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Guselkumab

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Related Policies (if applicable)
None

Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current peer-reviewed scientific literature. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and acceptable standards of medical practice. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Coverage

NOTE 1: Guselkumab (Tremfya®) may be self-administered. For self-administered medications, please refer to the applicable pharmacy benefit plan.

Ulcerative Colitis

Guselkumab (Tremfya®) **may be considered medically necessary** when **ALL** the following criteria are met:

- Adults (18 years of age or older) with moderate to severely active ulcerative colitis; AND

- Individual will not receive Guselkumab (Tremfya®) concurrently with other biologics used to treat ulcerative colitis (e.g., infliximab, vedolizumab, ustekinumab, risankizumab-rzaa).

NOTE 2: When meeting criteria noted above, adults with ulcerative colitis will receive the first three doses of Tremfya through a vein in the arm (intravenous infusion) in a healthcare facility by a healthcare provider at week 0, week 4 and week 8. Individuals may then receive Tremfya as an injection under the skin (subcutaneous injection) for maintenance every 4 or 8 weeks as recommended to maintain therapeutic response.

Crohn's Disease
Guselkumab (Tremfya®) **may be considered medically necessary** for adults with moderately to severely active Crohn's disease.

Other
Intravenous formulations of guselkumab (Tremfya®) **are considered experimental, investigational and/or unproven** for all other indications.

Policy Guidelines

None.

Description

Ulcerative Colitis
Ulcerative colitis is an inflammatory bowel disease that causes inflammation and ulcers or sores in the digestive tract. It usually develops over time and can cause diarrhea (often with blood or pus), rectal bleeding, abdominal pain and cramping, and weight loss. Treatment usually involves either medications or surgery.

Crohn's Disease
Crohn's disease is a chronic, systemic disease that manifests as inflammation within the gastrointestinal (or digestive) tract, causing persistent diarrhea and abdominal pain. It is a progressive disease, meaning it gets worse over time, and in many cases leads to surgery. Because the signs and symptoms of Crohn's disease are unpredictable, it causes a significant burden on people living with the disease.

Guselkumab
Guselkumab, an interleukin-23 antagonist, is a human immunoglobulin G1 lambda (IgG1λ) monoclonal antibody that selectively binds to the p19 subunit of interleukin 23 (IL-23) and inhibits its interaction with the IL-23 receptor. IL-23 is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Guselkumab inhibits the release of proinflammatory cytokines and chemokines.

Regulatory Status
Guselkumab (Tremfya®) was approved by the U.S. Food and Drug Administration (FDA) in 2017 for treatment of moderate to severe plaque psoriasis. In 2020, it received approval for active psoriatic arthritis; and in 2024 it was approved for adults with moderately to severely active ulcerative colitis. The FDA approved guselkumab for adults with moderately to severely active Crohn's disease in 2025. (1, 2)

NOTE 3: Guselkumab (Tremfya®) may be self-administered. For self-administered medications, please refer to the applicable pharmacy benefit plan.

Rationale

Ulcerative Colitis (1)
Induction Trial: UC1
In the 12-week induction study (UC1; NCT04033445), 701 subjects with moderately to severely active ulcerative colitis were randomized 3:2 to receive either Tremfya 200 mg or placebo by intravenous infusion at Week 0, Week 4, and Week 8. Disease activity was assessed by the modified Mayo score (mMS), a 3-component Mayo score (0-9) which consists of the following subscores (0 to 3 for each subscore): stool frequency (SFS), rectal bleeding (RBS), and findings on centrally reviewed endoscopy (ES). An ES of 2 was defined by marked erythema, lack of vascular pattern, friability, and/or erosions; an ES of 3 was defined by spontaneous bleeding and ulceration. Enrolled subjects with a mMS between 5 and 9 and an ES of 2 or 3 were classified as having moderately to severely active ulcerative colitis. Subjects with inadequate response, loss of response, or intolerance to corticosteroids, immunomodulators (azathioprine, 6-mercaptopurine), biologic therapy (TNF blockers, vedolizumab), and/or Janus kinase (JAK) inhibitors were enrolled.

