

# **Drug Coverage Policy**

# Multiple Sclerosis and Crohn's Disease (Injectable – Other) – Tysabri Prior Authorization Policy

• Tysabri® (natalizumab intravenous infusion – Biogen)

#### INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide quidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment quidelines. In certain markets, delegated vendor quidelines may be used to support medical necessity and other coverage determinations.

Page 1 of 9

## Cigna Healthcare Coverage Policy

### **Overview**

Tysabri, an integrin receptor antagonist, is indicated for the treatment of:1

- Relapsing forms of multiple sclerosis (MS) which include clinically isolated syndrome, relapsing remitting disease, and active secondary progressive disease in adults as monotherapy.
- **Crohn's disease**, inducing and maintaining clinical response and remission in adults with moderately to severely active disease with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional Crohn's disease therapies and inhibitors of tumor necrosis factor (TNF).

Tysabri increases the risk of progressive multifocal leukoencephalopathy (PML).¹ When initiating and continuing treatment with Tysabri in patients with MS, physicians should consider whether the expected benefit of Tysabri is sufficient to offset the risks. Tysabri should not be used in combination with immunosuppressants (e.g., azathioprine, 6-mercaptopurine, cyclosporine, methotrexate) or inhibitors of TNFa. The safety and effectiveness in patients with MS or Crohn's disease < 18 years of age have not been established.

# **Disease Overview Multiple Sclerosis**

MS is a chronic, inflammatory, demyelinating, autoimmune disease of the central nervous system that impacts almost 1,000,000 people in the US.<sup>2</sup> The condition is marked by inflammation and demyelination, as well as degenerative alterations. Patients usually experience relapses and remissions in their neurological symptoms. For most patients, the onset of MS symptoms occurs when patients are 20 to 40 years of age; however, children can get MS and new onset disease can occur in older adults. The MS disease course is heterogeneous but has some patterns. Approximately 85% to 90% of patients have a relapsing pattern at onset. However, this transitions over time in patients who are untreated to a worsening with very few or no relapses or magnetic resonance imaging (MRI) activity (secondary progressive MS). Around 10% to 15% of patients have a steady progression of symptoms over time (primary progressive MS), marked by some clinical manifestations or by MRI activity. Primary progressive MS is generally diagnosed in patients on the upper level of the typical age range (e.g., almost 40 years of age) and the distribution is equivalent among the two genders. Advances in the understanding of the MS disease process, as well as in MRI technology, spurned updated disease course descriptions in 2013,<sup>5</sup> as well as in 2017.<sup>6</sup> The revised disease courses are clinically isolated syndrome, relapsing remitting MS, primary progressive MS, and secondary progressive MS.<sup>2-4</sup> Clinically isolated syndrome is now more recognized among the course descriptions of MS. It is the first clinical presentation of MS that displays characteristics of inflammatory demyelination that may possibly be MS but has yet to fulfill diagnostic criteria.

#### Crohn's Disease

Crohn's disease is a chronic inflammatory disease of the gastrointestinal (GI) tract. Any GI tract segment can be impacted, but most common the terminal ileum and proximal colon in a discontinuous, patchy, segmental, and transmural manner. Common symptoms of Crohn's disease include abdominal pain, diarrhea, fatigue, weight loss, fever, anemia, and recurrent fistulas. Other extraintestinal manifestations may be present in up to 50% of patients (e.g., skin, joint, eye conditions). Notable associated manifestations are arthropathy (axial and peripheral), dermatological (e.g., pyoderma gangrenosum), ocular (uveitis, scleritis), and hepatobiliary disease (e.g., primary sclerosing cholangitis). Younger patients may experience growth failure. The chronic intestinal inflammation over time leads to intestinal complications such as strictures, fistulas, and abscesses. Only 20% to 30% of patients with Crohn's disease will have a

Page 2 of 9

nonprogressive or indolent course. Metabolic bone diseases, thromboembolic complications, osteonecrosis, cholelithiasis, and nephrolithiasis may be present as well. Previously, the condition was managed with 5-aminosalicylates, corticosteroids, methotrexate, and immunomodulators (e.g., azathioprine, 6-mercaptopurine). Now, other therapies include anti-TNF agents (e.g., infliximab products, adalimumab products, Cimzia<sup>®</sup> [certolizumab pegol subcutaneous injection]).

