rheumatoid bursitis, right shoulder
M06.212	Rheumatoid bursitis, left shoulder
M06.219	Rheumatoid bursitis, unspecified shoulder
M06.221	Rheumatoid bursitis, right elbow
M06.222	Rheumatoid bursitis, left elbow
M06.229	Rheumatoid bursitis, unspecified elbow
M06.231	Rheumatoid bursitis, right wrist
M06.232	Rheumatoid bursitis, left wrist
M06.239	Rheumatoid bursitis, unspecified wrist
M06.241	Rheumatoid bursitis, right hand

Diagnosis Code	Description
M06.242	Rheumatoid bursitis, left hand
M06.249	Rheumatoid bursitis, unspecified hand
M06.251	Rheumatoid bursitis, right hip
M06.252	Rheumatoid bursitis, left hip
M06.259	Rheumatoid bursitis, unspecified hip
M06.261	Rheumatoid bursitis, right knee
M06.262	Rheumatoid bursitis, left knee
M06.269	Rheumatoid bursitis, unspecified knee
M06.271	Rheumatoid bursitis, right ankle and foot
M06.272	Rheumatoid bursitis, left ankle and foot
M06.279	Rheumatoid bursitis, unspecified ankle and foot
M06.28	Rheumatoid bursitis, vertebrae
M06.29	Rheumatoid bursitis, multiple sites
M06.30	Rheumatoid nodule, unspecified site
M06.311	Rheumatoid nodule, right shoulder
M06.312	Rheumatoid nodule, left shoulder
M06.319	Rheumatoid nodule, unspecified shoulder
M06.321	Rheumatoid nodule, right elbow
M06.322	Rheumatoid nodule, left elbow
M06.329	Rheumatoid nodule, unspecified elbow
M06.331	Rheumatoid nodule, right wrist
M06.332	Rheumatoid nodule, left wrist
M06.339	Rheumatoid nodule, unspecified wrist
M06.341	Rheumatoid nodule, right hand
M06.342	Rheumatoid nodule, left hand
M06.349	Rheumatoid nodule, unspecified hand
M06.351	Rheumatoid nodule, right hip
M06.352	Rheumatoid nodule, left hip
M06.359	Rheumatoid nodule, unspecified hip
M06.361	Rheumatoid nodule, right knee
M06.362	Rheumatoid nodule, left knee
M06.369	Rheumatoid nodule, unspecified knee
M06.371	Rheumatoid nodule, right ankle and foot
M06.372	Rheumatoid nodule, left ankle and foot
M06.379	Rheumatoid nodule, unspecified ankle and foot
M06.38	Rheumatoid nodule, vertebrae
M06.39	Rheumatoid nodule, multiple sites
M06.4	Inflammatory polyarthropathy
M06.8A	Other specified rheumatoid arthritis, other specified site
M06.80	Other specified rheumatoid arthritis, unspecified site
M06.811	Other specified rheumatoid arthritis, right shoulder
M06.812	Other specified rheumatoid arthritis, left shoulder

Diagnosis Code	Description
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
M06.9	Rheumatoid arthritis, unspecified
M08.1	Juvenile ankylosing spondylitis
M45.0	Ankylosing spondylitis of multiple sites in spine
M45.1	Ankylosing spondylitis of occipito-atlanto-axial region
M45.2	Ankylosing spondylitis of cervical region
M45.3	Ankylosing spondylitis of cervicothoracic region
M45.4	Ankylosing spondylitis of thoracic region
M45.5	Ankylosing spondylitis of thoracolumbar region
M45.6	Ankylosing spondylitis lumbar region
M45.7	Ankylosing spondylitis of lumbosacral region
M45.8	Ankylosing spondylitis sacral and sacrococcygeal region
M45.9	Ankylosing spondylitis of unspecified sites in spine
M46.80	nr-axSpA, site unspecified
M46.81	nr-axSpA, occipito-atlanto-axial region
M46.82	nr-axSpA, cervical region
M46.83	nr-axSpA, cervicothoracic region
M46.84	nr-axSpA, thoracic region
M46.85	nr-axSpA, thoracolumbar region
M46.86	nr-axSpA, lumbar region
M46.87	nr-axSpA, lumbosacral region
M46.88	nr-axSpA, sacral and sacrococcygeal region