At baseline in UC1, the median mMS was 7, 64% of subjects had severely active disease (mMS ≥7), and 68% of subjects had an ES of 3. In UC1, 49% of subjects had previously failed (inadequate response, loss of response, or intolerance) treatment with at least one biologic therapy and/or JAK inhibitor, 48% were biologic and JAK inhibitor naïve, and 3% had previously received but not failed a biologic or JAK inhibitor. The median age was 39 years (ranging from 18 to 79 years); 43% were female; and 72% identified as White, 21% as Asian, 1% as Black or African American, <1% as American Indian or Alaskan Native, and <1% as multiple racial groups.

Enrolled subjects were permitted to use stable doses of oral aminosalicylates, immunomodulators (azathioprine, 6-mercaptopurine, methotrexate), and/or oral corticosteroids (up to 20 mg/day prednisone or equivalent). At baseline, 72% of subjects were receiving aminosalicylates, 21% of subjects were receiving immunomodulators, and 43% of subjects were receiving corticosteroids. Concomitant biologic therapies or JAK inhibitors were not permitted.

In UC1, the primary endpoint was clinical remission at Week 12 as defined by the mMS. Secondary endpoints at Week 12 included endoscopic improvement, clinical response, and histologic endoscopic mucosal improvement (see Table 1).

Table 1. Proportion of Subjects with Ulcerative Colitis Meeting Efficacy Endpoints at Week 12 in UC1

Endpoint	Placebo	Tremfya 200 mg Intravenous Infusion[a]	Treatment Difference (95% CI)
Clinical remission[b]			
Total Population	N=280 8%	N=421 23%	15% (10%, 20%)[c]
Prior biologic and/or JAK inhibitor failure[d]	N=136 4%	N=208 13%	
Without prior biologic or JAK inhibitor failure[e]	N=144 12%	N=213 32%	
Endoscopic improvement[f]			
Total population	N=280 11%	N=421 27%	16% (10%, 21%)[c]
Prior biologic and/or JAK inhibitor failure[d]	N=136 5%	N=208 15%	
Without prior biologic or JAK inhibitor failure[e]	N=144 17%	N=213 38%	
Clinical response[g]			
Total population	N=280 28%	N=421 62%	34% (27%, 41%)[c]
Prior biologic and/or JAK inhibitor failure[d]	N=136 20%	N=208 51%	
Without prior biologic or JAK inhibitor failure[e]	N=144 35%	N=213 71%	
Histologic endoscopic mucosal improvement (HEMI)[h]			
Total population	N=280 8%	N=421 24%	16% (11%, 21%)[c]
Prior biologic and/or JAK inhibitor failure[d]	N=136 4%	N=208 13%	
Without prior biologic or JAK inhibitor failure[e]	N=144 10%	N=213 33%	

CI: confidence interval; JAK: Janus kinase; UC: ulcerative colitis.

[a] Tremfya 200 mg as an intravenous infusion at Week 0, Week 4, and Week 8.

[b] A stool frequency subscore of 0 or 1 and not increased from baseline, a rectal bleeding subscore of 0, and an endoscopy subscore of 0 or 1 with no friability.

[c] $p < 0.001$, adjusted treatment difference (95% CI) based on Cochran-Mantel-Haenszel method (adjusted for stratification factors: biologic and/or JAK-inhibitor failure status and concomitant use of corticosteroids at baseline).

[d] Includes inadequate response, loss of response, or intolerance to biologic therapy (TNF blockers, vedolizumab) and/or a Janus kinase (JAK) inhibitor for ulcerative colitis.
[e] Includes subjects that were biologic and/or JAK inhibitor naïve and subjects with biologic and/or JAK inhibitor exposure who did not meet criteria for failure. Of these, 7 subjects in the placebo group and 11 subjects in the Tremfya group were previously exposed to, but did not fail, a biologic or JAK inhibitor.
[f] An endoscopy subscore of 0 or 1 with no friability.
[g] Decrease from induction baseline in the modified Mayo score by ≥30% and ≥2 points, with either a ≥1 point decrease from baseline in the rectal bleeding subscore or a rectal bleeding subscore of 0 or 1.
[h] An endoscopy subscore of 0 or 1 with no friability and Geboes score ≤3.1 (indicating neutrophil infiltration in <5% of crypts, no crypt destruction, and no erosions, ulcerations, or granulation tissue).

Study UC1 was not designed to evaluate the relationship of histologic endoscopic mucosal improvement at Week 12 to disease progression and long-term outcomes.