#### **Guidelines**

In September 2019, a consensus paper was updated by the MS Coalition that discusses the use of disease-modifying therapies in MS.<sup>2</sup> Many options from various drug classes, involving different mechanisms of action and modes of administration, have shown benefits in patients with MS.

The American College of Gastroenterology has guidelines on management of Crohn's disease in adults (2025). Tysabri has a limited role in the management of the condition. The recommendations are extensive. Generally, all of the advanced therapies are recommended for induction and maintenance of remission. Advanced therapies recommended include TNF inhibitors, Entyvio® (vedolizumab intravenous infusion and subcutaneous injection), interleukin (IL)-23 inhibitors, IL-12/23 inhibitors, and Rinvoq® (upadacitinib extended-release tablets). It is cited that treatment with Tysabri is best limited to patients who are not seropositive for anti-John Cunningham virus antibody; this should be checked before initiating therapy and at a minimum of once every 6 months thereafter. Due to the availability of other agents with more favorable safety profiles, the other **advanced therapies** that are indicated for moderate to severe Crohn's disease should be used instead of Tysabri.

#### Safety

Tysabri has a Boxed Warning regarding the risk of PML.<sup>1</sup> Tysabri is available only through a special restricted distribution Risk Evaluation and Mitigation Strategy (REMS) program called the TOUCH® Prescribing Program.

## **Coverage Policy**

### **Policy Statement**

Prior Authorization is required for benefit coverage of Tysabri. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Tysabri as well as the monitoring required for adverse events and long-term efficacy, approval requires Tysabri to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Tysabri is considered medically necessary when ONE of the following is met (1 or 2):

### **FDA-Approved Indications**

- **1. Multiple Sclerosis.** Approve for 1 year if the patient meets one of the following (A or B)
  - **A)** <u>Initial Therapy</u>. Approve if the patient meets all of the following (i, ii, iii, <u>and</u> iv):
    - i. Patient is ≥ 18 of age; AND
    - ii. Patient has a relapsing form of multiple sclerosis; AND

Page 3 of 9

<u>Note</u>: Examples of relapsing forms of multiple sclerosis include clinically isolated syndrome, relapsing remitting disease, and active secondary progressive multiple sclerosis

- **iii.** Patient meets ONE of the following (a <u>or</u> b):
  - According to the prescriber, the patient has experienced inadequate efficacy or significant intolerance to one disease-modifying agent used for multiple sclerosis;
     OR

Note: See Appendix A for examples.

- **b)** According to the prescriber the patient has highly active or aggressive multiple sclerosis by meeting ONE of the following [(1), (2), (3), or (4)]:
  - (1)Patient has demonstrated rapidly advancing deterioration(s) in physical functioning; OR

<u>Note</u>: Examples include loss of mobility or lower levels of ambulation and severe changes in strength or coordination.

- (2)Disabling relapse(s) with suboptimal response to systemic corticosteroids; OR
- (3) Magnetic resonance imaging (MRI) findings suggest highly active or aggressive multiple sclerosis; OR

<u>Note</u>: Examples include new, enlarging, or a high burden of T2 lesions or gadolinium-enhancing lesions.