Diagnosis Code	Description
M46.89	nr-axSpA, multiple sites in spine
M48.8X1	Other specified spondylopathies, occipito-atlanto-axial region
M48.8X2	Other specified spondylopathies, cervical region
M48.8X3	Other specified spondylopathies, cervicothoracic region
M48.8X4	Other specified spondylopathies, thoracic region
M48.8X5	Other specified spondylopathies, thoracolumbar region
M48.8X6	Other specified spondylopathies, lumbar region
M48.8X7	Other specified spondylopathies, lumbosacral region
M48.8X8	Other specified spondylopathies, sacral and sacrococcygeal region
M48.8X9	Other specified spondylopathies, site unspecified
N82.2	Fistula of vagina to small intestine
N82.3	Fistula of vagina to large intestine
N82.4	Other female intestinal-genital tract fistulae

Maximum Dosage Requirements

HCPCS Code Based Maximum Dosage Information

This section provides information about the maximum dosage per administration for certolizumab pegol administered by a medical professional.

Medication Name		Maximum Dosage per Administration	HCPCS Code	Maximum Allowed
Brand	Generic			
Cimzia	Certolizumab pegol	400 mg	J0717	400 HCPCS units (1 mg per unit)

Maximum Allowed Quantities by National Drug Code (NDC) Units

The allowed quantities in this section are calculated based upon both the maximum dosage information supplied within this policy as well as the process by which NDC claims are billed. This list may not be inclusive of all available NDCs for each drug product and is subject to change.

Medication Name		How Supplied	National Drug Code	Maximum Allowed
Brand	Generic			
Cimzia	Certolizumab pegol	2 x 200mg kit	50474-0700-62	2 vials
		2 x 200mg/ml prefilled syringe kit	50474-0710-79	2 mL
		6 x 200 mg/ml prefilled syringe kit	50474-0710-81	2 mL

Background

Cimzia (certolizumab pegol) is a recombinant, humanized antibody Fab' fragment, with specificity for human tumor necrosis factor alpha (TNF α). TNF α is a key pro-inflammatory cytokine with a central role in inflammatory processes. Certolizumab pegol selectively neutralizes TNF α but does not neutralize lymphotoxin α (TNF β). Certolizumab pegol does not contain a fragment crystallizable (Fc) region, which is normally present in a complete antibody, and therefore does not fix complement or cause antibody-dependent cell-mediated cytotoxicity in vitro. It does not induce apoptosis in vitro in human peripheral blood-derived monocytes or lymphocytes, nor does certolizumab pegol induce neutrophil degranulation.

TNF α induces the upregulation of cellular adhesion molecules and chemokines, upregulation of major histocompatibility complex (MHC) class I and class II molecules, and direct leukocyte activation. TNF α stimulates the production of downstream inflammatory mediators, including interleukin-1, prostaglandins, platelet activating factor, and nitric oxide. Elevated levels of TNF α have been implicated in the pathology of Crohn's disease and rheumatoid arthritis. Certolizumab pegol binds to TNF α , inhibiting its role as a key mediator of inflammation. TNF α is strongly expressed in the bowel wall in areas involved by Crohn's

disease and fecal concentrations of TNF α in patients with Crohn's disease have been shown to reflect clinical severity of the disease. After treatment with certolizumab pegol, patients with Crohn's disease demonstrated a decrease in the levels of C-reactive protein (CRP). Increased TNF α levels are found in the synovial fluid of rheumatoid arthritis patients and play an important role in the joint destruction that is a hallmark of this disease.

Clinical Evidence

Proven

Cimzia (certolizumab pegol) is indicated for:¹

- Reducing signs and symptoms of Crohn's disease and maintaining clinical response in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy
- Treatment of adults with moderately to severely active rheumatoid arthritis
- Treatment of adult patients with active psoriatic arthritis
- Treatment of adults with active ankylosing spondylitis
- Treatment of adults with active non-radiographic axial spondyloarthritis with objective signs of inflammation
- Treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy

Professional Societies

Crohn's Disease

According to the American College of Gastroenterology Practice Guidelines for the Management of Crohn's Disease in Adults (ACG Practice Guidelines) published in February 2009, patients with moderate-severe disease usually have a Crohn's Disease Activity Index (CDAI) of 220-450. They have failed to respond to treatment for mild-moderate disease, or have more prominent symptoms of fever, significant weight loss, abdominal pain or tenderness, intermittent nausea or vomiting (without obstructive findings), or significant anemia.