Rectal Bleeding and Stool Frequency Subscores
Decreases in rectal bleeding and stool frequency subscores were observed as early as Week 4 in subjects treated with Tremfya compared to placebo.

Endoscopic Assessment
Normalization of the endoscopic appearance of the mucosa (endoscopic remission) was defined as ES of 0. At Week 12 of UC1, a greater proportion of subjects treated with Tremfya compared to placebo-treated subjects achieved endoscopic remission (15% vs 5%).

Fatigue Response
In UC1, subjects treated with Tremfya experienced a clinically meaningful improvement in fatigue, assessed by the PROMIS-Fatigue Short form 7a, at Week 12, compared to placebo-treated subjects. The effect of Tremfya to improve fatigue after 12 weeks of induction has not been established.

<u>Maintenance Trial: UC2</u>
The maintenance trial (UC2) evaluated 568 subjects who received one of two intravenous Tremfya induction regimens, including the recommended 200 mg regimen, for 12 weeks in Studies UC1 or UC3 (induction dose-finding study) and demonstrated clinical response per mMS after 12 weeks. Subjects were re-randomized to receive a subcutaneous maintenance regimen of either Tremfya 100 mg every 8 weeks, Tremfya 200 mg every 4 weeks, or placebo for up to an additional 44 weeks.

In UC2, 42% of subjects had failed (inadequate response, loss of response, or intolerance) treatment with one or more biologics or JAK inhibitors.

The primary endpoint was clinical remission at Week 44 defined by mMS. Secondary endpoints included corticosteroid-free clinical remission, endoscopic improvement, histologic endoscopic mucosal improvement, all at Week 44 and maintenance of clinical remission at Week 44 in subjects who achieved clinical remission 12 weeks after intravenous Tremfya induction treatment (see Table 2).

Table 2. Proportion of Subjects with Ulcerative Colitis Meeting Efficacy Endpoints at Week 44 in UC2

Endpoint	Placebo	Tremfya 100 mg Every 8 Weeks SQ Injection[a]	Tremfya 200 mg Every 4 Weeks SQ Injection[b]	Treatment Difference vs Placebo (95% CI)	
				Tremfya 100 mg	Tremfya 200 mg
Clinical remission[c]					
Total population[d]	N=190 19%	N=188 45%	N=190 50%	25% (16%, 34%)[e]	30% (21%, 38%)[e]
Prior biologic and/or JAK inhibitor failure[f]	N=75 8%	N=77 40%	N=88 40%		
Without prior biologic or JAK inhibitor failure[g]	N=115 26%	N=111 49%	N=102 59%		
Corticosteroid-free clinical remission[h]					
Total population[d]	N=190 18%	N=188 45%	N=190 49%	26% (17%, 34%)[e]	29% (20%, 38%)[e]
Prior biologic and/or JAK inhibitor failure[f]	N=75 7%	N=77 40%	N=88 40%		
Without prior biologic or JAK inhibitor failure[g]	N=115 26%	N=111 49%	N=102 57%		
Endoscopic improvement[i]					
Total population[d]	N=190 19%	N=188 49%	N=190 52%	30% (21%, 38%)[e]	31% (22%, 40%)[e]
Prior biologic and/or JAK inhibitor failure[f]	N=75 8%	N=77 45%	N=88 42%		
Without prior biologic or JAK inhibitor failure[g]	N=115 26%	N=111 52%	N=102 60%		
Histologic endoscopic mucosal improvement (HEMI)[j]					
Total population[d]	N=190 17%	N=188 44%	N=190 48%	26% (17%, 34%)[e]	30% (21%, 38%)[e]

Prior biologic and/or JAK inhibitor failure[f]	N=75 8%	N=77 38%	N=88 39%		
Without prior biologic or JAK inhibitor failure[g]	N=115 23%	N=111 48%	N=102 56%		
Maintenance of clinical remission at week 44 in subjects who achieved clinical remission after 12 weeks of induction					
Total population[k]	N=59 34%	N=66 61%	N=69 72%	26% (9%, 43%)[l]	38% (23%, 54%)[e]
Prior biologic and/or JAK inhibitor failure[f]	N=15 27%	N=20 60%	N=18 56%		
Without prior biologic or JAK inhibitor failure[m]	N=44 36%	N=46 61%	N=51 78%		

CI: confidence interval; JAK: Janus kinase; SQ: subcutaneous; UC: ulcerative colitis.