- (4) Manifestations of multiple sclerosis-related cognitive impairment; AND
- **iv.** Medication is prescribed by or in consultation with a neurologist or a physician who specializes in the treatment of multiple sclerosis; OR
- **B)** Patient is Currently Receiving Tysabri. Approve if the patient meets ONE of the following (i or ii):
  - i. Patient has been receiving Tysabri for < 1 year. Approve if the patient meets ALL of the following (a, b, and c):
    - a) Patient is ≥ 18 years of age; AND
    - **b)** Patient has a relapsing form of multiple sclerosis; AND <a href="Note">Note</a>: Examples of relapsing forms of multiple sclerosis include clinically isolated syndrome, relapsing remitting disease, and active secondary progressive disease.
    - **c)** Medication is prescribed by or in consultation with a neurologist or a physician who specializes in the treatment of multiple sclerosis; OR
  - **ii.** Patient has been receiving Tysabri for 1 year or more. Approve if the patient meets ALL of the following (a, b, c, and d):
    - a) Patient is ≥ 18 years of age; AND
    - b) Patient has a relapsing form of multiple sclerosis; AND Note: Examples of relapsing forms of multiple sclerosis include clinically isolated syndrome, relapsing remitting disease, and active secondary progressive multiple sclerosis.
    - c) Patient meets ONE of the following [(1) or (2)]:
      - (1)Patient experienced a beneficial clinical response when assessed by at least one objective measure; OR

<u>Note</u>: Examples include stabilization or reduced worsening in disease activity as evaluated by magnetic resonance imaging (MRI) [absence or a decrease in gadolinium enhancing lesions, decrease in the number of new or enlarging T2 lesions]; stabilization or reduced worsening on the Expanded Disability Status Scale (EDSS) score; achievement in criteria for No Evidence of Disease Activity-

- 3 (NEDA-3) or NEDA-4; improvement on the fatigue symptom and impact questionnaire-relapsing multiple sclerosis (FSIQ-RMS) scale; reduction or absence of relapses; improvement or maintenance on the six-minute walk test or 12-Item Multiple Sclerosis Walking Scale; improvement on the Multiple Sclerosis Functional Composite (MSFC) score; and/or attenuation of brain volume loss.
- (2) Patient experienced stabilization, slowed progression, or improvement in at least one symptom such as motor function, fatigue, vision, bowel/bladder function, spasticity, walking/gait, or pain/numbness/tingling sensation; AND
- **d)** Medication is prescribed by or in consultation with a neurologist or a physician who specializes in the treatment of multiple sclerosis.

**Dosing.** Approve up to 300 mg given by intravenous infusion administered no more frequently than once every 4 weeks.

- **2. Crohn's Disease.** Approve for the duration noted below if the patient meets one of the following (A <u>or</u> B):
  - **A)** <u>Initial Therapy</u>. Approve for 6 months if the patient meets all of the following (i, ii, iii, <u>and</u> iv):
    - i. Patient is  $\geq$  18 years of age; AND
    - ii. Patient has moderately to severely active Crohn's disease; AND
    - **iii.** Patient has tried at least two advanced therapies indicated for use in Crohn's disease; AND

<u>Note</u>: Advanced therapies include biologics and a Janus kinase inhibitor indicated for Crohn's disease. Each biosimilar tried from the same chemical would only count as a trial of one product. Refer to <u>Appendix B</u> for examples of biologics and the Janus kinase inhibitor indicated for use in Crohn's disease.

- iv. Medication is prescribed by or in consultation with a gastroenterologist; OR
- **B)** Patient is Currently Receiving Tysabri. Approve for 1 year if the patient meets ALL of the following (i, ii, iii, and iv):
  - Patient has been established on therapy for at least 6 months; AND
     Note: A patient who has received < 6 months of therapy or who is restarting therapy is reviewed under criteria A (Initial Therapy).</p>
  - ii. Patient is ≥ 18 years of age; AND
  - iii. Patient meets at least ONE of the following (a or b):
    - a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating Tysabri); OR

      Note: Examples of objective measures include fecal markers (e.g., renal lactoferrin, fecal calprotectin), serum markers (e.g., C-reactive protein), imaging studies (magnetic resonance enterography [MRE], computed tomography enterography [CTE]), endoscopic assessment, and/or reduced dose of corticosteroids.
    - **b)** Compared with baseline (prior to initiating Tysabri), patient experienced an improvement in at least one symptom, such as decreased pain, fatigue, stool frequency, and/or blood in stool; AND
  - iv. Medication is prescribed by or in consultation with a gastroenterologist.