The CDAI is the sum of the following clinical or laboratory variables after multiplying by their weighting factor given in parentheses:

- Number of liquid or soft stools each day for seven days (2)
- Abdominal pain graded from 0-3 in severity each day for seven days (5)
- General well-being, subjectively assessed from 0 (well) to 4 (terrible) each day for seven days (7)
- Presence of complications where 1 point is added for each complication (20). Complications include:
 - The presence of joint pains (arthralgia) or frank arthritis
 - Inflammation of the iris or uveitis
 - Presence of erythema nodosum, pyoderma gangrenosum, or aphthous ulcers
 - Anal fissures, fistulae or abscesses
 - Other fistulae (e.g. Enterocutaneous, vesicle, vaginal)
 - Fever (>37.8° C) during the previous week
- Taking diphenoxylate/atropine [Lomotil®] or opiates for diarrhea (30)
- Presence of an abdominal mass where 0 = none, 2 = questionable, 5 = definite (10);
- Absolute deviation of hematocrit from 47% in males and 42% in females (6)
- Percentage deviation from standard body weight (1)

The 2018 ACG Practice Guidelines support the use of infliximab for treatment and maintenance of patients with moderate to severely active Crohn's disease which is resistant or refractory to corticosteroids, thiopurines or methotrexate. In addition, they state anti-TNF agents can be considered to treat severely active Crohn's disease.

Rheumatoid Arthritis

The 2015 American College of Rheumatology (ACR) RA treatment guideline addresses the use of DMARDs, biologics, tofacitinib, and glucocorticoids in early (<6 months) and established (\geq 6 months) RA and the use of various treatment approaches in frequently encountered clinical scenarios, including treat-to-target, switching between therapies, tapering of therapy, the use of biologics and DMARDs in high-risk RA patients, vaccination in patients with RA receiving DMARDs or biologics, TB screening with biologics or tofacitinib, and laboratory monitoring with DMARDs. The guideline recommendations apply to common clinical situations, since the panel considered issues common to most patients, not exceptions.

Recommendations are classified as either strong or conditional. A strong recommendation means that the panel was confident that the desirable effects of following the recommendation outweigh the undesirable effects (or vice versa), so the course of action would apply to most patients, and only a small proportion would not want to follow the recommendation. A conditional recommendation means that the desirable effects of following the recommendation probably outweigh the undesirable effects, so the course of action would apply to the majority of patients, but some may not want to follow the recommendation. As a result, conditional recommendations are preference sensitive and warrant a shared decision-making approach.

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

Recommendations for Early RA Patients

- The panel strongly recommends using a treat-to-target strategy rather than a non-targeted approach, regardless of disease activity level. The ideal target should be low disease activity or remission, as determined by the clinician and the patient. In some cases, another target may be chosen because risk tolerance by patients or comorbidities may mitigate the usual choices.
- For DMARD-naïve patients with early, symptomatic RA, the panel strongly recommends DMARD monotherapy over double or triple DMARD therapy in patients with low disease activity and conditionally recommends DMARD monotherapy over double or triple DMARD therapy in patients with moderate or high disease activity. Methotrexate should be the preferred initial therapy for most patients with early RA with active disease.
- For patients with moderate or high disease activity despite DMARD therapy (with or without glucocorticoids), the panel strongly recommends treatment with a combination of DMARDs or a TNFi or a non-TNF biologic, with or without methotrexate (MTX) in no particular order of preference, rather than continuing DMARD monotherapy alone. Biologic therapy should be used in combination with MTX over biologic monotherapy, when possible, due to superior efficacy.
- For patients with moderate or high disease activity despite any of the above DMARD or biologic therapies, the panel conditionally recommends adding low-dose glucocorticoids (defined as ≤ 10 mg/day of prednisone or equivalent). Low-dose glucocorticoids may also be used in patients who need a bridge until realizing the benefits of DMARD therapy. The risk/benefit ratio of glucocorticoid therapy is favorable as long as the dose is low and the duration of therapy is short.
- For patients experiencing a flare of RA, the panel conditionally recommends adding short-term glucocorticoids (< 3 months of treatment) at the lowest possible dose for the shortest possible duration, to provide a favorable benefit-risk ratio for the patient.

Recommendations for Established RA Patients

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

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

- For moderate or high disease activity despite TNFi therapy in patients currently not on a DMARD, the panel strongly recommends that one or two DMARDs be added to TNFi therapy rather than continuing TNFi therapy alone.
- If disease activity is moderate or high despite single TNFi biologic therapy, the panel conditionally recommends using a non-TNF biologic.
- If disease activity is moderate or high despite non-TNF biologic therapy, the panel conditionally recommends using another non-TNF biologic. However, if a patient has failed multiple non-TNF biologics and they are TNFi-naïve with moderate or high disease activity, the panel conditionally recommends treatment with a TNFi.