[a] Tremfya 100 mg as a subcutaneous injection every 8 weeks after the induction regimen.

[b] Tremfya 200 mg as a subcutaneous injection every 4 weeks after the induction regimen.

[c] A stool frequency subscore of 0 or 1 and not increased from induction baseline, a rectal bleeding subscore of 0, and an endoscopy subscore of 0 or 1 with no friability.

[d] Subjects who achieved clinical response 12 weeks following the intravenous administration of Tremfya in either induction study UC1 or induction dose-finding study UC3.

[e] p <0.001, adjusted treatment difference (95% CI) based on Cochran-Mantel-Haenszel method adjusted for randomization stratification factors.

[f] Includes inadequate response, loss of response, or intolerance to biologic therapy (TNF blockers, vedolizumab) and/or a Janus kinase (JAK) inhibitor for ulcerative colitis.

[g] Includes subjects that were biologic and/or JAK inhibitor naïve and subjects with biologic and/or JAK inhibitor exposure who did not meet criteria for failure. Of these, 7 subjects in the placebo group, 6 subjects in the Tremfya 100 mg group, and 6 subjects in the Tremfya 200mg group were previously exposed to, but did not fail, a biologic or JAK inhibitor.

[h] Not requiring any treatment with corticosteroids for at least 8 weeks prior to week 44 and also meeting the criteria for clinical remission at week 44.

[i] An endoscopy subscore of 0 or 1 with no friability.

[j] An endoscopy subscore of 0 or 1 with no friability and Geboes score ≤3.1 (indicating neutrophil infiltration in <5% of crypts, no crypt destruction, and no erosions, ulcerations, or granulation tissue).

[k] Subjects who achieved clinical remission 12 weeks following intravenous administration of TREMFYA in either induction study UC1 or induction dose-finding study UC3.

[l] p <0.01, adjusted treatment difference (95% CI) based on Cochran-Mantel-Haenszel method adjusted for randomization stratification factors.

[m] Includes subjects that were biologic and/or JAK inhibitor naïve and subjects with biologic and/or JAK inhibitor exposure who did not meet criteria for failure. Of these, 3 subjects in the placebo group, 3 subjects in the Tremfya 100 mg group, and 3 subjects in the Tremfya 200 mg group were previously exposed to, but did not fail, a biologic or JAK inhibitor.

Study UC2 was not designed to evaluate the relationship of histologic endoscopic mucosal improvement at Week 44 to disease progression and long-term outcomes.

Endoscopic Assessment
Normalization of the endoscopic appearance of the mucosa (endoscopic remission) was defined as ES of 0. In UC2, greater proportions of subjects treated with Tremfya 100 mg every 8 weeks or Tremfya 200 mg every 4 weeks achieved endoscopic remission at Week 44 compared to placebo-treated subjects (35% and 34%, respectively, vs. 15%).

Crohn's Disease (2)
The efficacy and safety of Tremfya were assessed in three randomized, double-blind, placebo controlled trials that enrolled adult subjects with moderately to severely active Crohn's disease who had a history of inadequate response, loss of response, or intolerance to oral corticosteroids, immunomodulators (azathioprine, 6-mercaptopurine, methotrexate), and/or biologic therapy (TNF blockers or vedolizumab). Moderately to severely active Crohn's disease was defined as a Crohn's Disease Activity Index (CDAI) score of ≥220 and a Simple Endoscopic Score for Crohn's Disease (SES-CD) of ≥6 (or ≥4 for subjects with isolated ileal disease). Subjects were permitted to use stable doses of oral corticosteroids (prednisone ≤40 mg/day or equivalent), immunomodulators (azathioprine, 6-mercaptopurine, methotrexate), and/or aminosalicylates.

Trials CD1 and CD2
In CD1 (NCT03466411), 361 subjects were randomized to receive intravenous Tremfya 200 mg at Weeks 0, 4, and 8 (N = 285) or placebo (N = 76). The median age of subjects enrolled into CD1 was 33 years (range: 18 - 83 years); 46% were female; and 75% identified as White, 22% as Asian, 1% as Black or African American, <1% as Native Hawaiian or Pacific Islander, and 2% did not report their racial group. The median baseline CDAI score was 285 (range: 220 - 442), and the median baseline SES-CD score was 11 (range: 4 - 39). Of the randomized subjects, 52% of subjects had previously failed (inadequate response, loss of response, or intolerance) treatment with at least one biologic therapy, 43% were biologic-naïve, and 6% had previously received but had not failed a biologic. At baseline, 37% of subjects were receiving oral corticosteroids and 30% of subjects were receiving immunomodulators (azathioprine, 6-mercaptopurine, methotrexate).