**Dosing in Crohn's Disease.** Approve up to 300 mg given by intravenous infusion administered no more frequently than once every 4 weeks.

Page 5 of 9

#### **Conditions Not Covered**

Tysabri for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. Concurrent Use with Other Potent Immunosuppressants. Co-administration with other potent immunosuppressive drugs has the risk of added immunosuppression and has not been evaluated in clinical trials.<sup>1</sup>

Note: Examples include 6-mercaptopurine, azathioprine, cyclosporine, and methotrexate.

- 2. Concurrent Use With a Biologic or with a Targeted Synthetic Oral Small Molecule Drug. This medication should not be administered in combination with another biologic or with a targeted synthetic oral small molecule drug used for an inflammatory condition (see Appendix B for examples). Combination therapy is generally not recommended due to a potentially higher rate of adverse events and lack of controlled clinical data supporting additive efficacy.
- **3.** Concurrent Use with Other Disease-Modifying Agents Used for Multiple Sclerosis. These agents are not indicated for use in combination (See Appendix A for examples). Additional data are required to determine if use of disease-modifying multiple sclerosis agents in combination is safe and provides added efficacy.
- 4. Non-Relapsing Forms of Multiple Sclerosis. The safety and efficacy of Tysabri have not been established in patients with primary progressive multiple sclerosis.
  Note: An example of a non-relapsing form of multiple sclerosis is primary progressive multiple sclerosis.
- **5. Ulcerative Colitis.** Efficacy data with use of Tysabri are limited. <sup>10</sup>

## **Coding Information**

- 1) This list of codes may not be all-inclusive.
- 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

# Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS	Description
Codes	
J2323	Injection, natalizumab, 1 mg

## References

- 1. Tysabri® intravenous infusion [prescribing information]. Cambridge, MA: Biogen; March 2025.
- 2. A Consensus Paper by the Multiple Sclerosis Coalition. The use of disease-modifying therapies in multiple sclerosis. Updated September 2019.
- 3. McGinley MP, Goldschmidt C, Rae-Grant AD. Diagnosis and treatment of multiple sclerosis. A review. *JAMA*. 2021;325(8):765-779.

Page 6 of 9

- 4. No authors listed. Drugs for multiple sclerosis. Med Lett Drugs Ther. 2021;63(1620):42-48.
- 5. Lublin FD, Reingold SC, Cohen JA, et al. Defining the clinical course of multiple sclerosis: the 2013 revisions. *Neurology*. 2014;83:278-286.
- 6. Thompson AJ, Banwell BL, Barkhof F, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *Lancet Neurol*. 2018;17(2):162-173.
- 7. Dolinger M, Torres J, Vermeire S. Crohn's disease. Lancet. 2024;403(10432):1177-1191.
- 8. Lichtenstein GR, Loftus EV, Afzali A, et al. ACG clinical guideline: management of Crohn's Disease in Adults. *Am J Gastroenterol*. 2025;120:1225-1264.
- 9. Gordon FH, Hamilton MI, Donoghue S, et al. A pilot study of treatment of active ulcerative colitis with natalizumab, a humanized monoclonal antibody to alpha-4 integrin. *Aliment Pharmacol Ther*. 2002;16:699-705.

## **Revision Details**

Type of Revision	Summary of Changes	Date
New	New policy	12/01/2024
Annual Revision	The name of the policy was changed to add "Injectable – Other". In addition, the following changes were made:  Multiple Sclerosis: Extavia was removed from Appendix A.  Crohn's Disease: For Initial Therapy, criteria was changed from "the patient has tried at least two biologics indicated for use in Crohn's disease" to "the patient has tried at least two advanced therapies indicated for use in Crohn's disease". An addition was made to the note that "advanced therapies include biologics and a Janus kinase inhibitor indicated for Crohn's disease. It was added that Appendix B now lists the Janus kinase inhibitor indicated for use in Crohn's disease. Appendix B was updated to note that biosimilars are available for IV and SC Stelara. New indications in Appendix B were updated.	11/01/2025

The policy effective date is in force until updated or retired.