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

Recommendations for RA Patients with High-Risk Comorbidities

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

- In patients with established RA with moderate or high disease activity and previously treated solid organ cancer, the panel conditionally recommends that they be treated for RA just as one would treat an RA patient without a history of solid organ cancer.
- Serious Infections:
 - In patients with established RA with moderate or high disease activity and previous serious infection(s), the panel conditionally recommends using combination DMARD therapy or abatacept rather than TNFi.

Plaque Psoriasis

American Academy of Dermatology (AAD)

In 2019, the AAD and the National Psoriasis Foundation published updated treatment guidelines for the management and treatment of psoriasis with biologic therapies. In regards to certolizumab and/or TNF inhibitors, the guidelines state:

- Certolizumab is likely to have class characteristics similar to those of other TNF- α inhibitors regarding treatment combination, efficacy in difficult-to-treat areas, and possibly, immunogenicity.
- The approved dosing for moderate-to-severe psoriasis is 400 mg (given as 2 subcutaneous injections of 200 mg each) every other week. Another dosing option may be considered for people who weigh 90 kg (198 pounds) or less: 400 mg (given as 2 injections of 200 mg each) initially and at week 2 and week 4, followed by a dose of 200 mg every other week.
- Definitive response (positive or negative) to treatment with most TNF- α inhibitors is best ascertained after 12 to 16 weeks of continuous therapy, except for infliximab, for which the best time is after 8 to 10 weeks.
- Consider dose escalation, an increase in frequency, or the addition of other modalities (such as topical corticosteroids or vitamin D analogues, methotrexate, acitretin, apremilast, or NB-UVB) in partially responding patients.

Psoriatic Arthritis

In 2019, the American Academy of Dermatology (AAD) and the National Psoriasis Foundation published updated treatment guidelines for the management and treatment of psoriasis with biologic therapies. In regards to psoriatic arthritis (PsA), certolizumab and/or TNF inhibitors, the guidelines state:

- All TNF- α inhibitors have long-established efficacy and FDA approval for PsA
- Improve the signs and symptoms of the disease
- Improve functional status and quality of life
- Inhibit progression of radiographically detected damage of joints
- Among the biologics TNF- α inhibitors should be considered as a preferred treatment option for patients with concomitant PsA

The 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 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).

Ankylosing Spondylitis

Evidence based recommendations for the management of ankylosing spondylitis (AS) were created as a combined effort of the 'ASsessment in AS' international working group and the European League Against Rheumatism (EULAR). Additionally, the American College of Rheumatology has provided recommendations for the treatment of ankylosing spondylitis. According to these comprehensive guidelines, anti-TNF treatment (infliximab, etanercept, adalimumab, and golimumab) should be given to patients with persistently high disease activity despite conventional treatments. There is no evidence to support the obligatory use of DMARDs before, or concomitant with, anti-TNF treatment in patients with axial disease. There is no evidence to support a difference in efficacy of the various TNF inhibitors on the axial and articular/enthesal disease manifestations; but in the presence of IBD a difference in gastrointestinal efficacy needs to be taken into account. Switching to a second TNF blocker might be beneficial especially in patients with loss of response.

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.

Cimzia (certolizumab pegol) is a tumor necrosis factor (TNF) blocker indicated for:

- Reducing signs and symptoms of Crohn's disease and maintaining clinical response in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy
- Treatment of adults with moderately to severely active rheumatoid arthritis
- Treatment of adult patients with active psoriatic arthritis
- Treatment of adults with active ankylosing spondylitis
- Treatment of adults with active non-radiographic axial spondyloarthritis with objective signs of inflammation
- Treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy

References

1. Cimzia [prescribing information]. Smyrna, GA: UCB, Inc; September 2019.
2. 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.
3. Lichtenstein GR, Hanauer SB, Sandborn WJ, et al. American College of Gastroenterology Practice Guidelines. Management of Crohn's Disease in Adults. *Am J Gastroenterol.* 2009;104(2):465-83.
4. Lichtenstein GR, Abreu MT, Cohen R, Tremaine W. American Gastroenterological Association Institute medical position statement on corticosteroids, immunomodulators, and infliximab in inflammatory bowel disease. *Gastroenterology.* 2006;130(3):935-9.
5. MCG™ Care Guidelines. Ambulatory Care, 24th Edition. Certolizumab.
6. Yee AM, Pochapin MB. Treatment of complicated sarcoidosis with infliximab anti-tumor necrosis factor-alpha therapy. *Ann Intern Med.* 2001;135(1):27-31.
7. Zochling J, van der Heijde D, Burgos-Vargas R, et al. ASAS/EULAR recommendations for the management of Ankylosing Spondylitis. *Ann Rheum Dis.* 2006 65:442-452.
8. Braun J, van den Berg R, Baraliakos X, et al. 2010 Update of the ASAS/EULAR Recommendations for the Management of Ankylosing Spondylitis. *Ann Rheum Dis.* 2011;70(6):896-904.
9. U.S. Food and Drug Administration Information for Healthcare Professionals: Tumor Necrosis Factor (TNF) Blockers (marketed as Remicade, Enbrel, Humira, Cimzia, and Simponi). <https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/information-tumor-necrosis-factor-tnf-blockers-marketed-remicade-enbrel-humira-cimzia-and-simponi>. Accessed July 1, 2013.
10. U.S. Food and Drug Administration Drug Safety Communication: UPDATE on Tumor Necrosis Factor (TNF) blockers and risk for pediatric malignancy. <http://www.fda.gov/Drugs/DrugSafety/ucm278267.htm>. Accessed July 1, 2013.
11. U.S. Food and Drug Administration Drug Safety Communication: Drug labels for the Tumor Necrosis Factor-alpha (TNF α) blockers now include warnings about infection with Legionella and Listeria bacteria. <http://www.fda.gov/Drugs/DrugSafety/ucm270849.htm>. Accessed July 1, 2013.
12. Takeuchi M, Kezuka T, Sugita S, et al. Evaluation of the long-term efficacy and safety of infliximab treatment for uveitis in Behçet's disease: a multicenter study. *Ophthalmology.* 2014 Oct;121(10):1877-84.
13. Kruh JN, Yang P, Suelves AM, et al. Infliximab for the treatment of refractory noninfectious Uveitis: a study of 88 patients with long-term follow-up. *Ophthalmology.* 2014 Jan;121(1):358-64.
14. Levy-Clark G, Jabs DA, Read RW, et al. Expert panel recommendations for the use of anti-tumor necrosis factor biologic agents in patients with ocular inflammatory disorders. *Ophthalmology.* 2014 Mar;121(3):785-96.
15. Lee FF, Foster CS. Pharmacology of uveitis. *Expert Opin Pharmacother.* 2010;11(7):1135-1146.

16. Menter A, Gottlieb A, Feldman SR, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 1. Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. *J Am Acad Dermatol* 2008; 58(5):826-50.
17. Gottlieb A, Korman NJ, Gordon KB, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Psoriatic arthritis: Overview and guidelines of care for treatment with an emphasis on the biologics. *J Am Acad Dermatol* 2008;58(5):851-64.
18. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 3. Guidelines of care for the management and treatment of psoriasis with topical therapies. *J Am Acad Dermatol* 2009;60(4):643-59.
19. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Guidelines of care for the treatment of psoriasis with phototherapy and photochemotherapy. *J Am Acad Dermatol* 2010;62(1):114-35.
20. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. *J Am Acad Dermatol* 2009;61(3):451-85.
21. Nast A, et al; European S3-Guidelines on the systemic treatment of psoriasis vulgaris – update 2015 – short version – EFF in cooperation with EADV and IPC, *J Eur Acad Derm Venereol* 2015;29:2277-94.
22. 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. 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.
23. [Lichtenstein GR, Loftus EV, Isaacs KL, Requeiro MD, Gerson LB, Sands BE](#). American College of Gastroenterology Practice Guidelines. Management of Crohn’s Disease in Adults. *Am J Gastroenterol*. 2018 Apr;113(4):481-517.
24. Ward MM, Deodhar A, Akl EA, Lui A, et al. American College of Rheumatology/Spondylitis Association of America, Spondyloarthritis Research and Treatment Network 2015 Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. *Arthritis Rheumatol*. 2016 Feb;68(2):282-98.