In CD2 (NCT03466411), 360 subjects were randomized to receive intravenous Tremfya 200 mg at Weeks 0, 4, and 8 (N = 288) or placebo (N = 72). The median age of subjects enrolled into CD2 was 33 years (range:18 - 72 years); 39% were female; and 73% identified as White, 23% as Asian, 1% as Black or African American, <1% as Native Hawaiian or Pacific Islander, and 2% did not report their racial group. The median baseline CDAI score was 286 (range: 220 - 442) and the median baseline SES-CD score was 11 (range: 4 - 42). Of the randomized subjects, 52% of subjects had previously failed (inadequate response, loss of response, or intolerance) treatment with at least one biologic therapy, 41% were biologic-naïve, and 7% had previously received but had not failed a biologic. At baseline, 36% of the subjects were receiving oral corticosteroids

and 31% of the subjects were receiving immunomodulators (azathioprine, 6-mercaptopurine, methotrexate).

The results of efficacy endpoints at Week 12 for CD1 and CD2 are shown in Table 3.

Table 3. Proportion of Subjects with Crohn's Disease Meeting Efficacy Endpoints at Week 12 in CD1 and CD2

	CD1			CD2		
Endpoint	**Placebo**	**Tremfya 200 mg Intravenous Infusion[a]**	**Treatment Difference vs Placebo (95% CI)[b]**	**Placebo**	**Tremfya 200 mg Intravenous Infusion[a]**	**Treatment Difference vs Placebo (95% CI)[b]**
Clinical remission[c] at Week 12						
Total population	N=76 20%	N=285 47%	27% (17%, 38%)[d]	N=72 15%	N=288 47%	31% (21%, 41%)[d]
Prior biologic failure[e]	N=39 21%	N=147 44%		N=39 15%	N=148 47%	
Without prior biologic failure[f]	N=37 19%	N=138 49%		N=33 15%	N=140 48%	
Endoscopic response[g] at Week 12						
Total population	N=76 9%	N=285 36%	27% (19%, 35%)[d]	N=72 13%	N=288 34%	21% (11%, 30%)[d]
Prior biologic failure[e]	N=39 3%	N=147 26%		N=39 8%	N=148 28%	
Without prior biologic failure[f]	N=37 16%	N=138 47%		N=33 18%	N=140 40%	
Clinical remission[c] at Week 12 and endoscopic response[g] at Week 12						
Total population	N=76 3%	N=285 20%	17% (11%, 23%)[d]	N=72 3%	N=288 21%	18% (12%, 24%)[d]
Prior biologic failure[e]	N=39 3%	N=147 14%		N=39 3%	N=148 19%	
Without prior	N=37 3%	N=138 26%		N=33 3%	N=140 24%	

biologic failure[f]						

CI: confidence interval; mg: milligram.
[a] Tremfya 200 mg as an intravenous infusion at Weeks 0, 4, and 8.
[b] The adjusted treatment difference and the confidence intervals (CIs) were based on the common risk difference test using Mantel-Haenszel stratum weights and the Sato variance estimator. The stratification variables used were baseline CDAI score (≤300 or >300), baseline SESCD score (≤12 or >12), BIO-Failure status (Yes or No), and baseline corticosteroid use (Yes or No).
[c] Clinical remission is defined as CDAI score <150.
[d] p <0.001
[e] Includes inadequate response, loss of response, or intolerance to biologic therapy (TNF blockers, vedolizumab) for Crohn's disease.
[f] Includes subjects that were biologic naïve and subjects with prior biologic exposure who did not meet criteria for failure. In CD1, 3 subjects in the placebo group and 18 subjects in the intravenous TREMFYA 200 mg group were previously exposed to but did not fail a biologic therapy. In CD2, 6 subjects in the placebo group and 19 subjects in the intravenous TREMFYA 200 mg group were previously exposed to but did not fail a biologic therapy.
[g] Endoscopic response is defined as >50% improvement from baseline in SES-CD score.