## **APPENDIX A**

Medication	Mode of Administration
Aubagio® (teriflunomide tablets, generic)	Oral
Avonex® (interferon beta-1a intramuscular injection)	Injection (self-administered)
Bafiertam® (monomethyl fumarate delayed-release capsules)	Oral
Betaseron® (interferon beta-1b subcutaneous injection)	Injection (self-administered)
Briumvi® (ublituximab-xiiy intravenous infusion)	Intravenous infusion
Copaxone® (glatiramer acetate subcutaneous injection,	Injection (self-administered)
generic) Gilenya® (fingolimod capsules, generic)	Oral
Glatopa® (glatiramer acetate subcutaneous injection)	Injection (self-administered)
Kesimpta® (ofatumumab subcutaneous injection)	Injection (self-administered)

Page 7 of 9

Lemtrada® (alemtuzumab intravenous infusion)	Intravenous infusion
Mavenclad® (cladribine tablets)	Oral
Mayzent® (siponimod tablets)	Oral
Ocrevus® (ocrelizumab intravenous infusion)	Intravenous infusion
Ocrevus Zunovo™ (ocrelizumab and hyaluronidase-ocsq	Subcutaneous Injection (not self-
subcutaneous injection)	administered)
Plegridy® (peginterferon beta-1a subcutaneous or	Injection (self-administered)
intramuscular injection)	
Ponvory® (ponesimod tablets)	Oral
Rebif® (interferon beta-1a subcutaneous injection)	Injection (self-administered)
Tascenso ODT® (fingolimod orally disintegrating tablets)	Oral
Tecfidera® (dimethyl fumarate delayed-release capsules,	Oral
generic)	
Tyruko® (natalizumab intravenous infusion)	Intravenous infusion
Tysabri® (natalizumab intravenous infusion)	Intravenous infusion
Vumerity® (diroximel fumarate delayed-release capsules)	Oral
Zeposia® (ozanimod capsules)	Oral

## APPENDIX B

	Mechanism of Action	Examples of Indications*			
Biologics	Biologics				
Adalimumab SC Products (Humira®, biosimilars)	Inhibition of TNF	AS, CD, HS, JIA, PsO, PsA, RA, UC			
Cimzia® (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, JIA, nr-axSpA, PsO, PsA, RA			
Etanercept SC Products (Enbrel®, biosimilars)	Inhibition of TNF	AS, JIA, PsO, PsA, RA			
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC			
Zymfentra® (infliximab-dyyb SC injection)	Inhibition of TNF	CD, UC			
Simponi®, Simponi Aria® (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC			
		IV formulation: AS, PJIA, PsA, RA			
<b>Tocilizumab Products</b> (Actemra® IV, biosimilar; Actemra SC, biosimilar)	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA			
		IV formulation: PJIA, RA, SJIA			
Kevzara® (sarilumab SC injection)	Inhibition of IL-6	RA			
Orencia® (abatacept IV infusion, abatacept	T-cell costimulation	SC formulation: JIA, PSA, RA			
SC injection)	modulator	IV formulation: JIA, PsA, RA			
Rituximab IV Products (Rituxan®, biosimilars)	CD20-directed cytolytic antibody	RA			
Kineret® (anakinra SC injection)	Inhibition of IL-1	JIA^, RA			
Omvoh® (mirikizumab IV infusion, SC injection)	Inhibition of IL-23	CD, UC			
<b>Ustekinumab Products</b> (Stelara® IV , biosimilar; Stelara SC, biosimilar)	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC			
		IV formulation: CD, UC			
Siliq® (brodalumab SC injection)	Inhibition of IL-17	PsO			
Cosentyx® (secukinumab SC injection; secukinumab IV infusion)	Inhibition of IL-17A	SC formulation: AS, ERA, nr-axSpA, PsO, PsA			
,		IV formulation: AS, nr- axSpA, PsA			
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA			
<b>Bimzelx</b> ® (bimekizumab-bkzx SC injection)	Inhibition of IL- 17A/17F	AS, HS, nr-axSpA, PsA, PsO			