Policy History/Revision Information

Date	Summary of Changes
09/01/2021	<p>Template Update</p> <ul style="list-style-type: none"> • Removed <i>CMS</i> section • Replaced reference to “MCG™ Care Guidelines” with “InterQual® criteria” in <i>Instructions for Use</i> <p>Coverage Rationale</p> <ul style="list-style-type: none"> • Revised medical necessity criteria for treatment of: <ul style="list-style-type: none"> <i>Crohn’s Disease</i> <ul style="list-style-type: none"> ○ Updated criteria for initial therapy: <ul style="list-style-type: none"> ▪ Replaced criterion requiring “history of failure to one of the [listed] conventional therapies at up to maximally indicated doses <i>within the last 3 months</i>, unless contraindicated or clinically significant adverse effects are experienced” with “history of failure to one of the [listed] conventional therapies at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced” ▪ Added criterion to allow coverage if the patient has been previously treated with a biologic DMARD FDA-approved for the treatment of Crohn’s disease [e.g., Humira (adalimumab), Stelara (ustekinumab)] ○ Removed criterion for continuation of therapy requiring Cimzia is prescribed by or in consultation with a gastroenterologist <i>Rheumatoid Arthritis</i> <ul style="list-style-type: none"> ○ Updated criteria for initial therapy:

Date	Summary of Changes
	<ul style="list-style-type: none"> ▪ Replaced criterion requiring “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 <i>within the last 6 months</i>, unless contraindicated or clinically significant adverse effects are experienced” with “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” ▪ Added criterion to allow coverage if the patient has been previously treated with a biologic DMARD FDA-approved for the treatment of rheumatoid arthritis [e.g., Humira (adalimumab), Simponi (golimumab)] ○ Removed criterion for continuation of therapy requiring Cimzia is prescribed by or in consultation with a rheumatologist <p>Psoriatic Arthritis</p> <ul style="list-style-type: none"> ○ Updated criteria for initial therapy: <ul style="list-style-type: none"> ▪ Replaced criterion requiring “history of failure to a 3 month trial of methotrexate at the maximally indicated dose <i>within the last 6 months</i>, unless contraindicated or clinically significant adverse effects are experienced” with “history of failure to a 3 month trial of methotrexate at the maximally indicated dose, unless contraindicated or clinically significant adverse effects are experienced” ▪ Added criterion to allow coverage if the patient has been previously treated with a biologic DMARD FDA-approved for the treatment of psoriatic arthritis [e.g., Humira (adalimumab), Simponi (golimumab), Stelara (ustekinumab), Tremfya (guselkumab)] ○ Removed criterion for continuation of therapy requiring Cimzia is prescribed by or in consultation with a rheumatologist or dermatologist <p>Ankylosing Spondylitis and Non-Radiographic Axial Spondyloarthritis</p> <ul style="list-style-type: none"> ○ Updated criteria for initial therapy: <ul style="list-style-type: none"> ▪ Replaced criterion requiring “history of failure to two NSAIDs (e.g., ibuprofen, naproxen) at the maximally indicated doses, each used for at least 4 weeks <i>within the last 3 months</i>, unless contraindicated or clinically significant adverse effects are experienced” with “history of failure to two NSAIDs (e.g., ibuprofen, naproxen) at the maximally indicated doses, each used for at least 4 weeks, unless contraindicated or clinically significant adverse effects are experienced” ▪ Added criterion to allow coverage if the patient has been previously treated with a biologic DMARD FDA-approved for the treatment of ankylosing spondylitis [e.g., Humira (adalimumab), Simponi (golimumab)] ○ Removed criterion for continuation of therapy requiring Cimzia is prescribed by or in consultation with a rheumatologist <p>Plaque Psoriasis</p> <ul style="list-style-type: none"> ○ Updated criteria for initial therapy: <ul style="list-style-type: none"> ▪ Replaced criterion requiring “history of failure to a 3 month trial of methotrexate at the maximally indicated dose <i>within the last 6 months</i>, unless contraindicated or clinically significant adverse effects are experienced” with “history of failure to a 3 month trial of methotrexate at the maximally indicated dose, unless contraindicated or clinically significant adverse effects are experienced” ▪ Added criterion to allow coverage if the patient has been previously treated with a biologic DMARD FDA-approved for the treatment of plaque psoriasis [e.g., Humira (adalimumab), Skyrizi (risankizumab-rzaa), Stelara (ustekinumab), Tremfya (guselkumab)] ○ Removed criterion for continuation of therapy requiring Cimzia is prescribed by or in consultation with a dermatologist <p>Supporting Information</p> <ul style="list-style-type: none"> ● Updated <i>References</i> section to reflect the most current information ● Archived previous policy version CS2020D0083D

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.