Stool Frequency and Abdominal Pain
Greater reductions in stool frequency and abdominal pain were observed as early as Week 4 in subjects treated with intravenous Tremfya compared to placebo.

Trial CD3
In CD3, 340 subjects were randomized in a 1:1:1 ratio to receive subcutaneous Tremfya 400 mg at Weeks 0, 4, and 8 followed by subcutaneous Tremfya 100 mg every 8 weeks (with the first dose given at Week 16); subcutaneous Tremfya 400 mg at Weeks 0, 4, and 8 followed by subcutaneous Tremfya 200 mg every 4 weeks (with the first dose given at Week 12); or placebo. The median age of subjects enrolled into CD3 was 36 years (range:18 - 83 years); 41% were female; and 66% identified as White, 22% as Asian, 3% as Black or African American, and 9% did not report their racial group. The median baseline CDAI score was 291 (range: 220 - 447), and the median baseline SES-CD score was 10 (range: 4 - 40). Of the randomized subjects, 46% of subjects had previously failed (inadequate response, loss of response, or intolerance) treatment with at least one biologic therapy, 47% were biologic naïve, and 7% had previously received but had not failed a biologic. At baseline, 30% of the subjects were receiving oral corticosteroids and 29% of the subjects were receiving immunomodulators (azathioprine, 6-mercaptopurine, methotrexate).

In CD3, the coprimary endpoints were clinical remission at Week 12 and endoscopic response at Week 12 compared to placebo. Additional efficacy endpoints included clinical response at Week 12, clinical remission at Week 24, clinical remission at Week 48, and endoscopic response at Week 48. The results of analyses of multiplicity-controlled efficacy endpoints in CD3 are shown in Table 4.

Table 4. Proportion of Subjects with Crohn's Disease Meeting Efficacy Endpoints in CD3

Endpoint	Placebo	Tremfya 400 mg Subcutaneous Injection at Weeks 0, 4, and 8[a]		Treatment Difference vs Placebo (95% CI)[b]	
Week 12					
Clinical Remission[c]					
Total population	N=115 22%	N=225 56%		34% (24%, 44%)[d]	
Prior biologic failure[e]	N=53 17%	N=104 60%			
Without prior biologic failure[f]	N=62 26%	N=121 52%			
Endoscopic Response[g]					
Total population	N=115 15%	N=225 34%		19% (10%, 28%)[d]	
Prior biologic failure[e]	N=53 11%	N=104 27%			
Without prior biologic failure[f]	N=62 18%	N=121 40%			
Clinical Response[h]					
Total population	N=115 33%	N=225 72%		39% (29%, 50%)[d]	
Prior biologic failure[e]	N=53 28%	N=104 76%			
Without prior biologic failure[f]	N=62 37%	N=121 69%			
Weeks 24 and 48					
Endpoint	**Placebo**	**Tremfya 100 mg Subcutaneous Injection every 8 weeks starting at Week 16**	**Tremfya 200 mg Subcutaneous Injection every 4 weeks starting at Week 12**	**Treatment difference vs Placebo (95% CI)[b]**	
				Tremfya 100 mg	**Tremfya 200 mg**
Clinical Remission[c] *at Week 24*					
Total population	N=115 21%	N=114 61%	N=111 58%	39% (28%, 51%)[d]	37% (25%, 48%)[d]
Prior biologic failure[e]	N=53 19%	N=54 63%	N=50 52%		

Without prior biologic failure[i]	N=62 23%	N=60 58%	N=61 62%		
Clinical Remission[c] at Week 48					
Total population	N=115 17%	N=114 59%	N=111 65%	41% (30%, 52%)[d]	47% (36%, 58%)[d]
Prior biologic failure[e]	N=53 9%	N=54 56%	N=50 60%		
Without prior biologic failure[i]	N=62 24%	N=60 62%	N=61 69%		
Endoscopic Response[g] at Week 48					
Total population	N=115 5%	N=114 39%	N=111 48%	34% (24%, 44%)[d]	42% (32%, 53%)[d]
Prior biologic failure[e]	N=53 0%	N=54 33%	N=50 52%		
Without prior biologic failure[i]	N=62 10%	N=60 45%	N=61 44%		

CI: confidence interval; mg: milligram.