Page 8 of 9 Coverage Policy Number: IP0690

Ilumya® (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
Skyrizi® (risankizumab-rzaa SC injection,	Inhibition of IL-23	SC formulation: CD, PSA,
risankizumab-rzaa IV infusion)		PsO, UC
		IV formulation: CD, UC
Tremfya® (guselkumab SC injection,	Inhibition of IL-23	SC formulation: CD, PsA,
guselkumab IV infusion)		PsO, UC
		IV formulation: CD, UC
Entyvio® (vedolizumab IV infusion,	Integrin receptor	CD, UC
vedolizumab SC injection)	antagonist	
Oral Therapies/Targeted Synthetic Oral S	Small Molecule Drugs	
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Cibinqo <sup>™</sup> (abrocitinib tablets)	Inhibition of JAK	AD
	pathways	
Olumiant® (baricitinib tablets)	Inhibition of JAK	RA, AA
	pathways	
Litfulo® (ritlecitinib capsules)	Inhibition of JAK	AA
	pathways	
Leqselvi® (deuruxolitinib tablets)	Inhibition of JAK	AA
	pathways	
<b>Rinvoq</b> ® (upadacitinib extended-release	Inhibition of JAK	AD, AS, nr-axSpA, RA, PsA,
tablets)	pathways	CD, UC
Rinvoq® LQ (upadacitinib oral solution)	Inhibition of JAK	PsA, PJIA
	pathways	
Sotyktu® (deucravacitinib tablets)	Inhibition of TYK2	PsO
Xeljanz® (tofacitinib tablets/oral solution)	Inhibition of JAK	RA, PJIA, PsA, UC
	pathways	
Xeljanz® XR (tofacitinib extended-release	Inhibition of JAK	RA, PsA, UC
tablets)	pathways	
Zeposia® (ozanimod tablets)	Sphingosine 1	UC
	phosphate receptor	
	modulator	
<b>Velsipity</b> ® (etrasimod tablets)	Sphingosine 1	UC
	phosphate receptor	
	modulator	

<sup>\*</sup> Not an all-inclusive list of indications. Refer to the prescribing information for the respective agent for FDA-approved indications; SC – Subcutaneous; TNF – Tumor necrosis factor; AS – Ankylosing spondylitis; CD – Crohn's disease; HS – Hidradenitis suppurativa; JIA – Juvenile idiopathic arthritis; PSO – Plaque psoriasis; PSA – Psoriatic arthritis; RA – Rheumatoid arthritis; UC – Ulcerative colitis; nr-axSpA – Non-radiographic axial spondyloarthritis; IV – Intravenous, PJIA – Polyarticular juvenile idiopathic arthritis; IL – Interleukin; SJIA – Systemic juvenile idiopathic arthritis; Off-label use of Kineret in JIA supported in guidelines; ERA – Enthesitis-related arthritis; DMARD – Disease-modifying antirheumatic drug; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; AD – Atopic dermatitis; AA – Alopecia areata; TYK2 – Tyrosine kinase 2.

<sup>&</sup>quot;Cigna Companies" refers to operating subsidiaries of The Cigna Group. All products and services are provided exclusively by or through such operating subsidiaries, including Cigna Health and Life Insurance Company, Connecticut General Life Insurance Company, Evernorth Behavioral Health, Inc., Cigna Health Management, Inc., and HMO or service company subsidiaries of The Cigna Group. © 2025 The Cigna Group.