[a] At baseline, subjects were randomized 1:1: 1 to receive subcutaneous Tremfya 400 mg at Weeks 0, 4, and 8 followed by subcutaneous Tremfya 100 mg every 8 weeks; subcutaneous Tremfya 400 mg at Weeks 0, 4, and 8 followed by subcutaneous Tremfya 200 mg every 4 weeks; or placebo. Because dosing is identical through Week 12, subjects in both Tremfya groups are combined for the analysis of the Week 12 endpoints.

[b] The adjusted treatment difference and the CIs were based on the common risk difference test using Mantel-Haenszel stratum weights and the Sato variance estimator. The stratification variables used were baseline CDAI score (≤300 or >300), baseline SES-CD score (≤12 or >12), BIO-Failure status (Yes or No). CI = confidence interval

[c] Clinical remission is defined as CDAI score <150.

[d] p <0.001

[e] Includes inadequate response, loss of response, or intolerance to biologic therapy (TNF blockers, vedolizumab) for Crohn's disease.

[f] Includes subjects that were biologic naïve and subjects with prior biologic exposure who did not meet criteria for failure. Of these, 8 subjects in the placebo group and 17 subjects in the subcutaneous Tremfya 400 mg group, were previously exposed to but did not fail a biologic therapy.

[g] Endoscopic response is defined as >50% improvement from baseline in SES-CD score.

[h] Clinical response is defined as ≥100-point decrease from baseline in CDAI total score.

[i] Includes subjects that were biologic naïve and subjects with prior biologic exposure who did not meet criteria for failure. Of these, 8 subjects in the placebo group, 7 subjects in the subcutaneous Tremfya 100 mg group, and 10 subjects in the subcutaneous Tremfya 200 mg group were previously exposed to but did not fail a biologic therapy.

Stool Frequency and Abdominal Pain
Greater reductions in stool frequency and abdominal pain were observed as early as Week 4 in subjects treated with Tremfya 400 mg subcutaneous compared to placebo.

Endoscopic Remission at Week 48
Endoscopic remission was defined as an SES-CD score ≤4 and at least a 2-point reduction from baseline and no subscore greater than 1 in any individual component. In CD3, a greater proportion of subjects treated with either Tremfya regimen (i.e., subcutaneous Tremfya 400 mg at Weeks 0, 4, and 8 followed by subcutaneous Tremfya 100 mg at Week 16 and every 8 weeks thereafter or subcutaneous Tremfya 400 mg at Weeks 0, 4, and 8 followed by subcutaneous Tremfya 200 mg at Week 12 and every 4 weeks thereafter) achieved endoscopic remission, compared to placebo-treated subjects (31% and 40%, respectively, vs. 6%).

Summary of Evidence
Based on the studies provided to the U.S. Food and Drug Administration (FDA) for approval, Guselkumab (Tremfya®) may be considered medically necessary for adults (18 years of age or older) with moderate to severely active ulcerative colitis; and the individual will not receive Guselkumab (Tremfya®) concurrently with other biologics used to treat ulcerative colitis (e.g., infliximab, vedolizumab, ustekinumab, risankizumab-rzaa). Guselkumab (Tremfya®) may be considered medically necessary for adults with moderately to severely active Crohn's disease. Intravenous formulations of Guselkumab (Tremfya®) are considered experimental, investigational and/or unproven for all other indications.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	None
HCPCS Codes	J1628

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

References

1. Tremfya® (guselkumab) FDA Approval History. Available at <https://www.drugs.com> (accessed September 25, 2024).
2. FDA Highlights of Prescribing Information Tremfya® (guselkumab). Revised March 2025. Available at <https://www.fda.gov> (accessed May 14, 2025).

Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <http://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
06/15/2025	Document updated with literature review. Coverage revised to indicate guselkumab (Tremfya®) may be considered medically necessary for adults with moderately to severely active Crohn's disease. References revised.
10/15/2024	New medical document. Guselkumab (Tremfya®) may be considered medically necessary when ALL the following criteria are met: Adults (18 years of age or older) with moderate to severely active ulcerative colitis; and Individual will not receive Guselkumab (Tremfya®) concurrently with other biologics used to treat ulcerative colitis (e.g., infliximab, vedolizumab, ustekinumab, risankizumab-rzaa). Intravenous formulations of Guselkumab (Tremfya®) are considered experimental, investigational and/or unproven for all other indications.